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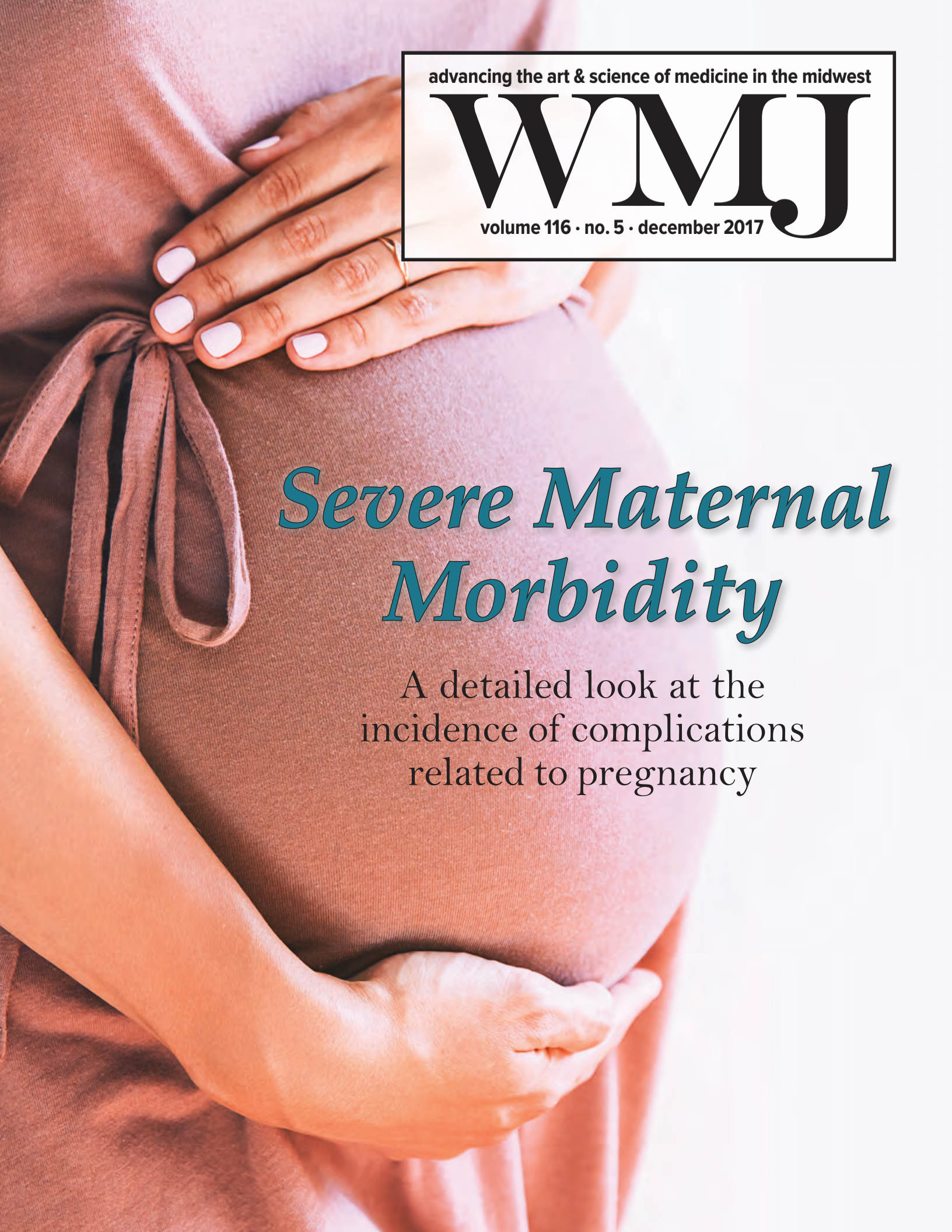

Severe Maternal Morbidity

A detailed look at the incidence of complications related to pregnancy

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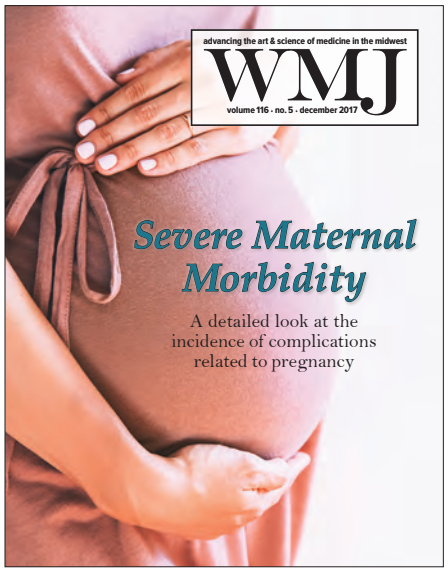

COVER THEME
Severe Maternal Morbidity

Severe maternal morbidities—which include 25 complications resulting from, or exacerbated by, pregnancy—have been on the rise over the past decade. A report in this issue of *WMJ* provides a detailed look at this trend to help identify opportunities for prevention and improvements in the quality of maternity care.

Cover design by Jane Lee

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WMJ

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The Wisconsin Medical Society designates this PI CME activity for a maximum of *20.0 AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This PI CME activity requires completion of two improvement cycles to qualify for Maintenance of Certification (MOC) Part IV. By completing the activity, physicians also earn an additional *10.0 AMA PRA Category 1 Credits*™ for a total of *30.0 AMA PRA Category 1 Credits*™.

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This Quality Improvement (QI) Effort meets Maintenance of Certification (MOC) Part IV Standards and Guidelines for the American Board of Medical Specialties (ABMS) Multi-Specialty Portfolio Approval Program Organization (Portfolio Program) and is eligible for MOC Part IV through participating ABMS Member Boards.

As an approved Portfolio Program Sponsor, the Wisconsin Medical Society has been approved by the ABMS Portfolio Program to approve QI Efforts for MOC Part IV through Oct. 1, 2020.

Wisconsin Medical Society

SHATTERING MYTHS

a story of addiction & hope

April 13, 2018
Wisconsin Medical Society Foundation
Fundraising Dinner and Silent Auction

Monona Terrace Community and Convention Center, Madison
5 p.m. hors d'oeuvres, cash bar and silent auction
7 p.m. dinner • 8 p.m. program

Join physicians and business leaders from across the state as the Wisconsin Medical Society Foundation presents a personal and deeply moving look at the epidemic of addiction. Journalist and best-selling author David Sheff will share his story of heartbreak, perseverance and hope as the father of a son battling addiction. Through years of research and interviews with numerous physician specialists, Sheff shatters the myths and stigma surrounding addiction and the mental illness that often accompanies it. Learn what you can do if a patient, friend or loved one may be struggling with a substance use disorder. Proceeds will help support programs that improve health in local communities and statewide.

David Sheff

For tickets or sponsorship information call Henry Thompson at 608.442.3756 or e-mail henry.thompson@wismed.org.

Wisconsin Medical Society Foundation

www.wisconsinmedicalsocietyfoundation.org

My Mentor

Leonard A. Mermel, DO

A cold winter morning
with snow piled high,
the storm had blown over
leaving a clear blue Wisconsin sky.

Rounding had ended
late the night before,
but I had to go see Dennis
to see what he had in store.

Dennis had said head on over
leaving little time to snore,
manuscripts were waiting
at 6 AM I was at his door.

We sat at his living room table
working the 15th draft or so,
his red felt tip marks were everywhere
pulling me along in tow.

When the last draft was written
he had a big grin on his face,
I could only imagine the next one
so I got 8 hours sleep just in case.

I'll never forget those mornings
watching the Master at his craft,
and when I mentor my students
they wonder why the 15th draft?

I can only look up and smile,
and tell them how fortunate I have been,
having worked with a true genius
opening my mind to the passion that lies within.

—for Dennis Maki, MD

• • •

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Beyond the Clinic: Making a Difference in the Lives of Others

Kay Simmons

There are some people who do more for others than seems possible given the number of hours in each day. Physicians are some of the busiest people around, working long hours to care for their patients, and yet some have the time and energy to reach out beyond the walls of their clinic or hospital to impact the health and well-being of those in their community, and in some cases, the state or nation.

Two physicians who have made significant differences in the lives of others are Paul Durbin, MD, of Racine, and Timthy Westlake, MD, of Oconomowoc, who were recipients of the Wisconsin Medical Society's 2017 Physician Citizen of the Year Award.

Paul Durbin, MD

Doctor Durbin, an internal medicine physician who practices with Ascension in Racine, was nominated for the award for his "exceptional kind and compassionate care, not only for his patients in clinic, but anyone he meets in the community."

In her nomination, colleague Kimberly Leslie called Dr Durbin a huge advocate for Racine's homeless community, noting that he volunteers monthly at the local homeless shelter. But she said what motived her the most to nominate Dr Durbin for this award was his involvement with Convoy of Hope, an organization headquartered in Missouri that brings together local churches, businesses, community services and health care organizations for one-day events that provide residents in need with groceries, medical and dental screenings, haircuts, children's shoes, job and career services, family portraits and more—at no charge.

Doctor Durbin's volunteerism began with his upbringing. It was the example of his parents, whom he said had a passion for serving the poor, and especially the homeless, that led him to want to serve the homeless in his community. When Dr Durbin and his family moved to Racine they wanted to volunteer as a family, and when they learned about the Homeless Assistance Leadership Organization (HALO) through their church they began volunteering once a month serving meals and providing music at the shelter.

In 2013, a friend's church in Kenosha was hosting an event with Convoy of Hope, and the friend asked Dr Durbin if he would be willing to help in the health service area. During that day a young man had a routine blood sugar finger stick that would not stop bleeding. He was referred to a hematologist and eventually diagnosed with a bleeding disorder, which six months later ultimately saved his life when he had emergency surgery. That young man's story, and so many others, moved Dr Durbin so much that he wrote a letter to Convoy of Hope to see if they would host an event in Racine.

It took two years of planning and organizing to pull the community together for the event, which was held at Walden School on September 17, 2016. Doctor Durbin recruited his church to be the host church and volunteered to set up and run the medical services. He also helped recruit the over 800 volunteers who worked at the event and helped fundraise the $35,000 it took to put on the event, all of which came from area organizations and donors.

> "As physician community leaders we have influence over others and can have a positive impact in the community using our knowledge and expertise. Ask yourself, 'what can I give back to my community?' Be willing to donate your time. "
>
> *—Paul Durbin, MD*

A variety of services, all free of charge, were provided to the 2,383 event participants. Services included 180 haircuts and 250 family portraits. Nearly 500 women were seen in the National Breast Cancer Foundation tent; over 1,500 pairs of shoes were distributed, 35,000 to 40,000 pounds of groceries and 12,000 Plum Organic products were given out, and 1,904 people were prayed over in the Connections Tent.

One hundred sixty people took advantage

of a multitude of services provided by 121 volunteers from Ascension All Saints, including adult medicine, pediatrics, family medicine, cardiology, physiatry, podiatry, physical therapy, dermatology, massage therapy, counseling, hearing, vision, blood pressure and blood sugar screenings, and flu shots. Participants received patient education for a variety of conditions and appropriate follow-up was arranged for the majority of the patients, many who did not have a doctor.

It was "an absolutely spectacular day, totally worth all the time and effort," said Dr Durbin. "The people I talked to who were there loved the event. The stories poured in of people who came to the event with needs, and came away with hope and dignity. Each guest was treated as a human being, made in the image of God, valued and treasured."

Despite being a such a huge undertaking, Dr Durbin said there is a lot of interest in putting on the event again. He felt that he and the other organizers learned a lot and developed excellent partnerships, but given what it takes to organize, it will most likely by three to five years before it can happen.

"I think it's clear Dr Durbin is a true champion for his patients and his community who exemplifies what we're looking for in a physician citizen of the year," said John Hartman, MD, vice chair of the Society's Board of Directors when presenting Dr Durbin with the award.

Reflecting on his time spent at the homeless shelter and volunteering with and coordinating Convoy of Hope events, Dr Durbin said, "As physician community leaders we have influence over others and can have a positive impact in the community using our knowledge and expertise. Ask yourself, 'What can I give back to my community?' Be willing to donate your time. Look at what's in your community and what volunteer opportunities are available in which you could give your time."

Paul Durbin, MD, of Racine, and Timothy Westlake, MD, of Oconomowoc, were honored with the Wisconsin Medical Society's 2017 Physician Citizen of the Year Awards for their efforts to improve health in their communities and state—beyond the clinic.

Tim Westlake, MD

Doctor Westlake is an emergency medicine physician who is the emergency department director at Oconomowoc Memorial Hospital. In addition to his emergency medicine work, Dr Westlake has dedicated himself to opioid reform efforts in Wisconsin and the nation.

Colleague Michael McNett, MD, said he nominated him for the award because of Dr Westlake's "commitment to addressing the prescription opioid abuse epidemic and expanding medication-assisted treatment throughout Wisconsin, resulting in Wisconsin being a paragon for all states."

Doctor Westlake said his passion and involvement in the opioid reform efforts began when he was appointed to the Medical Examining Board (MEB) in 2012.

"I wanted to be able to contribute to policy and have a voice in medical rule making with an emphasis on trying to rein in what I saw as over-regulation. I saw the critical importance of the people who are being regulated having a say in what the regulations actually were," he said.

In 2013, Dr Westlake's work in the opioid arena began when he took on the role of the MEB's Prescription Drug Monitoring Program (PDMP) liaison. For Dr Westlake, this was a natural fit because he saw the PDMP as a valuable tool he used daily as an emergency medicine physician, and he wanted to be able to guide its implementation.

Not long afterward Dr Westlake became Wisconsin team leader for the National

Governors' Association (NGA) Best Practice Policy Academy for Reducing Prescription Drug Abuse. While attending the NGA policy academy, he said he quickly realized the importance of taking a leadership role when, in a room of over 200 people working to craft the policies that would legislate and regulate opioid prescribing, he was the only person who actually prescribed them.

"I saw that there was going to be legislation and regulation in prescription opioid reform, and I saw that it would best be guided by someone who is in the trenches, actively practicing medicine and prescribing opioids on a regular basis," he said.

Doctor Westlake's work with the Wisconsin NGA team led to the idea for the enhanced PDMP (ePDMP). The team saw that getting the highest quality PDMP data and analytics to physicians in the quickest, least energy-consuming way possible was a must. Doctor Westlake challenged the managing director of the Wisconsin PDMP to build a new PDMP with the goal of seamless integration with the electronic medical record. What was created was beyond his expectations and is a national model for what is the ultimate expression of what a PDMP can be.

"I have been serving as the only physician on the Wisconsin ePDMP Design Team Executive Committee, and I'm proud to have been able to contribute from inception through implementation," he said.

After coming back from the NGA policy academy in 2014, Dr Westlake connected with Wisconsin State Representative John Nygren, who has been a leader in creating legislation to address the opioid crisis in Wisconsin. At the same time, Attorney General Brad Schimel had made addressing the opioid epidemic a plank of his policy agenda. Working together, they all agreed that what was needed was nothing less than a change in the culture of prescribing. With the help of Dr McNett, Rep Nygren, and Attorney General Schimel, the Wisconsin Health System Coalition for Prescription Drug Abuse Reduction was created to engage health systems and networks of physicians and prescribers to embed the cultural change within the fabric of medical practice, as well as increasing the availability of medication assisted treatment.

"I saw that there was going to be legislation and regulation in prescription opioid reform, and I saw that it would best be guided by someone who is in the trenches, actively practicing medicine and prescribing opioids on a regular basis."

—Tim Westlake, MD

In addition to state-level legislative efforts, Dr Westlake reached out to US senators with ideas on legislation that could make an impact nationally. He worked with Wisconsin Senator Ron Johnson on the Promoting Responsible Opioid Prescribing—or PROP Act—which untethered pain quality metrics from Medicare reimbursement, effectively ending the federal mandate of the pain scale. He also worked on sharing the Wisconsin opioid reform strategy with Senator Tammy Baldwin, who crafted Title IX of the recently enacted CARA Act, known as the Jason Simcakoski Memorial and Promise Act, which models the prescription opioid reforms in the Department of Veterans Affairs on Wisconsin reforms.

Along with all his other activities, Dr Westlake represents the MEB as its appointed member of the Controlled Substance Board (CSB). The CSB oversees the ePDMP and does all the scheduling of controlled substances for the state. Last year Dr Westlake saw an opportunity to develop catch-all fentanyl-related substance/analog language that would schedule all possible yet undeveloped fentanyl analogs with one law. He worked with State Representative Joel Kleefisch on the state version, which has been signed into law, and with Sen Johnson on the federal version, introduced as the Stopping Overdoses of Fentanyl Analogs (SOFA) Act.

"Thanks in no small part to these collaborative efforts and others, we are beginning to see real changes that are leading to positive outcomes for our patients and our communities, and for that, we honor him," said Dr Hartman when he presented Dr Westlake with the Society's Physician Citizen of the Year Award.

Alhtough Dr Westlake's dedication and hard work have led to legislation and reforms that promise to have a lasting impact on the opioid epidemic in Wisconsin and in the nation, he reminds his fellow physicians and other health care professionals that everyone can make a difference.

"Stay educated, stay engaged—the lion's share of the work happens when we educate ourselves, and more importantly our patients, in treating the cause of the pain, and not using treatments with little proven benefit but high potential risk.

"I lecture for a community educational program called 'Stairway to Heroin,' and my take-home point to the high school families is POP=H. Prescription opioid pills are the same thing as heroin/opium. If we as physicians have a similar understanding and respect/fear of opioids, then our prescribing would go back to where it used to be. There are times when prescribing opioids is appropriate, just as there always have been times when opium was appropriate, but we really all need to be self-circumspect with our prescribing habits."

• • •

Editor's Note: Awarded annually, the Wisconsin Medical Society's Physician Citizen of the Year award recognizes physicians who have volunteered their time and talents to improve their communities. It honors recipients for civic, economic, and charitable services they provide beyond their regular practice.

WMJ

Thank You to Our Reviewers

The *WMJ* would like to thank everyone who served as manuscript reviewers in 2017. Manuscript review is an important collegial act and is essential to the integrity of *WMJ*. We are grateful for the assistance of these individuals in ensuring authors receive objective and insightful feedback on their work.

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Clinical Medicine From 10,000 Feet

John J. Frey III, MD, Medical Editor

Many of the articles in this issue of the *WMJ* have a strong flavor of public health. Whether looking at the profile of drug resistance in Pseudomonas Aeruginosa in the largest health system in Wisconsin,[1] using statewide hospital discharge data to assess the frequency of serious maternal postpartum morbidity,[2] or the use of death certificates and Emergency Department visits to assess methods used for completed or attempted suicide,[3] investigators help clinicians think about these issues by reporting their studies with attention to the variations within the regions and populations in the state.

Wisconsin has wide variations in race and ethnicity, socioeconomic status, climate, geography, health systems, and many other factors that affect health.[4] The *WMJ* has published a great deal of work over the past 50 years that has taken the larger, statewide view or put local findings in the context of other regions of the state. The *WMJ/Wisconsin Medical Journal* has served as a repository of data on most of the public health issues that come up regularly in articles we publish today. For example, severe maternal mortality was discussed in a review by Hunter in 1949,[5] suicide has been a focus for many articles in the *WMJ*, going back to 1965,[6] and issues of bacterial drug resistance first came up with penicillin not long after it began to be widely used.[7]

Given that most of the delivery of medical care in Wisconsin is through large regional health systems, publishing articles that show statewide variations should help clinicians within those systems consider interventions that may be particular to their regions. A dramatic example of this came during the polio epidemic in the 1950s where authors examined the incidence of polio in relationship to the use and distribution of gamma globulin.[8] Local physicians, public health, and large clinics had to make plans for what might work, prior to the Salk vaccine. They concluded that the state would not have enough for the intervention to be useful. I have distinctly painful memories of the gamma globulin shot I got during that epidemic and certainly was one of the subjects of this study.

> It goes without saying, for example, that Green Bay is different than Chicago, but to effectively and efficiently take care of their patients, clinicians in both cities need specifics on how those populations differ, other than the NFL teams they support.

While the *WMJ* does publish well done research from a single hospital or local health system, we encourage authors to look at their results in the context of what might be known about the problem statewide. Wonderful resources have become available over the past 25 years to help clinicians who want to compare/contrast their populations and prevalence of conditions with other parts of the state or country. The County Health Rankings sponsored now by the Robert Wood Johnson Foundation (http://www.countyhealthrankings.org/) originated and were originally tested in Wisconsin and offer important comparative data on behavioral and chronic diseases by county and region. There are additional state and national sources of data that allow comparisons of quality, outcomes, and resources that authors should consult when writing up the results of their studies. A good example in this issue is the single clinic study on travel patterns of pregnant women, which references data from the Wisconsin Department of Health Services and the Centers for Disease Control and Prevention to help put their results into a larger context.[9]

We should expect authors to examine what they find from their data as it applies to other populations or to suggest the need to repeat a study in different populations to see whether what they have found is generalizable. Weiker and colleagues do just that in their study in this issue finding a lack of clinical value of Vitamin D supplementation for alleviating leg cramps by pointing out the need to extend their study to subjects that are not well represented in their study population.[10]

One of the most dramatic changes in medical education in the past decade has been the growing emphasis on physicians seeing themselves as population health managers. Whether family doctors in rural communities or subspecialty surgeons with statewide or regional network of patients, we all take care of populations and have the responsibility to know the characteristics of those populations and how they are similar to or different from others in the state or region. Knowing and understanding the characteristics of one's clinical populations should allow tailored interventions for those patients and communities. One potential value of electronic health records is to allow rich analyses of patient populations so that clinicians and clinical programs can use creative approaches to improving quality.

We are becoming accustomed to seeing maps of the state in relation to many health-related problems. The Dartmouth Atlas of Health Care (http://www.dartmouthatlas.org/) looks at cost and outcomes from region to region. We can now "see" what we do from a higher level. Both the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health have engaged in curricular reforms that emphasize longitudinal community-based education that seeks to integrate clinical training and community and population health. They also understand that data analysis and clinical epidemiology are basic sciences in the new curriculum. While still learning and practicing the skills of patient- and family-centered care, future physicians should also be expected to ask themselves and the systems in which they work how their individual patients differ from general populations. It goes without saying, for example, that Green Bay is different than Chicago, but to effectively and efficiently take care of their patients, clinicians in both cities need specifics on how those populations differ, other than the NFL teams they support.

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Differences in Methods of Self-Inflicted Injuries by Sex in Wisconsin, 2002-2014

Nivedita Nair, BS; Joseph Archer, BA; Alexa Statz, MPH; Ousmane Diallo, MD, MPH, PhD

ABSTRACT

Background: Despite suicide prevention efforts, there remains a high burden of self-inflicted injuries in Wisconsin.

Objective: Compare methods of suicide and nonfatal self-inflicted injury by sex in Wisconsin over a 12-year period.

Methods: Suicide and nonfatal self-inflicted injury rates in Wisconsin between 2002 and 2014 were compared by sex and method using data from the Wisconsin Interactive Statistics on Health. Percentages of total suicides by method of injury for each sex were calculated.

Results: Firearms and poisoning were the most common methods of suicide and nonfatal self-inflicted injuries, respectively. Rates of both suicide and nonfatal self-inflicted injuries differed significantly by sex and method.

Conclusions: Suicide prevention strategies in Wisconsin must account for the variability of method of self-inflicted injury between sexes.

INTRODUCTION

Suicide is an important public health issue in Wisconsin. Each year, over 700 residents die by suicide.[1] In addition to this burden, each year an additional 5,500 residents are hospitalized due to self-inflicted injuries, leaving them in need of extensive medical treatment or rehabilitation.[1] In Wisconsin, men have been shown to be at higher risk of completed suicide, while women have been noted to be at higher risk of self-harm.[2] Overall, the preventable burden of suicide and nonfatal self-inflicted injury in Wisconsin, in conjunction with the complications posed by discrepancies between men and women, present a critical public health problem. For the purpose of clarity, we will refer to nonfatal self-inflicted injury and self-harm synonymously throughout this paper.

The primary objective of this study was to compare the methods of self-inflicted injury between men and women, aggregated across 2002 to 2014, to provide an overview of the burden of suicide and self-harm in Wisconsin. This paper provides clinical utility in expanding the literature and providing accessible information to physicians about the need for targeted suicide prevention. Particularly, this study has relevance to mental health screening practices in the clinical setting.

METHODS

We used the Wisconsin Interactive Statistics on Health (WISH)[3] to examine data from 2002-2014 for both suicides and self-harm. We queried data on suicides using the Injury Related Mortality query—which gathers data from resident death certificates[3]—and queried data on self-harm using the Injury Related Emergency Department Visits query—which gathers data from the Wisconsin Hospital Association Emergency Department Discharge Billing Claims database on individuals treated and released from emergency departments (ED).[3] Suicides and nonfatal self-inflicted injuries were segregated from unintentional injuries, in their respective queries, based on International Classification of Disease (ICD) codes, which are assigned based on physician determination of the manner and/or intent of injury.[3]

Rates were age-adjusted to the 2000 US Standard Population and examined across the study period to identify trends for method of self-inflicted injury by sex, which proved consistent across the period. We then aggregated data across years for comparison and examined rates by sex in methods of suicide and self-harm. We used the categories of sex and method available

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in the WISH database for comparison and analysis (see Table 2). Percentages of self-inflicted injury by sex attributable to each method were calculated by dividing the number of injuries per method in each sex by the total number of injuries for that sex, over the period. We compared 95% confidence intervals provided by the query for method of injury across sexes to determine significant differences in method of self-inflicted injury for both suicide and self-harm between men and women.

RESULTS

Table 1 characterizes demographics of suicides and self-harm in Wisconsin between 2002 and 2014. During this period, men committed a greater number of suicides than women in Wisconsin; nearly 80% of all suicides were committed by men. However, women contributed to a greater number of ED admittances for self-harm than men; over 60% of ED visits for self-harm involved women. Overall, the most common method of suicide was firearms, followed by suffocation and poisoning. The most common method of self-harm overall was poisoning, followed by cutting or piercing objects and other specified cause of injury not elsewhere classifiable. Comparisons between suicide and self-harm by demographic factors, including age, race, and region of residence, are also included in Table 1. We determined age to be a possible confounder; therefore, age was adjusted for analysis of both suicide and self-harm. It is important to note that the rates of self-harm were 3-fold higher than the rates of suicide across both sexes. The total number of ED admissions for self-harm during this period was 37,733, whereas the total number of suicides was 9,287 (Table 1).

Table 1. Suicide/Self-Inflicted Mortality and Nonfatal Self-Inflicted Injury-Related Emergency Department Visits (Wisconsin, 2002-2014)

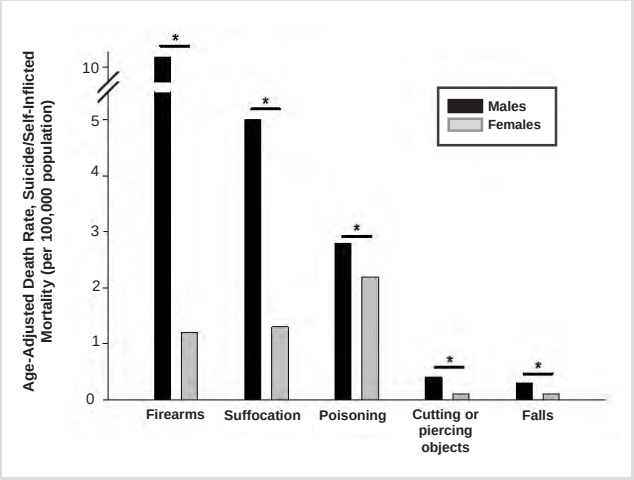
	Suicide		Nonfatal Self-Inflicted Injury	
	No. of Deaths	Age-Adjusted Death Rate (per 100,000 Population)	No. of Injury ED Visits	Age-Adjusted Rate of Injury ED Visits (per 100,000 Population)
All	9,287	12.7	37,733	52.8
Sex				
Male	7,357	20.2	14,857	40.8
Female	1,930	5.2	22,876	65.3
Age of injury				
0-17	337	2	9,993	98.5
18-24	1,032	14.1	10,093	137.7
25-34	1,470	15.8	7,881	84.8
35-44	1,759	17.5	5,284	52.7
45-54	2,132	19.4	3,229	29.3
55-64	1,302	15.4	899	10.7
65-74	628	12.3	216	4.2
75+	627	12.9	138	2.8
Race				
White	8,755	13.3	--	--
Black	297	6	--	--
American Indian	110	13.1	--	--
Asian	125	7.1	--	--
Region of residence				
Southern	1,808	12.9	9,048	64.2
Southeastern	3,068	11.3	12,929	49.0
Northeastern	2,151	13.6	7,897	52.2
Western	1,356	13.6	5,177	52.2
Northern	903	14.1	2,682	45.7
Underlying cause of injury				
Firearms	4,401	6	82	0.1
Suffocation	2,298	3.1	772	1.1
Poisoning	1,855	2.5	19,823	27.7
Cutting or piercing objects	174	0.2	12,140	17.0
Falls	161	0.2	160	0.2
Drowning	108	0.1	20	0.0
Fire, heat, chemical burns	48	0.1	211	0.3
Other specified cause of injury not elsewhere classifiable	51	0.1	3,577	5.0
Unspecified cause of injury	34	0	786	1.1

Abbreviation: ED, emergency department.

Table 2 characterizes the most common methods of suicide and self-harm based on percentage of total injuries between 2002 and 2014, separated by sex. The methods of suicide for men that carried the highest burden were firearms (53.9%), suffocation (24.8%), and poisoning (14.0%). The methods of suicide for women that carried the highest burden were poisoning (42.8%), suffocation (24.7%), and firearms (22.5%). For men, most suicides could be attributed to firearm use, while among women, most suicides could be attributed to poisoning. Comparison using 95% confidence intervals revealed that differences in age-adjusted death rates between men and women were statistically significant for the top five methods of suicide (Figure 1).

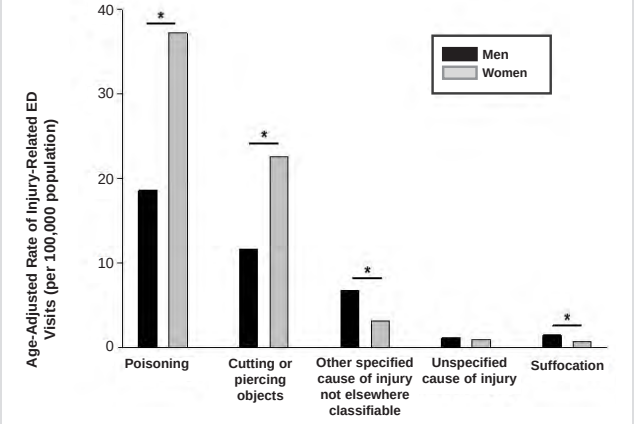
The 3 most common methods of self-harm for men were poisoning (45.5%), cutting or piercing objects (28.6%), and other specified cause of injury not elsewhere classifiable (16.6%). The 3 most common methods of self-harm for women were poisoning (57.1%), cutting or piercing objects (34.5%), and other specified cause of injury not elsewhere classifiable (4.9%) (Table 2). For both men and women, poisoning was the most common method of self-harm. The differences in age-adjusted rates of self-harm between men and women by suffocation, poisoning, cutting and piercing objects, and other specified cause of injury not elsewhere classifiable were statistically significant ($P < 0.05$) (Figure 2).

Figure 1. Top 5 Methods of Suicide by Sex, Wisconsin (2002-2014)



*Significant difference at *P*=0.05 level between men and women.

Figure 2. Top 5 Methods of Nonfatal Self-Inflicted Injury by Sex, Wisconsin, 2002-2014)



*Significant difference at 1=0.05 level between men and women.
Abbreviation: ED, emergency department.

DISCUSSION

Our findings confirm the significant burden of suicide and self-harm in Wisconsin. Additionally, there is a notable discrepancy in the rates of both suicide and self-harm between men and women. In Wisconsin, between 2002 and 2014, nearly 80% of all suicides were committed by men, while over 60% of ED visits for self-harm involved women. These findings are supported by the most recent Burden of Suicide in Wisconsin Report.[2]

The findings of our study also demonstrate the marked difference in the methods that men and women in Wisconsin employ to self-inflict injury. As mentioned above, the most common method of suicide for men was firearms (53.9%) and for women was poisoning (42.8%). This relationship is also reflected in national data; the Centers for Disease Control and Prevention (CDC) reported that in 2014, the most common method of suicide for American men was firearms (55.4%) and for American women was poisoning (34.1%).[4] In Wisconsin, men committed suicide at almost 10 times the rate of women using firearms and 5 times the rate of women using suffocation, while the rates of self-harm for women were almost double those for men when using poisoning and cutting or piercing objects. A variety of factors could explain these differences: substance abuse, prescription psychiatric drug use, history of mental illness, previous suicide attempts, and marital status have been noted to drive sex differences in suicide,[5] as have culturally assigned expectations of self-harm behaviors that differ between sexes.[6,7]

Due to the high burden of firearm use in completed suicides, the focus on self-harm reduction in Wisconsin historically has centered on firearms[8] because of the lethality of firearms and knowledge of the increased risk of firearm suicide with access to firearms.[9] While this focus is important, the results of our study suggest that this approach leaves significant gaps in addressing suicide in women and self-harm in both men and women. Moreover, trends in method across sex and overall rates for self-harm and suicide have remained largely unchanged in Wisconsin over the last decade. Public health priority in Wisconsin must address methods of self-inflicted injury beyond firearms, especially those responsible for high rates of self-harm. Self-harm must be accounted for in prevention initiatives; not only do high rates of self-harm pose short-term health burdens (ie, health care costs, preventable injury), but individuals whose self-harm has necessitated medical care are at significantly higher risk of both recurrences of nonfatal self-harm and future suicide.[10] Additionally, self-harm with methods other than poisoning or cutting/piercing objects, high medical severity, and repeat events increase the risk of suicide,[11] indicating potential risk factors.

Considering the method and sex issue may help Wisconsin health care professionals to augment suicide screening tools with sex-specific risk considerations.[12] For example, a suicide screening tool for men may incorporate questions about access to firearms as a risk assessment. Furthermore, Wisconsin public health advocates may utilize these findings to develop more specific prevention strategies.[13] Future studies should seek to unravel the sources of sex differences in method of self-inflicted injury in Wisconsin and to determine how residents gain access to given methods of self-inflicted injury, which would further inform public health interventions.

Three limitations must be considered when addressing the results of this study. First, we determined that querying nonfatal self-inflicted injury-related ED visits provided the most accurate estimate for our assessment of self-harm. While it cannot be assumed that those who nonfatally self-harmed had suicidal intent in their actions, we felt this to be an appropriate estimate because these intentional, nonfatal injuries were severe enough to warrant immediate and emergent medical attention. This assumption is backed by the progression of suicidal behavior developed in the

most recent Burden of Suicide Report.[2] Conversely, because this query only records individuals who visit the ED, it is possible this estimate is conservative. Our rate neglects any individual who engaged in serious self-harm but failed to seek medical attention, or sought it outside of an ED. Finally, a limitation to consider involves the classification of suicide. In some cases, a ruling of suicide may be obvious, but often the cause of death can be vague, due to incomplete or inaccurate details.[14] For example, it is possible that a death from opioid overdose that was classified as "accidental poisoning" could have instead been a suicide, which potentially could lead to an underestimation of suicide rates.

Table 2. Method of Self-Inflicted Injury by Sex, Wisconsin (2002-2014)

Underlying Cause of Injury	Suicides (%Total)		Nonfatal Self-Inflicted Injury ED Visits (%Total)	
	Male	Female	Male	Female
Firearms[a]	3,967 (53.9%)	434 (22.5%)	71 (0.5%)	11 (<0.1%)
Suffocation[a,b]	1,822 (24.8%)	476 (24.7%)	546 (3.7%)	226 (1.0%)
Poisoning[a,b]	1,028 (14.0%)	827 (42.8%)	6,767 (45.5%)	13,056 (57.1%)
Cutting or piercing objects[a,b]	140 (1.9%)	34 (1.8%)	4,254 (28.6%)	7,886 (34.5%)
Falls[a]	120 (1.6%)	41 (2.1%)	102 (0.7%)	58 (0.3%)
Drowning	71 (1.0%)	37 (1.9%)	5 (<0.1%)	15 (0.1%)
Non-traffic land transportation	63 (0.9%)	13 (0.7%)	--	--
Fire, heat, chemical burns	28 (0.4%)	20 (1.0%)	109 (0.7%)	102 (0.4%)
Other specified classifiable cause of injury	54 (0.7%)	27 (1.4%)	68 (0.5%)	23 (0.1%))
Other specified cause of injury not elsewhere classifiable[a,b]	43 (0.6%)	8 (0.4%)	2,467 (16.6%)	1,110 (4.9%)
Unspecified cause of injury	21 (0.3%)	13 (0.7%)	426 (2.9%)	360 (1.6%)
MVT - Self-inflicted/assault/ undetermined	--	--	32 (0.2%)	19 (0.1%)
Natural or environmental factors	--	--	10 (0.1%)	10 (<0.1%)

[a]Significant difference (P<0.05) between male and female age-adjusted death rate.
[b]Significant difference (P<0.05) between male and female age-adjusted rate of injury ED visits.
Abbreviations: ED, emergency department; MVT, motor vehicle traffic.

CONCLUSIONS

Self-inflicted injury, both fatal and nonfatal, remains an important public health issue in Wisconsin. Based on the results of this study, greater attention must be focused on specializing suicide prevention. Given the variability of method of self-inflicted injury between sexes found in this study, considerations should be made to tailor suicide screenings and prevention strategies based on sex and method. More evidence is needed to further evaluate differences in suicide trends to improve intervention strategies.

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Muscle Cramps Do Not Improve With Correction of Vitamin D Insufficiency

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ABSTRACT

Background: Minimal treatment options exist for idiopathic muscle cramps.

Objective: We evaluated whether correction of vitamin D insufficiency relieved muscle cramps in postmenopausal women.

Methods: We conducted a post hoc analysis of a randomized, double-blind, placebo-controlled trial at a single academic medical center in the Midwest to evaluate the benefits of treating vitamin D insufficiency. Two hundred thirty postmenopausal women participated. Eligible women were ≤75 years old, 5 years past menopause or oophorectomy, or ≥60 years if they had previously undergone hysterectomy without oophorectomy. Women had vitamin D insufficiency at baseline (25-hydroxyvitamin D 14-27 ng/mL). We excluded subjects with a glomerular filtration rate <45 mL/minute.

Interventions for Clinical Trials: Participants completed food diaries, laboratory studies, and functional tests including the Timed Up and Go test, Physical Activity Scale for the Elderly, Health Assessment Questionnaire (a measure of disability), and pain scores. Subjects recorded muscle cramp frequency and severity using a standardized form at 6 visits over 1 year.

Results: During the trial, over half of participants (n=121, 53%) reported muscle cramps. Despite unequivocal vitamin D repletion, vitamin D had no effect on muscle cramps. Pain levels, disability, and dietary potassium predicted presence of cramps. Serum albumin and physical activity were inversely associated with, and disability was positively associated with, severity of muscle cramps.

Conclusions: Further studies are needed to evaluate the link between pain, disability, dietary potassium intake, and muscle cramps.

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INTRODUCTION

Muscle cramps are defined as "sudden, uncomfortable squeezing or contraction of a muscle, lasting seconds to minutes."[1,2] In surveys,[3-6] between half and two-thirds of older adults experience muscle cramps, contributing to insomnia[6] and lower quality of life.[7] Some people describe muscle soreness or tenderness the following day.[7] Muscle cramps have diverse potential causes including lower motor neuron disorders; cirrhosis; dialysis; medications; and metabolic derangements including hypocalcemia, hypoglycemia, hyponatremia, and abnormal potassium levels.[1,8] However, most muscle cramps are idiopathic.[1]

Multiple interventions are suggested for muscle cramps, but few have proven effective in double-blind, placebo-controlled trials. In 1 clinical trial, stretching prior to bedtime reduced muscle cramp frequency.[9] Quinine moderately reduced frequency and severity of cramps, but its side effect profile prohibits routine use.[10] Other treatments, including vitamin B complex, diltiazem, vitamin E, magnesium, and gabapentin are of uncertain benefit.[2]

Identification of risk factors for muscle cramps might guide future treatment options. During a randomized, double-blind, placebo-controlled trial of vitamin D therapy in postmenopausal women,[11] we asked participants to complete a questionnaire during each of 6 visits over 1 year to assess the presence and severity of cramps as a function of vitamin D therapy. Because hypocalcemia causes tetany, and dialysis with disrupted vitamin D metabolism is a risk factor for muscle cramps, we hypothesized that vitamin D would reduce the

frequency and severity of muscle cramps in postmenopausal women with vitamin D insufficiency.

Herein, we report our planned post hoc analysis to evaluate the effect of vitamin D on muscle cramps, including associations between muscle cramps and subjects' clinical features, nutritional habits, total fractional calcium absorption, and functional measures.

METHODS

This study (clinicaltrials.gov NCT00933244) was approved by the University of Wisconsin Human Subjects Committee and all subjects provided written informed consent to participate.

Subjects participated in a single-center, randomized, double-blind, placebo-controlled trial[11] to evaluate the effect of vitamin D therapy on total fractional calcium absorption (TFCA), bone mineral density (BMD), and functional status. Participants were women ≤75 years old, at least 5 years past menopause or oophorectomy, or ≥60 years if they had undergone a prior hysterectomy without oophorectomy. Women had baseline 25-hydroxyvitamin D [25(OH)D] levels of 14 to 27 ng/mL by high performance liquid chromatography. Women were excluded if they had a glomerular filtration rate <45 mL/minute, estimated by the Modification of Diet in Renal Disease (MDRD) equation.[12] Complete exclusion criteria are described elsewhere.[11] During the trial, women were advised to consume 600 to 1400 mg of calcium per day.

To assess the frequency and severity of muscle cramps, subjects completed a questionnaire at each of the 6 study visits over 1 year (Table 1). We developed the questionnaire a priori and assigned point values to each answer, with higher scores indicating more frequent or severe cramps causing greater disturbance to daily activities and/or sleep. We calculated the composite muscle cramp score for each subject, using the sum of points from all 6 visits.

At baseline, all subjects underwent measurement of serum 25(OH)D, calcium, albumin, phosphorus, magnesium, creatinine, parathyroid hormone levels, TFCA, and BMD. Nutritional habits and supplement use were determined from analysis of 4- to 7-day food diaries by a research dietician, using Food Processor software (ESHA Research) prior to randomization. We measured subjects' total fluid intake, 24-hour urine calcium levels, and TFCA the day prior to randomization, as described elsewhere.[11]

We assessed subjects' measures of physical function and pain at each of 6 study visits. Participants completed the Timed Up and Go (TUG) and 5 sit-to-stand (5STS) tests twice per visit, and the final score was the better of 2 attempts. Subjects completed the Physical Activity Survey for the Elderly (PASE), with higher points indicating greater physical activity. Additionally, subjects completed the modified Stanford Health Assessment Questionnaire (HAQ),[13] with a possible score of 0 (no disability) to 3 (unable to perform or requiring assistance). Subjects marked their pain level due to any cause from 0 (no pain) to 10 (severe pain) on a 10 cm horizontal line in response to the question, "How much pain have you had in your muscles and bones in the past week?" We noted subjects' use of medications throughout the trial, including those known to cause or alleviate muscle cramps.

Table 1. Muscle Cramps Questionnaire

Question	Answer	Score
Do you have muscle cramps?	No	0
	Yes	1
If yes, how often?	Once or less a day	0
	2 to 5 times daily	3
	6 or more times daily	4
Do muscle cramps keep you from falling asleep?	No	0
	Yes	1
Do muscle cramps wake you during the night?	No	0
	Yes	1
Total		Range 0 to 7

After initial measurement of TFCA, subjects were randomized to 1 year of placebo, a low-dose vitamin D_3 regimen of 800 IU/day, or a high-dose vitamin D_3 regimen specifically designed to keep the 25(OH)D level >30 ng/mL throughout the trial. All subjects took a daily pill (placebo or 800 IU vitamin D_3) and intermittent yellow pills (placebo or 50,000 IU vitamin D_3 days 1 to 15 then every 15th day) to preserve the double-blind.

The CONSORT guidelines for the clinical trial were published with the parent paper.[11] Of relevance, 230 women were randomized into the trial including 76 assigned to placebo, 75 assigned to low-dose and 79 assigned to high-dose vitamin D therapy. Of the 230 women randomized, 221 women (96%) completed the trial including 73, 74, and 74 in the placebo, low-dose, and high-dose vitamin D arms, respectively.

Statistical Analysis

Data were entered in duplicate and accuracy confirmed prior to analysis. Variables included race and baseline age, height, weight, body mass index, tobacco use, nutrient intake from diet and supplements, laboratory results, TFCA, TUG and 5STS test times, and HAQ, PASE, and pain scores. All data were graphed to determine distributions (parametric or skewed) and then summarized using the mean ± standard deviation or median (interquartile range), as appropriate. We analyzed continuous data using independent t-tests or the Wilcoxon test, and categorical data using the chi-squared test. We used the "leaps" command to evaluate the top predictors of muscle cramps, focusing on the top 17 variables identified in initial analyses. In the subset of women with muscle cramps, we used Spearman correlation coefficients to assess relationships between subjects' characteristics and muscle cramp severity. The Benjamini-Hochberg correction[14] was employed to control the false positive discovery rate during univariate analyses; thus, a P-value ≤0.002 was considered significant. A P-value <0.05

Table 2. Characteristics of Subjects With and Without Muscle Cramps

Characteristic	All Subjects n=230	No Cramps n=109 (47%)	Cramps n=121 (53%)	*P*-Value
Clinical				
Age, years	61 ± 6	61 ± 6	61 ± 6	0.943
BMI, kg/m^2	30.8 ± 6.8	30.2 ± 6.1	31.4 ± 7.5	0.155
Race				
White	207 (90%)	101 (92%)	106 (88%)	
Black	14 (6%)	5 (5%)	9 (7%)	0.469
Other	9 (4%)	3 (3%)	6 (5%)	
Tobacco use	20 (9%)	6 (6%)	14 (12%)	0.158
Daily Nutrient Intake				
Calories, kcal	1,842 (1,539, 2,198)	1,839 (1,487, 2,226)	1,842 (1,572, 2,154)	0.816
Protein, g	75 (62, 86)	76 (63, 87)	74 (61, 86)	0.481
Fat, g	72 (60, 91)	68 (55, 92)	74 (61, 90)	0.327
Carbohydrates, g	222 (175, 266)	226 (179, 278)	209 (175, 259)	0.127
Fiber, g	19 (14, 25)	20 (15, 27)	18 (14, 24)	0.022
All calcium intake, mg	967 (752, 1,215)	1,026 (793, 1,264)	905 (731, 1,152)	0.034
Vitamin D, IU	196 (115, 266)	203 (134, 282)	169 (111, 259)	0.173
Magnesium, mg	306 (247, 370)	309 (251, 383)	301 (237, 356)	0.245
Iron, mg	13 (10, 16)	14 (10, 16)	13 (10, 16)	0.315
Phosphorus, mg	1,300 (1,086, 1,475)	1,318 (1,091, 1,565)	1,283 (1,081, 1,464)	0.412
Potassium, mg	2,775 (2,313, 3,249)	3,018 (2,453, 3,440)	2,665 (2,212, 3,053)	0.002
Total fluid intake, mL	2683 (2159, 3350)	2692 (2214, 3326)	2640 (2157, 3449)	0.993
Labs				
Calcium, mg/dL	9.1 ± 0.4	8.9 ± 0.3	8.9 ± 0.3	0.416
Albumin, g/dL	3.9 ± 0.3	3.9 ± 0.3	3.9 ± 0.3	0.813
GFR, mL/minute	79 ± 17	82 ± 17	76 ± 16	0.022
PTH, pg/mL	51 ± 21	51 ± 24	50 ± 17	0.740
25(OH)D, ng/mL	21 ± 3	21 ± 5	19 ± 5.0	0.045
Magnesium, mg/dL	2.1 ± 0.2	2.1 ± 0.2	2.1 ± 0.2	0.998
Phosphate, mg/dL	3.5 ± 0.5	3.4 ± 0.5	3.5 ± 0.4	0.285
1,25(OH)$_2$D, pg/mL	41 (31, 54)	43 (33, 55)	40 (29, 54)	0.131
Estradiol, pg/mL	48 (40, 56)	47 (41, 55)	49 (40, 57)	0.622
24-hour urine calcium, mg	180 ± 95	192 ± 108	167 ± 82	0.043
Calcium absorption	0.20 ± 0.07	0.20 ± 0.07	0.21 ± 0.07	0.467
Function				
Physical Activity Scale	171 ± 88	175 ± 93	166 ± 82	0.442
Timed Up and Go	8.1 ± 1.7	8.0 ± 1.8	8.2 ± 1.6	0.350
5 Sit-to-Stand Test	10 ± 2.7	9.7 ± 2.5	10.3 ± 2.8	0.143
HAQ	0.1 ± 0.3	0.06 ± 0.18	0.15 ± 0.30	0.008
Pain, 10-point scale	1.5 ± 1.9	0.9 ± 1.3	2.1 ± 2.2	<0.001

Abbreviations: BMI, Body Mass Index, GFR, glomeruler filtration rate; PTH, Parathyroid hormone; HAQ, Health Assessment Questionnaire.

Table 3. Medications Influencing Muscle Cramps

Medications Used to Treat Muscle Cramps	Medications Causing Muscle Muscle Cramps
Carisoprodol	Albuterol/ipratropium
Diltiazem	Intravenous iron sucrose
Magnesium	Levalbuterol
Orphenadrine	Pregabalin
Quinine	Selective serotonin reuptake inhibitors
Verapamil	
Vitamin B complex	

was considered significant in multivariate models. We used version 3.2.3 of "R" (The R Project for Statistical Computing, http://www.r-project.org) to perform statistical analyses.

RESULTS

We analyzed baseline data and muscle cramp questionnaires from all 230 subjects who participated in the study. The majority of participants were white (90%) with a mean age of 61 ± 6 years and body mass index of 30.8 ± 6.8 kg/m^2 (Table 2). More than half of subjects (n=121, 53%) reported muscle cramps during the trial. Among those with muscle cramps, the median composite cramp score was 4 (interquartile range 2-8).

High-dose vitamin D resulted in unequivocal vitamin D repletion to serum 25(OH)D levels ≥30 ng/mL throughout the trial.[11] However, vitamin D had no effect on the frequency of muscle cramps, with 32 of 76 subjects in the placebo, 34 of 75 in the low-dose vitamin D, and 31 of 79 subjects in the high-dose vitamin D arms during the trial experiencing muscle cramps (*P*=0.746). Likewise, vitamin D had no effect on muscle cramp severity. The composite cramp score was 3.2 ± 4.7 in the placebo, 3.5 ± 5.4 in the low-dose, and 2.7 ± 3.8 in the high-dose vitamin D arms (*P*=0.927).

Surprisingly, use of medications potentially causing or relieving cramps (Table 3) was similar between subjects with and without cramps. Causative medication use was noted in 18 of 103 women with cramps, and in 8 of 101 without cramps (*P*=0.111). Likewise, 24 of 97 women with cramps, and 18 of 91 women without cramps, took medications believed to alleviate cramps (*P*=0.631).

Women with muscle cramps had significantly higher pain levels (2.1 ± 2.2 vs. 0.9 ± 1.3, *P*<0.001) and consumed less potassium (2,665 mg/day [2,212 mg; 3,053 mg] vs 3,018 mg/day [2,453 mg; 3,440 mg], *P*=0.002) than those without cramps. Women with muscle cramps also reported greater disability (HAQ score 0.15 ± 0.30 vs 0.06 ± 0.18, *P* =0.008), although the *P*-value was above the false-positive discovery rate *P*-value of

0.002. Although clinicians often recommend hydration to treat muscle cramps, we found no significant difference in total fluid intake between women with and without cramps (Table 2).

We used the R program "leaps" to identify which of the top 17 variables from Table 2 predicted presence of muscle cramps. Candidate variables included tobacco use, body mass index, HAQ, pain, serum creatinine, calcium, phosphorus, 25(OH)D, $1,25(OH)_2D$, 24-hour urine calcium, TFCA, and dietary intake of carbohydrates, fiber, calcium, magnesium, potassium, and vitamin D. In this analysis, dietary potassium, serum creatinine, and pain levels were the only significant variables predicting the presence of muscle cramps (Table 4). Together these three variables predicted over 70% of the variability in presence of muscle cramps. Restricting the analysis to 10 or fewer variables did not alter these results.

Among women reporting muscle cramps (n=121), we used correlation coefficients to assess relationships between patient characteristics and the severity of muscle cramps (Table 5). In these analyses, serum albumin and physical activity were inversely associated with, and disability was positively associated with, severity of muscle cramps. Pain also was positively associated with severity of muscle cramps, but the *P*-value was >0.05.

Table 4. Variables Associated With Presence of Muscle Cramps

	Multivariate Model		
Characteristic	**Slope**	**Standard Error**	***P*-value**
Intercept	+0.0947	1.116	0.932
Creatinine, mg/dL	+1.9798	1.0944	0.070
Potassium intake, mg	-0.0007	0.0002	0.001
Pain, 10-point scale	+0.3413	0.0985	<0.001

Full model *P*<0.001, area under the curve = 0.708.

Dietary potassium, serum creatinine, and pain levels were the only significant variables predicting the presence of muscle cramps; they predicted over 70% of the variability in muscle cramps.

Table 5. Correlations Between Characteristics and Severity of Muscle Cramps

	Subjects With Muscle Cramps, n=121	
Characteristic	**ρ**	***P*-value**
Albumin, g/L	-0.19	0.039
Pain, baseline	+0.13	0.169
Pain, cumulative	+0.17	0.067
Health Assessment Questionnaire Score, baseline	+0.19	0.039
Health Assessment Questionnaire Score, cumulative	+0.21	0.026
Physical Activity Scale for the Elderly, baseline	-0.23	0.011
Physical Activity Scale for the Elderly, cumulative	-0.19	0.046

Pain was assessed using a 10-cm visual analog scale. Cumulative scores are the sum of individual scores obtained at each of 6 visits over 1 year. Data are not shown, for variables showing no significant correlation with muscle cramp score.

DISCUSSION

Muscle cramps commonly affect older adults and most cramps are idiopathic in nature. Understanding their pathophysiology could allow identification of new treatments for this common ailment, which is associated with insomnia and lower quality of life.[7] We therefore sought to identify potential novel causes of muscle cramps and were particularly interested in the effect of vitamin D.

In our randomized clinical trial, vitamin D therapy did not alter the frequency or severity of muscle cramps. However, women experiencing muscle cramps had significantly higher pain levels, greater disability by greater HAQ, and consumed less potassium than subjects without cramps. Although magnesium supplements and hydration are commonly suggested to treat muscle cramps, we found no relationship between muscle cramps and dietary or serum magnesium or fluid intake. We found that severity of muscle cramps was inversely associated with serum albumin and physical activity, and positively associated with disability and pain.

Additionally, women with muscle cramps had more pain and disability than those without muscle cramps. We cannot determine whether higher pain levels directly cause muscle cramps. However, consistent with the concept of central sensitization, subjects with higher pain levels might have increased nociceptive sensitivity[15] and therefore be more symptomatic when muscle cramps occur. Cramps might sensitize pain nerve fibers, reducing functional status.

We found that women with muscle cramps consumed less dietary potassium. While hypokalemia is a known cause of muscle cramps, we found no studies in which dietary potassium was identified as a risk factor for cramps. Further research is needed to evaluate whether increased potassium intake would reduce muscle cramps.

We could find no reports linking regular exercise with milder muscle cramps. Although muscle cramps are more common in people with liver disease, we likewise found no reports linking low albumin to greater risk of muscle cramps. However, one review[16] suggested that shifts in plasma volume contributed to muscle cramps in liver disease, which might relate to altered serum albumin levels.

Strengths and Limitations

Our study had a number of strengths. We analyzed a number of subjects' clinical features, nutritional habits, laboratory data, and functional measures. Additionally, our subjects were highly motivated, indicated by low attrition (4%) and excellent adherence to study pills (median ~99% to 100%).[11]

We also acknowledge some weaknesses of this study. First, this was a post hoc analysis of a single-center, randomized, double-blind, placebo-controlled trial focused on changes in TFCA, BMD, and functional status with correction of vitamin D insufficiency,

rather than on muscle cramps. Our study was limited to postmenopausal and mostly white women. Additionally, at the study's onset, we found no validated questionnaires developed to measure muscle cramps so created our own questionnaire. However, others[6] recently validated and published a questionnaire similar to our own. Finally, the observational nature of this study can only suggest, not prove, causes of muscle cramps.

CONCLUSIONS

Muscle cramps are highly prevalent in the general population. Our study provides good evidence that vitamin D does not reduce muscle cramps in postmenopausal women with baseline serum 25(OH)D levels equaling 21±3 ng/mL. In our study, muscle cramps were associated with higher levels of pain and disability and lower potassium intake. Given the high prevalence of muscle cramps and their impact on quality of life, future research is warranted to establish the causes of muscle cramps. Such knowledge could direct double-blind, placebo-controlled trials to identify effective treatments.

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Travel During Pregnancy: Results From an Ultrasound Unit-Based Questionnaire

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ABSTRACT

Background: The frequency of domestic and international travel among women residing in the United States, and specifically Wisconsin, during pregnancy is not known. Given the recent epidemic of Zika virus disease, clinicians should be aware of the frequency of travel during pregnancy and should inquire about travel by pregnant women, women of reproductive age, and their sexual partners.

Methods: Due to the Zika epidemic, our obstetric ultrasound center added questions about international and domestic travel to a general health form that is routinely distributed to all patients presenting for anatomic ultrasounds. The forms were then collected and recorded in order to provide an estimate of the frequency of travel during the first half of pregnancy.

Results: Of 1,256 women screened, 64 (5.1%) traveled internationally and 498 (39.6%) traveled domestically prior to their anatomic ultrasound. Additionally, 77 (6.1%) women screened reported international travel by their sexual partner. Among international travelers, 20 (28.1%) traveled to destinations with active ongoing transmission of Zika virus disease, and 16 (25%) traveled after the Centers for Disease Control and Prevention (CDC) issued a travel alert for the area. Among domestic travelers, Florida was the sixth most common destination, and Texas was the 10th most common.

Conclusions: In the population of women screened by this questionnaire, 5.1% traveled internationally and 39.6% traveled domestically prior to their anatomic ultrasound. Notably, Florida and Texas are common travel destinations among women at this clinic, and both have had active local transmission of Zika virus.

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INTRODUCTION

The Zika virus is an emerging mosquito-borne arbovirus that recently has migrated to the Americas. There are now at least 50 countries affected, including parts of the United States.[1,2] Zika also can be transmitted sexually and vertically.[3–5] While asymptomatic in the majority of the population, it can cause profound congenital anomalies including severe neurodevelopmental anomalies, most notoriously microcephaly.[6–9] This proclivity, combined with ongoing transmission in Central and South America, among other destinations, places an unprecedented number of pregnancies at risk. Because the genus of mosquito that transmits Zika is not found in Wisconsin, active transmission here does not seem probable at this time, but at the time of this writing, 67 travel-related cases have been reported.[10,11] It is also notable that 1,776 travelers have been tested in Wisconsin.[11] Testing is limited to travelers who are either pregnant or who exhibit symptoms of Zika virus disease, so this testing does not encompass all potentially exposed individuals.

In 2014, 68.2 million US citizens traveled internationally—a notable increase from 28.5 million in 2010.[12,13] Travel during pregnancy also is thought to be increasing in frequency, but the actual frequency of domestic or international travel among women residing in the United States during pregnancy is not known.[14–19] Clinicians who provide care to obstetric patients or their sexual partners need to be aware of any travel so that appropriate counseling may be offered. Notably, the recent Zika epidemic has transformed previously low-risk travel destinations, such as Miami, into high risk travel destinations.[1]

Table 1. Self-reported Traveler Demographics

Demographics	International n=64	Domestic Travelers n=498	All Travelers n=517
Advanced maternal age (n, %)	20 (31.3%)	164 (32.9%)	170 (32.9%)
Body mass index (mean, SD)	26.3 (4.3)	27.8 (6.2)	27.8 (6.2)
Diabetes (n, %)	1 (1.6%)	18 (3.6%)	19 (3.7%)
Cardiovascular disease (n, %)	2 (3.1%)	12 (2.4%)	12 (2.3%)
Tobacco, alcohol, drug, or radiation exposure (n, %)	1 (1.6%)	35 (7.0%)	36 (7.0)
Infectious disease, any (n, %)	1 (1.6%)	17 (3.4%)	17 (3.3%)
Multifetal gestation	0 (0.0)	16 (3.2%)	16 (3.1)
Assisted reproductive technology (n, %)	4 (6.3%)	44 (8.8%)	45 (8.7%)

Clinicians also should be aware that the Centers for Disease Control and Prevention (CDC) currently recommends that pregnant women avoid travel to areas with Zika.[3] Similarly, it recommends that if the sexual partner of a pregnant woman has traveled to an affected area, that the couple either abstain from intercourse or correctly and consistently use a condom for the remainder of the pregnancy.[4] The CDC suggests screening pregnant women at every prenatal visit for possible Zika virus exposure (ie, asking about travel history for the patient and her partner[s]).[20] It is also important to note that the map of affected areas is constantly changing, so both clinicians and pregnant travelers should periodically check updates, available online at http://www.cdc.gov/zika/geo/index.html.[1]

The purpose of this study is to describe current trends in travel during the first half of pregnancy among obstetric patients presenting for their anatomic ultrasound at a center for perinatal care. While there are no US data on international travel during pregnancy, studies in France and England found that 22% to 58% of women travel abroad.[21,22] Since the geographic composition of the United States differs from Europe, we estimated that fewer women would travel abroad from the United States than Europe, but that the rates of interstate travel may be similar to the rates of international travel in Europe. We were also mindful that our data collection method captured only the first half of pregnancy, thus would underestimate travel that occurred during pregnancy overall. Our hypothesis, therefore, was that both domestic and international travel were common, occurring among at least 30% and 10% of the population, respectively.

METHODS

This study was approved by the Meriter Hospital Internal Review Board (Meriter IRB# 2016-007). All patients who present to the Meriter Center for Perinatal Care for a fetal anatomic ultrasound evaluation (CPT code 76805 or 76811) complete a general health form inquiring about comorbid conditions and pregnancy exposures. As per our unit protocol, these fetal ultrasound evaluations are performed between 19 and 22 weeks of gestation. This health form supplements the history available from either the electronic medical record or faxed referral forms. Considering the recent Zika epidemic, questions regarding international travel by the pregnant woman or her sexual partner(s) were added to this form in February 2016, and questions about domestic travel outside the state of Wisconsin were added in May 2016. The purpose of adding questions about domestic travel was to proactively ensure that such travel was queried due to the potential for active transmission of the Zika virus in the southern United States. The questions simply query who traveled, the travel destination(s), and when travel occurred. The questions specifically queried travel during pregnancy itself. Travel prior to pregnancy was assessed separately and was not recorded for the purposes of this study. However, data on how many such travelers required counseling for potential Zika exposure were recorded for clinical purposes. Once completed, clinicians utilize data from these forms to ensure that the appropriate level of anatomy scan is performed and that appropriate counseling and testing is offered.

For this study, forms from all travelers were collected and recorded from May 6, 2016 through September 30, 2016. Data regarding the answers to questions about medical comorbidities and travel history were extracted from these forms and entered into a database. In July 2016, active transmission of Zika was identified in Dade County, Florida with a statement that transmission may have occurred as early as June 15, 2016.[23] The presence of this database also allowed us to retrospectively review the timing of travel to identify women potentially at risk of Zika who were seen for ultrasound before this warning was issued.

Statistical analysis was performed using SPSS version 23.0 (SPSS Incorporated, IBM Corp, Armonk, NY) and Excel 2013 (Microsoft Office 2013, Microsoft Corporation, Redmond, WA).

RESULTS

Between May 6, 2016 and September 30, 2016, 1256 patients presented to the Meriter Center for Perinatal Care for a fetal anatomic ultrasound evaluation (CPT code 76805 or 76811). Of these women, 64 (5.1%) reported a history of international travel, 498 (39.6%) reported a history of domestic travel; and 45 (3.6%) reported a history of both types of travel. Thus 517 (41.2%) women presenting for anatomic ultrasound had traveled prior to their appointment. In addition, 77 (6.1%) reported international travel and 408 (32.5%) reported domestic travel by their sexual partner(s).

In our ultrasound unit overall, 73% of the patients are white, 7.5% are African American, 6.9% are Asian, 1.8% are Hispanic, 2.4% are multiracial, and the remaining patients decline to report. Overall, 28.7% of women have advanced maternal age and the

average body mass index (BMI) is 28.2 kg/m^2. Self-reported demographics of travelers is shown in Table 1. Among all reported travelers, 32.9% had advanced maternal age and the average BMI was 27.8 kg/m^2. Rates of self-reported diabetes and cardiovascular disease were 3.7% and 2.3%, respectively. Overall, 8.7% of travelers underwent assisted reproductive technologies. No international travelers had multifetal pregnancies whereas 3.2% of domestic travelers did.

Among international travelers, 18 (28%) traveled to destinations with active ongoing Zika transmission. Fourteen (21.9%) traveled after the CDC issued a level 2 travel advisory for people traveling to regions and countries where Zika virus transmission is ongoing.[1,24]

Among domestic travelers, Figure 1 shows the frequency of travel destination by state. The 10 most frequently listed states are shown in Table 2. Of these 10 states, California, Florida, and Texas have reported the presence of *Aedes aegypti* in recent years.[10] Both Florida and Texas, the 6th and 10th most frequently visited states, respectively, have had active Zika virus transmission. Overall, 11.6% of domestic travelers visited these states. The majority of travel occurred prior to the time of active transmission of Zika virus, but 11 travelers to Florida traveled during the time of active transmission. Two women specified that they traveled to Miami and three indicated that they traveled to cities outside of Dade County, which was the specific county with active Zika virus transmission.[23] The remaining 6 women who traveled during the time of concern were either queried during their ultrasound visit or called to clarify the exact areas visited. Five had traveled to Miami and therefore had additional testing offered, as recommended. Of note, during the data collection period, there was not active Zika virus transmission in Texas; therefore no patients traveled during the time of active transmission in this dataset.

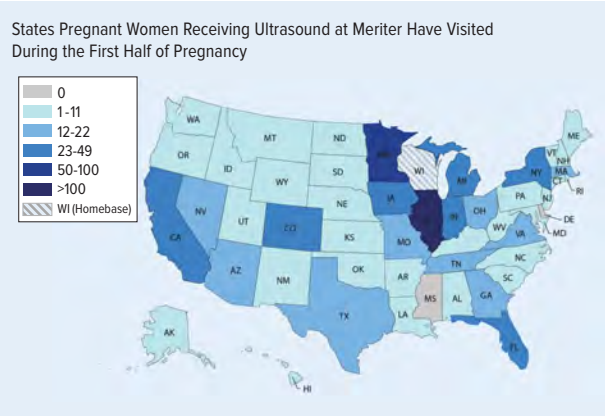
During the time of data collection, 30 women were tested for Zika; 12 of these women were tested due to travel that exclusively occurred prior to pregnancy.

Table 2. The Top 10 Most Frequently Visited States Among Pregnant Women Obtaining Anatomic Ultrasounds at the Study Site

State	Number of Travelers N= 1256
Illinois	179
Minnesota	71
California	43
Iowa	42
Michigan	41
Florida*	38
New York	30
Colorado	27
Indiana	24
Texas*	20

*Indicates states that have had active vector-borne transmission of Zika virus.

Figure 1. Number of Women Who Traveled to Each of the 50 States, May 2016 to September 2016



DISCUSSION

This study demonstrates that in the population of women obtaining anatomic ultrasounds in our ultrasound clinic, 5.1% traveled internationally and 39.6% traveled domestically prior to their ultrasound. During 2016, 28% of the international travelers and 11.6% of domestic travelers traveled to destinations with active ongoing transmission of Zika virus disease, although that risk was not necessarily known or present at the time of travel. Nevertheless, travelers continued to visit such areas: 21.9% of international travelers visited destinations with active Zika virus transmission after the travel warning.

There are no prior studies investigating the frequency of international travel during pregnancy performed in the United States. However, retrospective travel clinic studies suggest that when pregnant women travel, their destinations are similar to destinations of nonpregnant travelers, including travel to areas with endemic infectious diseases.[13,16,17] These findings are similar to ours, demonstrating that travelers visit destinations with known pregnancy risks.

In 2016, the CDC recommended that clinicians who care for pregnant women inquire about travel to areas with ongoing Zika transmission at every prenatal visit.[20] Here, we demonstrate that by adding 2 questions to an existing health form, we were able to identify women at risk of Zika. Additionally, by maintaining a database of travelers, we were able to retrospectively identify 5 women at risk of Zika after active Zika virus transmission was identified domestically. Strengths of this study include our ability to effectively screen patients presenting to our clinic for travel prior to their ultrasound appointment.

This study has notable limitations. By nature of the timing of the fetal anatomic evaluation, which, per unit protocol occurs at 19 to 22 weeks of pregnancy, this history form only captures travel

that occurs during the first half of pregnancy. Thus, all travel that occurred after the fetal anatomic ultrasound is missed by this study, which results in an underestimation of travel frequency. Second, travel history is self-reported onto a form that patients may only partially complete. For example, 11.7% of travelers did not complete the height and weight section of the form, which implies that other portions of the form may be similarly incomplete. Travelers who do not understand the rationale for asking about travel may be less inclined to answer these questions completely, therefore some travelers may have been missed. Additionally, travelers who completed Zika screening prior to their ultrasound may not have fully completed this form because they knew they had already been tested. They also may have not fully completed the form due to concerns about judgment from clinical staff. Because our clinic is staffed by maternal-fetal medicine specialists, our ultrasound unit sees a high proportion of patients with maternal comorbidities or fetal concerns. Given the higher medical risk of our clinic population, patients may be less inclined to travel than in a general obstetric population, which would result in an underestimation of travel. Because we did not record information from the health forms of patients who did not travel, we were not able to perform statistics to describe any clinical characteristics of travelers versus non-travelers. The frequency of travel also may be overestimated here, due to referrals for the indication of maternal Zika exposure. Finally, the health form, due to its brevity, did not capture information about mode of transportation (air vs ground), the reasons for travel (work, family, or leisure), or any other travel-related details. We also did not previously request information on the specific cities or regions visited within a state. However, as travel warnings specify cities and counties, we have subsequently modified our form to request more specific information about domestic travel.

Travel during pregnancy is reported to be increasingly common.[14–19] Obstetric clinicians, therefore, should ask pregnant women about whether travel is planned during pregnancy, and should also be prepared to discuss basic travel considerations or refer to a travel clinic.[19,25] Obstetric clinicians also should ask whether travel has already occurred so that relevant post-travel testing may be offered for infectious diseases such as Zika virus.[20] Finally, counseling regarding recommendations on the timing of pregnancy after travel should be discussed with both men and nonpregnant women during routine care, such as physical examinations or well woman examinations.

This study sought to describe current trends in travel by pregnant women who receive their ultrasound examinations at a perinatal care center in Madison, Wisconsin, which is a medium-sized city in the Midwest. Travel patterns in the United States may vary widely between coastal cities and rural areas. While the majority of patients in this population did not travel internationally prior to their anatomic ultrasound, a significant proportion of those who did travel internationally visited areas with ongoing Zika transmission, which poses pregnancy risks. Additionally, among women who traveled domestically, two of the top 10 travel destinations have had active Zika virus transmission in the past year. Ideally, future studies should focus on capturing data from the duration of pregnancy and ascertain additional details about the timing of travel, reason for travel, and whether any pretravel discussion occurred between the obstetric patient and her provider.

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Risk Factors Associated With Carbapenem-Resistant *Pseudomonas aeruginosa*

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ABSTRACT

Introduction: *Pseudomonas aeruginosa* infections resistant to carbapenem antimicrobials have increased. Traditional risk factors for non-carbapenem resistance include intensive care unit stay, mechanical ventilation, previous hospitalization, and major comorbidities. As microbes evolve, our understanding of their risk factors for resistance also should evolve.

Methods: We conducted a retrospective study of adult inpatients and outpatients with a positive *Pseudomonas aeruginosa* culture during 2014. Cultures were obtained from system laboratories and medical records were reviewed through our electronic medical record. Pearson's chi-squared test with Yates correction and 2-sample t-tests were performed on categorical and continuous variables, respectively. Binary regression was used for multivariable modeling.

Results: Patients (N=1,763), of mean age 68.0 years and body mass index (BMI) 30.4 kg/m^2, were more likely to be women (51.3%) and were predominately white (89.3%). Resistance to imipenem or meropenem (14.0%) on univariable analysis was associated with several variables of interest. Non-white race (odds ratio [OR] =1.67; *P*=0.009), respiratory cultures (OR=1.95; *P*=0.003), recent institutional transfer (OR=2.50; *P*<0.0001), vasopressor use (OR=1.98; *P*=0.001), central line placement (OR=1.55; *P*=0.036), and peripherally inserted central catheter placement (OR=1.74; *P*=0.002) remained significant predictors of carbapenem resistance in multivariable modeling.

Conclusion: Demographic and traditional risk factors, as well as respiratory cultures, were predictive of carbapenem resistance and may guide initial antibiotic treatment. Use of "last resort" antibiotics for *Pseudomonas aeruginosa* based solely on patient chronic conditions may not be necessary. Fortunately, <1% of strains were resistant to all drugs tested. Ongoing efforts to face drug-resistant organisms are warranted.

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INTRODUCTION

Over the last decade, infections with gram-negative bacteria have become a growing global concern due to increased resistance to widely accepted empiric therapies and new resistance mechanisms.[1-3] *Pseudomonas aeruginosa* (*P aeruginosa)* is a common gram-negative bacteria associated with nosocomial infections.[2-5] In 2013, an estimated 51,000 healthcare-associated *P aeruginosa* infections occurred in the United States, of which more than 13% were secondary to multidrug-resistant strains that resulted in nearly 400 deaths.[6] Infections with multidrug-resistant *P aeruginosa* have been correlated with higher treatment costs, increased mortality/morbidity, and additional care needs (ie, discharge to chronic care facilities).[2,3,5]

Risk factors for acquiring resistant organisms like *P aeruginosa* vary depending on patient characteristics and temporospatial factors.[1,2] Studies suggest that traditional risk factors for the acquisition of multidrug-resistant organisms include intensive care unit (ICU) admission, use of invasive medical devices (ie, mechanical ventilation), previous treatment with broad spectrum antibiotics (like cephalosporins, aminoglycosides, or carbapenems), length of hospital stay, and underlying diseases or comorbidities.[1,2,4,5,7]

Limited studies have investigated whether these risk factors for multidrug resistance can be used to predict carbapenem resistance in patients diagnosed with *P aeruginosa*.[8] As microbes evolve, our understanding of their risk factors also should evolve. This study aimed to determine whether traditional risk factors were predictive of carbapenem-resistant *P aeruginosa*.

METHODS

Study Design

We retrospectively studied all adult patients (inpatients and outpatients) with a positive *P aeruginosa* culture during the 2014 calendar year who presented to any of the 15 hospitals and 159 outpatient clinics in the Aurora Health Care system, an integrated medical system located primarily within eastern Wisconsin. Patients with a positive *P aeruginosa* culture were identified by ACL Laboratories, and culture site and antimicrobial susceptibility test records were obtained. The study population was inclusive of both colonized and infected patients with *P aeruginosa*. There was no way to differentiate colonization or infection based on culture results. Patient characteristics and demographics were obtained through Aurora Research Analytics and reviewed through the electronic medical record. Duplicate patient records were excluded and only the most recent positive culture susceptibility results were included in the analysis for each patient. The Aurora Institutional Review Board approved this study.

The outcome of interest, carbapenem-resistant *P aeruginosa*, was defined as resistance to either imipenem or meropenem as identified by antimicrobial susceptibility testing. Ertapenem was not included in this definition as it is not an effective treatment against *Pseudomonas*.[9] Additionally, multidrug-resistant *P aeruginosa* was defined as resistance to ceftazidime, cefepime, aztronam, ciprofloxacin, piperacillin, and gentamicin.[4] For the purpose of this study, pandrug-resistant *P aeruginosa* was defined as resistance to the 6 traditional non-carbapenem drugs associated with multidrug-resistant *P aeruginosa* and both carbapenems. These definitions were also based on antimicrobial susceptibility testing.

Variables hypothesized as risk factors for carbapenem-resistant *P aeruginosa* included age, race/ethnicity, history of chronic medical conditions, history of infections with other multidrug-resistant pathogens, recent ICU stay, recent transfer from an institution, and recent procedures that may require a hospital stay. Race/ethnicity was categorized into 4 groups: white non-Hispanic, black non-Hispanic, white Hispanic, and other. Due to the low number of patients who identified as either Asian, Alaskan native or American Indian, and 2 or more race/ethnicities, they were categorized as other race/ethnicity. Data also were categorized by institutional source of the culture, including 14 system hospitals and the one system-wide network of clinics. Recent events (ie, ICU admission) were identified from electronic medical record encounters and were defined as events that occurred up to 1 year prior to the most recent culture positive for *P aeruginosa*. Additionally, we hypothesized that cultures obtained within a hospital facility for inpatient or emergency department care also may be associated with resistance.

Statistical Analysis

Analyses were performed using MINITAB statistical software (Version 13; State College, PA). To describe demographic characteristics of our study population, frequencies with percentages and odds ratios (OR) with 95% confidence intervals (CI) were computed. To determine which risk factors were predictive of carbapenem resistance, we used the Pearson chi-squared test of independence with Yates correction and 2-sample t-tests, as appropriate. Significance was defined as $P< 0.05$. Only variables demonstrating significance in univariable analyses were included in multivariable logistic regression models. A P value cutoff of <0.20 for single variables was also explored to minimize bias associated with a P value cut off of <0.05.[10]

RESULTS

During the study period, data were collected on a total of 1,763 inpatients and outpatients with a positive *P aeruginos*a culture who met inclusion criteria. Across all of those identified with *P aeruginosa*, patients of mean age of 68.0 years and BMI 30.4 kg/m^2, were predominately white (89.3%), more likely to be women (51.3%), and from the outpatient setting (51.5%). *P aeruginosa* was isolated from non-respiratory surface or deep body tissue sites (44.9%), urinary tract (42.8%), respiratory tract (9.9%), and blood (2.4%).

Overall, 14.0% of cultures were resistant to imipenem or meropenem and were deemed carbapenem-resistant. Univariable analyses identified several variables that were significantly associated with carbapenem resistance (Table 1). Multivariable analyses revealed that the odds of carbapenem resistance were greater among those with a respiratory culture and who were of black or non-Hispanic race, as well as those who had a recent transfer from an institution, vasopressor use, central line placement, and peripherally inserted central catheter placement. All predictors remained in the multivariable model when single variables with a P value <0.20 were included.

While a mixture of inpatient and outpatient culture sources were present in each of the 14 system hospital locations, the proportions of carbapenem-resistant strains varied widely from a low of 3/58 (5.2%) at a small suburban Milwaukee County hospital to a high of 114/488 (23.36%) at a large, tertiary Milwaukee hospital. The proportion of resistant strains was 30/535 (5.6%) in cultures obtained system-wide from our outpatient clinic network. Despite these differences, when location of culture source was added to models or substituted for inpatient versus outpatient status, with either the tertiary hospital or the clinic network used as a reference "location," there was no significant change to the multivariable results listed in Table 1, with the exception of black race, which changed from borderline significant (P=0.042) to nonsignificant (P=0.06).

Overall, 9.0% of strains were resistant to both imipenem and meropenem. Additionally, only 0.62% and 0.57% of strains were deemed multidrug-resistant and pandrug-resistant *P aeruginosa*, respectively.

Table 1. Predictors of Carbapenem-Resistant *Pseudomonas aeruginosa* on Univariable and Multivariable Analyses

	Carbapenem-Resistant *P aeruginosa*					
Predictors	**Resistant (N=246)**	**Nonresistant (N=1517)**	**Univariable OR (95% CI)**	**Univariable *P* value**	**Multivariable OR (95% CI)**	**Multivariable *P* value**
Demographic Characteristics		68.3				
Younger Age (years), mean (SD)[a]	65.9 (15.5)	(16.8)	0.99 (0.98-1.00)	0.027	0.99 (0.98-1.00)	0.108
BMI (kg/m2), mean (SD)[a]	30.7 (11.1)	30.3 (9.7)	1.00 (0.99-1.02)	0.671	--	--
Male, N (%)	138 (56.1)	723 (47.7)	1.40 (1.07-1.84)	0.017	1.22 (0.91-1.64)	0.191
Race/Ethnicity[b]		1316				
White, non-Hispanic	185 (77.1)	(88.0)	*ref*	*ref*	*ref*	*ref*
Black, non-Hispanic	36 (15.0)	119 (8.0)	2.15 (1.44-3.22)	<0.0001	1.61 (1.02-2.55)	0.042
White Hispanic	11 (4.6)	36 (2.4)	2.17 (1.09-4.34)	0.028	1.84 (0.87-3.89)	0.113
Other	8 (3.34)	24 (1.61)	2.37 (1.05-5.36)	0.038	1.61 (0.63-4.11)	0.324
Hospitalized patients, N (%)	168 (68.3)	687 (45.3)	2.60 (1.95-3.47)	<0.0001	1.20 (0.85-1.72)	0.303
Culture Type						
Nonrespiratory surface or deep tissue culture, N (%)	103 (41.9)	688 (45.4)	*ref*	*ref*	*ref*	*ref*
Respiratory culture, N (%)	54 (22.0)	121 (8.0)	2.98 (2.03-4.37)	<0.0001	1.80 (1.13-2.88)	0.013
Blood culture, N(%)	7 (2.9)	35 (2.3)	1.34 (0.58-3.09)	0.498	1.08 (0.43-2.70)	0.875
Urine culture, N (%)	82 (44.4)	673 (33.3)	1.23 (0.90-1.67)	0.191	1.20 (0.83-1.72)	0.323
History of:						
Diabetes mellitus, N (%)	97 (39.4)	527 (34.7)	1.22 (0.93-1.61)	0.153	--	--
Stage 4 or 5 kidney disease, N (%)	79 (32.1)	412 (27.2)	1.27 (0.95-1.70)	0.108	--	--
Chronic obstructive pulmonary disease, N (%)	55 (22.4)	229 (15.1)	1.62 (1.16-2.26)	0.005	1.09 (0.74-1.60)	0.679
Congestive heart failure, N (%)	54 (22.0)	236 (15.6)	1.53 (1.10-2.13)	0.016	1.13 (0.77-1.65)	0.535
Infections with other multidrug-resistant pathogens, N (%)	11 (4.5)	22 (1.5)	3.18 (1.52-6.65)	0.003	1.89 (0.84-4.27)	0.126
Recent Events						
Transfer from an institution, N (%)[c]	119 (48.4)	352 (23.3)	3.09 (2.34-4.08)	<0.0001	2.52 (1.80-3.52)	<0.0001
Chronic steroid use, N (%)	2 (0.8)	17 (1.1)	0.72 (0.17-3.15)	0.665	--	--
Surgery, N (%)[d]	100 (40.7)	461 (30.5)	1.56 (1.18-2.06)	0.002	1.14 (0.83-1.57)	0.412
Foley catheter placement, N (%)	133 (54.1)	535 (35.3)	2.16 (1.65-2.84)	<0.0001	1.15 (0.82-1.61)	0.412
Vasopressor treatment, N (%)	93 (37.8)	190 (12.5)	4.25 (3.15-5.73)	<0.0001	1.96 (1.28-2.99)	0.002
Central line placement, N (%)	99 (40.2)	242 (16.0)	3.55 (2.66-4.74)	<0.0001	1.55 (1.03-2.33)	0.035
Peripherally inserted central catheter, N (%)	157 (63.8)	494 (32.6)	3.65 (2.76-4.84)	<0.0001	1.69 (1.18-2.40)	0.004
Mechanical ventilation, N (%)	34 (13.8)	78 (5.1)	2.96 (1.93-4.54)	<0.0001	1.04 (0.62-1.75)	0.875
ICU admission, N (%)	146 (59.4)	524 (34.5)	2.77 (2.10-3.64)	<0.0001	1.18 (0.79-1.75)	0.408
Dialysis, N (%)	38 (15.5)	190 (12.5)	1.28 (0.87-1.86)	0.205	--	--
Bedridden status, N (%)[e]	61 (24.8)	161 (10.6)	2.77 (1.99-3.87)	<0.0001	1.20 (0.81-1.78)	0.368

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; ICU, intensive care unit.
[a] Continuous variable.
[b] Missing variables of interest; numbers used for analysis: Resistant (N=240) and Nonresistant (N=1495).
[c] Missing variables of interest; number used for analysis: Nonresistant (N=1514).
[d] Missing variables of interest; number used for analysis: Nonresistant (N=1513).
[e] Missing variables of interest; number used for analysis: Nonresistant (N=1515).

DISCUSSION

Several studies have identified respiratory culture sites as an independent risk factor for infections with *P aeruginosa*.[3,11,12] The flagellar cap and outer core of lipopolysaccharide molecules of *P aeruginosa* are advantageous for adhesion to mucins within the lungs and rapid development of resistant strains.[13,14] Unsurprisingly, we found that carbapenem-resistant *P aeruginosa* was significantly associated with respiratory culture sites, which was consistent with the findings of Dantas et al.[12] As *P aeruginosa* is a common cause of ventilator-associated pneumonia,[14] we were surprised to find no association of multidrug-resistant *P aeruginosa* with mechanical ventilation on multivariable analyses. Patients requiring mechanical ventilation occasionally require other aggressive management modalities (ie, peripherally inserted central catheter, central line,

vasopressors, etc). It is possible that the risk for infections with resistant organisms in mechanically ventilated patients is only a perceived risk, given their disease state and treatments being utilized. Further studies of multidrug-resistant *P aeruginosa* in mechanically ventilated patients are warranted.

It is well known that healthcare facilities (ie, hospitals, subacute care facilities and nursing homes) provide an environment where selective pressure due to broad spectrum antibiotic use results in the selection of highly resistant pathogens.[4,5,15] Our findings of elevated risk for carbapenem-resistant *P aeruginosa* in patients who had a recent transfer from an institution were consistent with this phenomenon. Individual risk factors (vasopressor treatment, central line placement, and peripherally inserted central catheter placement) identified by Aloush et al for multidrug-resistant *P aeruginosa* were consistent with our findings for carbapenem-resistant *P aeruginosa* on both univariable and multivariable analyses.[4] Such invasive treatments are often reserved for very sick patients requiring invasive modalities for disease management. These patients may already have a compromised immune system due to disease burden, and added insult of invasive treatments provides pathogens with an opportunity for access. Additionally, invasive treatments may be proxies for length of stay, which may be an independent factor influencing the development of resistance. Further study is necessary.

Overall, there are many useful clinical implications that can be drawn from this study: (1) it is likely that the coalition of the above-mentioned risk factors, rather than individual factors, increase the risk of carbapenem resistant *P aeruginosa* infections; (2) patients who have multiple risk factors for resistance should minimize carbapenem use,[1,8] and empiric therapies from other antibiotic groups with known activity against *Pseudomonas* should be utilized; and (3) history of an infection with other resistant pathogens or chronic medical conditions were not risk factors for carbapenem-resistant *P aeruginosa*. Additionally, increased implementation of antibiotic stewardship programs is needed to ensure the appropriate use of antimicrobials in an effort to minimize the development and spread of drug resistance among microbes.[1,9]

Our study has several strengths. First, this study investigated a large cohort of individuals who had a positive *P aeruginosa* culture, giving us the statistical power needed to detect any effects or patterns associated with our outcome of interest. Thus, we were able to derive a stronger sense of what risk factors may predict or correlate with resistance. Identification of risk factors has become increasingly important within our specific region of Wisconsin, as *P aeruginosa* isolates seem to have decreased susceptibility, not only to carbapenems, when compared to other nearby regions.[16] Additionally, antimicrobial susceptibility testing was very comprehensive, allowing us to identify carbapenem, multidrug, and pandrug resistance. Secondly, even though in practice chronic medical conditions such as diabetes or chronic kidney disease are thought to increase the risk of resistance, this was not confirmed by our study. Our results may positively impact clinical practice by reducing unwarranted use of last resort antibiotics based solely on a patient's chronic conditions.

Our study also has some limitations. First, this was a retrospective study design in which information or observer bias could be introduced. Electronic medical records (EMR) are only as accurate as the recorder and not all data collected may be available. This is particularly true when identifying recent events (ie, surgery), as patients may not have had a documented surgery in our EMR if the surgery was conducted outside of our hospital system. Additionally, there could be sampling biases due to the nonrandom selection of the population studied, although all patients meeting criteria during the period were used. Further prospective studies are needed to minimize these biases. Secondly, this study focused on a population of individuals from a single hospital system and geographic region, which may impact the generalizability of our findings. Additionally, our study could not identify specific mechanisms associated with resistance given the retrospective study design.

CONCLUSION

Demographic and traditional risk factors, as well as isolation of *P aeruginosa* from respiratory culture sites, were predictive of carbapenem resistance. Further understanding of these risk factors with prospective studies and evidence-based scoring systems involving well studied risk factors, may provide an invaluable tool for the prevention and management of carbapenem resistant *P aeruginosa*. Emergence and spread of antimicrobial resistance is an increasing challenge among healthcare systems across the world. Ongoing efforts to face drug-resistant organisms are vital to the future care of patients.

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Severe Maternal Morbidity During Delivery Hospitalizations

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ABSTRACT

Introduction: Severe maternal morbidities include 25 complications resulting from, or exacerbated by, pregnancy. Nationally, in the last decade, these rates have doubled.

Objective: This study describes trends in the rates of severe maternal morbidities at the time of hospitalization for delivery among different groups of Wisconsin women.

Methods: Hospital discharge data and ICD-9-CM diagnosis and procedure codes were used to identify delivery hospitalizations and rates of severe maternal morbidity among Wisconsin women from 2000 to 2014. Subsequent analyses focused on recent years (2010-2014). Rates of severe maternal morbidity were calculated per 10,000 delivery hospitalizations for all 25 severe maternal morbidity conditions as well as 24 conditions (excluding blood transfusions). Rates and rate ratios were calculated overall and for racial/ethnic groups, age groups, public health region of residence, and hospital payer. Median hospital length of stay and median hospital charges were compared for delivery hospitalizations with increasing severe maternal morbidities.

Results: Severe maternal morbidity rates increased 104% from 2000 to 2014 (*P* for trend <0.01). After excluding blood transfusions, rates increased 15% (*P* for trend <0.05). From 2010 to 2014, overall rates were stable over time, but varied by maternal age, race/ethnicity, payer, and public health region of residence. Median hospital charges and length of stay increased as the number of morbidities increased.

Conclusions: Monitoring severe maternal morbidities adds valuable information to understanding perinatal health and obstetric complications in order to identify opportunities for prevention of severe morbidities and improvements in the quality of maternity care.

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INTRODUCTION

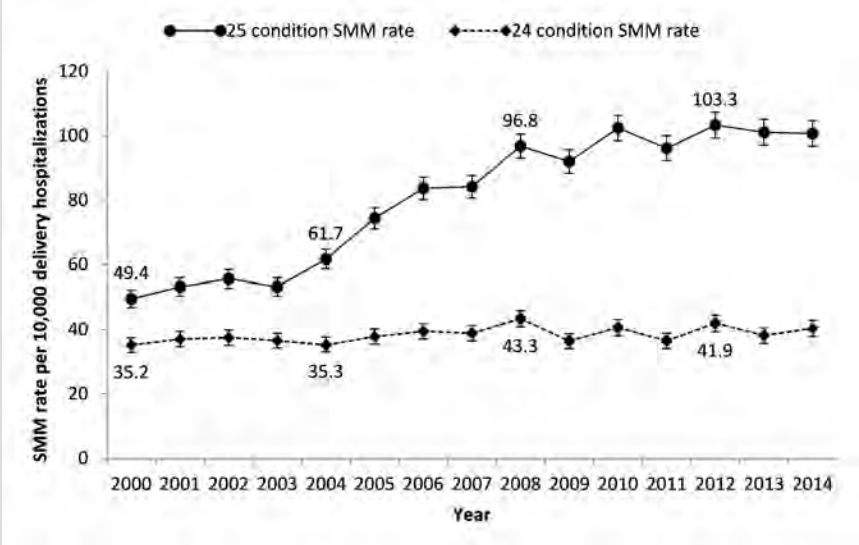
Considerable progress has been made in the United States to reduce pregnancy-related deaths.[1] This is reflected in Wisconsin, where maternal mortality remains below the national average (16.0 per 100,000 live births) at 5.9 deaths per 100,000 live births.[2] Though maternal deaths are relatively rare, it is estimated that for each death another 50 women experience serious complications related to pregnancy.[3] While maternal deaths traditionally have been the key indicator for maternal outcomes, the prevalence of serious pregnancy complications—or severe maternal morbidities—can provide a more comprehensive picture of perinatal health issues when examined along with maternal deaths.[3,4]

Nationally, there are efforts to expand maternal health surveillance beyond maternal death to severe maternal morbidity, which may have both short- and long-term consequences for childbearing women.[5] Included in these efforts is the development of a standardized measure that utilizes diagnostic codes from hospital data to identify delivery hospitalizations with at least 1 of 25 severe conditions.[3-5] These conditions often are associated with long hospital stays and high medical costs at the time of delivery and, for some women, well into the postpartum period.[4]

In the past decade, reported severe maternal morbidity nationally has increased from 79 to 163 per 10,000 delivery hospitalizations—a 106% increase—suggesting a need to improve the quality of maternal care and identify high-risk women for targeted interventions in the perinatal period.[4,6] Estimating severe maternal

morbidity at the state level is an important extension of this work, since state health departments are well-positioned to share the information with multiple partners who work closely with and within health-care systems. To date, statewide surveillance of severe maternal morbidity has not been put into practice in Wisconsin, but may offer insights for identifying opportunities to prevent maternal deaths and address quality in perinatal care.[3] This analysis utilizes the standardized measure for severe maternal morbidity to describe temporal trends and identify groups at increased risk in Wisconsin.

Figure. Severe Maternal Morbidity Rate, Wisconsin 2000-2014



Abbreviation: SMM, severe maternal morbidities.

METHODS

Wisconsin's hospital discharge data was used to identify delivery hospitalizations to Wisconsin women from 2000 to 2014. This data contains hospital admission and discharge encounters in Wisconsin facilities regardless of payer. In addition, delivery hospitalizations for Wisconsin residents in Minnesota facilities were included, as approximately 1,200 Wisconsin resident births (2%) and as many as 98% of births to women residing in some western Wisconsin counties occur in Minnesota facilities. Any hospitalizations of out-of-state residents in Wisconsin facilities were excluded from analysis. Delivery hospitalizations were identified with pregnancy-related International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes using methods previously described by Kuklina and colleagues.[6]

To identify delivery hospitalizations with severe maternal morbidity, 25 conditions present at the time of delivery hospitalization among Wisconsin residents were identified with ICD-9-CM diagnosis and procedure codes using methods described by Callaghan and colleagues.[4] A severity recalculation was applied to account for implausibly short length of hospital stay, such that delivery hospitalizations identified by diagnosis codes were reclassified as non-severe maternal morbidity delivery hospitalizations if the length of stay was less than the 90th percentile.[4]

The severe maternal morbidity rate was calculated as the number of delivery hospitalizations with at least 1 condition per 10,000 delivery hospitalizations, and the Cochran-Armitage test for linear trend was used to examine changes from 2000 to 2014. To statistically test apparent stabilization in more recent years, Joinpoint software was used to identify the best fit line for trends, including detection of any changes in the slope of the trend line over time.[7]

To provide a more detailed look at trends and disparities in recent years, delivery hospitalizations from 2010 to 2014 were the focus of subsequent analyses. Rates were calculated separately for each condition as well as hospital stay payer (private, Medicaid, and other—eg, all other payers including Medicare, other governmental payer, self-pay, or unknown), age categories (less than 20 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, and 40 or more years), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic American Indian/Alaska Native, non-Hispanic Asian/Pacific Islander, and non-Hispanic other), delivery type (vaginal, primary cesarean, and repeat cesarean) and public health region of residence (western, northern, northeastern, southeastern, and southern). Crude rate ratios were calculated to compare rates within these categories.

Delivery hospitalizations with severe maternal morbidity were categorized as having 0, 1, 2, or 3 or more conditions. In addition, median hospital length of stay and median total hospital charges for delivery hospitalizations with no severe maternal morbidity were compared to delivery hospitalizations across these categories. The Wilcoxon Rank Sum test was used to compare median length of stay and charges for each category compared to the category with fewer severe maternal morbidities as the comparison group (eg, 1 vs 0, 2 vs 1, and 3+ vs 2).

Two severe maternal morbidity rates were calculated across all analyses: (1) a morbidity rate including all 25 conditions, and (2) a 24-condition morbidity rate excluding blood transfusion. The 25-condition rate usually is dominated by transfusion as the leading severe maternal morbidity condition, so an examination of the 24-condition rate allows for an assessment of trends and other findings independent of the impact of transfusion.[5] This comparison is valuable, as hospital discharge data does not include information about the number of units of blood transfused, and transfusions of less than 4 units may inappropriately classify delivery

hospitalizations as those with severe maternal morbidity. *P*-values of less than 0.05 were interpreted as statistically significant for all comparisons and statistical tests. All statistical analyses were conducted in SAS version 9.4 (SAS Institute, Cary, North Carolina) and Joinpoint version 4.3.1.0.

RESULTS

A total of 995,179 delivery hospitalizations occurred among Wisconsin women between 2000 and 2014. Of those, 7,999 were identified with severe maternal morbidity (overall rate=80.4 per 10,000 delivery hospitalizations, 95% CI=78.6, 82.2), but 1,894 (19.1%) were reclassified as non-severe maternal morbidity hospitalizations due to length of stay less than the 90th percentile. The severe maternal morbidity rate increased 103.6% between 2000 and 2014 (*P* for trend <0.01; see Figure), and we identified 1 point where the slope of the trend line changed significantly. While the rate increased from 2000 to 2007 (*P*<.01), there was no significant change from 2008 to 2014 (*P*=0.14). After removing blood transfusions, there were 3,812 delivery hospitalizations with severe maternal morbidity from 2000 to 2014 (overall rate=38.3, 95% CI=37.1, 39.5), with a 14.7% increase during this time period (*P* for trend=0.04). No changes in the slope of the trend line were identified.

From 2010 to 2014, there were 320,745 delivery hospitalizations. Of those, 3,229 were identified with severe maternal morbidity (rate=100.7, 95% CI=97.2, 104.1), and 572 (15.0%) were reclassified as non-severe maternal morbidity hospitalizations due to length of stay less than the 90th percentile. This rate remained stable during the time period (*P* for trend=0.90). After removing blood transfusions (24-condition rate), there were 1,266 delivery hospitalizations with severe maternal morbidity (rate=39.5, 95% CI=37.3, 41.7), a rate that remained virtually stable (percent decrease=0.6%, *P* for trend=0.88).

Table 1 shows the number and rate of each condition, ordered by highest rate. Among delivery hospitalizations with severe maternal morbidity, 12.8% (n=414) had more than 1 condition. Both hospital charges and length of stay increased significantly with each additional severe maternal morbidity for the 25-condition analysis (*P*<0.01 for each comparison), and results were similar for the 24-condition analysis with the exception of 3+ vs 2 conditions (Table 2). Table 3 shows rates and rate ratios by demographic and geographic subgroups. We observed disparities by age, race, payer, mode of delivery, and region.

Table 1. Severe Maternal Morbidity Rates by Condition for Delivery Hospitalizations, 2010–2014

	Delivery Hospitalizations		
		Rate Per 10,000	
Condition	No.	Delivery Hospitalizations	95% CI
Blood transfusion	2,214	69.0	66.2, 71.9
Operations on heart, pericardium, and other vessels[a]	271	8.4	7.4, 9.5
Hysterectomy	245	7.6	6.7, 8.6
Disseminated intravascular coagulation	221	6.9	6.0, 7.8
Heart failure during procedure or surgery	147	4.6	3.8, 5.3
Acute renal failure	130	4.1	3.4, 4.7
Adult respiratory distress syndrome	122	3.8	3.1, 4.5
Ventilation	99	3.1	2.5, 3.7
Eclampsia	85	2.7	2.1, 3.2
Shock	81	2.5	2.0, 3.1
Sepsis	62	1.9	1.5, 2.4
Puerperal cerebrovascular disorders	35	1.1	0.7, 1.5
Cardio monitoring	28	0.9	0.5, 1.2
Pulmonary edema	27	0.8	0.5, 1.2
Thrombotic embolism	27	0.8	0.5, 1.2
Sickle cell anemia with crisis	18	0.6	0.3, 0.8
Internal injuries of thorax, abdomen and pelvis	14	0.4	0.2, 0.7
Amniotic fluid embolism	12	0.4	0.2, 0.6
Cardiac arrest or ventricular fibrillation	12	0.4	0.2, 0.6
Conversion of cardiac rhythm	12	0.4	0.2, 0.6
Severe anesthesia complications	11	0.3	0.1, 0.5
Intracranial injuries	5	[b]	[b]
Acute myocardial infarction	4	[b]	[b]
Aneurysm	1	[b]	[b]
Temporary tracheostomy	1	[b]	[b]

[a]Category has been renamed to clarify the inclusion of operations on other vessels.
[b] Rates and CIs not calculated for severe maternal morbidity with fewer than 10 events.

Table 2. Median and Range of Length of Hospital Stay and Hospital Charges by Number of Severe Maternal Morbidities Among Delivery Hospitalizations, Wisconsin, 2010-2014

	25-Condition SMM		24-Condition SMM	
	LOS (Days)	Hospital Charges	LOS (Days)	Hospital Charges
0 SMM	2	$8,954	2	$8,983
1 SMM	3[a]	$18,891[a]	4[a]	$23,619[a]
2 SMM	5[b]	$34,975[b]	6[b]	$52,426[b]
3+ SMM	6[c]	$68,895[c]	7	$78,874[c]

Abbreviations: SMM, severe maternal morbidity; LOS, length of hospital stay.
[a]Significantly different from 0 SMM, *P*<0.01.
[b]Significantly different from 1 SMM, *P*<0.01.
[c]Significantly different from 2 SMM, *P*<0.01.

DISCUSSION

Our observations for the most commonly documented severe maternal morbidity conditions and increasing trend over time

Table 3. Severe Maternal Morbidity Rate by Demographics, Payer, and Public Health Region of Residence, Wisconsin, 2010-2014

	25-Condition SMM			24-Condition SMM		
	Delivery With SMM	Rate Per 10,000 Delivery (Hospitalizations (95% CI)	Rate Ratio (95% CI)	Delivery With SMM	Rate Per 10,000 Delivery Hospitalizations (95% CI)	Rate Ratio (95% CI)
Age						
< 20	290	139.6 (123.6, 155.7)	**1.6 (1.4, 1.9)**	79	38.0 (29.6, 46.4)	1.2 (0.9, 1.5)
20-24	670	98.8 (91.3, 106.2)	1.2 (1.0, 1.3)	190	28.0 (24.0, 32.0)	0.9 (0.7, 1.0)
25-29	866	85.4 (79.7, 91.1)	Reference	332	32.7 (29.2, 36.3)	Reference
30-34	833	93.3 (87.0, 99.7)	1.1 (1.0, 1.2)	366	41.0 (36.8, 45.2)	**1.3 (1.1, 1.5)**
35-39	443	128.4 (116.5, 140.4)	**1.5 (1.3, 1.7)**	227	65.8 (57.2, 74.4)	**2.0 (1.7, 2.4)**
40+	127	181.4 (149.8, 212.9)	**2.1 (1.8, 2.6)**	72	102.8 (79.1, 126.6)	**3.1 (2.4, 4.1)**
Race/ethnicitya						
Non-Hispanic white	1,922	86.2 (82.3, 90.0)	Reference	775	34.7 (32.3, 37.2)	Reference
Non-Hispanic black	476	148.0 (134.7, 161.3)	**1.7 (1.6, 1.9**)	197	61.3 (52.7, 69.8)	**1.8 (1.5, 2.1)**
Hispanic	347	126.3 (113.0, 139.6)	**1.5 (1.3, 1.6)**	116	42.2 (34.5, 49.9)	1.2 (1.0, 1.5)
Non-Hispanic Asian/Pacific Islander	172	135.7 (115.4, 156.0)	**1.6 (1.3, 1.8**)	61	48.1 (36.0, 60.2)	**1.4 (1.1, 1.8)**
Non-Hispanic American Indian/Alaska Native	56	158.9 (117.3, 200.5)	**1.8 (1.4, 2.4)**	14	39.7 (18.9, 60.5)	1.1 (0.7, 1.9)
Non-Hispanic Other	29	100.5 (63.9, 137.1)	1.2 (0.8, 1.7)	16	55.5 (28.3, 82.6)	1.6 (1.0, 2.6)
Payer						
Private	1,551	85.1 (80.9, 89.3)	Reference	652	35.8 (33.0, 38.5)	Reference
Medicaid	1,548	120.9 (114.9, 126.9)	**1.4 (1.3, 1.5)**	543	42.4 (38.8, 46.0)	**1.2 (1.1, 1.3)**
Other	130	125.8 (104.2, 147.4)	**1.5 (1.2, 1.8)**	71	68.7 (52.7, 84.7)	**1.9 (1.5, 2.5)**
Public health region of residence						
Western	310	75.3 (66.9, 83.7)	Reference	131	31.8 (26.4, 37.3)	Reference
Northeastern	663	98.2 (90.7, 105.7)	**1.3 (1.1, 1.5)**	202	29.9 (25.8, 34.0)	0.9 (0.8, 1.2)
Northern	271	113.9 (100.3, 127.4)	**1.5 (1.3, 1.8**)	94	39.5 (31.5, 47.5)	1.2 (1.0, 1.7)
Southeastern	1,259	101.7 (96.1, 107.4)	**1.4 (1.2, 1.5)**	538	43.5 (39.8, 47.2)	**1.4 (1.1, 1.7**)
Southern	726	112.8 (104.6, 121.0)	**1.5 (1.3, 1.7)**	301	46.8 (41.5, 52.0)	**1.5 (1.2, 1.8)**
Delivery type						
Vaginal	606	57.9 (54.9, 61.0)	Reference	306	17.2 (15.6, 18.9)	Reference
Primary cesarean	1,250	273.4 (258.6, 288.9)	**4.7 (4.4, 5.1)**	553	121.0 (111.2, 131.4)	**7.0 (6.2, 8.0)**
Repeat cesarean	1,373	159.6 (147.3, 172.7)	**2.8 (2.5, 3.0)**	407	80.6 (71.9, 90.0)	**4.7 (4.0, 5.4)**

Abbreviations: SMM, severe maternal morbidity.

Bold type indicates a statistically significant difference from a ratio of 1.0.

[a]18,927 hospitalizations missing race/ethnicity (5.9%).

are consistent with other studies.[3] Blood transfusions, which accounted for most of the increase in severe maternal morbidity over time, may relate to postpartum hemorrhage.[3,4] It is well understood that prior cesarean delivery increases the risk for abnormal placentation in subsequent deliveries, potentially leading to hemorrhage. Further, placental abnormalities, labor induction, cesarean deliveries, and instrumental delivery have increased, which may be related to prenatal obesity and advanced maternal age.[5,8-13] Increases in severe maternal morbidity nationally have been attributed to maternal factors such as obesity, cesearean delivery, and chronic health conditions.[14] Publicly available data from the Wisconsin Department of Health Services indicate that the proportion of cesarean delivery births increased from 17% to 25% from 2000 to 2007 but remained stable from 2008 to 2014 (25% vs. 26%).[15] Further, the Centers for Disease Control and Prevention's Pregnancy Risk Assessment Monitoring System, a population-based survey targeting mothers with a live birth, indicates that the proportion of Wisconsin women who were obese prior to pregnancy has remained stable since 2008.[16] While previous studies have identified higher risk of severe maternal morbidity for cesarean deliveries,[5,14] it is unclear whether severe maternal morbidity increases the risk for cesarean delivery or vice versa. Future examination of prepregnancy maternal health may assist in understanding the relationship between severe maternal morbidity and mode of delivery.

A challenge in understanding blood transfusion trends relates to how the ICD-9-CM code is used in practice in events such as postpartum hemorrhage. This condition is often clinically defined as blood loss greater than 500 ml for a vaginal delivery and 1,000 ml for cesarean delivery,[5,17] thresholds that are good predictors of

the need for blood transfusion.[17] However, the ICD-9-CM code for blood transfusion does not include information for important contextual details such as units of transfused blood, which may be an important indicator of severity, particularly as calls for in-hospital reviews of severe maternal morbidity suggest reviewing cases where women receive 4 or more units of blood.[18] In addition, lack of detailed clinical information and changes in clinician use of blood transfusion over time further limits our ability to fully explain the increase in blood transfusions in Wisconsin.[19]

Our findings for median length of stay and hospital charges likely reflect that women with multiple severe maternal morbidities may tend to have more severe or complex medical complications during delivery hospitalization, which may require longer and more expensive hospital care. Of interest, median length of stay and charges were lower for 25-condition vs 24-condition severe maternal morbidity. This may reflect the predominance of blood transfusions in the 25-condition definitions such that some of those hospitalizations with only blood transfusion may be relatively minor in comparison to the other 24 conditions.

Disparities for severe maternal morbidity by demographic characteristics followed very similar patterns to those recently reported for maternal mortality in Wisconsin.[2] The rare occurrence of maternal death and small population size for some racial/ethnic groups in the state prevent the ability to examine disparities in maternal mortality across all groups. Thus, severe maternal morbidity can provide a mechanism for identification of these disparities in maternal health and outcomes.

Some limitations of this study should be noted. First, we included only delivery hospitalizations; consequently, women hospitalized prenatally or postpartum for any of the 25 severe maternal morbidity conditions are not captured in our estimation of severe maternal morbidity burden if these conditions were not also present at delivery. Further, though we utilized a validated method for identifying severe maternal morbidity, the use of ICD-9-CM codes for the analysis may result in misclassification as coding practices can vary among medical coders by facility or over time. In addition, the severe maternal morbidity conditions described here each include multiple ICD-9-CM codes, which might obscure whether a few codes disproportionately account for the events in some categories. For example, Wisconsin's rate for operations on the heart, pericardium, and other vessels category was substantially higher than the US rate.[4] Upon examination of the ICD-9-CM codes contributing to this category, we observed that suture of artery (39.31) was the most common code within this category and very few codes were related to the heart or pericardium. Finally, hospital data does not include contextual information that could enhance the analysis. For example, there are few fields within the dataset that allow for adjustment for potential confounders beyond basic demographic information, including risk factors such as obesity, poverty status, late or no prenatal care, prior cesarean delivery, or prepregnancy medical condition.[1,20-22] Consequently, differences identified by geography, demographics, and hospital payer should be interpreted cautiously, as we did not conduct analyses to adjust for confounders. Analyses utilizing hospital discharge data linked to the newborn hospitalization and birth certificate would enable a more complete exploration of contributors to differences and trends in severe maternal morbidity.[1]

CONCLUSIONS

Despite these limitations, our analysis of severe maternal morbidities adds to the understanding of perinatal complications in Wisconsin. The Wisconsin Maternal Mortality Review Team has been able to glean some limited information about the increased risk of chronic disease on maternal health, but continued surveillance of severe maternal morbidities would provide more in-depth understanding.[2] In addition, it is important for physicians and hospitals to be aware of the trends and current distribution of severe maternal morbidities among Wisconsin mothers as they identify needs for quality improvement related to perinatal care. The American College of Obstetricians and Gynecologists recommends that hospitals or birth facilities develop and maintain their own severe maternal morbidity review process to address opportunities for system and caregiver improvement.[14] Our analyses provide important information about groups of women at risk for severe pregnancy complications, which could help identify areas for targeted intervention. Further, our use of a standard approach for identifying and tracking maternal complications provides clinicians and public health partners with a framework for exploring opportunities to improve perinatal care and outcomes.

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Case Report of Metronidazole-Induced Encephalopathy

Adam Clements, DO

ABSTRACT

This report describes the case of an 83-year-old woman who was admitted to a hospitalist service with weakness and falls. She was transferred from an outside facility where she was treated with 3 courses of metronidazole for diagnosed *Clostridium difficile* colitis and presumed reoccurrences. Magnetic resonance imaging (MRI) demonstrated T2 enhancement of the dorsal pons and dentate nuclei consistent with metronidazole-induced encephalopathy. Her metronidazole was stopped and her symptoms resolved. This condition is rare, poorly understood, and causes reversible changes in the brain that are detectable through T2-weighted MRI. It will need ongoing study with current widespread use of metronidazole.

BACKGROUND

Metronidazole is an antibiotic available for oral or intravenous (IV) use typically used to treat protozoan or anaerobic bacterial infections. One of its important and common uses is as the first-line treatment for *Clostridium difficile*. Metronidazole crosses the blood brain barrier and, since animal experiments in the 1960s, it has been known to potentially cause neurotoxicity in animal models.[1,2] In 1995 metronidazole was first described as a cause of neurotoxicity in the brain of a human patient.[3] Lesions occur in similar areas in nearly all patients and are seen as bright areas on T2-weighted magnetic resonance imaging (MRI). They are most commonly seen in the dentate nucleus of the cerebellum and in the pons. Most published cases describe resolution of symptoms and MRI changes after metronidazole is stopped. Poor neurologic outcomes and death attributable to metronidazole-induced encephalopathy (MIE) have been reported. One case report from 2015 described a patient whose MRI revealed expected changes after a 3-week course of metronidazole for cholecystitis; however, despite appropriately stopping metronidazole and providing supportive care, her neurological impairment progressed. She was placed on hospice care and died 12 days later. Near the time of her hospice enrollment the T2 MRI enhancement had spread throughout brainstem, corpus callosum, subcortial white matter, and spinal cord.[4]

CASE REPORT

An 83-year-old woman was transferred to our institution after 7 days of progressive weakness, ataxia, and falls. Her symptoms were exclusively of her truncal muscles and on exam, her limbs had normal strength and coordination. Her muscles were normal in appearance, but she was unable to maintain an upright posture when sitting. When she was assisted to a sitting position she fell backwards or to the side if unsupported. No mental status changes or other neurological symptoms were reported by nursing or on the review of symptoms, and no other focal neurological or muscular symptoms were found by the hospitalist or the neurologist.

The patient had a relevant past medical history of spinal stenosis in her lumbar spine, protein calorie malnutrition, rheumatoid arthritis, chronic prednisone use, and *Clostridium difficile*. She had undergone lumbar spine laminectomy and fusion approximately 3 months prior to admission and had been doing well post-operatively. She lived independently, performed all her activities of daily living, and walked unassisted.

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Figure 1. Axial Magnetic Resonance Imaging Demonstrating Enhancement of the Dentate Nucleus Bilaterally

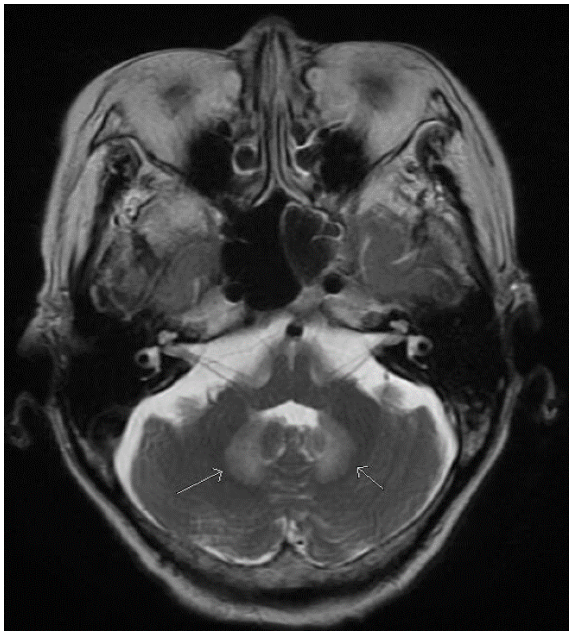
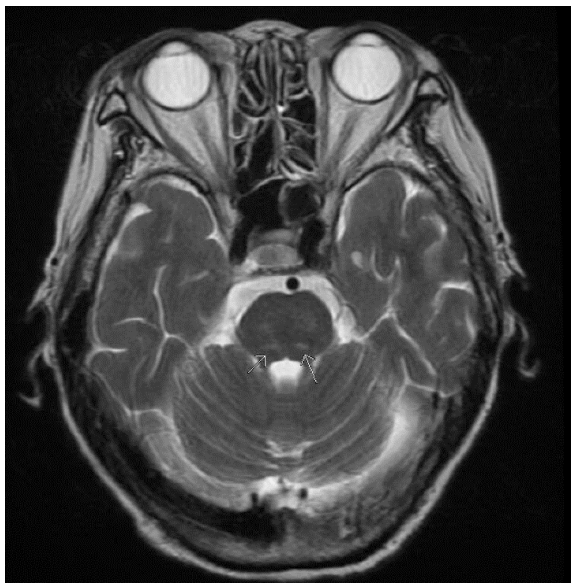


Figure 2. Axial T2 Magnetic Resonance Imaging Demonstrating Enhancement in the Bilateral Posterior Pons



One month after surgery she developed diarrhea. Stool testing was positive for toxigenic *Clostridium difficile* and she was treated with metronidazole 500mg 4 times daily orally for 10 days. She had complete resolution of her diarrhea and reportedly had returned to her normal state of health. Two weeks after treatment was completed she developed a recurrence of diarrhea and was started on 500mg 4 times daily orally for 21 days. A second stool test was not performed to verify relapse. On day 17 of treatment she was taken to her local hospital after a fall with a prolonged downtime. On admission, she was started on 500mg IV metronidazole 3 times daily instead of her oral dose. She received 11 doses of IV at the referring hospital prior to discontinuation. The total amount of metronidazole she received was 56 grams by mouth and 5.5 grams IV with a treatment duration of 31 days. Approximately 44 grams orally were taken over 22 days before the onset of weakness and ataxia.

On admission, an MRI of the brain was obtained without IV contrast. It demonstrated bilateral T2 bright signal symmetrically in the dentate nuclei and dorsal pons. The most likely differential included MIE, Wernicke encephalopathy, methyl bromide intoxication, and enteroviral encephalomyelitis.

She was treated with IV vitamin supplementation for potential Wernicke encephalopathy and the metronidazole was discontinued. Neurology was consulted and an electromyogram found no evidence of peripheral neuropathy or myopathy. One day after discontinuation of metronidazole she was feeling stronger and her ataxia was improved enough that she sat up in bed unassisted. On day 2, she could stand with a walker and the assistance of a physical therapist. Three days after discontinuation she was able to walk in the hallways with a wheeled walker and without help from a therapist. She was discharged on day 6 to a skilled nursing facility for ongoing rehabilitation.

Fifteen months after her initial episode of *Clostridium difficile*, the patient was contacted via phone for follow up. She had recovered fully from her truncal weakness and ataxia after a short stay in a rehabilitation facility. At the time of our call, she was living in her own home and independent in all her activities of daily living.

DISCUSSION

Imaging Findings

This patient had symmetrical T2 bright lesions located in the dentate nucleus of her cerebellum and posterior pons (Figures 1 and 2). In 2007, Kim et al described a case series of 7 patients who had reversible symmetrical lesions on MRI after prolonged treatment with metronidazole. Lesions varied from patient to patient but all had involvement of the dentate nucleus and pons.[5] These findings are consistent with other smaller case reports of MIE. Lesion locations vary and have included the dorsal pons, the splenium of the corpus callosum, the inferior olivary nuclei bilaterally or unilaterally, the cerebral white matter, and the anterior commissure.[6]

Symptoms and Resolution

Our patient had symptoms of truncal weakness and ataxia. Reported symptoms in previous cases include dysarthria, ataxia,

vertigo, nausea, vomiting, weakness, confusion, and tingling of the extremities. Case reports describe resolution of symptoms about 1 to 2 weeks after stopping the metronidazole,[5] although there are isolated case reports of symptoms persisting past 2 weeks. The earliest case reported was in 1995, which describes peripheral nerve pain that persisted longer than 6 weeks.[3] Peripheral neuropathy is a known side effect of metronidazole, so it is likely that the reported pain is unrelated to the central nervous system changes seen on MRI. A majority of patients, including the patient described in this report, experience the onset of symptoms during their treatment with metronidazole. A 2012 report describes a patient who had the onset of symptoms 12 days after stopping therapy. The patient had MRI changes and symptoms consistent with MIE, confirming the diagnosis despite having stopped metronidazole treatment.[7]

Table. Metronidazole Dosing, Duration, and Time to Neurologic Recovery in Reviewed Case Reports

Paper	Daily Dose (Grams)	Total Dose (Grams)	Duration of Treatment (Days)	N	Time to Recovery or Discharge (Days)
Ahmed A, et al, 1995[3]	.75-2.25	35	30	1	7
Hobbs K, et al, 2015[4]			21	1	N/A
Kim E, et al, 2007[5]	1.5	58.1 (average)	38.7 (average)	7	6.7 (average)
Kalia V, et al, 2010[6]	1.2	67.2		1	
Huang YT, et al, 2012[7]	1.5	32.6 (average)	25-28	2	
Kim H, et al, 2011[8]	1.5	45.5	31	1	
Moriya M, 2013[9]	2			1	14
Shah H, 2014[10]	2.4	75	27	1	10
Our patient	2	44	22	1	6

Metronidazole Dosage

The dosage received and duration of metronidazole treatment varied among case reports. Most authors discuss larger dosages or longer duration as key risk factors for development of MIE. The Table identifies several typical case reports and the duration of metronidazole. Although the amount and duration of metronidazole treatment was different in each case, the total exposure for each patient is higher than the current recommendation for initial treatment of *Clostridium difficile*, which suggests 1.5 grams daily for 10 to 14 days, for a total dose of 15 to 21 grams. The patient in this report was treated with 2 grams daily for 10 days—a total of 20 grams. Relapses after initial therapy are common, in which case a second course of metronidazole is often tried. This gives the patient a total of 30 to 42 grams of metronidazole and 28 days of treatment, which could put the total dose and duration in the range known to have caused MIE.

CONCLUSIONS

Metronidazole-induced encephalopathy is a rare but potentially serious neurologic syndrome presenting with typical symptoms and imaging findings in patients with a history of metronidazole exposure. The diagnosis can be made based on the history, exam, and constellation of MRI findings. With increasing prevalence of *Clostridium difficile* infection and metronidazole as a first-line agent, primary care and hospital clinicians should be aware of MIE and how to treat it.

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Proceedings from the 2016 Annual Meeting of the American College of Physicians, Wisconsin Chapter

The following abstracts were presented during the 61st Annual Meeting of the Wisconsin Chapter of the American College of Physicians in 2016. Internal medicine residents from each of Wisconsin's 5 residency programs presented their research and/or unusual clinical experience via case-and research-based vignettes and posters. All of the vignettes as well as the winning posters are published here. Additional poster presentations are available online in an appendix and can be accessed at https://www.wisconsinmedicalsociety.org/_WMS/publications/wmj/pdf/116/5/16_ACP_Abstract_Book.pdf.

RESEARCH-BASED VIGNETTES

1st Place

Blood-Based Genomic Testing for Newly Diagnosed Lung Cancer Patients to Facilitate Rapid Treatment Decisions

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Background: Despite advances in lung cancer treatment, its management remains challenging. Several patients present at an advanced stage where systemic therapy and biomarker testing are required. From studies on non-small-cell lung cancer (NSCLC), 21% of patients had biomarker results available at their initial oncology consultation, which led to shorter median time from consultation to treatment decision (0 vs 22 days, *P*=0.0008) and time to treatment start (16 vs 29 days, *P*=0.004). Of those patients with positive estimated glomerular filtration rate (eGFR) or ALK results, 19% started chemotherapy before biomarker results were available. Our institution's multidisciplinary team used blood-based genomic testing to expedite treatment decisions and facilitate more informed conversations with lung cancer patients.

Methods: Commercially available, blood-based genomic testing was ordered for all clinical patients. Testing included genomic test GeneStrat, a targeted panel for eGFR sensitizing and resistance mutations, ALK fusions, KRAS and BRAF mutations.

Results: Of the patients (n=32) submitted for genomic testing, results were available within 72 hours of blood draw. Among this cohort of patients who were diagnosed with adenocarcinoma between January and June, 2016, approximately 28% (n=9) had a mutation identified by GeneStrat (KRAS G12D=4, eGFR T790M=4, EML4-ALK=1, eGFR L858R=1). One patient had dual eGFR L858R/EML4-ALK mutations. There was 1 patient for whom the test was not able to identify G719A (exon 18) as it looks only for exon 19, 20, and 21. The sample size was limited for positive predictive value but the negative predictive value is 94%.

Conclusions: Blood-based genomic testing provides valuable treatment information regardless of disease stage. Early identification of the mutations will benefit the patient with early initiation of specific chemotherapy.

2nd Place

Utility of a Remote Image Acquisition and Feedback Tool in Promoting Point-of-Care Ultrasound Skills Among Critical Care Trainees

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Introduction: Point-of-care ultrasound (POCUS) is increasingly incorporated into both clinical practice and training programs. Implementation of POCUS curricula is challenged by a limited number of experts available to teach ultrasound skills and oversee interpretation at the bedside. Recent image database software products now allow faculty members to remotely supervise and teach learners by reviewing recorded, interpreted studies followed by provision of feedback on the POCUS skill components of image acquisition, image interpretation, and clinical application skills. We sought to assess the level of basic critical care echocardiography (BCCE) skills attained among critical care trainees after introduction of a remotely supervised POCUS curriculum.

Methods: A POCUS curriculum incorporating hands-on training was introduced in July 2015. A structured BCCE exam with required image set was taught along with a process for using an ultrasound archiving and quality assurance software product to record, interpret, and submit performed exams. In September 2015, trainees began wirelessly submitting independently performed exams for remote over-read by a faculty member who was an expert in critical care ultrasonography. After a 6-month period, an analysis of all submitted and over-read studies was performed with a primary focus on appropriateness of clinical application of ultrasound findings. Image quality and interpretation scores were also evaluated.

Results: Eighty-one BCCE exams were performed and submitted for over-read; 72% of the submitted studies were graded as having good or excellent image quality. Overall diagnostic accuracy was 77%. Accurate interpretation of ultrasound exams was associated with appropriate clinical application in greater than 90% of cases. In cases of inac-

curate interpretation of ultrasound images, 25% were associated with inappropriate clinical application. Incorrect clinical applications included inappropriate fluid management (60%) and use of inotropic agents (40%).

Conclusions: After introduction of a POCUS curriculum founded upon remote image over-reading with written electronic feedback, critical care trainees achieved high levels of image acquisition, interpretation accuracy, and appropriateness of clinical application.

Bias in the Eyes of Resident Physicians

Abel Irena, MD, Kern Reid, MD, Richard Battiola, MD; Aurora Health Care, Milwaukee, Wis

Introduction: The utilization of patient characteristics can allow clinicians to arrive at diagnosis or decide on treatment options; however, the subjective nature of patient characterization can negatively affect patient care. A 2003 Institute of Medicine report, *Unequal Treatment*, recognized that bias or stereotyping may affect provider-patient communication or the care offered. We investigated residents' recognition of bias.

Methods: We indirectly assessed recognition of bias among resident physicians by asking their opinion in an anonymous manner about their fellow residents. We asked residents the following 2-step question; "Have you observed a colleague of yours SAY, PORTRAY, or ACT in a biased manner towards a patient while providing inpatient service?" If the answer was yes, we subsequently asked them to elaborate on the bias.

Results: The survey was sent to 39 postgraduate (PG) internal medicine residents in their 1st to 3rd year of training. Half of the respondents (20/39) were female. The response rate was 100%. Forty-six percent (18/39) reported observing their colleague(s) being biased toward patients. Of those who reported bias, 77.8% (14/18), reported one or more examples about the content of the perceived bias. The largest category, 42.8% (9/21), was about bias towards patients with past or current "drug/substance abuse" or "narcotic seeking" behavior; 14.3% (3/21) involved patients with repeated admissions or so-called "frequent fliers;" 9.5% (2/21) related to race/ethnicity; 14.3% (3/21) indicated providers not wanting to care for patients who were perceived to be "difficult." Interestingly, another 9.5% (2/21) reported witnessing preferential service for "affluent/VIP" patients. Other examples included bias against obese patients, female patients, and general stereotyping with no specifics given.

Conclusions: Given the evidence that implicit bias can be recognized and improved upon, this study reinforces the need for implicit bias training/discussion to be included in residency programs.

Reducing Central Line-Associated Blood Stream Infections in Pediatric Oncology Patients

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Background: Central line-associated blood stream infections (CLABSI) are preventable, hospital-acquired conditions that increase morbidity, mortality, length of stay, and health care costs. Implementation of central line insertion and maintenance bundles have reduced but not completely eliminated these infections. Daily treatment with chlorhexidine gluconate (CHG) antiseptic has been shown to reduce them in a variety of populations including adult, pediatric, and neonatal intensive care, burn, adult medical and surgical, and long-term acute care units. We hypothesized that daily CHG treatments would reduce the incidence of CLABSIs in pediatric oncology and bone marrow transplant (BMT) patients.

Methods: All pediatric oncology and BMT patients received daily treatment with 2% CHG-impregnated cloths during the 1-year intervention period unless contraindicated. All primary blood stream infections in patients with a central line during this period (wCHG) and the preceding 12 months (pre-CHG) were recorded as a CLABSI. CLABSI rate was calculated as events per 1,000 central line days. Cultured pathogen, microbe sensitivity, and CHG compliance were also collected. Patient characteristics were evaluated to determine relationship to mucosal barrier injury (MBI) per the Centers for Disease Control and Prevention criteria.

Results: Compliance with CHG treatment remained >90% over the wCHG period. The CLABSI rate did not improve with CHG use (2.90 preCHG vs 3.39 wCHG). Most patients affected were undergoing treatment for hematologic malignancy (*hematologic* 11 preCHG vs 15 wCHG, *BMT 2* preCHG vs 3 wCHG, *solid tumor* 3 preCHG vs 2 wCHG). There was no alteration in the type of pathogens isolated (*Gram positive* 6 preCHG vs 6 wCHG, *Gram negative* 7 preCHG vs 13 wCHG, *Fungus* 3 preCHG vs 0 wCHG) or incidence of antibacterial-resistant infections (*Vancymycin resistant enterococcus* 1 preCHG vs 0 wCHG). A large proportion of CLABSIs qualified as an MBI in both intervention periods (11/16 preCHG vs 15/20 wCHG). The non-MBI CLABSI rate still remained unchanged with CHG use (0.91 preCHG vs 0.85 wCHG). However, 100% of non-MBI CLABSIs in the wCHG period had mucositis or neutropenia and were not classified as an MBI based only on growth of nonintestinal organisms (*mucositis or neutropenia 100%* all MBIs, 40% preCHG Non-MBI, 100% wCHG Non-MBI).

Discussion: CHG did not appear to reduce CLABSIs based on strict infection-source definitions. However, all patients with CLABSIs in the wCHG period had severe neutropenia and/or mucositis. There were few CLABSIs in immunocompetent patients receiving CHG treatment, specifically, patients undergoing chemotherapy for a solid tumor. This suggests an endogenous source of bacteremia in severely immunocompromised patients.

CASE-BASED VIGNETTES

1st Place

Platypnea-Orthodeoxia Secondary to Patent Foramen Ovale: A Rare But Dramatic Cause of Respiratory Failure

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Introduction: Platypnea-orthodeoxia syndrome is a rare disorder characterized by both dyspnea (platypnea) and arterial desaturation (orthodeoxia) in the upright position with improvement in the supine position.

Case: The patient is a 73-year-old woman with a past medical history significant for sudden cardiac death status post single chamber implantable cardioverter-defibrillator, mitral regurgitation, patent foramen ovale (PFO), and chronic lymphoid leukemia who was sent from the primary care clinician for evaluation of hypoxia and chest discomfort. She reported dyspnea when she is upright, improved when she lay flat. Initial evaluation showed oxygen saturation of 85% on room air; this did not improve with nasal cannula or non-rebreather mask necessitating admission to intensive care unit (ICU) on bilevel positive airway pressure. Physical examination was benign, electrocardiogram showed left atrial enlargement, computed tomograpy (CT) angiogram ruled out pulmonary embolism. Cardiology was consulted, transthoracic echocardiogram was remarkable only for a positive bubble study. Transesophageal echocardiogram demonstrated a PFO with large right-to-left shunt, aneurysmal interatrial septum, and a prominent eustachian valve directing blood towards the PFO. Right and left heart catheterization ruled out pulmonary hypertension and Eisenminger syndrome or other cardiac pathology. The patient underwent percutaneous PFO closure under guidance of fluoroscopy and intracardiac echocardiography via the right femoral vein using a 30mm Gore septal occluder. She had immediate and complete resolution of her symptoms, normal oxygen saturation on room air, and was discharged home in 2 days.

Discussion: Platypnea-orthodeoxia is a rare manifestation of PFO, and closure of the atrial defect is curative. Few cases are reported in the literature, but the severity of presentation is rarely as dramatic as this case.

2nd Place

A Typical Presentation of an Atypical Problem

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Introduction: Cryptogenic organizing pneumonia is a rare and diffuse idiopathic organizing form of interstitial pneumonia. The disease is characterized by acute to subacute onset of vague systemic and pulmonary complaints often leading to a difficult clinical diagnosis of exclusion.

Case: We describe the case of a 77-year-old farmer with a 1-month history of a persistent minimally productive cough with associated fatigue, malaise, dyspnea, and orthopnea found to be hypoxic in clinic in the setting of previously failed macrolide and fluoroquinolone therapy. Admission review of chest x-rays indicated a progression from atypical infiltrates and pulmonary edema to bilateral peripheral infiltrates. A chest CT confirmed parenchymal reticulation, septal thickening, and ground glass opacities consistent with cryptogenic organizing pneumonia. Clinical diagnosis and treatment with high dose steroids led to improved pulmonary function and exercise capacity.

Discussion: Cryptogenic organizing pneumonia is characterized by a variable clinical course and a time to treatment dependent disease severity. Timely diagnosis and early intervention is key to abating a destructive and potentially reversible disease process. The induction of alveolar injury, recruitment of fibroblasts, and excessive proliferation of granulation tissue leads to intraluminal plugs and polyps. The resulting airway consolidation injury often led to the presenting clinical picture of a nonproductive cough, fevers, dyspnea, malaise, and weight loss. Further investigation frequently identifies peripheral pulmonary infiltrates on imaging as well as a reduction in oxygen saturation and functional capacity of the patient. Pulmonary function tests frequently indicate a reduction in diffusion capacity as well as a restrictive flow pattern. Treatment with glucocorticoids early in the disease course reverses identifiable pulmonary deficits in approximately 66% of patients. Overall prognosis remains positive with early recognition and treatment.

5-Oxoproline (Pyroglytamic Acid) Associated Increased Metabolic Anion Gap Acidosis: Role of Acetaminophen

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Introduction: Acute acetaminophen hepatotoxicity is associated with anion gap metabolic acidosis secondary to lactic acidosis and renal failure. However, severe anion gap metabolic acidosis in patients consuming acetaminophen at therapeutic levels, secondary to 5-oxoprolinemia, is rare and seldom reported.

Case: A 63-year-old severely malnourished woman with history of osteoporosis, chronic pancreatitis, Type 2 diabetes mellitus, anemia of chronic disease fibromyalgia, and depression was brought in unresponsive by emergency medical services. En route, she was intubated since she was found to have agonal breathing and unresponsiveness. She had elevated white blood cell count, acute kidney injury, elevated anion gap metabolic acidosis, and elevation in her beta-hydroxybutyrate of 4.04 initially consistent with diabetic ketoacidosis, as well as septic shock secondary to pneumonia diagnosed on a CT scan performed to rule out pulmonary embolism. She was started on vancomycin and levofloxacin for sepsis. Initial arterial blood gas analysis showed a pH of 6.81, partial pressure of carbon dioxide of 27, bicarbonate of 3 with an anion gap of 23. Rapid blood screen was negative for alcohol. Salicylate levels were 2.5 (2.0-29.9) and acetaminophen levels were slightly elevated at 13 (0-10). Patient had been taking acetaminophen for chronic pain. Diabetic ketoacidosis treatment protocol was initiated with regular insulin drip and frequent monitoring of fluid status and serum electrolytes. Bicarbonate drip was given for metabolic acidosis. Despite above measures, anion gap failed to correct although blood glucose levels returned to less than 200. N-acetylcysteine was started suspecting acetaminophen-related liver toxicity while awaiting urine 5-oxoproline levels. For renal failure and electrolyte disorders, continuous renal replacement therapy was initiated. She continued to stay unresponsive and neuron specific enolase was elevated at 34. Vasopressors (norepinephrine and vasopressin) were started for hypotension refractory to volume resuscitation. Urine 5-oxoproline came back elevated at 8800 µmol/mol creatinine (reference range: <50).

Conclusions: In severely malnourished patients, chronic ingestion of acetaminophen can cause high anion gap metabolic acidosis secondary to elevated blood levels of 5-oxoproline.

Hickam's Dictum or Occam's Razor? Use PRN!

Hari Pokhrel, MBBS, Rachel Hawker, MD, FACP; Gundersen Heath System, La Crosse, Wis

Introduction: Decision making in medicine relies a lot upon heuristics. We present a case in which Hickam's dictum was used initially to explain multiple issues the patient had. In hindsight, however, it appeared that Occam's razor would have been more appropriate for explanation.

Case: A 63-year-old woman with a history of alcoholic liver disease, presented to her primary care clinician with concerns for acute mental status changes and inability to perform activities of daily living. She was referred to an emergency department (ED) where she was found to have severe hypercalcemia (corrected calcium: 14.98) and elevated ammonia. She was given intravenous fluids, calcitonin, and zoledronic acid and transferred to our hospital. A thorough evaluation of hypercalcemia did not reveal anything specific. Complete blood cell count (CBC) showed pancytopenia; so did the peripheral blood smear. Serum protein electrophoresis showed a polyclonal gammopathy with normal light chain ratio. Hematology was consulted due to high suspicion for an underlying bone marrow malignancy. Hematology advised that the polyclonal gammopathy was likely a consequence of liver disease and the pancytopenia was likely a consequence of splenomegaly. They further recommended to right upper quadrant ultrasound and screening for liver malignancy due to history of liver cirrhosis. Both these tests were negative. However, the next day, the shifts changed and a different hematologist saw the patient and recommended a bone marrow biopsy to evaluate the cause of hypercalcemia and pancytopenia and rule out underlying bone marrow disorder or lymphoma. The final pathology report for bone marrow biopsy was read as noncaseating granulomas consistent with sarcoidosis. Further evaluation revealed that her sarcoidosis was only limited to her bone marrow. She has been following rheumatology and is being treated with steroids.

Conclusions: Medical decision making is a complex process and physicians certainly should be aware of the cognitive errors and biases. Although we may be able to explain clinical cases using either Occam's razor or Hickam's dictum, we should certainly be willing to reconsider our preassumptions and challenge ourselves until we find a satisfactory explanation and see actual clinical improvement in our patients.

HSV in Eczema's Clothing

Christopher R. Lindholm, MA, Sean O'Neill, MD; Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wis

Case: A 20-year-old woman 3 months postpartum with past medical history significant for asthma, allergies, and atopic dermatitis presented to the ED with 2 weeks of fatigue, fever to 103º F, nausea, and a progressively worsening rash involving the face, hands, legs, and back. On presentation, temperature was 99.9º F, blood pressure 82/40 mm Hg, SpO2: 92% on room air, white blood cell count 4.0, C-reactive protein 18.9, and chest x-ray was clear. She was fluid resuscitated and started on ceftriaxone and vancomycin. She was transferred to another hospital 2 days later for continued hypotension increasing oxygen requirements and concern for sepsis secondary to skin and pulmonary source. Chest x-ray now revealed bilateral patchy infiltrates and she was given a single dose of IV acyclovir for concern of herpetic rash. She was transferred to our facility the following day for persistent hypoxemia and specialty care. There, she reported a similar rash all her life, usually limited to face and hands. The rash had worsened during pregnancy for which she received oral steroids within last 3 months but had progressed over preceding 2 weeks. Rash was tender without pruritis. She denied a history of herpes simplex virus (HSV) and had chicken pox as a child.

On exam, thick erythematous plaques with punched out bases and overlying yellow crusts were noted on her forehead, cheeks, nose and chin, and forearms. Her lower legs had many 2 to 3 mm monomorphic vesicles with eroded centers and an umbilicated appearance. Some vesicles coalesced into larger plaques with hemorrhagic crusts. HSV1 PCR of fresh lesions was positive and Tzanck was positive for multinucleated giant cells. She was diagnosed with eczema herpeticum and continued on IV acyclovir. Mupirocin 2% ointment was applied for secondary impetigenization and moisturization with white petrolatum was used. Oxygen requirements slowly improved over the course of her 7-day hospital stay, no pathogen was ever identified for her bibasilar pneumonia but she did receive IV zosyn for 5 days. The erosions and plaques eventually sloughed off revealing denuded skin and she was ultimately discharged on oral valacyclovir for 7 days.

Conclusions: This case illustrates eczema herpeticum as one of the dermatological emergencies and the importance of recognizing the characteristic presentation of fever and clusters of pustular vesicles and/or punched out erosions that most often occurs as a complication of atopic dermatitis. It also highlights the importance of prompt lab tests and treatment with acyclovir as this condition has high rates of morbidity and mortality.

Hypertension in a Pregnant Woman

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Case: This case report describes a 25-year-old G3P0020 woman at 36 weeks and 2 days gestation presenting with severe hypertension. She had a 2-year history of hypertension treated with labetalol. She was noted to be hypertensive from the 140s to 170s systolic at multiple office visits starting at 11 weeks. She developed episodes of dizziness, sweating, and tachycardia during her second trimester. Holter monitor showed sinus tachycardia and transthoracic echocardiogram was normal. Testing returned positive for elevated urine normetanephrine, 24-hour norepinephrine and dopamine levels, and normal metanephrine, 24-hour epinephrine and vanillylmandelic acid levels. Twenty-four hour urine protein excretion also was elevated. Of note, she has a positive family history for paraganglioma in her mother. She was started on phenoxybenzamine. Given persistent severe hypertension at 36 weeks, she was admitted

to the ICU. MRI abdomen was concerning for extra-adrenal paraganglioma. Nicardipine drip was started, phenoxybenzamine was uptitrated, and propranolol was added on hospital day 2. She underwent a caesarean delivery at 37 weeks and 1-day gestational age. This patient remained inpatient at the time this report was prepared.

Discussion: Catecholamine-secreting tumors are a rare but life-threatening cause of hypertension, particularly during pregnancy. Pheochromocytomas are intra-adrenal masses, while paragangliomas are extra-adrenal. Diagnosis is made by measurement of urinary and/or plasma fractionated metanephrines and catecholamines; family history also may be of assistance. Strict blood pressure control is essential, particularly in pregnancy, via obtaining alpha blockade before beta blockade. Untreated, this condition causes maternal and fetal mortality rates of 8% and 17%, respectively. Timing of surgical intervention is more controversial. In this case, caesarean delivery was pursued prior to tumor resection.

Localized Ocular Amyloidosis: A Case Series

Lindsay Hammons, Anita D'Souza, MD, MS; Pinky Jha, MD; Medical College of Wisconsin, Milwaukee, Wis

Introduction: Immunoglobulin light chain amyloidosis (AL) is a clonal plasma cell neoplasm in which clonal immunoglobulin light chains, either λ or κ, misfold into amyloid and deposit in tissues. The pathogenesis of AL depends on the degree of systemic deposition of amyloid fibrils into vital organs. Localized ocular amyloidosis without systemic involvement is rare.

Cases: (A) A 31-year-old woman presented to eye clinic with left ptosis, watery eyes, a left inner eyelid lesion, and a foreign body sensation (FBS) in her left eye. Physical exam was unremarkable except for left eye ptosis. Laboratory findings were significant for Congo red positive staining on left upper lid conjunctival excision with liquid chromatography-tandem mass spectrometry (LCTMS) positive for AL (lambda) type amyloid deposition. Workup for systemic amyloidosis was within normal limits.

(B) A 49-year-old woman with migraine headaches presented to eye clinic with left-sided proptosis, left-sided FBS, limited eye movement, and binocular horizontal diplopia. Past MRI showed enlargement of left extraocular muscles (EOM) thought to be secondary to orbital pseudotumor and treated with a course of prednisone that did not seem to help. Physical exam was unremarkable except for left eye proptosis, diplopia, and enlarged EOM on left side. Laboratory findings were significant for anterior orbitotomy with medial rectus muscle biopsy and Congo red positive staining with LCTMS positive for AK (kappa) type amyloid deposition. Workup for systemic amyloidosis was within normal limits with the exception of mildly elevated κ levels in serum.

(C) A 69-year-old man with history of coronary artery disease, atrial fibrillation, and stroke presented to his primary care clinician with left ptosis for the past month with a change in vision. Physical exam was unremarkable except for left upper lid ptosis with significant visual field changes. Laboratory changes were significant for left orbicularis muscle and full-thickness wedge left upper lid excision with immunohistochemistry subtyping suggestive of AA, however weak staining for λ and κ also was present. Workup for systemic amyloidosis (no serum immunofixation or bone marrow biopsy) was within normal limits.

(D) A 66-year-old man with history of posterior vitreous detachment, cataract, and dermatochalasis of bilateral eyelids presented to eye clinic with new floaters and flashes in left eye with restricted right EOM. Physical exam was unremarkable. Imaging showed right inferior rectus mass and laboratory changes were significant for Congo red positive right inferior rectus biopsy with LCTMS positive for AL (lambda) type amyloid deposition. Workup for systemic amyloidosis was within normal limits.

Discussion: Patients with localized ocular amyloidosis do not appear to be at an increased risk of developing systemic involvement; watchful waiting is appropriate.

New Onset Psychosis in Young Man

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Introduction: Anti-N-methyl-D-asparate receptor (NMDAR) encephalitis is a neurologic syndrome with prominent psychiatric manifestations. This autoimmune encephalitis is often paraneoplastic, post viral, or idiopathic, and leads to limbic encephalitis and frontal lobe dysfunction that can mimic a primary psychiatric disorder. Diagnosis requires a high level of clinical suspicion in order to guide prompt recognition and initiation of appropriate therapy.

Case: We discuss a 23-year-old high functioning graduate student with no significant past medical or psychiatric history who presented to the ED after a diarrheal illness with progressive agitation, psychosis, euphoria, and suicidal ideation. The patient initally was triaged to psychiatry and discharged on olanzapine. He returned to the ED following a suicide attempt. Urine drug screen was negative; lumbar puncture demonstrated >100 white blood cell with lymphocyte predominance with subsequent negative viral serology and bacterial cultures. Magnetic resonance imaging (MRI) showed bilateral temporal lobe hyperintesity and leptomeningeal enhancement concerning for meningoencephalitis. Patient initially was treated for presumed herpes simplex encephalitis with acyclovir despite negative herpes simplex virus polymerase chain reaction (PCR). Two weeks after presentation, cerebrospinal fluid returned a positive NMDAR antibody, confirming anti-NMDAR encephalitis. Patient was started on high-dose steroids and intravenous immunoglobulin (IVIG) with improvement though he continued to experience episodes of agitation, psychosis, and catatonia, alternating with periods of lucidity. During episodes of agitation, he demonstrated Kluver-Bucy syndrome, as he would sporadically become hypersexual and impulsive. Due to continued agitation, he was started on rituximab with significant improvement, though far from his baseline. Patient was discharged to neurocognitive rehabilitation. Primary malignancy was never identified despite extensive radiologic and serologic workup.

Discussion: Anti-NMDAR encephalitis is part of an expanding group of autoimmune

encephalitides that generally affect younger patients (median age of 21 years). Given association with paraneoplastic syndromes, this diagnosis should prompt workup for a primary malignancy. The majority of patients with underlying neoplasm are women with an ovarian teratoma. When present, tumor resection with immunotherapy leads to favorable outcomes. In men, it is common that no tumor is discovered. First-line treatment for those without identifiable tumors is immunotherapy with IVIG, glucocorticoids, or plasma exchange. For those failing first-line treatment, therapy with rituximab or cyclophosphamide showed improved outcomes, as well as significant reduction in relapses. Despite severity of disease, patients often improve with supportive care, immunotherapy, and lengthy recovery with multidisciplinary care.

Rapid Dissemination of Blastomycosis in Late Pregnancy

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Introduction: Blastomycosis is widely prevalent in the lungs of those living in the Great Lakes region and is widely known to disseminate in the immunocompromised, such as those with AIDS or solid organ transplant recipients. However, in rare cases, a latent infection is activated by the partially immunocompromised state of pregnancy. Given the life-threatening nature of this disease complication, early diagnosis is critical.

Case: A 38-year-old woman at 35 weeks pregnancy presented to a local ED with 2 weeks of right knee pain, a cutaneous left thigh lesion, and new-onset dyspnea. MRI of knee revealed large effusion with findings consistent with tibial osteomyelitis while CT chest revealed bilateral infiltrates. The patient was taken to the operating room for urgent caesarean delivery and incision and drainage of both the right knee and left thigh cutaneous lesion. Postoperatively, she failed to respond to antibacterial therapy and developed severe acute respiratory distress syndrome (ARDS). She was transferred to a tertiary care center, where she underwent bronchoscopy and was diagnosed with pulmonary blastomycosis. Retrospective review of original tibial biopsy confirmed the presence of osteomyelitis secondary to blastomycosis, confirming suspicions of dissemination. She later experienced seizures thought to be due to central nervous system infection with blastomycosis, as MRI findings were consistent with such a diagnosis. She was treated with amphotericin and voriconazole with subsequent improvement. She was discharged with plan to complete 8 weeks of amphotericin and 1 year of voriconazole.

Discussion: This case presents an uncommon primary manifestation of blastomycosis in a pregnant patient. The peripartum state of immunosuppression can lead to rapid dissemination and ARDS. Blastomycosis must be considered in the differential of both native joint osteomyelitis and disseminated ARDS among immunocompromised patients in the Great Lakes region.

Successful Treatment of Lupus Mesenteric Vasculitis With Cyclophosphamide

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Introduction: Lupus mesenteric vasculitis (LMV) is one of the most serious gastrointestinal complications in systemic lupus erythematosus (SLE). Steroids are considered as a first-line therapy; in only few steroid unresponsive cases cyclophosphamide has been tried. We present a case of LMV that carried therapeutic challenge with pulse dose steroid with ongoing risk for sepsis, but cyclophosphamide treatment provided symptom improvement.

Case: A 39-year-old man with a past medical history of antiphospholipid antibody syndrome and SLE presented with acute onset abdominal pain and diarrhea. On examination, he had stable vital signs, diffuse abdominal tenderness, no rebound tenderness. The following were normal: CBC, comprehensive metabolic panel, lipase, infectious, autoimmune, and vasculitic workup. International normalized ratio was 4.5. CT of abdomen showed generalized small bowel edema with perienteric fluid around terminal ileum consistent with enteritis, no large vessel thrombosis. Gastroscopy shows severe scalloping and villous loss in duodenum, erythematous friable terminal ileal mucosa with ulcers/exudate and granular colonic mucosa. Histopathology showed mucosal capillary vasculitis and excessive plasma cells in lamina propria, consistent with autoimmune and/or small vessel vasculitis related enteritis. He was started on 1mg/kg/day steroids. He developed worsening abdominal pain, fever, and hypotension. Repeat CT showed no bowel perforation. Repeat infectious workup was negative. After stabilization over 72 hours, he received 1 dose of cyclophosphamide 800mg with concomitant steroids. His symptoms improved within a few days and he was discharged home with plan to continue cyclophosphamide therapy for 3 to 6 months and slowly wean steroids.

Discussion: The relevance of LMV in SLE patients is 0.2% to 6.4%. LMV-related ischemia carries high risk for infarction and mortality. There are no return to clinic recommendations or guidelines in literature regarding LMV treatment; nevertheless, based on high steroid responsiveness in retrospective studies, it has been considered first-line treatment. Cyclophosphamide have been tried in few rare steroid unresponsive situations. LMV carries high risk for gut bacterial translocation and sepsis, and use of pulse dose steroids can be challenging. In that situation cyclophosphamide use can help improve symptoms and mortality.

Supradiaphragmatic Ectopic Hepatic Tissue

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Introduction: Ectopic liver tissue is a rare developmental anomaly most commonly found incidentally during surgery in intra- and retroperitoneal spaces. Only a few cases of supradiaphragmatic ectopias are reported in the literature. Detection of an abnormality by imaging before surgery or autopsy is also unusual. Most of the reported supradiaphragmatic cases are found in neonates causing respiratory distress or hydrothorax. Erroneous dorsal budding of hepatic tissue before closure of the pleuroperitoneal membranes may explain how ectopic liver develops in the thoracic cavity.

Case: A 38-year-old generally healthy woman

presented with a productive cough of 4 days duration with acute dyspnea. She had no chest or calf pain, fever, or chills. Vital signs were stable but she demonstrated decreased breath sounds in the right lung field on exam. Chest x-ray and subsequent CT revealed a right loculated hydropneumothorax with a small fluid component and several nonparenchymal 1.2 to 1.4 cm lesions above the right hemidiaphragm. The patient denied any occupational exposures or travel. Pulmonology contemplated a parapnuemonic fluid collection, hepatic deposits, or catamenial pneumothorax, however unlikely since she had menstruation 3 weeks prior. Infectious Disease did not believe this to be infectious. She underwent video-assisted thoracoscopy with decortication. Pathology was positive for benign liver tissue with hemosiderin. No malignancy or endometrial tissue was seen. α-fetoprotein was normal.

Discussion: This is an extremely rare case of ectopic hepatic tissue. Not only are the patient's age and diaphragmatic ectopic location impressive, but the majority are found incidentally in asymptomatic adult patients; this ectopia caused a symptomatic hydrothorax, making this even more unusual. Most importantly, ectopic deposits have a higher incidence of hepatocellular carcinoma, independent of disease or tumor in the regular liver. Small ectopic liver tissue is thought to have an incomplete functional architecture leading to longer exposure to carcinogenic factors. Awareness of this entity is important for prevention of future malignancies. This patient, therefore, will have close monitoring with consideration for future surgical resection.

An Underrecognized Cause of Anion Gap Metabolic Acidosis

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Introduction: The causes of pure anion gap metabolic acidosis are taught early in medical education through the mnemonic MUDPILES. However, this mnemonic overlooks other causes of metabolic acidosis such as oxoprolinemia. Oxoprolinemia is directly linked to the use of acetaminophen, and its diagnosis is likely limited by awareness of clinicians and by availability of testing.

Case: A 72-year-old woman with a history of chronic kidney disease stage 3 and chronic back pain presented to the ED with a chief complaint of back pain after running out of hydrocodone/acetaminophen, acetaminophen/codeine, and acetaminophen. The patient's daughter reported that the patient was acting confused and somnolent. Review of medications revealed chronic intake of at least 4000 mg of acetaminophen from 3 different sources per day for the past year. A basic chemistry panel revealed a bicarbonate of 9 mmol/L with a serum creatinine of 1.63 mg/dL, a serum urea nitrogen of 38 mg/dL, and an anion gap of 31. A subsequent arterial blood gas revealed a pH of 7.25, CO_2 < 20 mmHg. Her workup was negative for lactic acid, volatile alcohols, or other ingestions; there was no evidence of diabetic ketoacidosis, and a drug screen was negative for salicylates. She was found to be appropriately compensating via Winter's Formula and her Delta-Delta indicated a pure metabolic acidosis. She was started on a bicarbonate infusion, which corrected her bicarbonate but her anion gap remained elevated. A urine sample was sent for organic acid evaluation given her long-term use of acetaminophen and found to be highly positive for 5-oxoproline. She was started on n-acetylcysteine and IV fluids, acetaminophen was held, and her anion gap slowly recovered over 10 days in the hospital, but did not fully normalize for another 7 days after discharge.

Discussion: 5-oxoproline is a byproduct of acetaminophen metabolism that builds up in the blood with continued acetaminophen use. Glutathione depletion and cysteine deficiency occur secondary to chronic use of acetaminophen. Alongside malnutrition, these factors result in the depletion of ATP stores, which leads to the inability to convert oxoproline to glutamic acid. Oxoprolinemia is most likely to be seen in elderly women with chronic kidney disease, and with the increasing prevalence of kidney disease due to diabetes and hypertension, and the ubiquity of acetaminophen-containing pain relievers used daily, it is likely that oxoprolinemia anion gap metabolic acidosis is underdiagnosed due to lack of awareness and access to testing. There is no defined treatment; per case reports n-acetylcysteine is often used given the physiology of glutathione depletion, as well as bicarbonate infusions, with no clear benefit of either. The only proven treatment is abstaining from acetaminophen. High clinical suspicion and awareness remains the key for diagnosis as confirmatory labs tests are not readily available and can take weeks for a final result.

POSTER PRESENTATIONS

1st Place

Autoimmune Thyroid Disease: A Rare Presentation of a Common Condition

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Introduction: Hashimoto encephalopathy (HE) is a rare, possibly underreported, autoimmune condition associated with Hashimoto thyroiditis (HT). The association is not well known, but HT is the most common cause of hypothyroidism making this case an imperative demonstration of recognizing a life-threatening and sometimes irreversible condition that can easily be mistaken for other common disorders.

Case: A 67-year-old woman was admitted for worsening altered mental status. She had a 3-week history of mild cognitive decline and complained of headaches. CT and MRI demonstrated no acute ischemia but cerebral atrophy and extensive hyperintense white matter changes were evident. Infectious etiology was ruled out. Thyrotropin was severely elevated at 258. Antithyroid peroxidase antibody (TPOAb) and antithyroglobulin antibody (TgAb) were both elevated at 3,548 and 1,858. She was started on levothyroxine but her mental status continued to worsen. Electroencephalogram showed generalized slowing consistent with moderate diffuse encephalopathy. She developed myoclonus and somnolence. Hyperreflexia was present. Myxedema coma was considered, but she did not demonstrate signs of hypothermia, hypotension, bradycardia, or hypoglycemia. HE was considered and the patient was given IV methylprednisolone; within 24 hours her myoclonus and somnolence resolved, her mentation

improved and she was able to converse again.

Discussion: This case emphasizes the challenge of diagnosing a rare condition in a patient presenting with altered mental status, a common diagnosis in emergency departments nationwide. This was a particularly difficult case because HE does not always present as hypothyroidism; thyroid status varies tremendously. This misled suspicion for other differentials such as severe HT and myxedema coma. Although HE is rare, thyroid dysfunction along with a similar clinical presentation to this patient should cause high suspicion for HE. Mild cognitive impairment persisted after treatment, but it is well documented that HE may take up to 1 year to resolve. In some cases, if left untreated, encephalopathy will not improve making recognition paramount for timely and effective treatment.

2nd Place
Steroids and Ritonavir: A Case of Drug-Induced Cushing's Syndrome

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Introduction: Managing comorbidities in HIV-infected patients can be complicated given the numerous drug interactions with antiretroviral (ART) medications. Ritonavir (RTV) is a protease inhibitor (PI) that is a potent inhibitor of cytochrome P450 CYP3A4, CYP3A5 and CYP2D6. Glucocorticoid medications are metabolized by the CYP34A enzyme system. Taken concurrently, RTV can increase the area under the concentration versus time curve (AUC) and half-life of glucocorticoid medications resulting in iatrogenic Cushing's syndrome.

Case: A 54-year-old man with 23-year history of HIV, calcium pyrophosphate disease (CPPD) and chronic obstructive pulmonary disease (COPD) presented with an 11-pound weight gain, facial swelling, new onset dyspnea with increased abdominal girth over the past 3 weeks. His HIV was well controlled on darunavir, etravirine, raltegravir, and RTV with a CD4 count of 448 and undetectable viral load. Prior to these symptoms, he received 120 mg intra-articular (IA) triamcinolone (TMC) injections in his knees over 2 months relieving his CPPD. Additionally, he was taking beclomethasone nasal spray and formoterol/mometasone. His exam showed facial plethora, moon facies, hoarseness, lateral eyebrow loss, and mild bilateral hand tremor. He had no abdominal striae, an enlarged pannus with internal umbilicus without lower extremity edema. A cortisol level was < 0.8 for 4 months. Over the next 5 months his symptoms resolved and his cortisol remained low at 1.2 with a relatively low corticotropin level of 9 with post-cosyntropin cortisol of 6.5. He was placed on anakinra and colchicine for his CPPD, his beclomethasone nasal spray was discontinued, and formoterol/mometasone inhaler dose was lowered to reduce his glucocorticoid exposure.

Discussion: This patient presented with iatrogenic Cushing's Syndrome secondary to the interaction between RTV and TMC injections for his CPPD. The TMC injections required no entry in the electronic medical record prior to use as this was readily available in the clinic, thus evading the drug interaction warning. There are case reports describing similar instances in HIV patients taking glucocorticoids; however, different steroids vary in their metabolism making some safer than others. HIV patients are susceptible to osteoporosis, infection and DM highlighting the importance of this interaction. This case illustrates the importance of monitoring drug interactions in HIV patients on ART and speaks to the systems issue of having the ability to dispense medications and bypass the EMR drug interaction warnings.

3rd Place
'Experimental' Ingestion of Cerberin

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Introduction: Cerberin is an active ingredient found in the seeds of the Cerbera odollam tree, also known as the "suicide tree." Cerberin mimics digoxin and is commonly used as a suicide and homicide drug in South Asia. However, its use is relatively uncommon in the western world.

Case: A 25-year-old-man with a past medical history of depression and prior suicide attempts presented to the ED with confusion, lip numbness, nausea, vomiting, palpitations, and diarrhea. He admitted to ingesting a seed containing cerberin, which he purchased online. He reported experimenting with the seed in the event he was sentenced to prison. In the ED, he was found to have an irregular pulse with heart rate of 106 and blood pressure of 94/55. Electrocardiogram (ECG) revealed sinus tachycardia, Mobitz type I 2nd degree AV block, and T wave inversions in inferolateral leads. His labs were significant for a potassium of 5. His urine drug screen was positive for cannabinoids. Toxicologist at Poison Control recommended Digibind, a digoxin-specific antibody. The patient's overall condition remained stable. A repeat ECG 24 hours later was normal sinus rhythm.

Discussion: Cerberin ingestion is responsible for 50% of plant poisonings in South Asia. Since cerberin poisoning is uncommon in the western world, its diagnosis presents a challenge to physicians. Cerberin and digoxin are cardiac glycosides that inhibit the Na-K-ATPase pump in the myocardium. Overdose may present with a variety of systemic symptoms including nausea, vomiting, diarrhea, and any dysrhythmias of which AV block is more commonly seen. Physicians must suspect cerberin poisoning in patients with unexplained digoxin-overdose like presentation. Management includes appropriate administration of Digibind and monitoring on telemetry for any further arrhythmias.

Jody Silva, MEd

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Women's Health Care in Wisconsin: A Closer Look

Jody Silva, MEd; Ellen Hartenbach, MD; Robert N. Golden, MD

Of Wisconsin's 72 counties, 26 have no board-certified obstetrics and gynecology (Ob/Gyn) physicians. This is an alarming situation. Adding to the problem, the number of Ob/Gyn doctors who retire each year is higher than the number who graduate from residency training programs in Wisconsin. By 2030, the state's female population will have increased by 7.8%.[1] In addition, an increasing number of rural hospitals are closing their maternity services, and many family medicine physicians are dropping their obstetrical practices.[2,3] Women are forced to drive long distances to seek care when their local hospitals no longer offer maternity services.

Key reproductive health issues

Ob/Gyn physicians have an enormous impact on women's health across the lifespan in areas ranging from reproductive health concerns (eg, contraception and obstetrical care) to the unique gynecologic needs of aging women (eg, menopause and pelvic floor disorders). Cancer prevention, detection, and care are important areas of focus for women of all ages.

Women who live in rural communities face special challenges to their health and well-being due to the higher rates of poverty and unemployment in rural regions compared to urban and suburban areas. These factors can make access to and affordability of perinatal care extremely difficult. Women in rural counties are less likely than their non-rural peers to seek first-trimester care. They have a higher risk of hospitalization due to pregnancy complications and higher rates of preterm and low-birth-weight infants.[4] A concerning recent trend is the increasing number of babies born to opioid-addicted mothers in rural communities. These babies suffer from neonatal abstinence syndrome, which includes gastrointestinal dysfunction, temperature instability, and central nervous system problems such as tremors, high-pitched crying, and seizures.

The absence of local Ob/Gyn physicians in rural settings has a negative impact across the life cycle. The number of women over 65 years of age will double in the next 20 years.[1] As women age they have an increased need for incontinence evaluation and treatment, and the barriers to early evaluation and intervention are greater if they need to travel outside of their local community to obtain care. Rural women are at greater risk for pelvic cancer compared with women in other communities. Without a local Ob/Gyn physician, women are less likely to have preventive education and annual well-women exams that could detect cancer in its early stages.

Women who live in rural communities face special challenges to their health and well-being... These factors can make access to and affordability of perinatal care extremely difficult.

A strategic approach to women's health equity in rural Wisconsin

In recognition of the critical importance of this issue, the Department of Obstetrics and

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Gynecology at the University of Wisconsin School of Medicine and Public Health (SMPH) developed a novel approach for expanding the pipeline of Ob/Gyn physicians in rural Wisconsin: it created the nation's first Ob/Gyn Rural Residency Program. The concept of rural residency training is well established in primary care fields including family medicine; however, it is new territory for Ob/Gyn.

Working with SMPH partners in rural sites, the Department of Obstetrics and Gynecology designed the residency track to recruit and train physicians who are interested in future practice in rural Wisconsin communities. The Wisconsin Rural Physician Residency Assistance Program supported the development of this novel training program. It is a logical extension of the SMPH's Wisconsin Academy for Rural Medicine (WARM) that attracts and trains medical students who want to develop careers in rural medicine.

The Ob/Gyn rural training track is a new component of our well-established Ob/Gyn Residency Program, which is accredited by the Accreditation Council for Graduate Medical Education. Residents in the rural track receive approximately 80% of their training in Madison and spend the remaining 20% of their time at 4 rural community hospitals in Wisconsin. During the rural rotations, these residents gain valuable insight and experience in rural Ob/Gyn care. A broad evidence base has documented a strong relationship between where new residency graduates establish their practices and the geographic location of their residency training experiences. We predict that our rural training track residents will develop the skills necessary for successful practice in rural settings and will settle in rural communities after completing their training.

We believe this program, which already has drawn national attention, may serve as a model and inspire other Ob/Gyn residency programs to develop similar rural training tracks. In this way, we hope to address the growing need for more Ob/Gyn physicians in rural Wisconsin and beyond.

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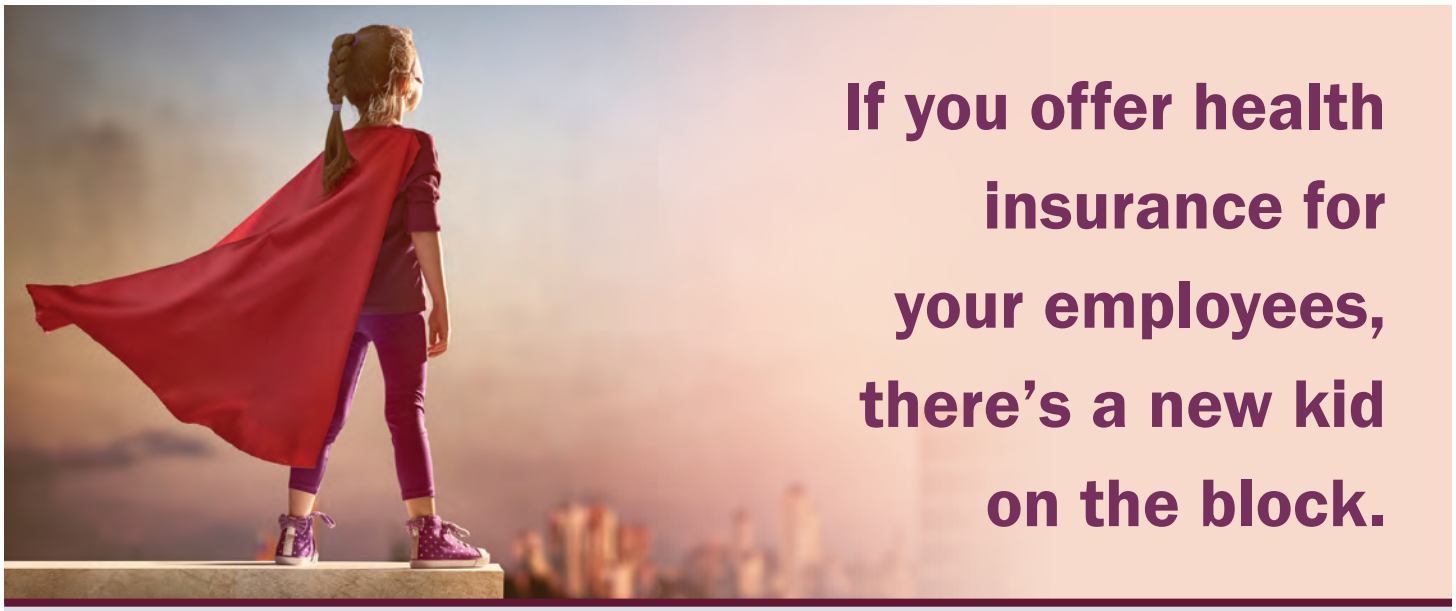

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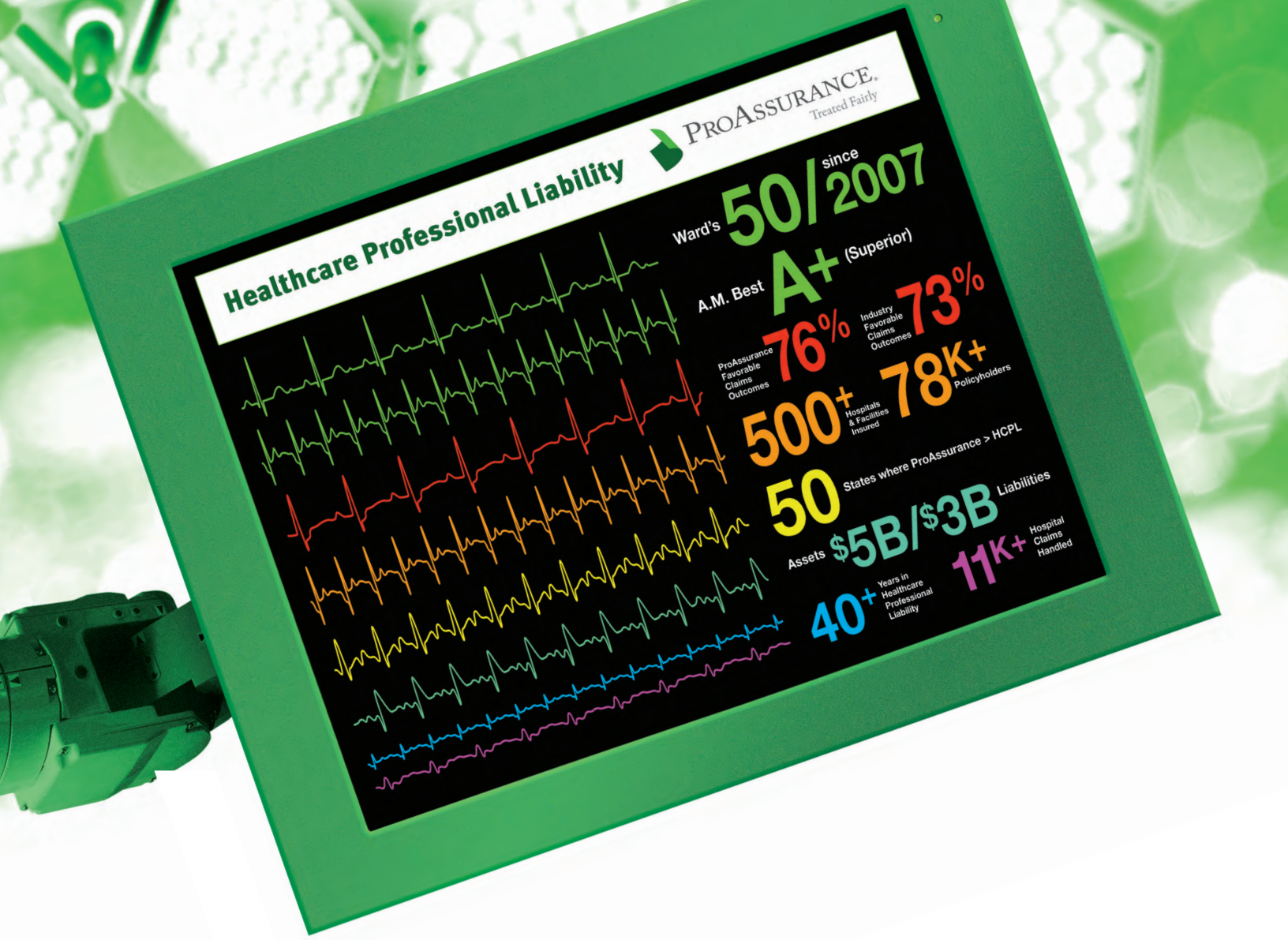

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