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#### COVER THEME Hidden in Plain Sight: Ticks & other potential health risks emerge as warm weather returns

Forty years ago, many clinical topics focused on infection and infectious diseases rather than cancer, genomics, and chronic illness—the subjects of much of today's medical literature. While a great deal has changed, much remains the same: infectious diseases are still important health concerns. This issue of *WMJ* highlights tick-borne illnesses and other infectious diseases found in our region, serving as a reminder to readers of some of nature's hidden dangers.

#### Cover design by Mary Kay Adams-Edgette.

The mission of *WMJ* is to provide a vehicle for professional communication and continuing education for Midwest physicians and other health professionals. *WMJ* is published by the Wisconsin Medical Society.

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### Be a Wisconsin Medical Society Foundation CHAMP

The Wisconsin Medical Society Foundation (Foundation) welcomes all physicians to be a CHAMP in advancing Wisconsin's health care. CHAMP (Community Health Action via Medical Partnerships) participants will work to advance health within Wisconsin communities through action teams comprised of physicians, medical students, other health care professionals, foundations, businesses and public health agencies.

The Foundation has rolled up its sleeves, put on its running shoes and plans to engage physicians to action. Through newly developed Foundation Ambassadors who will serve as the eyes and ears for the organization and physician-led CHAMP teams, our goal is to bring together a variety of professionals and individuals to improve community health throughout Wisconsin.

Working within the Wisconsin Medical Society's framework of over 12,000 physician members statewide provides a significant asset that the Foundation plans to leverage. In certain communities, the CHAMP teams may take on a leadership role helping to guide grassroots community improvement efforts while in other communities the teams may provide guidance or input to existing initiatives that could benefit from physician involvement. Assisting with implementing certain aspects of the state's health plan is another CHAMP team objective.

While we are making strong strides as a nation toward advancing health, we know that many opportunities exist to improve health beyond payment and policy reform. We believe that great energy and creative solutions may be gathered from professionals who engage in direct health care service on a daily basis. Through its focus on community health efforts, the Foundation will strive to be the conduit for sharing both new and existing positive programs that work to advance health. Stay tuned for a section of our website dedicated to community health innovation.

Please join us and **Be A CHAMP For Wisconsin!** For more information or ways to get involved, please contact Foundation Executive Director Rebecca Thompson at 866.442.3800, ext. 3720, or e-mail rebecca. thompson@wismed.org.





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# Infectious Diseases Still Cause for Concern

John J. Frey, III, MD, Medical Editor

or a project I am working on, I have been reading through journals from 1970, the year I graduated from medical school. What is revealing, of course, is both how much has changed and, conversely, how much is still the same. Rather than cancer, genomics, and chronic illnesses that are the subjects of today's medical literature, the clinical topics from 40 years ago focused on infection and infectious diseases. Interestingly, though, infectious diseasesboth ones that were known 40 years ago and those that weren't-are still around and still cause problems. This issue of WMJ highlights some of the infectious diseases that are found in our region.

Two articles on tick-borne illnesses should catch readers' attention as spring and the woods beckon. To the chant that Dorothy and her friends repeated as they crept through the woods on the way to Oz—"Lions and Tigers and Bears! O My!"-we should add "and ticks." The first is a case report of a severe complication of an infection with Anaplasma phagocytophilum in a patient who is on a statin, creating a life-threatening condition of potential renal failure from rhabdomyolysis.1 Fortunately a more complete history from the patient's wife secured enough of a concern to look for tick-borne disease, and the patient recovered. With the almost universal presence of statins in adults these days, it might be a good case to remember. The second article by Maloney is a review of the recommendations for diagnosis and management of Lyme disease as well as the possible transmission of Anaplasma phagocytophilum and Babesiosis via the

same ticks as the case report.<sup>2</sup> Maloney feels that the recommendations for diagnosis and treatment should be broadened to give clinicians more leeway in diagnosing and managing potential tick-borne diseases, which might decrease the potential for chronic form of Lyme disease or the more severe acute consequences of the other diseases.

Blastomycosis is not anywhere near as prevalent as Lyme disease but is a human

have previously shown, there are good reasons that they should.<sup>4</sup> A family doctor friend from New Mexico got a call from his patient who had flown to the East Coast and then developed a severe illness. My friend told his patient, "Tell the doctors to look for the plague," which, of course was what the patient had—and which is less common in New York than New Mexico.

Edwards and colleagues look at the atti-

Rather than cancer, genomics, and chronic illnesses that are the subjects of today's medical literature, the clinical topics from 40 years ago focused on infection and infectious diseases. Interestingly, though, infectious diseases...are still around and still cause problems.

pathogen that should be on our minds in both rural and urban areas where exposure to rivers and lakes exists. Baumgardner and colleagues, who have done work on establishing the water-borne risks for blastomcyosis, show how, despite clinical scenarios that are highly suggestive of that infection, most primary care clinicians do not put it among their most likely diagnoses.<sup>3</sup> Even when presented with clinical descriptions that are grounded in environmental situations, most clinicians have a hard time imagining diagnoses that do not fit with their usual experience. While urban doctors didn't think of blasto as frequently as rural doctors from endemic areas, perhaps, as the authors

tude of pediatricians toward immunizations and discovered some provocative data.5 The reassuring aspect of their study is that most pediatricians follow immunization recommendations for their patients. However, these same doctors come up short when recommending immunizations to family members of their at-risk patient. Children live in families, and the medical home for children should somehow contain the ability to deal with parents and other relatives of at-risk children. One confounder for the practicing community is that the size and location of practices affect both accessibility consistency of primary care and access to immunization. A recent article pointed

out that family doctors in small practices and rural areas did not consistently provide a high level of routine immunizations for children and adults in their practices because of cost and access to vaccines.<sup>6</sup> Edwards and colleagues also point out that the continuing controversy over thimerosol-free immunizations will affect physician and patient behavior regarding adhering to national guidelines. Changing beliefs might require more work and more conversation than it has to this point.

This issue also contains a study of chest pain in adolescents by Hanson and Hokanson from the view of the consulting clinician rather than the referring clinician.<sup>7</sup> Their nicely done retrospective study is very reassuring in that a good history, physical exam, a screening electrocardiogram, and an echocardiogram will help primary care clinicians distinguish adolescents who have the likelihood of a cardiac origin for their chest pain from those who don't. This study looks at a 2-year period of referrals to a pediatric cardiology clinic, and fewer than 1% of the patients were found to have a cardiac etiology for chest pain.

Finally, Ahrens reviews the experience of lobbying around the health bill in Wisconsin that created statewide regulations eliminating smoking in workplaces.<sup>8</sup> Why in 2010, one might ask, are there any arguments at all about the health effects of cigarettes on smokers or those exposed to secondary smoke? The facts did not sway a wide variety of lobbyists trying to influence the bill: the pro-tobacco groups used money and those in favor of a smoking ban used time and energy. It might be refreshing at some point to see discussion and debate about a public health problem and how best to accomplish it rather than whether it should be a goal at all.

Finally, this issue of *WMJ* contains a CME opportunity that we plan to include periodically. Readers may review the designated manuscript, in this case the Maloney article, and take the quiz for CME credit. *WMJ* Editorial Board member Richard

Reynerston, MD, has taken the lead on this idea, and we are grateful to Dick and his efforts at improving the journal.

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# Etiology of Chest Pain in Children and Adolescents Referred to Cardiology Clinic

Carleen L. Hanson, MD; John S. Hokanson, MD

#### ABSTRACT

**Objective:** To determine the proportion of children referred to pediatric cardiology clinic for chest pain diagnosed with a cardiac cause for the pain.

**Design:** Medical records of patients evaluated for chest pain at the University of Wisconsin Children's Hospital from 2004 to 2006 were reviewed, including the studies performed and final diagnosis.

**Results:** A total of 135 patients, including 78 boys, ranging from 4 to 17 years were evaluated. Eighty-four (62%) patients had pain for at least 1 month. All patients had an electrocardiogram (ECG), and most had an echocardiogram performed. Only 1 patient (0.7%) was found to have a cardiac cause for the pain. In 6 patients (4.3%), there was possible supraventricular tachycardia based on history, but no evidence of abnormality on subsequent testing. Ninety-five percent of the patients were diagnosed with noncardiac chest pain.

**Conclusion:** The incidence of cardiac chest pain in our study population is less than previously reported. Many patients were referred to cardiology clinic despite having had normal testing by the referring physician. Primary care physicians should be reassured when patients have a normal history, physical examination, and testing. Referral to pediatric cardiology usually is not necessary under these circumstances.

INTRODUCTION

Although a cardiac cause for chest pain is uncommon in children, concern for this possibility by family and primary care physicians prompts referral to the pediatric cardiologist. It has been reported that the complaint of chest pain accounts for 5.2% of all pediatric cardiology consults in an inpatient and emergency room setting.<sup>1</sup>

Multiple retrospective<sup>2-4</sup> and prospective<sup>5-11</sup> studies have been performed in the past to evaluate the etiology of chest pain in children; a cardiac etiology is reported in 0% to 15% of

. . .

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patients. However, few studies2,9,10 have reported on patients referred to a cardiology clinic. In addition, most studies were completed in the 1970s and 1980s.2-8 Subsequent to these earlier reports, there have been substantial advances in the ability to assess the cardiovascular system with noninvasive techniques. Children evaluated in a pediatric cardiology clinic in recent years would be the most likely to have the presence of cardiac abnormalities detected. The objective of this study was to determine the proportion of patients referred to a pediatric cardiology clinic for the complaint of chest pain who were diagnosed with a cardiac etiology for their pain.

#### **METHODS**

We performed a retrospective medical record review of patients evaluated for chest pain from January 1, 2004, through December 31, 2006, at the University of Wisconsin Children's Hospital Pediatric Cardiology Clinic. Patients up to but not exceeding 18 years were included if they were evaluated for the chief complaint of chest pain during the study period.

Patients were identified using 2 modalities: billing codes and echocardiogram records. In addition to the diagnosis of "chest pain," our billing code search also included other diagnoses that may be related to or might cause chest pain, including precordial pain, hypertrophic obstructive cardiomyopathy, dilated cardiomyopathy, coronary artery anomalies, myocarditis, pericarditis, arrhythmia, long-QT syndrome, Wolff-Parkinson White (WPW) syndrome, palpitations, asthma, gastroesophageal reflux disease (GERD), vocal cord dysfunction, and anxiety. We searched echocardiogram records for a study indication of chest pain.

This study was approved by the Institutional Review Board of the University of Wisconsin School of Medicine and Public Health.

#### RESULTS

Two hundred thirty patient encounters were identified by echocardiogram indication and 1180 patient encounters were found by the billing code search, for a total of 1410 encounters. One hundred thirty-five patient visits met the inclusion criteria; 1275 patient visits were excluded.

The study population included 78 boys and 57 girls, with ages ranging from 4 to 17 years (average 11.5 years). Seventy-five percent of children were at least 9 years of age. Between 40 and 50 children with the complaint of chest pain were evaluated in each year of the study. Sixty-nine percent of children were greater than the 50th percentile for body mass index (BMI).

Chest pain characteristics are shown in Table 1. Eighty-four (62%) patients had pain for at least 1 month. The frequency and duration of the pain were variable. Forty-three (32%) patients described their pain as sharp, which was the most common descriptor. The most common locations of the pain were the left chest (52 patients, 39%) and sternum (43 patients, 32%).

The most common event precipitating chest pain was exercise, reported in a total of 76 patients (56%). Forty patients (30%) reported having pain only with exercise, and 36 patients (27%) had pain both with exercise and at rest. Twenty-six patients (19%) reported taking a deep breath as preceding the pain. Less-reported triggers were movement (4 patients); after exercise concluded (3 patients); illness, palpitations, and anxiety (2 patients each); and eating (1 patient). Some patients reported multiple precipitating events. In 25 patients, no precipitating event was identified; in 11 patients, no precipitating event was documented.

Palpitations, the most common symptom associated with chest pain, were reported in 57 (42%) patients. Dyspnea and dizziness were the other commonly associated symptoms, with reports by 44 (33%) patients and 35 (26%) patients, respectively. Syncope was reported in 4 (3%) patients. No associated symptoms were reported in 40 (30%) children.

On physical exam, 5 (4%) patients had elevated blood pressure (above the 95th percentile for age, sex, and height). Eight patients had reproducible chest pain on palpation of their chest. Fifty-one patients had murmurs or clicks heard on physical exam in the cardiology clinic. Eight (16%) of them had findings on echocardiogram consistent with the exam findings. Four of the patients had mitral valve abnormalities, and 1 each had pulmonary valve stenosis, subaortic membrane, ventricular septal defect, and bicuspid aortic valve. The remaining patients were felt to have innocent murmurs.

Patients underwent various testing modalities in the course of their work-up for chest pain. Some of the testing was performed by the referring physician and interpreted at his or her clinic; some of these interpretations were completed by the

	Number (N = 135)	Percent (totals may not equal 100% due to rounding
Duration of symptoms		
Single episode	10	7
<1 week	1	1
1 week to 1 month	17	13
> 1 month to 6 months	50	37
> 6 months	37	27
Not documented	20	15
Frequency of pain		
Single episode	10	7
< 1 per month	11	8
1/month to < 1 per week	22	16
1/week to < 1 per day	19	14
Once or more per day	22	16
Not documented	51	38
Length of episodes		
< 1 minute	12	9
1 to 5 minutes	31	23
6 – 15 minutes	19	14
16 minutes – 1 hour	18	13
2 hours – 1 day	10	7
>1 day	4	3
Not documented	41	30
Quality of pain <sup>a</sup>		
Sharp	43	32
Pressure	17	13
Tightness	8	6
Squeezing	7	5
Burning	6	4
Dull	4	3
Other	29	21
Not documented	37	27
Location of pain <sup>a</sup>		
Left	52	39
Sternal	43	32
Right	14	10
Diffuse	11	8
Epigastric	5	4
Other	4	3
Not documented	34	25

referring physician and some were by specialists. These tests are useful in identifying children and adolescents with clearly normal or abnormal studies. However, obtaining and interpreting electrocardiograms (ECGs) and echocardiograms on pediatric patients can be challenging, and at times, studies that were initially interpreted as abnormal or possibly abnormal were repeated and interpreted as normal by the pediatric cardiologist.

All of the patients had an ECG performed at least once during their evaluation. Of the 74 ECGs performed by the referring physician, 48 (65%) were normal, and 26 (35%) were thought to be abnormal. The most common abnormality 
 Table 2. Abnormalities Found on Electrocardiograms (ECGs) in Children with Chest Pain from Referring Physicians and in Cardiology Clinic

	Number	Percent (of 135)
Abnormal ECGs from referring physician	26/74	19
Chamber hypertrophy	8 (31%)	
Axis deviation	4 (15%)	
Premature atrial contractions	3 (12%)	
Pre-excitation/Wolff-Parkinson-White syndrome	3 (12%)	
First degree atrioventricular (AV) block	2 (8%)	
Right ventricular (RV) conduction delay	2 (8%)	
Possible faulty lead placement	2 (8%)	
J-point elevation	1 (4%)	
Low atrial rhythm	1 (4%)	
Nonspecific T wave changes	1 (4%)	
Abnormal ECGs from cardiology evaluation	40/89	30
Chamber hypertrophy	15 (38%)	
Axis deviation	6 (15%)	
Pre-excitation/Wolff-Parkinson-White syndrome	5 (13%)	
Low atrial rhythm	3 (8%)	
Incomplete right bundle branch block (RBBB)	2 (5%)	
Borderline first degree block and RV conduction delay	2 (5%)	
Chamber hypertrophy with premature ventricular contraction (PVC)	1 ( 3%)	
Borderline first degree block	1 (3%)	
Possible Brugada with chamber hypertrophy	1 (3%)	
Axis deviation with intraventricular conduction delay	1 (3%)	
Bradycardia with early repolarization	1 (3%)	
T-wave abnormality	1 (3%)	
Borderline prolonged QTc	1 (3%)	
Possible Brugada vs early repolarization	1 (3%)	
Intraventricular conduction delay	1 (3%)	

Some patients had more than 1 type of abnormality detected.

detected was possible chamber enlargement. Eighty-nine ECGs were obtained in the cardiology clinic. Of these, 49 (55%) were normal, and 40 (45%) were thought to be abnormal. Again, the most commonly detected abnormality was possible chamber enlargement. One patient with Wolff-Parkinson-White syndrome had this diagnosis before evaluation for chest pain in the cardiology clinic. Table 2 details the abnormalities noted on the ECGs.

Thirty (22%) patients had echocardiograms ordered by the referring physicians prior to the cardiology appointment; 12 were thought to be abnormal. The most common abnormal finding was a possible coronary abnormality (either possible coronary artery fistula or abnormality of a coronary artery origin). Coronary arteries in children can be difficult to clearly delineate and, if they are not well visualized or if there is artifact, this may be interpreted as a possible coronary artery abnormality. Ninety-three (69%) patients had echocardiograms performed during the cardiology visit; 21 were abnormal. The most common finding was an abnormality of the mitral valve. In total, 108 patients (80%) had an echocardiogram performed as part of their evaluations; none was found to have echocardiographic findings related to the chest pain. Five patients with previously known echocardiographic abnormalities had the abnormality again demonstrated on echocardiogram during their work-up (1 each of mitral valve abnormality, pulmonary valve stenosis, ventricular septal defect, atrial septal defect, and bicuspid aortic valve). Table 3 provides further details on the echocardiogram results.

A follow-up cardiology evaluation was recommended in 19 patients based on their incidental cardiac findings (either by ECG or echocardiogram). Twelve patients received a recommendation for bacterial endocarditis prophylaxis based on their incidental cardiac findings, as all patients were seen prior to the 2007 revision of the American Heart Association guidelines. However, following the 2007 AHA guidelines, this recommendation would no longer be necessary in any of these patients.<sup>12</sup>

Seventeen percent (5/30) of patients with abnormalities suspected on the initial echocardiogram later were found to have normal echocardiograms. These included 1 patient with possible coronary artery fistula, 1 patient with pos-

sibly elevated right-sided pressures, 1 patient with possible subaortic membrane, 1 patient with enlarged aortic root, and 1 patient with possible mitral valve abnormality.

The diagnoses of the patients with chest pain are shown in Table 4. Only 1 patient (0.7%) was determined to have a cardiac cause for his chest pain (pericarditis). Eighteen patients (13%) were diagnosed initially as having a possible cardiac cause for their chest pain, but on further testing, only 6 were still thought to have a possible cardiac cause. (In these 6 patients, a tachyarrhythmia was suspected based on history, but was not demonstrated on either a Holter and/or event monitor). One-hundred sixteen patients (86%) were diagnosed with noncardiac chest pain after the initial visit. At the conclusion of their cardiac evaluation, 128 patients (94.8%) were diagnosed with noncardiac chest pain.

The single patient deemed to have a cardiac cause for his chest pain was a 16-year-old boy who presented after a 2- to 3-day history of chest pressure starting in his upper-chest bilaterally and then moving more centrally. The discomfort was preceded by less than 1 day of a vomiting illness that had also affected other members of his family. There were no complaints of fever, dizziness, or shortness of breath, although he did have 1 episode of a brief sensation of skipped heartbeats. An ECG was obtained that demonstrated ST segment changes in the inferior leads. Chest radiograph was normal. A troponin I level was elevated at 5.07 (normal 0-0.05). He was diagnosed with pericarditis, but no significant pericardial effusion was seen on his echocardiogram. He was treated with ibuprofen, and within 3 days his troponin I level was normal.

Twenty-nine patients (21%) were determined to have cardiac findings that were not thought to explain their chest pain by the consulting pediatric cardiologist. Mitral valve abnormalities were the most common incidental finding, in 8 patients (6%). Hypertension was documented in 5 patients, and Wolff-Parkinson-White syndrome in 4 patients. There were 3 patients each with borderline prolonged PR-interval and atrial septal defect, and 2 patients were found to have a small ventricular septal defect. Finally, there was 1 patient each with mild aortic dilation, possible coronary artery fistula, pulmonary valve stenosis, bicuspid aortic valve, and mildly elevated right-sided pressures. One patient had 2 incidental findings.

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	Number	Percent (of 135)
Abnormal echocardiograms from referring physician	12	9
	Number (n = 12)	Percent (of abnormal referring echocardiograms) <sup>a</sup>
Possible coronary artery abnormality	7	58
Elevated right-sided pressure	2	17
Atrial level shunt	2	17
Mildly dilated right ventricle	1	8
Increased left ventricular wall thickness	1	8
Decreased function	1	8
Mitral valve prolapse	1	8
Pulmonary insufficiency with increased wall thickness	1	8
	Number	Percent (of 135)

Table 3. Abnormal Echocardiograms in Children with Chest Pain from Referring Physicians and in

Abnormal initial echocardiograms from cardiology evaluation	21	16
	Number (n = 21)	Percent (of abnormal cardiology clinic echocardiograms) <sup>a</sup>
Mitral valve abnormality	7	33
Small ventricular septal defect	2	10
Small secundum atrial septal defect	2	10
Possible coronary artery fistula	2	10
Right coronary origin slightly high (potential normal variant)	2	10
Possible subaortic membrane	1	5
Mild pulmonary valve stenosis	1	5
Bicuspid aortic valve	1	5
Mild-moderate tricuspid regurgitation	1	5
Mild aortic dilation	1	5
Right-sided pressures upper limits normal/mildly elevated	1	5

#### DISCUSSION

This is the largest study to evaluate chest pain in a pediatric cardiology clinic. Previous studies have reported between 50 and 100 patients.<sup>2,9,10</sup> In this study, all of the patients had at least 1 ECG performed, and 80% of the patients had an echocardiogram performed as part of their evaluation. The high percentage of patients with this comprehensive testing should increase the likelihood of documenting the presence of cardiac pathology, if it is present. Additionally, we did not exclude patients who had known cardiac abnormalities if they were referred for evaluation of chest pain. This also would be expected to increase the likelihood of finding patients with a cardiac cause for their chest pain.

There is an obvious selection bias present in our subjects. The frequency of a cardiac cause for chest pain would be expected to be lower in the primary care physician's office than in the cardiologist's office. Presumably, children with a clinical history suggesting a noncardiac etiology, including a reassur
 Table 4. Diagnosis in Children with Chest Pain at Time of Initial Cardiology

 Clinic Visit

	Number of patients (N = 135)	Percent
Cardiac	1	0.7
Possibly cardiac	18	13
Diagnosis after follow-up		
Non-cardiac	12 (67%)	
Possibly cardiac	6 (33%)	
Noncardiac	<b>116</b> ª	86
Musculoskeletal	25 (22%)	
Respiratory	16 (14%)	
Gastrointestinal/Gastroesophagea reflux disease	l 13 (11%)	
Anxiety	3 (3%)	
Precordial catch	2 (2%)	
Not specified/idiopathic	63 (54%)	

ing personal and family history and a normal physical examination, would not have been referred to pediatric cardiology. Therefore, this study population excludes those children for whom a cardiac cause was already excluded by their primary provider. Accordingly, referral to cardiology would be more likely if an abnormality were detected on the initial evaluation by the primary care provider, even if that finding did not suggest an etiology likely to cause chest pain. Therefore, we expected the incidence of cardiac abnormalities to be higher in this study population than in the general population.

Of interest, the incidence of a cardiac cause for chest pain of 1/135 (0.7%) in this study is lower than that reported by most previous studies. Even if the 6 patients with a possible, but non-documented arrhythmia are included, the overall incidence of cardiac-induced chest pain is 7/135 (5.2%).

One possible explanation for the low incidence of cardiacinduced chest pain in our population is a decreasing threshold for referral to the pediatric cardiology clinic from the primary care physician. In recent years, news and media coverage of sudden deaths in athletes has created heightened concern among both families and physicians. Primary care physicians may be fearful of missing cardiac pathology and assuming responsibility for clearing athletes to participate in sports. This hypothesis is supported by the fact that there were 50 (37%) patients referred who had no abnormalities on the cardiac tests ordered by the primary care physician (1 or more of ECG, echocardiogram, chest radiograph, Holter monitor, or event monitor). Additionally, 11 (8%) of those patients had both a normal ECG and echocardiogram before referral to pediatric cardiology.

Another potential reason that more children with chest pain are being referred to pediatric cardiology is the increased number of overweight and obese pediatric patients. It is possible that with increasing concern for premature coronary disease in overweight children, primary care physicians have fears of early atherosclerotic heart disease as a possible cause of chest pain. Our study population included a higher number of patients with an increased body mass index (BMI) than might have been expected (69% of patients had a BMI greater than the 50th percentile, 24% had a BMI greater than the 85th percentile, and 10% had a BMI greater than the 95th percentile) although these numbers may be reflective of the referral population in general.

The sensitivity and specificity of ECG evaluation of the child with chest pain have not been studied previously. The pretest probability of ischemia or other cardiac causes of chest pain in this population is low, and our data suggests that the specificity of ECG testing is poor. Of the 163 ECGs performed, 24 suggested ventricular hypertrophy or enlargement. All patients with these findings on ECG had an echocardiogram, none of which demonstrated cardiac chamber enlargement or hypertrophy. Of the 163 ECGs performed, 42 demonstrated some other form of electrical abnormality, but only 1 of these abnormalities was thought to be related to the presenting complaint of chest pain. Similarly, incidental findings on echocardiography unrelated to the presenting complaint of chest pain were common. In our population, the only change in clinical care was the now outdated recommendation for bacterial endocarditis prophylaxis in 12 patients.

#### CONCLUSION

Chest pain is a common complaint in children. Although a pediatric cardiology referral may provide reassurance to the family and primary care physician, this study suggests that the outpatient evaluation of chest pain in children only rarely identifies a cardiac origin for the chest pain. Primary care physicians should be reassured that when patients have a normal history, physical examination, and testing, referral to pediatric cardiology is usually not necessary.

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# Attitudes of Wisconsin Pediatricians Toward Influenza Immunization

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#### ABSTRACT

**Objective:** Determine the influenza immunization practices of Wisconsin pediatricians in response to evolving influenza prevention strategy in the United States.

**Design:** Two hundred fifty members of the Wisconsin Chapter of the American Academy of Pediatrics were surveyed prior to the 2004-2005 influenza season about their expectations for implementing the latest and future influenza vaccination recommendations for children and their use of trivalent inactivated influenza vaccines free of thimerosal as a preservative.

**Results:** Ninety-two percent of respondents expected to vaccinate most medically high-risk children against influenza, but only 53% would recommend influenza vaccine for most of their household contacts. Although 57% planned to vaccinate most healthy children ages 6 months to 23 months, just 27% thought the majority of household contacts of healthy infants under 23 months of age would be vaccinated. Fewer than 24% favored universal influenza vaccination for the majority of healthy school-aged children. Seventy percent had little or no concern about recommending thimerosal-containing influenza vaccines, but 60% agreed or strongly agreed thimerosal-free vaccine availability would increase parental acceptance of vaccinating their children.

**Conclusion:** Although Wisconsin pediatricians are aware of the importance of preventing influenza disease in children, barriers to universal influenza vaccination of children and key household contacts remain.

#### INTRODUCTION

Pediatric deaths due to influenza complications are unusual but not inconsequential<sup>1</sup> with infants aged 0 to 6 months having the highest mortality rate from influenza among all children.<sup>2</sup> Eighty percent of influenza-associated hospitalizations under 5 years of age occur in healthy children less than 2 years old,<sup>3</sup> and the rate of influenza-related hospitalizations for children aged 0 to 1 years eclipses that of the elderly.<sup>4</sup> Influenza also may play an important role in the pathogenesis of acute otitis media with influenza com-

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plications accounting for a 10% to 30% increase in the number of antimicrobial courses during the influenza season.<sup>5</sup>

Children appear to be important in disease propagation during influenza epidemics as a consequence of significantly higher attack rates approaching 40% and protracted high levels of influenza viral shedding.<sup>6.7</sup> During pandemics, the elderly are often at the end of a community transmission chain that begins with children.<sup>8</sup>

In 2004, the Advisory Committee on Immunization Practices (ACIP) expanded the recommendations for annual influenza vaccination to include healthy children 6 months to 23 months of age in recognition of their increased morbidity due to influenza.<sup>9</sup> These recommendations were broadened in 2006 to include all healthy children aged 6 months to 59 months.<sup>10</sup> By August 2008, the Centers for Disease Control

and Prevention (CDC) recommended all children 6 months through 18 years of age be immunized yearly against influenza beginning no later than the 2009-2010 influenza season.<sup>11</sup> Despite the increased emphasis on immunizing healthy children against influenza, success has been elusive in immunizing even the highest risk patients in the United States.<sup>12</sup> In the 2006-2007 influenza season, only 35% of children aged 5 to 17 years with high risk medical conditions had received influenza vaccine, and just 26% of household contacts of persons of high risk including children under 5 years of age had been immunized against influenza.<sup>13</sup> Less than 30% of children in the United States aged 6 months through 18 years received influenza vaccine during the 2009-2010 pandemic and less than 25% of those under 9 years of age given their first dose of influenza vaccine received the recommended 2-dose regimen.<sup>14</sup>

Current influenza prevention strategy requires intensive surveillance, the availability of antiviral drugs, and the attainment of sustained levels of immunity with vaccine against the influenza virus, particularly in children. Mass immunization of susceptible school children has been shown to provide protection against influenza disease for unvaccinated adults, including the elderly.<sup>15</sup>

Modern trivalent inactivated influenza vaccine (TIV) has been demonstrated to be safe and effective in healthy and medically at-risk children greater than 6 months of age.<sup>16</sup> Live attenuated influenza vaccine (LAIV) is now recommended for healthy children and adults ages 2 to 49 years as an effective and safe intranasal option for patients who desire an injectionfree regimen.<sup>17</sup>

Many parents remain skeptical of influenza vaccine safety due to an ongoing disinformation campaign on the Internet and in the popular media. As of summer 2004, up to 12% continued to refuse to vaccinate their children against influenza because of concerns the vaccine causes influenza or contains thimerosal.<sup>18</sup> The balance of safety research on thimerosal fails to support any association with neurodevelopmental or autism spectrum disorders.<sup>19,20</sup> Supplies of TIV vaccines free of thimerosal as a preservative continue to be limited.

Because physician recommendation for use of vaccination has been shown to strongly predict influenza vaccination status in children,<sup>21</sup> we surveyed Wisconsin pediatricians at the onset of the 2004-2005 influenza season to assess: (1) their knowledge about influenza prevention in children; (2) their past and anticipated influenza immunization practices; and (3) their use of thimerosal-free influenza vaccine preparations.

#### **METHODS**

This study was approved and funded by the Executive Committee of the Wisconsin Chapter of the American Academy of Pediatrics (WI-AAP).

#### **Subjects and Design**

The WI-AAP comprises more than 900 pediatricians. Two hundred fifty members were selected randomly from a list of nearly 400 actively practicing general pediatricians who historically provide routine immunization services. The WI-AAP Executive Committee determined the study was in compliance with AAP regulations governing projects involving AAP membership. Pediatricians selected were sent a 1-page, 2-sided survey by postal mail along with return postage and a cover letter explaining the study. The survey was sent September 16, 2004; 4 weeks later members who had not returned a survey were sent an e-mail reminder or a postcard if e-mail contact was not possible.

#### **Survey Instrument**

The survey contained closed-ended questions about expected influenza vaccination plans for the 2004-2005 season, identification of populations who would receive influenza vaccine, and whether there was agreement with national policy statements targeting pediatric populations with influenza vaccine in current and future influenza seasons. They were also polled about their past experience with and future plans for use of thimerosal-free TIV in their practices. Survey answer options used were: "percentage of patients in the practice expected to receive influenza vaccine" (1 choice allowed for 4 options: <25%, 25%-50%, 50-75%, and >75%) and Likert formats with 5-point selection scales (1 = strongly disagree or worse to 5 = strongly agree or best) for questions concerning immunization practices. Selected ranges of percentages were used for proportions of children who would receive thimerosal-free vaccines. Returned surveys were assigned a unique numerical identifier to facilitate targeted reminders. No identifying data of individual pediatricians were maintained.

#### **Statistical Analysis**

Categorical data were summarized as frequencies and percentages. All quantitative data were summarized by medians and ranges. Respondents who no longer routinely vaccinated children were excluded in the final results. The Wilcoxon Signed Rank test was used to compare response patterns of physicians' past experience with their future plans for use of the thimerosal-free influenza vaccine. Comparisons of categorical data between groups were performed using a chi-square test or Fisher's exact test whenever appropriate. The Wilcoxon rank sum test was used to compare quantitative data. All statistical tests were 2-sided, and P values of <.05 indicated statistical significance. Statistical analyses were performed using SAS version 6.12 software (SAS Institute, Cary, NC).

#### RESULTS

Of 250 surveys sent, 136 (54%) were returned, with 5% of respondents no longer vaccinating children. The survey collected respondent ZIP codes and determined all 5 Wisconsin health regions were proportionally represented relative to urban, suburban and rural practices in the state. Ninety-five percent of respondents agreed or strongly agreed that children contribute substantially to the transmission of influenza within the community, and 84% agreed or strongly agreed that children under the age of 2 years had a high risk of hospitalization with influenza infection. Ninety-eight percent of respondents agreed or strongly agreed TIV is safe for children, 94% agreed or strongly agreed that TIV effectively prevents influenza in children, while 97% agreed or strongly agreed that TIV reduces the severity of influenza in the vaccinated child.

When asked to whom they would administer TIV during the coming season, 86% of respondents expected to vaccinate at least three-fourths of children in their practices with "high-risk" medical conditions (Figure 1). Fifty-seven percent expected to vaccinate at least three-fourths of their healthy patients aged 6 months to 23 months while another 26% believed they would reach between one-half and three-fourths of their patients in that age group. Fiftythree percent expected to administer TIV to at least three-fourths of the pediatricaged household contacts of "high-risk" children, and an additional 28% of pediatricians expected to vaccinate between half and three-fourths of their patients in the high-risk contacts group. Twentyseven percent of respondents planned on vaccinating at least three-fourths of their patients in the group of household contacts of healthy children from birth to 23 months of age while an additional 23% of the pediatricians expected to immunize between half to three-fourths of their patients in households within that same cohort. Twenty-four percent



expected to receive trivalent inactivated influenza (TIV) in each of 131 respondent practices.

of respondents planned to vaccinate the majority of older healthy children, aged 24 months to 18 years in their practices. Eighty-seven percent of Wisconsin pediatricians reported vaccine availability would strongly influence which cohorts would receive influenza vaccine.

Seventy percent of respondents indicated they had little or no concern about recommending the use of TIV that contained thimerosal as a preservative (Figure 2). However, 60% of respondents agreed or strongly agreed that thimerosal-free TIV availability would increase parental acceptance of vaccinating their children. When asked what percentage of children ages 6 months to 23 months received thimerosal-free TIV during the 2003-2004 season, 56% (60 out of 108 respondents) reported at least 10% of their patients received it. When asked about anticipated use of thimerosal-free TIV during the 2004-2005 influenza season, 78% of respondents (89 of 114) expected to give it to 10% or more of the children in their practice, a significant increase over the 2003-2004 season (P<0.001).

#### DISCUSSION

The results from this survey suggest Wisconsin pediatricians enjoy a solid knowledge base with regard to pediatric influenza disease epidemiology and severity. However, despite strong pediatric influenza vaccine recommendations from ACIP and the American Academy of Pediatrics Committee on Infectious Diseases (AAP-COID) for the 2004-2005 season, this survey revealed a high degree of variability as to who is likely to receive influenza vaccine in the office setting.

Wisconsin pediatricians appeared to respond positively to the case made for immunizing the cohort age 6 months to 23 months but were less likely to pursue a "cocooning strategy"

to routinely recommend vaccination of other groups such as healthy household members of the medically high-risk children or healthy children less than 23 months of age. If the United States hopes to pursue a universal influenza vaccination program and promote a cocooning concept to protect vulnerable cohorts, efforts must be made to: (1) further increase and stabilize the influenza vaccine supply appropriate for pediatric use; (2) educate physicians and nurses on the rationale for universal influenza vaccination in the context of pandemic planning, cocooning, and containing influenza within the community; (3) assist the medical home in developing efficient models of immunization delivery during influenza season that include a means to provide a 2-dose regimen when recommended for children 6 months to 9 years old; and (4) provide financial incentives to make immunization services economically desirable for the private sector.<sup>22-24</sup>

A paradox also exists in physician behavior concerning the safety of influenza vaccine containing thimerosal as a preservative when compared to actual usage in practice. Although most Wisconsin pediatricians reported little concern about the safety of TIV containing thimerosal, they anticipated an increase in the use of thimerosal-free vaccine during the 2004-2005 influenza season in response to pressure from parents with concerns about thimerosal. Discussing the difference between good science and the pseudoscience that permeates the thimerosal controversy is time-consuming and emotionally charged. Wisconsin pediatricians appear willing to use thimerosal-free influenza vaccine to defuse this issue.

The conclusions drawn from this survey are supported by a number of strengths in design. A decade of repeated WI-AAP immunization practices surveys has shown that response rates



over 50% are typical and exceptional for private practice surveys in general. The respondents represent a diverse collection of practice styles in urban, suburban, and rural communities. Wisconsin pediatricians historically work closely with their public health counterparts, and together they have substantial influence on how quickly national recommendations are adopted. This survey was performed in the late summer when community and state influenza vaccination promotion programs are most active.

This survey is subject to a number of limitations. The survey was completed within a time frame when there were major problems with the influenza vaccine supply. Although nearly all surveys were returned before this issue was publicly acknowledged, rumors about impending influenza vaccine shortages could have influenced some of the respondents' answers. There is a potential for response and recall bias because the sponsoring organization had engaged in an aggressive influenza vaccination education campaign through a chapter newsletter published 3 times a year. Non-responders may opt out of responding to a survey that might reflect their disagreement with AAP immunization policies. The survey was given only to pediatricians in Wisconsin; therefore, the conclusions may not be representative of pediatricians nationally or other Wisconsin health care professionals who vaccinate children.

#### CONCLUSION

Although Wisconsin pediatricians appear knowledgeable about the consequences of influenza disease in children, there is inconsistency in the provision of influenza vaccine to children in the state. Clearly, barriers need to be identified and overcome if the goal of yearly influenza vaccination of children 6 months through 18 years is to be realized. Physician advocacy for any new vaccine initiative is often driven by factors beyond good vaccine science. The economic and infrastructure strain on pediatric offices attempting to comply with a seasonal universal influenza immunization campaign may require consideration of alternate immunization sites such as schools and pharmacies that could displace, to some degree, the traditional medical home as the preferred site of immunization delivery.

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# The Differential Diagnosis of Pulmonary Blastomycosis Using Case Vignettes: A Wisconsin Network for Health Research (WiNHR) Study

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#### ABSTRACT

**Purpose:** Pulmonary blastomycosis is an uncommon but serious fungal infection endemic in Wisconsin. Clinician awareness of the protean presentations of this disease may reduce diagnostic delay. This study addressed the diagnostic accuracy of physicians responding to case vignettes of pulmonary blastomycosis and the primary care differential diagnosis of this disease.

**Methods:** Eight pulmonary blastomycosis cases were developed from case files. From these, 2 vignettes were randomly selected and mailed to primary care physicians in the Wisconsin Network for Health Research. Respondents were asked to list the 3 most likely diagnoses for each case.

**Results:** Respondents listed Blastomycosis as the most likely diagnosis for 37/227 (16%) case vignettes, and 1 of the 3 most likely diagnoses for 43/227 (19%). When vignettes included patient activity in counties with an annual incidence rate of blastomycosis greater than 2/100,000, compared to counties with lower incidence rates, diagnosis was more accurate (28/61 [46%] vs 15/166 [9%]; P<0.001). Physicians with practice locations in counties with annual blastomycosis incidence rates >2/100,000 listed blastomycosis more commonly than physicians from other counties (16/36 [44%] vs 27/177 [15%]; P<0.001). This difference in accurate diagnosis remained significant in a multivariate model of practice demographics. Based on responses to the vignettes, pneumonia, cancer, non-infectious pulmonary disease, and tuberculosis emerged as the most-frequently noted diagnosis in the differential diagnosis of blastomycosis.

**Conclusion:** Blastomycosis was not listed as 1 of 3 primary diagnoses in a majority of cases when Wisconsin primary care physicians considered case vignettes of actual pulmonary blastomycosis cases. Diagnosis was more accurate if the patient vignette listed exposure to a higher incidence county, or if the physician practiced in a higher incidence county. In Wisconsin, failure to include blastomycosis in the differential diagnoses of illnesses associated with a wide variety of pulmonary symptoms suspected to represent infectious or non-infectious pulmonary, cardiac, or neoplastic disease, regardless of geographic exposure, could result in excess morbidity or mortality.

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#### INTRODUCTION

Blastomycosis is an uncommon but serious infection caused by the dimorphic fungus, Blastomyces dermatitidis, which primarily affects the lungs and skin.1 Infected individuals may present with variable symptoms, ranging from no symptoms, mild-severe respiratory problems, to progressive illness involving multiple organ systems or acute fulminating pulmonary infection.<sup>2</sup> Pulmonary blastomycosis can clinically be divided into 4 broad categories: (1) asymptomatic, associated with only serological evidence of prior infection or granulomas, often in the lung, which can be confused with other lung nodules; (2) acute localized pneumonia; (3) severe acute respiratory distress syndrome (ARDS), seen in 2 of our cases, often confused with congestive heart failure, pulmonary emboli, or other causes of ARDS; (4) subacute to chronic infiltrates and/or cavitary disease, confused with cancer, tuberculosis, bacterial abscess, and Wegener's granulomatosis. In addition, acute or chronic dissemination of B dermatitidis to skin, brain, genitourinary (GU) system, or bone, including illnesses that mimic pso-

riasis, lung cancer with metastases, or other malignancies, may occur at any stage of any category.

In highly endemic areas of Wisconsin (generally northern and north central Wisconsin), where clinicians more commonly encounter blastomycosis,<sup>3,4</sup> a large proportion of cases are discovered in the earlier pulmonary stage. Even in these areas, significant delay may occur between onset of pulmonary symptoms and diagnosis and treatment.<sup>5</sup> This disease may mimic a variety of pulmonary, infectious, or malignant diseases.<sup>1,6,7</sup> Delay in diagnosis of blastomycosis is well described in the literature,<sup>6,8</sup> and can often be fatal in patients with delayed 

 Table 1.
 Summary of Descriptions of Blastomycosis Case Vignettes, Percentage of Respondent Wisconsin Primary Care Physicians Diagnosing Blastomycosis, and

 Top 3 Diagnoses Suggested for Each Vignette

Patient Characteristics			Director				
Age	Gender	County of Residence <sup>a</sup>	Other Counties Visited <sup>a</sup>	Case Scenario in Brief	mycosis Clinical Category <sup>b</sup>	Respondents Diagnosing Blastomycosis <sup>c</sup>	Top 3 Diagnoses
42	М	"Fox Valley" (1-4)	Washburn (3) "Northern Wisconsin" (1-4)	1 month cough, sore throat, dyspnea, chest congestion, low-grade fever, weight loss; RML infiltrate; computer technician; camping, canoeing and pets	2	13/26 (50%)	Pneumonia, cancer, blastomycosis
31	М	Manitowoc (4)	"Northern Wisconsin" (1-4)	11 weeks of cough and rib/back pain, weight loss, no fever; smoker; painter; mold exposure; hunting and fishing; LLL consolidation	4	15/35 (43%)	Pneumonia, blastomycosis, "fungal"
54	F	Racine (4)	None mentioned	3 weeks of cough, febrile, night sweats, dyspnea, fatigue; obesity; rheumatoid arthritis on prednisone/ methotrexate; unemployed; became hypoxemic, had signs of ARDS	3	3/25 (12%)	Pneumonia; noninfectious, nonmalignant pulmonary process; complication of non pulmonary disease
56	М	Milwaukee (4)	None mentioned	Skin lesions and progressive dys- pnea, cough, chills, weight loss; no fever; history of sarcoidosis; truck driver, no recent outdoor activities; LUL mass, mediastinal adenopathy	4, D	2/26 (8%)	Noninfectious, nonmalignant pulmonary process; cancer; pneumonia
31	М	Kewaunee (5)	None mentioned	2-3 weeks of cough, hemoptysis, dyspnea, chest/back discomfort, fatigue, weight loss; works outdoors as welder; fume exposure; LML/LLL infiltrates	2	5/36 (14%)	Pneumonia; cancer; noninfectious, nonmalignant pulmonary process
29	М	Milwaukee (4)	None mentioned	Pleuritic chest, back and scapular pain, productive cough, night sweats; afebrile; machine tool and steel fabri- cator; LUL mass	4	2/25 (8%)	Cancer, pneumonia, tuberculosis/mycobacterium
48	М	Kenosha (4)	None mentioned	2 months of cough, low-grade fever, chest congestion, weight loss; then night sweats, chills, hemoptysis; en- gineer, works indoors; lung abscess, pulmonic process and hemoptysis	4	3/31 (10%)	Pneumonia. tuberculosis/mycobacterium. cancer
47	М	Milwaukee (4)	None mentioned	4 days of dyspnea, cough; diabetes, hypertension, hyperlipidemia; com- puter technician; bilateral lung infil- trates, increased pulmonary vascular congestion with normal heart size	3	0/23 (0%)	Cardiac disease; pneumonia; noninfectious, nonmalignant pulmonary process

Abbreviations: LUL, left upper lobe; LML, left middle lobe; LLL, left lower lobe; RML, right middle lobe; ARDS, acute respiratory distress syndrome <sup>a</sup> Categories of county specific mean annual reported blastomyosis incidence per 100,000 population adapted from reference 14: Category 1 county incidence

is > 20 cases/100,000 population; category 2 is > 5 to 20; category 3 is > 2 to 5; category 4 is <2; category 5 is no cases.

<sup>b</sup> Clinical category of blastomycosis corresponding to illness presented in the vignette. Blastomycosis clinical categories: category 1 – Asymptomatic (no vignettes sent in this category); category 2 – Acute localized pneumonia; category 3 – ARDS; category 4 – Subacute to chronic infiltrate and/or cavitary disease; D – Dissemination from lungs to other organs, bone, or skin.

<sup>c</sup> Number of respondents who included blastomycosis as a diagnosis for this vignette divided by the number of reviews of this vignette (%).

Editor's Note: See appendix on page 73 for the complete text of 3 case vignettes. The text of all 8 vignettes used in this study is available online at www.wmjonline.org/\_WMS/publications/wmj/pdf/110/2/68vignettes.pdf.

diagnosis.<sup>9,10</sup> One review<sup>8</sup> states, "Improving the awareness of clinicians to the possibility of *B dermatitidis* infection is a key step to resolving the problem of delayed diagnosis." Therefore, it is essential to obtain a better understanding of how primary care physicians initially diagnose the various clinical presentations of blastomycosis.

The purpose of this study was to determine the rate at which clinicians currently practicing medicine in distinct geographic regions of Wisconsin correctly diagnose *B dermatitidis* infection when given brief descriptions of actual cases.

#### METHODS

During March and April 2010, primary care physicians affiliated with the Wisconsin Network for Health Research (WiNHR)11 (N=1064) were mailed a survey to be completed anonymously and returned using an enclosed metered, preaddressed envelope. The survey packet invited the recipient to participate in "a research study of the differential diagnosis of pulmonary disease," and contained questions regarding the county of practice, gender, specialty, and years in practice of the respondent; and 1 of 28 possible fixed combinations of 2 clinical case vignettes selected from a set of brief descriptions of 8 pulmonary blastomycosis cases on a rotating basis. The vignette pairs were always ordered the same, but identified by fictitious numbers from 1 to 56. The vignettes were described in the cover letter as "2 randomly selected (actual) clinical case histories that resulted in the diagnosis of a pulmonary condition." The letters were sent on behalf of WiNHR by the third author (EG), and the name of a specific person involved in the research program at the particular institution was included in the cover letter (for questions concerning the study). Participants were not informed of the names of the 2 primary authors as their identity, based on reputation, may have biased responses toward blastomycosis (DJB) or influenza or anthrax (JLT).

De-identified vignettes were selected from a case series of blastomycosis from eastern Wisconsin. The case series was a continuation of a recently published study<sup>12</sup> that used the same methods. The cases (Table 1) were chosen to represent the variety of patient presentations, ages, and geographic areas of exposure in the case series. The demographic, geographic, clinical, laboratory, and radiologic data were those obtained and considered at the time of each presentation, according to the medical record. Patients with the case illnesses were initially examined between January and August 2009. The only information excluded was the clinician impressions and the nature and result of the definitive diagnostic test. A summary of the 8 case vignettes is included in Table 1; details are available at www.wmjonline.org/\_WMS/publications/wmj/ pdf/110/2/68vignettes.pdf. For each case, respondents were asked to write down their 3 most likely diagnoses, in order, based on their experience and the clinical vignette. Similar methods have been used by one of the principal investigators to study the differential diagnosis of anthrax.<sup>13</sup>

Diagnostic responses were coded by one of the physician authors (DJB) into 1 of 11 categories (Table 2). Counties of respondent practice location and case vignette residence and exposure were placed into 5 ranked categories based on blastomycosis incidence rates as published for 1999-2003 by the Wisconsin Division of Public Health.<sup>14</sup> MINITAB statistical software (State College, Penn) was used for data analysis. Categorical data was analyzed using chi-square tests, or Fisher exact test, as appropriate. Multivariate analysis was performed using binary logistic regression models.

For Aurora Health Care, Marshfield Clinic Research Foundation, and University of Wisconsin, the project was reviewed and approved by the Wisconsin IRB Consortium. The project was exempted from oversight by the Gundersen Lutheran Medical Foundation review board.

#### RESULTS

The survey had an 11% response rate, with 227 case vignette surveys returned by 114 physicians. Sixty-six percent were male (compared to 63% in the survey mailing, P=0.7), and included 147 (65%) family medicine, 63 (28%) general internal medicine, 9 (4%) internal medicine/pediatrics and 6 (3%) hospitalist physicians (1 physician did not identify specialty). Thirteen percent of respondents had been in practice less than 5 years, 11% for 5 to 10 years, 31% for 11 to 20 years and 46% for 21 years or more.

Respondent practice locations included 30 of the 72 Wisconsin counties. Survey responses, by county, could not be compared to the mailing distribution due to extensive use of non-clinic addresses. However, survey response by county of practice regarding blastomycosis incidence rate categories 1-5, as listed in Table 1, is similar to the population distribution (US Census 2006 estimate) of counties in these categories, respectively (3%/10%/4%/75%/8% vs 1%/9%/5%/73%/13%, P=0.7, actual vs expected).

Overall, blastomycosis was listed as the most likely diagnosis for 37/227 (16%) case vignettes, and 1 of the 3 most likely diagnoses for 43/227 (19%). There was, however, considerable variation in accuracy of diagnosis between vignettes (Table 1) and between respondents. Vignettes 1 and 2 that described patient residence or exposure within 1 of the 20 counties with higher annual incidence rates (>2/100,000) of blastomycosis<sup>14</sup> much more commonly included blastomycosis as 1 of the 3 most likely diagnoses (28/61 [46%] vs 15/166 [9%] for counties with annual incidence rates < 2/100,000; P=0.001). Physicians with practice locations in the higher incidence counties listed blastomycosis more commonly as a potential diagnosis than did those from other counties (16/36 [44%] vs 27/177 [15%]; P<0.001). Physicians with >20 years in practice were associated with increased blastomycosis diagnosis on univariate analysis (26/103 [25%] vs 17/122 [14%]; P=0.05).

In multivariate analysis with blastomycosis listed in top 3 diagnoses as outcome, and clinician gender, internal medicine vs family medicine specialty, practice >20 years and practice location in higher incidence county as predictors, practice location was significantly associated with blastomycosis diagnosis (P<0.001) as was internal medicine specialty (P<0.04).

When "blastomycosis" and "fungal pneumonia" were combined, these diagnoses were listed in the top 3 suggested diagnoses for 78/227 (34%) case vignettes; associations with highincidence case and respondent county of exposure or practice, respectively, remained similar to blastomycosis alone (internal medicine specialty was no longer significant). Only 4/227 (2%) respondent vignette results listed both "blastomycosis" and "fungal disease" for the top 3 diagnoses. Responses for 97/227 vignettes (43%) listed either "blastomycosis," "fungal disease," or a specifically named fungus, eg, *Histoplasma* (proposed diagnoses that may have resulted in a blastomycosis diagnosis if a non-specific test such as fungal stain and culture were ordered in actual clinical practice).

When only vignettes 1 and 2 (which together included blastomycosis as 1 of the 3 most likely diagnoses in 28/61 [46%] of cases) are considered, blastomycosis was listed in only 1/10 (10%) instances when these vignettes were paired with each other, compared to 27/51 (53%) instances when vignette 1 or 2 was paired with any of vignettes 3 through 8 (P<0.02). When only vignettes 1 and 2 were considered, blastomycosis was listed as a top 3 diagnosis by 7/10 (70%) physicians from high incidence counties, compared to 21/48 (44%) by physicians from low incidence counties, but this difference was not significant (P = 0.17).

Table 1 includes the top 3 listed diagnoses for each scenario. Table 2 summarizes all diagnoses, by category, for all vignettes combined (total suggested diagnoses = 657; some listed fewer than 3).

#### DISCUSSION

When confronted with masked cases of diagnosed blastomycosis, Wisconsin physicians provided a very wide constellation of diagnoses. Pneumonia, cancers, noninfectious pulmonary disease, and tuberculosis accounted for 69% of diagnoses offered **Table 2.** Differential Diagnosis of Pulmonary Blastomycosis Based on the 3Diagnoses Provided by Respondent Wisconsin Primary Care Physicians forEach of the 227 Reviews of Clinical Vignettes

Disease category	Number of respondent diagnoses
Pneumonia	186
Viral etiology listed	4
Cancer	108
Noninfectious pulmonary	83
Sarcoidosis	28
Hypersensitivity/autoimmune	11
Tuberculosis/mycobacteria	78
Blastomycosis	43
Other specific fungal/fungal-like	42
Aspergillosis	15
Histoplasmosis	11
Pneumocystis	6
"Fungal disease"	39
Cardiac disease	33
Congestive heart failure	14
Complication of systemic process	19
Sepsis	12
Trauma/toxin	14
Pulmonary embolism	13
Total suggested diagnoses = 657. Diagnoses are grouped into 11 disea	ise categories.

compared to 19% with a fungal diagnosis considered and 6% with blastomycosis specifically listed. Accordingly, the primary care differential diagnosis for blastomycosis is quite broad and diverse, features that are likely to contribute to difficulty in an accurate clinical diagnosis.

The diagnosis of an uncommon infectious disease relies on high clinical suspicion, which can be enhanced through experiential or educational exposure. Low recognition of blastomycosis as seen in our study can contribute to delayed diagnosis and may result in poor outcome, similar to the delayed recognition of inhalational anthrax in 2001.<sup>15</sup>

Clinical clues and experience can contribute to higher recognition. In this study, geographic location played such a role in recognition. This was seen in that vignettes involving patients residing in or with activities in Wisconsin counties with high blastomycosis incidence were significantly more likely to have correct diagnoses than vignettes that detailed other locations. Physicians working in high incidence counties had significantly higher rates of correctly diagnosing blastomycosis than did peers from lower incidence counties. In a study of the differential diagnosis of inhalational anthrax, Lyme disease appeared in the differential of inhalational anthrax cases of upper Midwest physicians while hantavirus pulmonary syndrome was included by physicians in the 4 corners area of the southwest.<sup>13</sup>

This study was limited by the low rate of response to the survey; however, the gender and geographic distribution of responses appear to be representative of Wisconsin primary care practices, and the number of responses to clinical vignettes yielded a robust differential diagnosis. Nonetheless, the estimate of likelihood of correct diagnosis is suspect. One could surmise that clinicians more interested in pulmonary or infectious disease would be more inclined to respond, which could bias this estimate upward. In addition, specific case scenarios may have biased the differential diagnosis (ie, history of rheumatoid arthritis and sarcoidosis, respectively, in the 3rd and 4th case listed in Table 1). As evidenced by our data, respondents may have been unwilling to name blastomycosis for both case scenarios, disbelieving that both would be the same. Considering that blastomycosis is an uncommon disease with protean manifestations, it is perhaps not surprising to find it infrequently listed as a potential diagnosis in a case vignette when the physician is limited to 3 diagnoses.

Strengths include the broad geographic and demographic representation of respondents and an adequate number of responses per case that facilitates "saturation" of diagnostic possibilities. This study used a master of public health student as the corresponding investigator with the respondents since this limited any bias toward infectious agents that may have resulted if the primary authors had sent the contact letter.

Despite limitations, this study indicates that blastomycosis is frequently not included in the differential diagnosis by clinicians seeing patients with pulmonary disease. Undoubtedly, this is because of the infrequency of blastomycosis among pulmonary diseases, even in Wisconsin. Despite this rarity, blastomycosis should be considered, as it is a curable infection. In addition, if this diagnosis is not considered in a case in which steroid therapy is initiated, catastrophic complications could occur. In absolute numbers, urban-origin cases contribute significantly to the burden of blastomycosis in Wisconsin. For example, while Vilas County<sup>14</sup> has a much higher reported annual incidence rate than Milwaukee County<sup>12</sup> (approximately 38 vs 1/100,000) the much larger Milwaukee County population leads to similar numbers of cases (approximately 9) per year. Despite this, physicians in urban areas are much less likely to correctly diagnose blastomycosis.

Increased awareness of the protean manifestations and complete geographic distribution of pulmonary blastomycosis should increase the frequency with which blastomycosis is properly considered in the differential diagnosis of respiratory illness throughout Wisconsin.

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#### CASE 1

A 42-year-old male presented to urgent care in August with a 1-month history of cough, sore throat, chest congestion and some shortness of breath. A week ago he experienced a syncopal episode due to an intractable cough. Chest x-ray revealed an abnormal opacity near the right cardiac border. A week later his symptoms worsened. His cough persisted, was worse with activity and after waking up in the morning, and was associated with scant phlegm, chest discomfort, tickles in throat, low-grade fever and occasional sweats. A repeat chest x-ray showed an increase in the right lung middle lobe infiltrate. He was started on levofloxacin. Ten days later he returned to urgent care again with complaints of continuous cough, which made it difficult to breathe or laugh, a decrease in activity and appetite. He was fatigued and felt as if something was stuck in his throat. In the past few weeks, he had lost 5 to 6 pounds and had a constant dull chest pain, which was aggravated by coughing.

The patient has never been a smoker and drinks rarely. He had a history of gastroesophageal reflux disease (GERD). He went canoeing and camping in Spooner and Northern Wisconsin around mid-July for a week, and a week or two later developed this cough. He also mentioned inhaling some dust while cleaning his computer. He lives in the Fox Valley and does computer-imaging/editing, and owns a pet snake, dog, and cat.

Physical examination revealed a temperature of 99.4°F, blood pressure of 122/72, pulse 100, respiratory rate 20. Lungs revealed decreased breath sounds in the right axillary area and lower right posterior chest. Bronchophony was detected on the right posterior chest at the bases and in the axillary area on the right.

#### CASE 2

A 31-year-old male presented in May with an 11-week history of worsening cough, left-sided rib and back discomfort. Six weeks into his illness he was seen in the emergency department for left mid-back pain radiating to left axilla, shortness of breath and nonproductive cough. He denied any fevers or chills. A chest x-ray taken at that time revealed a left middle lobe infiltrate. He was given hydrocodone/ acetaminophen, oral azithromycin and IM ceftriaxone. A month later his cough was now mostly nonproductive, except in the mornings it appeared brownish. He recently lost approximately 15 pounds of weight, and stated that he normally loses weight in spring when he starts working full-time as a painter. Several weeks prior to becoming ill he was exposed to "pipes with molds" at work. He had a lump on his left cheek and occasionally experienced wheezing and shortness of breath. He denied any nausea, vomiting, diarrhea, chills, fever, skin lesions, and rashes but had night sweats. He is single and lives with his parents in a small settlement near a river in Manitowoc County. He enjoys fishing and hunting. He had not traveled outside the country but went to Northern Wisconsin in January for bow hunting. Patient admitted to smoking 1 pack per day and drinking alcohol.

Physical examination revealed a temperature of 98.6°F, blood pressure of 104/68, heart rate of 81, pulse oximetry 98% on room air. Lungs had coarse rhonchi noted posteriorly throughout and bronchial vascular sounds were heard over the left mid-zone.

Chest x-ray now revealed consolidation of the superior segment of the lower lobe of the left lung.

#### CASE 3

A 54-year-old morbidly obese woman presented to the emergency department in July with a 3-week history of nonproductive cough, night sweats, shortness of breath, and fatigue. She had a fever which resolved in the first 2 weeks but in the past 4 to 5 days she had increased shortness of breath along with marked swelling in her lower extremities and pain in her knees. She experienced nausea and vomiting with eating. She had a rash on her body, mainly on the torso.

The patient had a history of rheumatoid arthritis (RA) and had undergone cholecystectomy, appendectomy and fibroid surgery in the past. She had been taking prednisone and methotrexate for her RA and was allergic to penicillin. She had a greater than 10 packs per year smoking history but had quit smoking. She denied any alcohol and drug use. She lived in a house in a subdivision in Racine.

Physical examination revealed a temperature of 101°F, blood pressure 125/59, pulse of 110-120, and respirations of 20-30. She was profoundly hypoxic, saturation range 60%. Bilaterally diffuse rhonchi and tubular breath sounds were detected. There were erythematous pustules and lesions on her face, forehead, legs, and nares, and an indurated abscess on her back. She had 2+ pitting edema in her lower extremities.

Laboratory data included WBC count of 20,000 (absolute neutrophils 19,000), sedimentation rate 48, hemoglobin 11.0, platelets 537,000, sodium 138, potassium 5.4, CO2 24, BUN 25 and creatinine 0.8. Liver function test revealed elevated alkaline phosphatase level of 224, AST 220, ALT 66, myoglobin 102, C-reactive protein 1.6, and lactic acid levels of 5.6. Chest x-ray revealed bilateral fluffy infiltrates, right greater than left. Large bacteria were found in the urine.

Additional case vignettes are available online at www.wmj online.org/\_WMS/publications/wmj/pdf/110/2/68vignettes.pdf.

# An Analysis of Lobbying Activity on Tobacco Issues in the Wisconsin Legislature

David Ahrens, MS; Nathan Jones, PhD; Kyle Pfister, BS; Patrick L. Remington, MD, MPH

#### ABSTRACT

**Background:** Although public and media attention has focused on the federal role in the regulation of tobacco products, state government remains an important arena for changing tobacco control policies. Lobbying state officials by public health and the tobacco industry is a commonly used mechanism to influence public policy.

**Methods:** Major bills of the 2007-2008 and 2009-2010 Wisconsin legislative sessions related to tobacco use regulation were analyzed by the hours engaged in lobbying and the estimated expenditures by supporters and opponents of tobacco control legislation in reports submitted to the Government Accountability Board.

**Results:** In the 2007-2008 legislative session, anti-tobacco control organizations reported lobbying expenditures of more than \$2 million (2627 hours) while opposing bills to raise tobacco excise taxes and enact smoke-free legislation; pro-tobacco control organizations reported lobbying expenditures of \$623,000 (3997 hours) while supporting these bills. In the first 6 months of the 2009 session, anti-tobacco control groups spent \$1.25 million (1472 hours) and pro-tobacco control groups spent \$172,000 (1727 hours).

**Conclusion:** In the 2007-2008 legislative session, the proposal to increase the tobacco tax by \$1 per pack was passed. However, the smoke-free indoor air bill was defeated. Anti-tobacco control organizations outspent pro-tobacco control organizations by a margin of over 3:1. In 2009 anti-tobacco control groups outspent health groups by a ratio of 7:1. Legislation for smoke-free workplaces and an increase in the cigarette tax was enacted. However, fund-ing for tobacco prevention and treatment programs was substantially reduced.

#### BACKGROUND

Thousands of bills are introduced and debated in the legislature each year, but few garner as much attention year after year as tobacco-related policies. Because of the interest in the Food and Drug Administration's (FDA) regulation of tobacco and other federal actions, the role of state government in tobacco

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use is often overlooked. The state has an important role in establishing the price of tobacco products through its ability to tax, regulating access to tobacco products and establishing rules about smoking in public places.

These changes in regulation are also political issues because they must be approved by Wisconsin's legislature and governor. One of the key indicators of tobacco's importance as a political issue is the amount of money spent lobbying the legislature.<sup>1</sup> The process of lobbying plays a critical role in the introduction, formation, and potential for passage of legislation. For this reason, Wisconsin and national organizations spent more than \$58 million in the 2005-2006 legislative session for lobbying services.

For decades at the state and national level, the tobacco industry had one of the largest and most effective lobbying forces.<sup>2</sup> The industry is credited with preventing the effective regulation

of tobacco products, as well as their taxation, in the period between the first Surgeon General's Report on smoking (1964) and the Master Settlement Agreement (1998).<sup>3</sup> During the past decade, however, public health organizations have developed and fielded relatively large lobbying operations to influence tobacco control policymaking and contest the power of the tobacco industry.

#### PURPOSE

The purpose of this report is to describe the lobbying expenditures of anti-tobacco control organizations (including the tobacco industry and other tobacco-related industries and organizations) and pro-tobacco control organizations (including voluntary and health care organizations) with declared interests in: (1) the budget proposal to increase the tobacco excise tax; and (2) legislation to require all workplaces to be smoke-free in the 2007-2008 and 2009 Wisconsin legislative sessions.

#### METHODS

Registered lobbyists are required by law to submit semi-annual reports on their activities and expenditures.<sup>4</sup> Lobbying reports submitted to the Wisconsin Government Accountability Board (GAB) for the 2007-2008 legislative and the January through June 2009 floor period of the 2009-2010 session were collected and analyzed for activities related to tobacco. Review of the data on expenditure and hours of effort indicated that 2 issues were far more extensively lobbied than all others: increasing the tobacco excise tax and legislation requiring smoke-free workplaces.

The GAB website (http://ethics.state. wi.us/) lists registered lobbyists who declare an interest in specific legislation. The lobbying reports of organizations identifying Senate Bill (SB) 150 and Assembly Bill (AB) 834 (prohibiting smoking in places of employment) for the 2007-2008 session and the budget bill and Senate Bill (SB) 181 and Assembly Bill (AB) 253 (prohibiting smoking in places of employment) for the 2009-2010 session as items of interest were analyzed.5 Lobbying reports detail the effort of the registrant on each bill as a percentage of their overall effort. Overall effort is represented by the total expenditure and hours expended.

Reports of anti-tobacco control and

pro-tobacco control organizations were reviewed to determine the overall effort and the percentage of effort related to increasing the tobacco excise tax. Reports that indicated a small or minimal level of activity (<\$10,000) were grouped together in a single category of "others."<sup>6</sup> While the amount of funds spent on lobbying or the number of hours of effort often is not the most important factor in the passage of legislation, the substantial growth of lobbying activity indicates its important political effect.

#### RESULTS 2007 - 2008 Session

Anti-tobacco control organizations expended over 3 times more than pro-tobacco control organizations on lobbying on



Figure 1. Lobbying expenditures on tobacco issues: Wisconsin 2007-2008. Source: Reports of Government Acct. Board, 2007-2008, Wisconsin Government Accountability Board.



**Figure 2.** Hours of lobbying on tobacco issues: Wisconsin 2007-2008. Source: Reports of Government Acct. Board, 2007-2008, Wisconsin Government Accountability Board.

the 2 primary tobacco-related legislative proposals. Proponents of low tobacco taxes and opponents of SB 150 (the "smoke-free" bill) spent \$2,070,817 in the session. In contrast, supporters of higher tobacco taxes and the smoke-free workplace legislation spent a total of \$623,671 (Figure 1).

Two tobacco corporations, Philip Morris and Reynolds American, spent \$1,426,000 or 69% of all anti-tobacco control funds. The expenditure of each of these companies exceeded the funds spent by all pro-tobacco control groups combined. The focus of their lobbying was opposition to the governor's proposed \$1 per pack increase in the cigarette tax and proportionate increases in other tobacco products. Swisher, a low-cost cigar manufacturer; UST, a maker of smokeless tobacco; and







the Cigar Association also focused their activities on opposing the tobacco tax and spent a combined total of \$318,000.

The pro-tobacco control organization expenditure of \$623,671 was fairly evenly divided between support of the tobacco tax and the smoke-free workplace legislation. SmokeFree Wisconsin devoted more of its resources in support of the smoke-free workplace legislation, while the American Cancer Society and the American Lung Association focused on increasing taxes on tobacco products.

The primary opponent of smoke-free workplaces was

the Tavern League of Wisconsin, which reported expenditures of nearly \$195,000 in opposition to the proposed legislation.

The lobbying hours expended by the 2 groups of organizations show the opposite relationship to their fiscal expenditures. Pro-tobacco control organizations expended 3997 hours in the legislative session while the anti-tobacco control organizations expended 2627 hours. (Hours expended by both groups only describes the hours of effort by registered lobbyists. It does not include the greater efforts of advocate-volunteers such as tavern owners and physicians.) (See Figure 2.)

While most of the public health organizations lobbied for both higher taxes and smoke-free public places, tobacco organizations focused one proposal or the other. For example, Philip Morris lobbied on taxes, while the Tavern League focused on opposition to smoke-free workplaces. The tobacco industry's efforts cost an average of \$788 per hour, while the cost per hour for the public health organizations was \$156.

#### 2009 - 2010 Session

Expenditures for the January through June 2009 floor period focused on the biennial budget. The budget was important to anti-tobacco control and health groups because Wisconsin Governor Jim Doyle included an increase of 75 cents in the cigarette excise tax (along with related taxes on other tobacco products) and the smoke-free workplace legislation.

Tobacco companies (Altria/Philip Morris and Reynolds American) spent \$985,366 in the first 6 months. These 2 companies were the 2nd and 6th highest spenders for lobbying services during the period. Tobacco retailers and distributors spent an additional \$142,551. The Tavern League and other opponents to the smoke-free legislation spent less than \$100,000 for lobbying expenses (Figure 3).

Pro-tobacco control groups, who spent just over \$172,000, were outspent by tobacco groups 7:1. The American Cancer Society had the highest lobbying expenditure with \$68,000. Similar to the 2007-2008 period, pro-tobacco control groups reported many more lobbying hours than the anti-tobacco control groups (1727 hours vs 1472, respectively). Health organizations spent an average of \$100 per hour for lobbying while the tobacco organizations spent an average of \$848 per hour (Figure 4).

#### DISCUSSION

More than \$2.5 billion worth of tobacco products were sold in Wisconsin in 2008. More than half of those dollars went to tobacco manufacturers while the remainder was received by state and local government and retail and wholesale distributors.<sup>7</sup> Because sharp increases in tobacco taxes are related to reduction in tobacco product sales,<sup>8</sup> the tobacco industry spent relatively large amounts of money on lobbying fees to eliminate or reduce the tax increases. However, the efforts of anti-tobacco control organizations to lower or eliminate the governor's proposal to increase cigarette taxes by \$1 per pack in January 2008 and a 75-cent increase in September 2009 were unsuccessful.

The legislation to prohibit smoking in workplaces was introduced in both legislative houses and passed in Senate and Assembly committees in 2008. However, the bill was not voted on by either house. While it is arguable how much of the decision to withhold the legislation was due to the lobbying of anti-tobacco control organizations, it is likely that these efforts affected the behavior of some Senate members. In the following session, the proposal for smoke-free workplaces was passed in May 2009 and took effect in July, 2010.

Lobbying expenditures, including hours spent lobbying for legislation, is only 1 measure of legislative activity and impact. The ability of an organization to mobilize its members, sway public opinion, and gain media attention are also critical factors in influencing legislators. One cannot say with certainty which part of a legislative effort was most important in achieving a legislative victory. However, it appears that given the sharp increases in lobbying expenditures, organizations that are experienced in public policy understand its value to the overall process.

While the legislature enacted significant tobacco control policies, it also reduced funding for tobacco control by 55%—from \$15 million per year to \$6.85 million per year. This is despite a 135% increase in tobacco revenues the past 3 years, from \$318 million per year to \$741 million per year. Other states have found that the loss of effective tobacco control programs leads to future increases in tobacco use.<sup>9</sup>

#### CONCLUSION

Nearly a half century after the first surgeon general's report, efforts to reduce tobacco's health and economic costs remain controversial. Despite a strong scientific consensus on the negative health effects of secondhand smoke, political and economic forces often are paramount when public policy is made. Although the tobacco companies have suffered setbacks in the last decade, they continue to employ significant financial resources to oppose policies that reduce the affordability, access, or use of their products. This report highlights the tobacco industry's willingness and ability to outspend pro-tobacco control organizations in lobbying for its agenda. However, the data also indicate that despite significant industry expenditures, pro-tobacco control organizations are able to expend more hours of effort and succeed in achieving much of their agenda.

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# The Management of *Ixodes scapularis* Bites in the Upper Midwest

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#### ABSTRACT

*Ixodes scapularis*, commonly referred to as the deer tick, is the vector of Lyme disease and anaplasmosis; both illnesses are endemic to the upper Midwest. Avoidance of *I scapularis* bites is the primary preventative strategy for both infections. Antibiotic prophylaxis has been demonstrated to prevent Lyme disease, but similar studies have not investigated antibiotic prophylaxis for the prevention of anaplasmosis. Thus, recommendations regarding the management of *I scapularis* bites are focused on the prevention of Lyme disease.

This paper reviews the prevailing antibiotic prophylaxis recommendation for Lyme disease and the evidence supporting it. Given the additional risk of acquiring anaplasmosis from an *I scapularis* bite in the upper Midwest, this paper proposes an alternative regimen for antibiotic prophylaxis in this region.

#### INTRODUCTION

Lyme disease, the most common vector-borne illness in the northern hemisphere, is endemic to much of Wisconsin and Minnesota.<sup>1</sup> In these areas, more than 20% of the *Ixodes scapularis* populations harbor *Borrelia burgdorferi*, and in many regions *I scapularis* has expanded its range.<sup>2,3</sup> Primary and secondary prevention of Lyme disease assumed greater importance following the withdrawal of the only commercially available vaccine in 2002. *I scapularis* also transmits *Anaplasma phagocytophilum*, the bacterial agent of human granulocytic anaplasmosis (HGA), and species of *Babesia*, red blood cell parasites similar to malaria.<sup>2-6</sup> The presenting symptoms and signs of HGA are generally nonspecific and include fever, headache, myalgia, cough, nausea, and abdominal pain; disease severity can range from an asymptomatic infection to death.<sup>5,6</sup> Diagnosis is usu-

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ally based on positive polymerase chain reaction (PCR) or serologic results. PCR is most sensitive, 67% to 90%, in the first week of illness;<sup>6</sup> serologic testing looks for a 4-fold rise in IgM or IgG antibody titers between acute and convalescent specimens.<sup>6</sup> HGA is usually treated with 10 days of doxycycline.<sup>5,6</sup> The acute symptoms of babesiosis include fever, chills, sweats, myalgia, arthralgia, anorexia, nausea, and vomiting. The diagnosis is based on positive blood smears, serology, or PCR. Treatment is with either a combination of quinine and clindamycin or

atovaquone and azithromycin.<sup>5</sup> Both HGA and babesiosis are endemic to the upper Midwest, and vaccines to prevent either illness are lacking.<sup>5,6</sup> The upper Midwest is also seeing increased cases of human monocytic ehrlichiosis (HME), caused by *Ehrlichia chaffeensis*, and a new Ehrlichia muris-like agent (EML) was recently discovered in Wisconsin and Minnesota.<sup>6,7</sup> HME is transmitted by *Amblyomma americanum* (Lone Star tick);<sup>5,6</sup> the vector for EML is unknown.<sup>7</sup>

Central to the primary prevention of Lyme disease, HGA, and babesiosis is the avoidance of *I scapularis* bites. The risk of these infections may be reduced by avoiding known tick habitat, wearing appropriate clothing (long-sleeved shirts and pants), the judicious use of insecticides (permethrin) and repellents (DEET), and performing body-wide tick checks to find and promptly remove ticks after spending time in tick environs.<sup>5</sup>

When those measures fail and an attached tick is found, antimicrobial prophylaxis assumes a greater role in disease prevention. Recommendations regarding antibiotic prophylaxis for Lyme disease have been formulated;<sup>8</sup> similar recommendations for the prevention of anaplasmosis or babesiosis have not been made. The purpose of this paper is to review the prevailing recommendation for Lyme disease antibiotic prophylaxis following an *I scapularis* bite and the evidence supporting it. This paper will also discuss an alternative prophylaxis strategy that addresses the risk of acquiring *A phagocytophilum* from an *I scapularis* bite in the upper Midwest.

#### **IDSA Recommendation for Lyme Disease Prophylaxis**

The Infectious Diseases Society of America's (IDSA) guidelines on Lyme disease contain recommendations regarding the management of *I scapularis* bites.<sup>5</sup> To prevent the development of Lyme disease following a bite, while avoiding the costs and adverse events associated with prophylactic antibiotics, the 2006 IDSA guidelines recommend a single 200-mg dose of oral doxycycline to prevent Lyme disease. This dose should be given only to patients who meet these, and other, criteria:<sup>5</sup> (1) the involved tick was identified as an adult or nymphal *I scapularis* by a reliable source, and the tick attachment time, based on observed engorgement or known time of bite, was greater than 36 hours; and (2) the bite occurred in an area where greater than 20% of the ticks are infected.

The above criteria were drawn from what was known about disease transmission. The risk of acquiring Lyme disease from any given bite is related to the duration of tick attachment and the *B* burgdorferi infection rate among ticks in the area where the bite occurred. Studies in animal models demonstrate that the risk of disease transmission increases with increasing durations of tick attachment times.9 In general, attachment times under 24 hours have little chance of transmitting *B burgdorferi*; at 60 hours, 50% of infected nymphs will transmit B burgdorferi. Feeding to repletion (96 hours or more) results in 94% transmission rates.9 Lyme-endemic areas of the upper Midwest and Northeast are thought to have tick infection rates consistently higher than 20%, and many areas report infection rates above 40%.<sup>2,3,5</sup> Thus, if a nymphal tick is allowed to feed for 60 hours in an area where the local tick infection rate is 30%, that particular bite has a 15% chance of transmitting B burgdorferi to a human host. Ticks transmit A phagocytophilum in a matter of hours.6

The prophylaxis regimen recommended in the 2006 IDSA guidelines is drawn from a study by Nadelman et al.<sup>5</sup> This randomized, placebo-controlled trial reported that administering a single 200-mg dose of oral doxycycline within 72 hours of an *I scapularis* bite prevented the development of Lyme disease with a treatment efficacy of 87%.<sup>8</sup>

The risk of adverse effects related to antibiotic prophylaxis was also a factor in the recommendation, presumably favoring the single oral dose doxycycline approach. The guidelines cited 2 earlier prophylaxis trials, noting the placebo groups' risk of developing Lyme disease was roughly equal to the risk of an antibiotic-associated rash in the treatment groups.<sup>5</sup>

There are several problems with the IDSA recommendation. The application of the required criteria to primary care practices in Wisconsin and Minnesota may be problematic. Medical professionals are encouraged to acquire the ability to identify ticks and assess engorgement, but physicians lack opportunities to do so. The assessment criteria are based on a study that employed a medical entomologist;<sup>8</sup> community physicians are not likely to have, or develop, this level of expertise. External validity is the ability of the cause-and-effects relationships in an experimental study to be generalized to a clinic setting. External validity is "poor" if the study situation differs from the typical clinical situation in ways likely to affect outcomes,<sup>10</sup> as is the case here. Furthermore, bites from ticks damaged or discarded following identification by non-medical personnel would not receive prophylaxis, yet withholding treatment solely on those grounds exposes patients to the risk of infection. In addition, physicians would need to know the current infection rates for various tick populations, but this data is often unavailable and tick infection rates in the same general locale vary significantly from year to year,<sup>11</sup> potentially leading to inaccurate risk assessments.

The antibiotic regimen recommended by the IDSA is based on the single-dose doxycycline trial, but that trial cannot inform physicians regarding Lyme disease prevention. Lyme disease is a multi-systemic illness having both early and late manifestations;<sup>12-16</sup> patients may be asymptomatic early in the infection only to develop symptoms of late disease after a latent period lasting months to years.<sup>17-19</sup> The single-dose doxycycline trial employed a 6-week follow-up period,<sup>8</sup> too short a timeframe to allow for the development of late Lyme disease. Thus, the ability of a single 200-mg dose of oral doxycycline to prevent Lyme disease following a tick bite was not demonstrated.

Nor did the study investigate the effectiveness of single-dose oral doxycycline on the prevention of early Lyme disease. Data from the Centers for Disease Control and Prevention indicates that 30% of all Lyme disease patients fail to exhibit an erythema migrans rash in the course of their illness, yet the trial's primary endpoint was strictly limited to the development of an erythema migrans rash at the bite site.<sup>8,20</sup> Three study subjects (1 in the doxycycline group and 2 in the placebo group) had clinical and laboratory evidence consistent with early Lyme disease, but because they lacked an erythema migrans, they were not considered "disease positives" when treatment efficacy was calculated.<sup>8</sup>

The trial's short observation period and narrow disease definition limit the scope of its findings. A single 200-mg dose of oral doxycycline successfully prevented the development of erythema migrans at the bite site, but its ability to prevent all stages of Lyme disease remains unknown.

While the risks of adverse events associated with antibiotic prophylaxis need to be considered, they should not be given undue weight. The risks for developing Lyme disease and an antibiotic-induced rash may be equal but the conditions themselves are not; a simple drug eruption and Lyme disease differ significantly in their potential to harm patients. There is substantial evidence detailing both the outstanding clinical safety of doxycycline, amoxicillin, and cefuroxime (other potential prophylactic agents) and the consequences of late Lyme disease, which can be quite severe and irreversible.<sup>21-26</sup> It is concerning that the guidelines' developers based their prophylaxis recommendation on the single-dose doxycycline study, knowing it was unable to assess the risks of treatment failure.<sup>5</sup>

Single-dose doxycycline carries a risk that was not discussed in the original trial or the IDSA guidelines:<sup>5,8</sup> namely, the risk of developing seronegative Lyme disease. One subject in the doxycycline arm of the trial developed an erythema migrans but remained seronegative by enzyme-linked immunosorbent assay (ELISA) testing. First described by Dattwyler et al and confirmed by others,<sup>27-30</sup> seronegative Lyme disease may be induced by administering insufficient antibiotics early in the course of the infection, thereby altering the immune response and diminishing antibody production such that these patients, though ill, have negative results on serologic testing. This is an important consideration because seronegative patients who remain ill will likely experience treatment delays, which have been associated with poorer outcomes.<sup>31,32</sup>

The IDSA recommendation on antibiotic prophylaxis does not address the realities of the upper Midwest, namely, the possibility that an *I scapularis* bite might transmit *A phagocytophilum* or simultaneously transmit *B burgdorferi* and *A phagocytophilum*.<sup>2,3,33</sup> In a dual-exposure model, single-dose oral doxycycline was only 20% and 30% effective in preventing infection by *B burgdorferi* and *A phagocytophilum*, respectively;<sup>34</sup> its effect on serologic testing for HGA is unknown.

In summary, the IDSA recommendation for antibiotic prophylaxis of *I scapularis* bites using single-dose doxycycline may not be appropriate for use in the upper Midwest because: (1) it mandates clinical criteria that may be difficult to meet; (2) it is based on a poorly designed trial that was unable to demonstrate treatment effectiveness for Lyme disease prevention but did document the development of seronegative Lyme disease when treatment failed; (3) it assessed risk by comparing the number of adverse events from antibiotics to the number of treatment failures instead of discussing the relative significance each risk poses for a patient's health; and (4) the effects and effectiveness of this strategy on the diagnosis and treatment of patients with anaplasmosis alone is unknown, while the ineffectiveness of this approach for dual-exposure has been demonstrated in animal models.

### An Alternative Recommendation for the Management of *Ixodes Scapularis* Bites

Given that the rate of *B burgdorferi*-infected ticks in the upper Midwest is high,<sup>2,3</sup> that physicians may be unable to determine attachment times based on tick engorgement, and that the optimum regimens for the prophylaxis of Lyme disease and anaplasmosis are unknown, physicians may offer doxycycline 100-mg twice daily for 10 to 20 days to patients with *I scapularis* bites. The evidence supporting this recommendation is limited, and the duration of treatment is deductive. The absence of prophylaxis trials for anaplasmosis and the limited understanding of the mechanisms underlying Lyme disease latency and persistence introduce significant uncertainties. Three prospective trials on Lyme disease prophylaxis, using 10 days of antibiotic therapy, were unable to demonstrate treatment efficacy.<sup>35-37</sup> Thus, the shorter end of the duration range simply represents an accepted duration of treatment for HGA and the minimum treatment duration for early Lyme disease.<sup>5,6</sup>

Justification for 20 days of treatment comes from animal studies of prophylaxis. A sustained-release, injectable form of doxycycline, with measurable plasma levels for 19 days, was 100% effective for preventing Lyme disease alone. In a dual-exposure model, this regimen was also 100% effective for preventing *B burgdorferi* and *A phagocytophilum* infections.<sup>34,38</sup>

Doxycycline is the preferred antibiotic in appropriate patient populations because amoxicillin and cefuroxime are not effective for HGA.6 However, given their effectiveness in early Lyme disease and contraindications for the use of doxycycline in children and pregnant women, amoxicillin and cefuroxime may be appropriate alternatives in some circumstances. However, patients would require continued observation to detect a potential A phagocytophilum infection.29,39,40 Recommending 10 to 20 days of antibiotics for an I scapularis bite creates an increased risk for adverse events, especially for those patients who have multiple bites in a single season;8 the increased risk may make this approach appear excessive to some. Taking doxycycline with food and administering probiotics should reduce or eliminate many of the minor adverse effects (nausea, vomiting, abdominal pain, and diarrhea) encountered in the singledose doxycycline trial.41

#### CONCLUSION

Lyme disease and anaplasmosis are significant and endemic illnesses in the upper Midwest. Antibiotic prophylaxis is an appropriate response to *I scapularis* bites in this region.<sup>2-6</sup> The differences between the alternative and IDSA recommendations for the management of tick bites reflect the uncertainty of clinical practice when the evidence is scant or absent and the limited usefulness of generalized guidelines in specific clinical situations.<sup>42</sup> While some physicians may prefer to follow the IDSA recommendation on prophylaxis, others may accept the increased risk of adverse events to gain improved efficacy and, therefore, will wish to follow the alternative recommendation. In keeping with the American Medical Association principles of informed consent and patient autonomy,<sup>43,44</sup> physicians should fully explain each prophylaxis strategy and consider the patient's goals and values before making their selection. **Acknowledgments:** The author would like to thank Bea Szantyr, MD, and Ralph Magnusson, MD, for their assistance.

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# Rhabdomyolysis-induced Acute Kidney Injury Secondary to *Anaplasma phagocytophilum* and Concomitant Statin Use

Stephen R. Talsness, BA; Sanjay K. Shukla, PhD; Joseph J. Mazza, MD; Steven H. Yale, MD

#### ABSTRACT

We report the case of a patient with rhabdomyolysis-induced acute renal failure occurring in the setting of *Anaplasma phagocytophilum* infection based on the presence of morulae in neutrophils and concomitant statin use. Although the pathogenesis is unknown, we believe the combination of concurrent statin use in the setting of the infection promoted this complication. We describe proposed mechanisms including cytokine activation, alteration of the muscle membrane components, and ionic balance as contributing factors.

#### INTRODUCTION

*Anaplasma phagocytophilum* is a tick-borne pathogen that is endemic in the midwestern and eastern United States, although it has been reported in other parts of the world. This obligate intracellular pathogen shows leukocyte-specific tropism, infects granulocytes, and commonly causes human granulocytic anaplasmosis (HGA).<sup>1</sup> Symptoms of HGA include undifferentiated febrile illnesses, rigors, myalgias, and generalized malaise accompanied by leukopenia and thrombocytopenia. Rhabdomyolysis, a disease affecting the integrity of the skeletal muscle, is a rare complication of infection with *A phagocytophilum*.<sup>2.4</sup> Herein, we report a case of rhabdomyolysis in an elderly man living in a tick-endemic area.

#### **CASE REPORT**

An 84-year-old man from northern Wisconsin presented with symptoms including confusion, weakness, and diarrhea. Two days earlier he was admitted to a non-affiliated health care

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facility after his wife found him on the floor exhibiting weakness, confusion, and urinary incontinence. On initial evaluation his temperature was 39.4°C. Initial blood cultures, urine culture, and chest x-ray were all negative. Tests for influenza A and B were negative. A lumbar puncture was attempted twice, unsuccessfully. He was initially treated with ceftriaxone,

based on a presumptive diagnosis of meningitis, but because of persistent fever, his antibiotics were changed to imipenem and vancomycin. Overnight, the patient developed diarrhea and pancytopenia. He was subsequently transferred to our hospital.

Upon arrival and further interview, his wife recalled removing a tick from the patient's right groin approximately 5 days prior to presentation. The duration of the tick attachment was unknown. The patient denied any vision change, headache, neck stiffness, photophobia, nausea, vomiting, or trauma. On initial evaluation, his temperature was 38.4°C, pulse rate was 71 bpm, and blood pressure 161/70 mm/Hg. Examination was significant for memory loss for recent events, round erythematous 1.5-cm rash in the right groin, and the absence of hepatosplenomegaly. He continued to be febrile with wheezing, confusion, and complaints of generalized weakness. Medications on admission included simvastatin 40 mg daily, hydrochlorathiazide 25 mg daily, valsartan 320 mg daily, aspirin 81 mg daily, and warfarin 5 mg daily.

Laboratory estudies revealed the following: white blood cell count, 3.6 x 10<sup>3</sup>/uL with neutrophil cytoplasmic inclusions morphologically consistent with *Anaplasma* morulae; platelet count 57 x 10<sup>3</sup>/uL; estimated glomerular filtration rate 42 mL/ min; troponin I 0.5 ng/mL; blood urea nitrogen (BUN) 34 mg/ dL; creatinine 1.6 mg/dL; aspartate aminotransferase 220 U/L; alanine aminotransferase 43 U/L; uric acid 6.5 mg/dL, ionized calcium 4.6 mg/dL, phosphorous 3.2 mg/dL; creatine kinase 9299 U/L; and urinalysis with 1+ protein, 3+ blood (without red blood cells present), 1+ leukocytes. Blood, urine, and stool cultures showed no bacterial growth. Renal ultrasound was normal. Anaplasma antibody <1:64, *Babesia Ab* <1:16, and Lyme serology were nonreactive. He was treated initially with doxycycline 100 mg intravenous twice daily and intravenous hydration with sodium bicarbonate for rhabdomyolysis. Over the course of the hospitalization, the patient's renal function and mental status improved and he was discharged to a nursing home.

#### DISCUSSION

Rhabdomyolysis is a disease characterized by the breakdown of skeletal muscle and the release of electrolytes, myoglobin, and other muscle proteins into the systemic circulation. Acute renal failure is a serious complication that develops in as many as 33% of patients with rhabdomyolysis.<sup>5</sup> Free myoglobin is filtered in the kidney, damaging the nephron as a consequence of renal tubule obstruction and oxidative injury.5,6 The risk of acute kidney injury in rhabdomyolysis is low, with creatine kinase levels less than 15,000 to 20,000 U/L, but may occur with levels as low as 5000 U/L, especially in the presence of other contributing factors such as sepsis, intravascular volume depletion, acidosis, and renal vasoconstriction.6 Intravascular volume depletion causes intrarenal vasoconstriction due to activation of the renin-angiotensin, vasopressin, and sympathetic nerves.6 Other mediators that reduce vascular tone and renal homeostasis include endothelin-1, thromboxane A2, tumor necrosis factor  $\alpha$ , and F<sub>2</sub>-isoprostanes;<sup>7,8</sup> nitric oxides are released in response to myoglobin induced oxidative stress.6

The etiology of rhabdomyolysis secondary to A phagocytophilum infection is still unknown. Proposed mechanisms of rhabdomyolysis caused by other infections include tissue hypoxia, reduced or activated enzymatic responses, and endotoxic effects.5 Direct invasion of skeletal muscle resulting in rhabdomyolysis has been identified in certain bacterial infections including Streptococci, Salmonella, and Staphylococcus aureus.<sup>9,10</sup> This mechanism, however, is not likely in a case of A phagocytophilum, since in vitro investigation of A phagocytophilum-infected neutrophils showed reduced adhesion to endothelial cells.7 Additionally, while Legionella spp is associated with rhabdomyolysis, it is not found in muscle biopsies, suggesting an alternative cytochemical pathway.11 Cytokines, including tumor necrosis factor-alpha (TNF-a) and interleukin-1 (IL-1), have been implicated in causing rhabdomyolysis-associated skeletal muscle damage.<sup>12</sup> Though a clear association is lacking, elevation of cytokines involved in the innate immune response and macrophage activation, including gamma interferon (IFN-y), IL-12, and IL-10 have been described in A phagocytophilum infection.13

Statin-associated myopathy also may have played a role in this patient's development of rhabdomyolysis. The mechanisms through which infectious agents contribute to, or exacerbate, statin-induced myositis are not fully understood. Statins are believed to induce myocyte injury through the disruption of membrane components and ionic balance.<sup>11</sup> Additionally, incidence of statin-induced rhabdomyolysis associated with other infectious agents including *Enterococcus faecalis* has been reported.<sup>14,15</sup> In a reported case of myositis with creatine kinase (CK) elevation, both statin use and HGA infection were identified as potential contributing factors.<sup>16</sup>

*A phagocytophilum*, the suspected agent in this case, is transferred by vector host of *Ixodes scapularis* in Wisconsin.<sup>17,18</sup> This tick also serves as the zoonotic vector for *Borrelia burgdorferi* (the cause of Lyme borreliosis) and *Babesia microti* (the cause of babesiosis).<sup>17-19</sup> Genetic variants of *A phagocytophilum* have been reported among isolates collected in Rhode Island, Connecticut, and Washington.<sup>8,20</sup> It has been postulated that disparity in disease incidence, severity, seroprevalence, and manifestation could be due to genetic differences in *A phagocytophilum* strains.<sup>20</sup>

Transmission of the pathogen usually occurs after a minimum of 24 hours of tick attachment and an incubation period 7 to 10 days.<sup>16,21</sup> Though most infections are related to tick exposure, additional transmission modalities may exist including mother to child transplacental transmission and exposure to infected deer blood.<sup>17</sup> Between 1994 and 2005 over 2900 cases of HGA have been reported to the Centers for Disease Control and Prevention (CDC)<sup>22</sup> with a reported incidence of 8.79 per million in Wisconsin.<sup>23</sup> However, more recent active surveillance has shown an incidence of more than 500 per million. Additionally, seroprevalence studies suggest that asymptomatic infection is common, and the principal risk factor for contracting HGA is the length of residence in endemic areas.<sup>17,22</sup>

A presumptive diagnosis of HGA may be made by the presence of unexplained fever, nonspecific symptoms (eg, headache and generalized myalgias), and laboratory values showing leukopenia and thrombocytopenia in resident(s) in an area endemic for the vector.<sup>17</sup> In addition, the observation of granulocytic morulae by experienced pathologists adds weight to the diagnosis. In this particular case, presence of morulae in the granulocytes of blood samples from the patient living in an endemic area was quite relevant. Laboratory diagnosis should not delay treatment, given the rapid progression of this potentially fatal infection.24 Differentiation between probable and confirmed HGA may be based on case definitions established by Walker et al<sup>25</sup> that include a combination of clinical symptomology and laboratory tests including polymerase chain reaction, blood culture, and demonstration of antibody titers specific for HGA in serum. However, the sensitivity of the various laboratory tests varies with phase of the illness.<sup>24</sup> In our case, the serologic testing was negative for HGA. The false negative result may be attributable to testing during the first week of illness when sensitivity for this test is at its lowest. Ultimately, the laboratory diagnosis was made based on the presence of infected neutrophils (morulae) identified during differential evaluation of the peripheral blood smear. Laboratory diagnosis based upon blood smear interpretation has a reported sensitivity of 25% to 75%.<sup>24</sup> Confirmed presence of infected neutrophils defined this case as consistent with probable HGA.

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# Quiz: The Management of *Ixodes scapularis* Bites in the Upper Midwest

#### **EDUCATIONAL OBJECTIVES**

- 1. To understand the range of diseases transmitted by the *Ixodes scapularis* (deer tick).
- 2. To understand the Infectious Diseases Society of America's current guidelines for the prevention of Lyme Disease and some of the limitations of these recommendations.
- 3. To understand an alternative treatment for *Ixodes scapularis* (deer tick) bites in the upper Midwest as proposed by the author.

#### PUBLICATION DATE: April 1, 2011

#### **EXPIRATION DATE:** April 1, 2012

#### **QUESTIONS**

- 1. The following diseases may be transmitted by the *Ixodes scapularis* (deer tick):
  - A. Lyme disease
  - B. Human monocytic ehrlichiosis (HME)
  - C. Human granulocytic anaplasmosis (HGA)
  - D. Babesiosis

#### Answer:

- □ A and B
- $\Box$  A and C
- A and D
- $\Box$  A, C, and D
- □ All of the above
- 2. The Infectious Diseases Society of America's (IDSA) current guidelines for the prevention of Lyme disease following a tick bite include the following:
  - A. The involved tick should be an adult or nymphal *Ixodes scapularis* (deer tick).

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You may earn CME credit by reading the designated article in this issue and successfully completing the quiz (75% correct). Return completed quiz to WMJ CME, 330 East Lakeside St, Madison, WI 53715 or fax to 608.442.3802. You must include your name, address, telephone number, and e-mail address.

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- B. The tick attachment time based on engorgement or known time of bite is greater than 12 hours.
- C. The bite occurred in an area where greater than 10% of the ticks are known to be infected with *Borrelia burgdorferi*, the etiologic agent of Lyme disease.

Answer:

- AA and B
- $\Box$  A and C
- □ All of the above
- 3. Problems concerning the IDSA's current guidelines for antibiotic prophylaxis of *Ixodes scapularis* (deer tick) bites using a single dose of doxycycline include the following:
  - A. It is based on a clinical trial that was unable to demonstrate treatment effectiveness for Lyme disease prevention but did document the development of seronegative Lyme disease when treatment failed.
  - B. The effectiveness of this strategy on the diagnosis and treatment of patients with anaplasmosis is unknown.
  - C. The identification of the tick species and the documentation of the attachment time may be difficult to establish in a clinical setting.

Answer:

- $\hfill\square$  A and B
- **D** B and C
- $\Box$  A and C
- □ All of the above
- 4. The author of this article suggests that the clinician who is practicing in the upper Midwest consider treatment for an *Ixodes scapularis* (deer tick) bite with a full course of doxycycline (100 mg twice daily for 10 to 20 days) in those patients in whom there is no contraindication in view of the concern of adequate treatment for *Borrelia burgdorferi* with a single dose of doxycycline and the possible coexistent infection with *Anaplasma phagocytophilum*.
- Answer:
  - □ False

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# A Tough Act to Follow: Wisconsin's Quality Improvement Act Great for Health Care Providers

Sarah E. Coyne, JD

n January 27, 2011, Wisconsin Governor Scott Walker signed into law the Quality Improvement Act (QIA) as part of 2011 Wisconsin Act 2.

hesitant to critique each other even in the most confidential of circumstances. The ageold battle to keep the record of that process private (and out of the hands of potential

Physicians and other medical professionals may feel less pressure providing open and honest information to regulatory agencies without the fear of being forced to testify in a civil or criminal proceeding...

Act 2 amended Wisconsin's statute protecting the review of health care services for quality issues, more commonly known as "peer review,"<sup>1</sup> as well as other relevant statutes. The QIA, part of a larger "tort reform" package, became effective February 1, 2011. The short version of the story is that the QIA enhances peer review protections, which is a good thing for health care professionals.

The revisions to this law are intended to encourage open and honest peer review (toward the ultimate end of improving quality and safety of patient care) by addressing the natural reluctance health care professionals have to speak freely if their comments are at risk of being disclosed to regulators or plaintiffs' attorneys. Providers are understandably

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plaintiffs in particular) added to that inevitable discomfort.

The revised law provides greater protection for peer review records including any investigations, inquiries, proceedings, and conclusions generated from individuals, organizations, or evaluators who review health services to improve health care quality, avoid overuse of services, or determine reasonable charges for services.<sup>2</sup> The term "health care provider" is expanded to include individuals; facilities, organizations and business entities; persons working under the supervision of individuals; and parents, subsidiaries and affiliate organizations.<sup>3</sup>

#### **Confidentiality Protections**

The new law provides significantly greater confidentiality protections to peer review records than previous Wisconsin peer review law. For example, peer review records may not be used in a criminal proceeding against a health care provider—even under subpoena. Also, peer review records may not be used in a civil action against any health care provider.<sup>4</sup>

The new law also affords protection to incident and occurrence reports. Incident reports are defined in the law as "written or oral statements—made to notify a person, organization or evaluator who reviews or evaluates the services of health care professionals or charges for such services of an incident, practice, or other situation—that becomes the subject of such a review or evaluation."<sup>5</sup> Incident and occurrence reports are given parallel protections to that of peer review records; these reports cannot be used in any civil or criminal action against any health care provider.<sup>6</sup>

Even peer review records and incident/ occurrence reports that have been disclosed to an outside party must remain confidential and cannot be used in actions against any health care provider.

Peer review records and incident/occurrence reports may be disclosed to others under limited circumstances. Some of these circumstances remain intact from the prior law (with minor amendments<sup>7</sup>), some were repealed, and others were created.<sup>8</sup> The new law also makes technical changes to the reporting of information gleaned in a review process in statistical form in order to facilitate large studies of clinical practices.

#### Shared Records and Processes among Multiple Entities

Historically there has been ambiguity surrounding the sharing of peer review process and records between separate entities, eq, the employing physician clinic and a hospital at which that physician holds privileges. Many systems have addressed the problem by obtaining consent from each provider. The new law significantly eases this process by specifying that the protection applies to records of evaluators from multiple entities to help improve the quality of health care, avoid improper utilization of services of health care providers, or determine reasonable charges for such services. This language also appears to protect the records of joint processes between providers and payors. The law specifically allows disclosure of peer review records to the provider's employers, or the parent, subsidiary, or affiliate of that employer.9

#### **Evidentiary Protections**

The QIA includes improved evidentiary protections for health care professionals; data information collected by a regulatory agency (eg, Department of Health Services or Department of Regulation and Licensing) from a health care provider may no longer be admitted into evidence during a civil or criminal action against that provider.<sup>10</sup> Physicians and other medical professionals may feel less pressure providing open and honest information to regulatory agencies without the fear of being forced to testify in a civil or criminal proceeding or of having their testimony used against themselves or a colleague in court.

The QIA also prevents the use in criminal or civil procedures of reports or written statements provided to regulatory agencies. There is an important exception to this rule, which is that administrative proceeding reports, statements and records collected by a regulatory agency may be used against a health care provider in any **administrative** proceeding.<sup>11</sup> An example of an administrative proceeding is an action regarding state licensure of a provider.

#### **Negligence Is not Criminal**

Another benefit of the new law—which should allow physicians and medical professionals

to breathe a sigh of relief—is that they cannot be criminally liable for their negligence if it occurred within the scope of their duties.

A provider who negligently harms a patient or who acts with inefficiency or unsatisfactory conduct, or who fails in good performance as a result of inability, incapacity, inadvertency, ordinary negligence, or good faith error in judgment or discretion, cannot be held criminally liable for these unintentional medical errors.<sup>12</sup> Negligence by health care professionals within the scope of their duties is now a matter only for civil court. The law applies to acts or omissions committed on and after February 1, 2011.

### Public Information Related to Quality Indicators

The revised peer review law permits data collection entities—which gather health care information for the Department of Administration—to report (to DOA) quality indicators that specifically identify individual hospitals (based on the data the entity collects pursuant to Wis. Stat. Chapter 153).<sup>13</sup> The previous law prohibited these reports from identifying individual hospitals with quality indicators.

#### Conclusion

Taking a good hard look at problematic patient care outcomes and unprofessional conduct is the only tried and true route to quality improvement. You have to know what's "broke" before you can "fix it." Such review has been hampered for many years by the inevitable litigation demands as well as pressure from (well-intended) regulators. Health care professionals did not want to participate in meaningful peer review if they were essentially dooming themselves or a colleague to a malpractice verdict or a licensing restriction. Right or wrong, this is human nature. The QIA recognized and addressed this problem head on. This legislation will go a long way toward effecting robust and meaningful peer review and hopefully improved quality of care.

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**1.** Wisconsin Statute Section 146.38, entitled "Health care services review; confidentiality of information," in conjunction with Wis. Stat. § 146.37, are commonly known as Wisconsin's "peer review" statutes. Section 146.37 protects individuals participating in peer review of health care services from liability such that the reviewers are immune from lawsuits based on their participation in the peer review process. Wis. Stat. § 146.37 works together with Wis. Stat. § 146.38 which protects the confidentiality of information used and created in connection with the peer review process.

- 2. Wis. Stat. § 146.38(2).
- 3. Wis. Stat. § 146.38(1)(b).
- 4. Wis. Stat. §§ 146.38(2); 148.38(3t).
- 5. Wis. Stat. § 146.38(1)(bm)
- 6. Wis. Stat. §§ 146.38(2); 148.38(3t).
- 7. Wis. Stat. §§ 146.38(3)(a)-(c).
- 8. Wis. Stat. § 146.38(3m).
- 9. Wis. Stat. §§ 146.38(3), (3m).
- 10. Wis. Stat. § 904.16(2).
- 11. Wis. Stat. § 904.16(3).
- 12. Wis. Stat. §§ 940.03(3), 940.24(1), 940.24(3),
- 940.295.
- 13. Wis. Stat. § 153.05(3m).



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# Addressing Physician Workforce Needs in Wisconsin

Robert N. Golden, MD

s I write this column, we anticipate that 68 of our 4th-year medical students will match in primary care residencies in the upcoming annual residency match. This will be a significant increase compared to last year, when 53 students matched in the primary care fields of family medicine, internal medicine, medicine/pediatrics, and pediatrics. These are disciplines in which we face immediate and growing needs—both in Wisconsin and nationally.

While 1 year does not make a trend, we are gratified by this increase and believe it reflects the deliberate planning and hard work in our ongoing efforts to address Wisconsin's physician workforce needs in underserved areas. I was recently invited to testify before the Legislative Council Study Committee on Health Care Access to brief them on this urgent problem and describe our efforts to address it. The committee, consisting of Wisconsin legislators and public members, is studying potential solutions to the problem of health care provider shortages, particularly in rural areas and inner cities.

There are many root causes of physician shortage areas in the Badger State and across the country, including a disconnection

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Doctor Golden is the Robert Turell Professor in Medical Leadership, Dean of the School of Medicine and Public Health, and Vice Chancellor for Medical Affairs at the University of Wisconsin-Madison. between the geographic distribution of physicians and population needs, and the selection of specialty fields of practice by graduating medical students. Medical student debt burden and the current compensation models in primary care perpetuate these issues.

The School of Medicine and Public Health

TRIUMPH, or Training in Urban Medicine and Public Health, is our central-city Milwaukee counterpart to WARM. TRUIMPH medical students receive much of their clinical training at sites that serve disadvantaged populations, including Aurora Sinai Hospital, Milwaukee Health Services, Sixteenth

Research shows—and students report—that debt repayment has a meaningful impact on career choices, and primary care incomes are significantly lower than those of many other specialties.

(SMPH) is addressing these challenges in several innovative ways. Four years ago, we welcomed our inaugural class into the Wisconsin Academy for Rural Medicine (WARM); next fall, we will complete the planned expansion in class size to include 25 students in WARM each year. The selection criteria for WARM students include those factors that predict a career in rural medical practice. WARM medical students receive much of their clinical training in rural community sites, in partnership with our Marshfield Academic Campus, based in the Marshfield Clinic system, our Western Academic Campus, based in the Gundersen Lutheran Health System and, beginning this July, in Green Bay and the surrounding area based with Aurora Health Care and BayCare. To date, the program's performance has exceeded our expectations, and has received national recognition.

Street Community Health Center, Westside Healthcare Association, and the Bread of Healing free clinic. A cornerstone of the experience is a community service learning project in which each medical student works with a community organization on a project aimed at a specific public health challenge and opportunity. This training track was launched 2 years ago, and currently 8 students participate each year. We have begun planning for a possible expansion, but the availability of training sites and resources is the rate-limiting step.

In fact, clinical training site capacity is the rate-limiting step for both WARM and TRIUMPH. This is why we are very concerned about the ongoing discussion of the possible creation of a new medical school in the state. While this might seem to be a viable approach to expanding the physician workforce, we believe it would, in fact, squeeze out students from current training sites unless new training capacity is created. The incredibly high costs associated with creating a new medical school, compared with the more modest costs involved in class size expansion in an existing school, is only one of the many reasons why this approach would be unwise, and in some ways counter-productive.

RUSCH, our Rural and Urban Scholars in Community Health program, is a pipeline program created in partnership with UW-Milwaukee, UW-Platteville, and Spelman College. It is designed to attract and train college students for entry into WARM and TRIUMPH, and also to increase the diversity of our physician workforce. Stellar college sophomores receive summer enrichment experiences at our school, and when they return to their campuses, are given the opportunity to shadow community physicians.

Another strategy for increasing the diversity of the physician workforce focuses on increasing the diversity of our faculty. The SMPH Centennial Scholars program offers substantial support for the recruitment of faculty who represent segments of the Wisconsin population in which substantial health disparities have been identified. Launched in the spring of 2009, the program has already attracted 6 new faculty to our campus, and several additional recruitments are in process.

Medical student debt burden is an important challenge that must be addressed as part of an overall strategy for increasing the workforce of primary care physicians in underserved areas of the state. Our average medical student debt hovers around \$135,000 for medical school loans, and many of these students carry additional college loans. Research shows-and students report-that debt repayment has a meaningful impact on career choices, and primary care incomes are significantly lower than those of many other specialties. For this reason, we have identified need-based financial aid as our top fundraising priority with our alumni. We are very excited about the current UW Foundation "Great People" campaign, in which every dollar contributed

towards need-based financial aid for medical students receives a 50-cent match.

In addressing work force issues, we must remember that retention is just as important as recruitment. If we successfully recruit new physicians into underserved areas, but they experience a sense of professional isolation and lack of support, then we will lose them and will need to restart the process. The statewide medical and hospital community needs to design effective approaches for supporting clinicians in underserved areas, including support for multidisciplinary health care teams, strategies for sharing on-call duties and offering vacation coverage, and provision of ongoing professional development and consultation services.

Physician workforce issues are extremely important. They require immediate action, as well as long-term planning. We are pleased with the initial results of the innovative strategies our school has launched, and we will continue to carefully monitor their impact. But much more needs to be done. The health of our most vulnerable populations is at stake.



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# MetaStar Achieves High Performance on Medicare Contract

Jay A. Gold, MD, JD, MPH

I n 2008, when MetaStar began work on its most recent 3-year contract with Medicare, known as the 9th Statement of Work, we described the contract in this space. That contract will end in July 2011, and the Centers for Medicare & Medicaid Services (CMS) has found that MetaStar has met all requirements of all themes and tasks in the contract. As a result, CMS is renewing without competition MetaStar's status as the Medicare Quality Improvement Organization (QIO) for Wisconsin.

*WMJ* readers may be interested in what has been accomplished under this contract for Medicare beneficiaries in Wisconsin. As precise measure definitions and interventions have been described in this space<sup>1</sup> for many of these topics, I will not describe them again here; further information about any of them is available upon request.

The contract has required MetaStar to work in 3 broad areas: prevention, patient safety, and beneficiary protection.

#### Prevention

The prevention portion of the contract required MetaStar to work with 14 participating clinics on 4 clinical topics: mammogra-

• • •

Doctor Gold is senior vice president and chief medical officer for MetaStar, Inc. This material was prepared by MetaStar, the Medicare Quality Improvement Organization for Wisconsin, under contract with the Centers for Medicare & Medicaid Services (CMS), an agency of the US Department of Health and Human Services. The contents presented do not necessarily reflect CMS policy. 9SOW-WI-PS-10-81. phy, colorectal cancer screening, influenza immunization, and pneumococcal immunization. From baseline until February 15, 2011, we have seen relative improvements (RI) in the rates of these measures for our participating providers (Table 1).

Note that the relative improvement rate for influenza immunization is relatively low. Probably the most important reason is that this measure, unlike the others, is seasonal, and all the data from the 2010-2011 influenza season are not yet available; indeed, at this writing, the season has 5 weeks remaining. On the basis of our experience in past years, we expect the influenza immunization RI to be substantial once all data are in.

In addition, we have worked successfully with our participating providers on reporting their quality data to MetaStar and to CMS.

#### **Patient Safety**

There are several components of the patient safety portion of the contract. It required MetaStar to work with 36 identified-participant (IP) nursing homes to improve care for high-risk pressure ulcers (HRPU), and with 19 IP nursing homes to decrease the use of physical restraints (PRs). Furthermore, we worked intensively with 3 nursing homes felt to be in particular need of intervention on their HRPU and PR rates. In addition, we worked with 5 hospitals on a surgical care improvement project (SCIP), which also included measures on venothromboembolism (VTE) prophylaxis and heart failure. The measures for SCIP were as follows:

• Timeliness of prophylactic antibiotic

• Appropriate selection of antibiotic

Participants in 4 Clinical Areas, 2008-2011.				
Measure	RI			
Colorectal cancer screening	231.19%			
Influenza immunization	7.90%			
Pneumococcal immunization	59.11%			

25 37%

Table 4 Dalats

Mammography

Abbreviations: RI=Relative Improvement

**Table 2.** Relative Improvement Demonstrated in

 Patient Safety Measures

Measure	RI
High risk pressure ulcers (HRPU) for I	P* 4.19%
Physical restraints for IP*	70.75%
HRPU for nursing homes in need	32.76%
of intervention (NHIN)	
Physical restraints for NHIN	100%
Surgical care improvement project	22.88%
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	91.7%
Potentially inappropriate medications	21.4.%
Drug-drug interactions	8.51%

Abbreviations: RI=Relative Improvements; IP=Identified Participant

- Timely cessation of prophylactic antibiotic
- Appropriate hair removal
- VTE prophylaxis ordered
- Timeliness of VTE prophylaxis
- Continuation of beta blocker
- Angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blockers (ARB) for left ventricular systolic dysfunction (LVSD)

We also have worked with 12 hospitals to decrease methicillin-resistant *Staphylococcus* 

*aureus* (MRSA) transmission and infection through data reporting. And we completed a project to decrease prescription rates of potentially inappropriate medications and medications apt to be involved in drug-drug interaction. Table 2 shows these results.

#### **Beneficiary Protection**

In the area of Beneficiary Protection, MetaStar investigates complaints from Medicare beneficiaries. The contract looks to such matters as timely completion of case review, beneficiary satisfaction with the complaint process, beneficiary completion of satisfaction surveys, and system-wide quality improvement activities where there are confirmed quality-of-care concerns. MetaStar scored highly on all of these measures.

#### What's Next?

CMS's upcoming QIO contract is expected to be made public in late March. MetaStar expects that the contract will ask us to continue to work in many of the areas discussed above and is apt to add some other areas as well. For example, there has been talk of a project to decrease hospital readmissions by improving transitions of care, and to expand our work with hospitals to decrease hospitalacquired conditions. Wisconsin physicians will be essential to success in the new contract, as they have been essential to success in the current one. We look forward to updating *WMJ* readers about the new contract when it becomes available.

#### Reference

**1.** Gold J, Simmons K. MetaStar to begin new Medicare contract. *WMJ*. 2008;107(3):145-146.

#### ERRATUM

In a listing thanking advertisers published in the February 2011 issue of *WMJ*, ProAssurance Wisconsin was incorrectly identified as ProAssurance Pronational (*WMJ*. 2011;110[2]:47). We regret the error.

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