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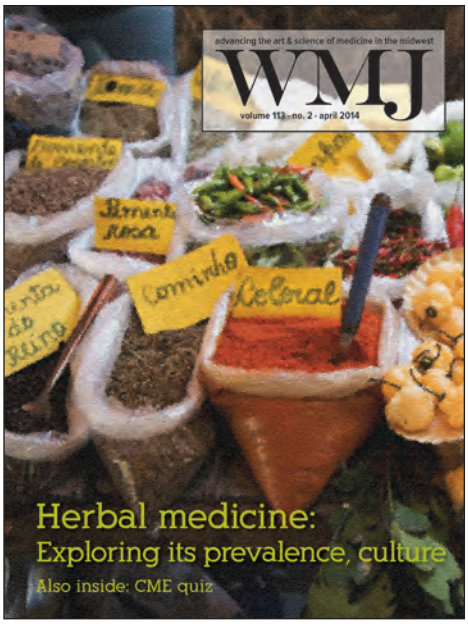

COVER THEME
Herbal medicine: Exploring its prevalence, culture

It's estimated that approximately 20% of the US population regularly uses herbal medicine, and that percentage may be much higher among some ethnic and cultural groups. Meanwhile, understanding of such plant use is incomplete. A pilot study in this issue of *WMJ* explores herbal medicine use among a small Midwest Latino population, seeking to bring clarity to the issue and making a case for further research.

Cover design by Mary Kay Adams-Edgette.

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Burning Issue

D. N. Goldstein, MD, Editorial Director

Editor's note: The following editorial was published in WMJ, *Volume 63, p. 169, March 1964.*

Now that the Surgeon General's report on smoking has confirmed to the public what had been general knowledge for a long time, it will be interesting to see what action the federal government will take against a demonstrated health hazard.

Obviously, a ban on the sale of cigarettes can't be legislated: the sad experience of the Volstead act suggests that making the use of cigarettes illegal might lead to an era of smoke-easies, butt-leggers, and secret inhaling. By printing a message of warning on each package, the cigarette manufacturer would merely underline the hazard the smoker chose to ignore when he bought the pack of cigarettes in the first place. In fact, the only reasonably positive measures the government can undertake are educational in nature. Against the counter-education of the Madison Avenue professors, who work for much higher wages, the government's warnings would probably have the effect of a flute in a windstorm.

The government can, however, take certain negative measures through the Federal Trade Commission and the Federal Communication Commission. Within legal limits, the advertising of tobacco companies could have the same limitations imposed upon it as has the liquor industry's advertising. As no ad ever shows a person drinking beer, wine or whisky, so ads should be prevented from depicting anybody actually smoking a cigarette. Suppression of advertising copy to the effect that smoking is a concomitant of enjoyment, a hallmark of glamor, or a mark of virility should go a long way toward making cigarette puffing attractive only to confirmed smokers. It's the occasional smoker, the beginning smoker, the non-habitual smoker who can be saved from cigarette addiction, and the ban of no-holds-barred advertising might do the trick.

Whatever measure the government takes, the action of our media of communication with regard to tobacco advertising will be a significant note on their sense of responsibility toward the health and welfare of the public. In the face of the proven fact that cigarette smoking may be injurious to many people, will newspapers, radio and television networks, and magazines continue to accept the same kind of cigarette advertising as they have done in the past? Or will they have the integrity to sacrifice a part of their income for the sake of the public good? Will they do it voluntarily or will it require a legal decision?

—D.N.G.

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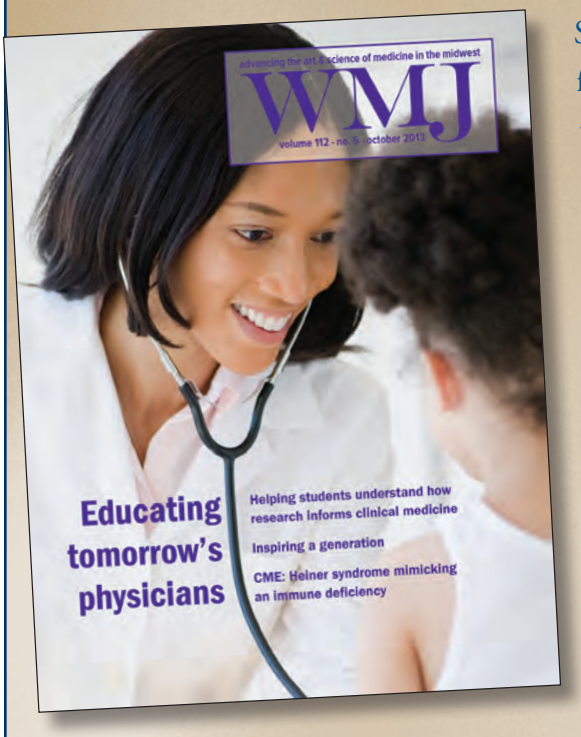

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Bugs, Drugs, Hospitalists, and a New Chapter

John J. Frey III, MD, Medical Editor

The decision of health systems and hospitals to parse the care of patients into smaller and smaller pieces has used the argument that more intensive management by fewer people will improve outcomes and increase efficiency. Most visibly the hospitalist—who has been taking the place of generalist and, increasingly, specialist physicians—has expanded from community hospitals to academic health centers. While changing the career trajectory of many physicians toward more limited practice areas (the term "nocturnalist" conjures for me the image of doctors who come from Transylvania with long capes) the research on hoped-for results has not been convincing. However, this train has left the station, since the large majority of young general internists are populating the hospitalist groups.

The study by Raghavendra and colleagues[1] sheds some light on the process through a very nice analysis of the role of hospitalists on a very narrow, specialty-heavy, topic: neutropenic fever. Their natural experiment at the Gundersen Health System used chart review to look at changes in patient care management as the system migrated from hematologists/oncologists to hospitalists over almost 6 years. They found that adherence to treatment guidelines for neutropenic fever was much higher in the hospitalist era than previously, and antibiotic treatment was more aggressive and consistent. Hospitalists got more consults in the process, as well. However, the drastic changes in the underlying pathology of patients treated—from lymphoma to other more serious malignancies—makes some of the hard outcomes difficult to interpret. The success of generalists managing what had been subspecialist diseases seems to indicate that there is an important role for them in large tertiary hospitals in more than general admissions.

The article from the State Public Health Department by Harless and colleagues[2] demonstrates the value of having a statewide look at MRSA antibiotic sensitivity, a serious and increasingly common problem in all practice settings. They found a pocket of MRSA resistance in Southern Wisconsin that should raise an alarm for all physicians who practice there. I was encouraged by a recent interaction with one of our residents when we were discussing antibiotic choice in a patient we suspected might have MRSA. He knew of the local increase in clindamycin resistance through the hospital bulletins, so data are being shared and disseminated. The question raised by Harless's article, however, is why Southern Wisconsin is so different from the rest of the state? To find the answer, public health and the practicing community must work together. The presence of a single EHR dominating the region should make a chart review possible to look at patients and physician behavior that might have led to this trend. We are all aware of the challenges of electronic charting on daily work, but this might be one example of how it could help understand a dangerous trend.

When I was a senior medical student in a remote town on the US/Mexico border in the 1960s, I had the humbling experience of finding out that a "folk medicine" tea used for treating diarrhea, which I felt had no scientific basis, produced the same results with fewer side effects than the stuff I was prescribing. While some traditional medicines are now being subject to randomized trials to test their effectiveness, those that have endured and are widely used are products of a different type of research—trial and error over centuries. So Kiefer and colleagues' article[3] describing widely used traditional treatments in the Wisconsin Latino community is of great value, not only as information that can be used when we populate our patients' medication lists correctly, but as a stimulus to know more about less potentially toxic ways we can treat patients in their cultural context.

> The movement of immigrants into areas far from their countries of origins and the urge to travel that seems to affect Americans…raise the risk of seeing diseases that are not exotic in many countries around the world but are quite exotic in the Midwest.

The world being flat usually refers to the movement of information across borders and languages that knit us together, for better or worse. However the movement of immigrants into areas far from their countries of origins

and the urge to travel that seems to affect Americans—global health visits are a big part of most medical schools these days—raise the risk of seeing diseases that are not exotic in many countries around the world but are quite exotic in the Midwest. Naddaf and colleagues[4] report 3 cases of unanticipated neurocystocercosis and review its etiology and management. During my 1960s time in the border community, I saw a case of neurocystocercosis—it was endemic there—but none since. As I am always having to remember, zebras occur and this journal often alerts us to that fact.

McLimore and colleagues[5] don't discuss rare bugs, but reasonably common diagnoses that appear at unusual times. The case of neurofibromatosis first manifesting itself in a 69-year-old woman should cause us to do more than look for keratoses and potential malignancies on our skin scans of patients. It should make us take a more detailed family history on everyone. One would hope this patient's doctor asked about funny bumps or other neurological manifestations so that the dermatologists are confirming what has been suspected, not surprising everyone with an unsuspected diagnosis.

The commentary by Baeseman and Corden[6] on the need for a much wider approach to bicycle injury prevention is especially important as communities are encouraging more bicycle traffic as one approach to weight loss and environmental improvement. The "messaging" has to be consistent about injury prevention and the teaching has to be consistent from doctors' offices, home, schools and workplaces. Bicycle injuries still account for a very large portion of emergency department and urgent care visits and are both expensive to society and even more expensive to those who suffer them.

Finally, after serving as Medical Editor of *WMJ* the past 8 years, I've decided it's time for a transition. I've enjoyed serving as your editor and have appreciated the support the journal has received over the years. It remains one of the few state medical society-sponsored journals that publishes a significant amount of research, and it's been rewarding to see the journal evolve and expand. We hope to name my successor this summer and the search is underway. More information about that process is available below and at www.wmjonline.org.

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A Social-Ecologic Framework for Improving Bicycle Helmet Use by Children

Zachary J. Baeseman, MD, MPH; Timothy E. Corden, MD

An estimated 67 million bicyclists in the United States ride roughly 15 billion hours per year[1] for recreation, exercise, and transportation. Each year, serious bicycle-related injuries result in lifelong debilitation and fatalities. These injuries account for more than 1.2 million physician visits, 580,000 emergency department (ED) visits, 23,000 hospital admissions, and approximately 900 deaths each year at an estimated cost of more than $8 billion.[2]

If riders simply wore a standard bicycle helmet many of these injuries may have been prevented. Wearing a standard bicycle helmet reduces a cyclist's risk of injury by 88% and reduces the risk of a serious injury by a minimum of 75%.[1] Helmet use can specifically reduce bicycling-associated head injuries, which account for 62% of bicycle fatalities, 33% of ED visits, and 67% of hospital admissions.[3]

The social-ecologic theory is a strategy for behavioral modification that addresses numerous social and ecologic factors that affect risky behavior. This commentary reviews the literature for interventions shown to increase the prevalence of helmet use among children and present a social-ecologic public health framework to increase helmet use and reduce bicycle-associated head injuries among children.[4] The 4 levels explored include individual factors, relationships, community, and societal opportunities (Figure).

• • •

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SOCIAL-ECOLOGIC THEORY BASE

Individual

Bicycling is nearly ubiquitous among children; close to 85% own a bicycle, yet only about 38% actually own a bicycle helmet, and even fewer regularly wear them.[5] Thus, the barriers to increase helmet use must include helmet ownership and the associated obstacles to using them. Research demonstrates that programs supplying free or subsidized helmets have success at increasing use, which is particularly important in economically challenged communities—both rural and urban.[6]

Relationships: Peers

Children generally know that wearing a helmet could save their lives and that a helmet is an effective way of protecting their heads.[5] Nevertheless, they often have negative feelings toward helmet use, and usage is further decreased through negative peer pressure. In 1 survey, 60% of children specified that they discontinued bicycle helmet use because it was "ugly," "silly," "uncomfortable," or "inconvenient."[5] Additionally, there is a gap in perception regarding what children believe about their peers, and what they actually report as a group. Although the vast majority of children (75%) felt their peers stopped using bicycle helmets due to the fear of being teased, only 1% to 3% of children actually reported this as the reason they stopped wearing a helmet. Similarly, most children (80%) believe their peers stop wearing helmets because friends did not use them, but again as a group, only about 10% actually reported this as their reason for ceasing helmet use.[5] Educating children and adults about their role and dispelling the misperceptions surrounding bicycle helmet practices may be an opportunity to remove some barriers to using helmets.

> By establishing a multifaceted social-ecologic prevention program, the state could move to reduce the burden of childhood bicycle related head injuries.

Relationships: Parents/Clinicians

Parenting approaches can affect helmet use among children. Parents generally misper-

Figure. Social-ecologic Model for Increasing Childhood Bicycle Helmet Use

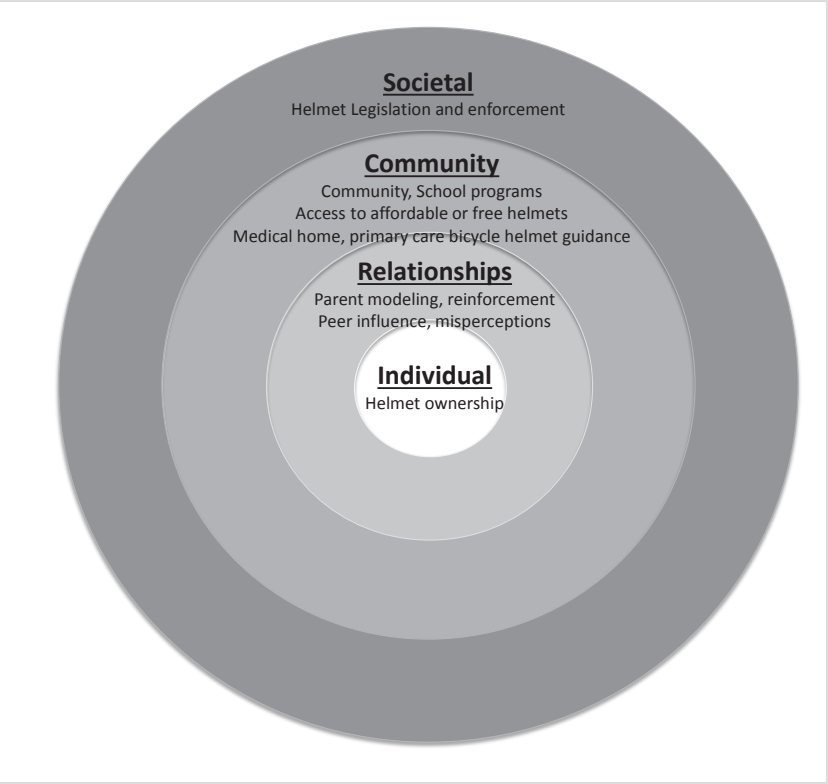

Table. Meta-analysis of Nonlegislative Helmet Interventions[a]

Study	Observed Helmet Use OR (95% CI)	Self-reported Helmet Ownership OR (95% CI)	Self-reported Helmet Use OR (95% CI)
Community-based programs	4.30 (2.24-8.25)[c]	5.56 (0.82-38.98)	—
School-based programs	1.82 (0.94-3.52)	0.84 (0.47-1.49)	4.73 (1.09-20.49)[c]
Free helmet programs[b]	4.35 (2.13-8.89)[c]	5.56 (0.82-38.98)	6.05 (0.91-40.09)
Subsidized helmet programs	2.02 (0.98-4.17)	—	—
Composite analysis	2.30 (1.37-3.85)[c]	1.69 (0.65-4.38)	3.90 (1.42-10.69)[c]

[a]Table compiled by author using the data presented in Royal, et al systematic review.[6]
[b]All of the studies with free helmets were community-based.
[c]Statistically significant ($P = < 0.05$)

ceive their children's helmet use, reporting that their children wore a helmet 90% of the time, when the children actually indicate a 61% use. Conversely, children consistently report parent helmet usage in line with parents' self-reported use (40%).[7] It is not surprising that a child's helmet habits correlate with parental practice. The presence of a parent at home during the work week strongly correlates with increased bicycle helmet use by children in the family, further illustrating the value of parental influence in general.[8]

Clinicians should educate parents about their role in helping children make good helmet choices and help parents recognize that their own helmet use can set an example. Counseling a parent about injury prevention may have a valuable influence on helmet use as well. Simply including bicycle safety preventative guidance during medical visits increased children's likelihood of using a bicycle helmet by 87% (OR 1.87, 95% CI 1.29-2.71).[9] In the same study, only 42.5% of children aged 5 to 14 years had received bicycle safety counseling during an office visit with a clinician within the preceding 12 months.[9]

Community

The findings of a Cochrane Collaboration review examining nonlegislative interventions promoting childhood bicycle helmet use are summarized in the Table.[6] A nonlegislative program included 1 or all 3 of the following elements: health education, subsidized or free helmet distribution, or a media campaign. If an intervention took place at school, it was classified as a "school-based program;" all others were categorized as "community-based." All reviewed programs show that both observed and self-reported helmet use increases with the interventions, but subgroup analyses show that the most robust influence comes from community-based efforts that provide subsidized or free helmets and free helmet distribution programs have the greatest overall effect. Education-only programs that do not offer helmet assistance have no statistical effect on helmet use (OR = 3.08, 95% CI 0.69-13.80).[6] These findings show that providing bicycle helmets for children appears to be an integral component for a successful helmet adherence program.

Society

Laws calling for the mandated use of bicycle helmets have proven to be the most effective means of improving helmet use. While some countries have adopted universal legislation, laws in the United States range from those in local municipalities to those covering an entire state. A systematic Cochrane Review (Macpherson and Spinks) found that legislation is effective at both increasing use of bicycle helmets (45% to 84%) and in reducing bicycle-related head injuries in children 17 years and younger (45% to 82%), when compared to non-mandated adult populations in the targeted jurisdictions.[10] Another systematic review by

Karkhaneh, et al found a significant increase in child use of bicycle helmets post-legislation (OR 4.22, 95% CI 2.03-8.76).[11] The increases in helmet adherence after legislation were modest (OR = 1.24) to very substantial (OR = 22.25). Multiple factors inherent to each jurisdiction may explain the post-legislation variation. The strongest factors influencing increased helmet use post-legislation include lower baseline helmet use prelegislation and mandates that encompass universal enforcement.[11] The effect of a mandate was less in communities with high prelegislation helmet use.[11] The value of helmet legislation appears clear and well supported by evidence.[5,10-14] To move legislation forward, it may be helpful for communities to establish coalitions in order to make state legislators aware of the issue.

CONCLUSION

Our review outlines a framework of evidence using a social-ecologic approach to both explain low helmet use and factors that might increase use in communities. In Wisconsin, brain injury caused by not wearing a bicycle helmet results in 1 in 5 of the lives lost by children under age 14.[15] By establishing a multifaceted social-ecologic prevention program, the state could move to reduce the burden of childhood bicycle-related head injuries. To attain this goal, Wisconsin coalitions for injury prevention and primary care clinicians should focus on programs that are community-based, provide free or subsidized helmets, move to dispel the peer assumptions of helmet use among children, encourage helmet use role-modeling by parents, and advocate to pass mandatory statewide bicycle helmet legislation.

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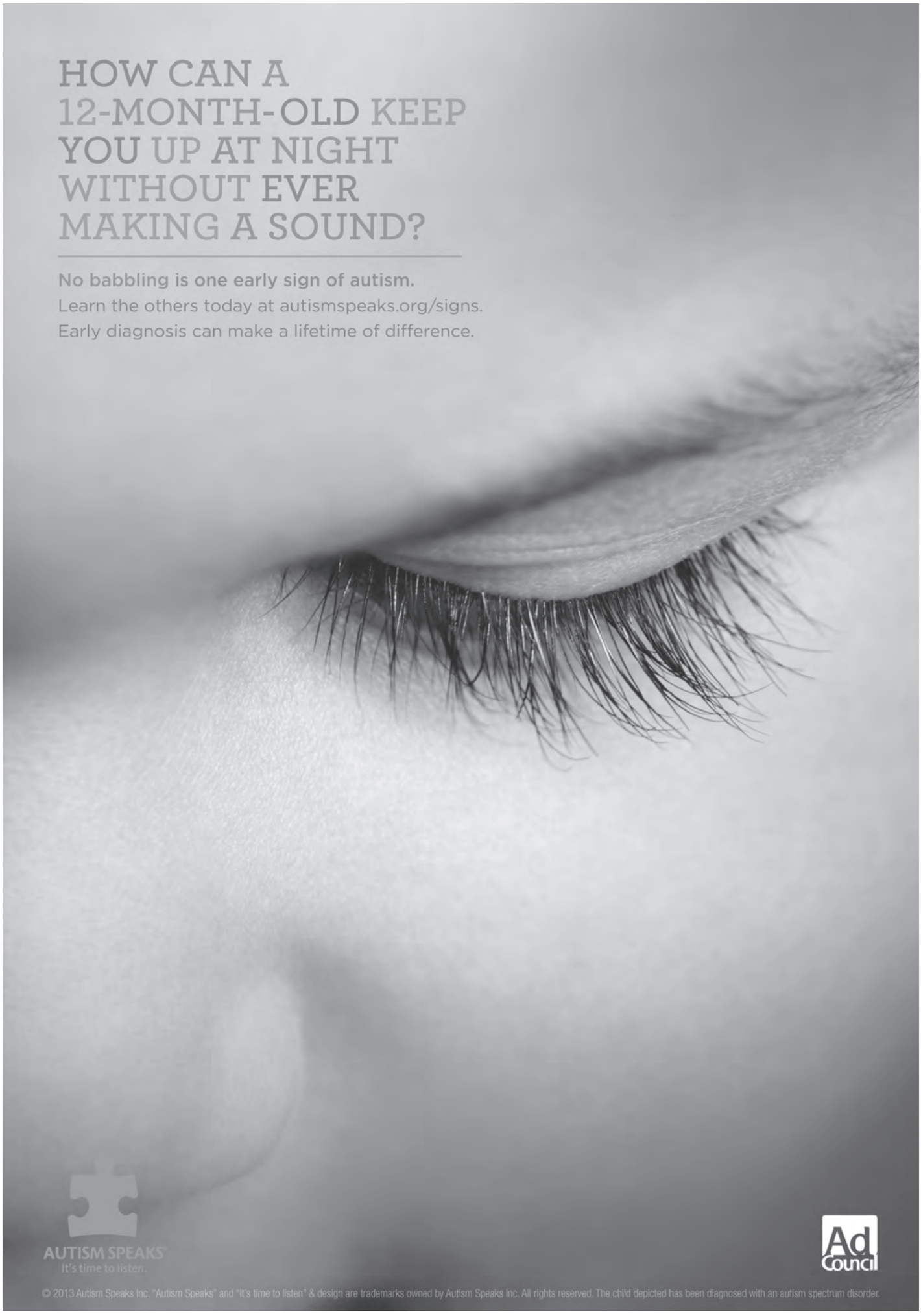
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Management of Neutropenic Fever During a Transition from Traditional Hematology/Oncology Service to Hospitalist Care

Meghana Raghavendra, MD; Rasmus T. Hoeg, MD; Wayne A. Bottner, MD; William A. Agger, MD

ABSTRACT

Objectives: Increasingly, hospitalists across the United States provide primary inpatient care for almost all subspecialty patients, including hematology and medical oncology. Febrile neutropenia (FN) is a serious condition often seen as a complication of cytotoxic chemotherapy or in patients with underlying bone marrow defects. The purpose of this study was to document the change of inpatient management of a common admission diagnosis during a transition of providers from hematologists/oncologists to the use of hospitalists in a tertiary care medical center, and to compare the appropriateness of treatment and outcomes over a period of 5.5 years of this transition.

Methods: The medical records of all patients with neutropenia at a community-based teaching hospital during a period of conversion from hematologist/oncologist to hospitalist coverage were retrospectively reviewed. Patients with fever and absolute neutrophil counts of less than 500/μL (.5 x 10^9/L) on admission were included. Study cases were divided into 3 groups by admission date, roughly demarcating the nascent hospitalist era, the era of transition to hospitalist, and the mature hospitalist era. Management of FN during these eras was compared.

Results: Three hundred ninety-nine inpatients were identified as neutropenic. Of these, 184 did not meet case-inclusion criteria. The remaining 215 cases were included in the study. The internal medicine hospitalist service admitted less than 10% of this population in 2003, but by 2007-2008 it admitted over 90%. The use of 4th-generation cephalosporins and carbapenems increased over time ($P = .027$), and the infectious disease service was consulted more frequently over time ($P = .007$). Outcomes varied due to changes in underlying disease states, use of hospice services, and changes in the types of patients hospitalized with FN. Morbidity decreased due to the change in the type and nonantibiotic therapy of cases, but inappropriate antimicrobial treatment was unusual, and septic morbidity or mortality related to inappropriate therapy was too rare to compare through these eras.

Conclusion: Over the 3 eras compared, care of most neutropenic fever patients was transferred from specialists to hospitalists. Care became more uniform, guideline based, and used more infectious disease consultation, and mortality decreased. Complex changes in the types and treatments of cancer, neutropenia therapy, and in the types of patients hospitalized with FN prevent any conclusion of added value for this change in the type of primary provider management.

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INTRODUCTION

In patients receiving cytotoxic chemotherapy with significant myelosuppressive effects, febrile neutropenia (FN) is a common but serious occurrence that, if unrecognized, can result in significant morbidity and mortality. FN is usually defined as a body temperature of >38.3°C in a patient with an absolute neutrophil count (ANC) <500/μL (.5 x 10^9/L). FN often mandates hospitalization and treatment with intravenous antibiotics. This not only has a detrimental effect on the patient's quality of life but could also result in inferior treatment outcomes, such as decreased overall survival due to subsequent reduction in the dose of chemotherapy.[1-3] In most institutions, neutropenic fever is treated in accordance with the guidelines of the Infectious Diseases Society of America (IDSA) and the American Society of Clinical Oncology (ASCO). In addition, treatment should always be guided by local resistance patterns. Depending on many clinical factors (ie, patient wishes, type and location of infection if known, degree of neutropenia, type of cancer, and chemotherapy administered), treatment can range from outpatient treatment with oral antibiotics to broad-spectrum intravenous antibacterials and antifungals.

In the last 2 decades, hospitalists have emerged as a new physician group in the United States. Transition of inpatient care to hospitalists has been bolstered by several studies showing that hospitalist programs decrease length of stay and cost, as well as improve quality of care.[3-5] These studies have compared hospitalists with primary care physicians, that is, physicians who see both in- and outpatients. The disease groups in the studies have generally been internal medicine diagnoses.

A secondary effect of this evolution has been a broadening of the clinical scope of the hospitalists. As hospitalists are caring for an increasing number of general medicine patients, they are also increasingly managing patients with subspecialty internal medicine and noninternal medicine illness and are now increasingly taking a primary role in the care of patients who, in the past, were not considered within the scope of internal medicine.[3] It is unknown to what degree hematology and oncology patients are managed by hospitalists in the United States, but there is little doubt that this number is growing steadily.

Our institution underwent a transition from subspecialty primary teams to hospitalist teams for management of hospitalized hematology and medical oncology patients from 2004 to 2006. Since FN is a common occurrence in this particular patient population, we decided to retrospectively compare the outcomes of patients with FN over these specific time periods in order to determine whether any difference in outcomes existed between the 2 practice groups. To our knowledge, our study is the first to compare outcomes of FN and to compare outcomes between subspecialists and hospitalists in the management of FN.

METHODS

Setting

Gundersen Health System is centered around a 325-bed community-based, tertiary-care, teaching hospital in La Crosse, Wisconsin. In 2002, the first hospitalist service was implemented and, since then, 5 more hospitalist services have been added. These services are staffed by full-time hospitalists and by primary care internists doing 7-day blocks of hospitalist medicine.

Since 2003, the hospitalist services have admitted an increasingly large percentage of our hospitalized patients. When one disregards same-day admissions, that is, admissions for transfusions or invasive studies, most internal medicine subspecialty departments have stopped admitting patients altogether. The cardiology and pulmonary services continue to be primary providers for approximately 50% of admitted patients with heart or lung conditions, but hematology, oncology, gastroenterology, endocrinology, infectious disease, and neurology now function as consultation services only.

The incidence of neutropenic patients with fever is relatively high for a medium-sized tertiary-care hospital due to an active Center for Cancer and Blood Disorders that treats most solid tumors, lymphoma, and leukemia. Patients are transferred to larger centers only for autologous and allogeneic hematopoietic cell transplants, where immediate complications of these transplant procedures are treated.

After obtaining Institutional Review Board approval, we retrospectively reviewed the medical records of FN patients hospitalized from January 2003 through July 2008. The following data were extracted from the records of patients who fit the case definition: presence of fever >38.3˚C, admitting service, length of stay, type of malignancy, intent of chemotherapy (palliative vs curative), ANC on admission and discharge, primary antibiotics (those used within 24 hours of admission), secondary antibiotics (those added >24 hours after admission), type and outcome of infections, outcome of hospitalization (death/hospice vs discharge), and use of the infectious disease consult service. Cases without both fever and neutropenia were excluded from further study. We also excluded patients admitted solely for chemotherapy administration even if they developed fever during their hospitalization because most of these patients were already on prophylactic antibiotics at the time they developed neutropenic fever.

We then divided the study period into 3 eras: *Prehospitalist,* during which hematologists and medical oncologists admitted and managed patients with FN (January 2003 through June 2004); *Transitional,* during which the hospitalist service admitted some of these patients (July 2004 through May 2007); and *Hospitalist,* during which the hospitalist services admitted all of these patients (June 2007 through July 2008).

We analyzed whether length of stay, use of antibiotics, and use of the infectious disease consult service had changed over the 3 eras and determined appropriateness of the antibiotic regimen by comparing national guideline recommendations for neutropenic fever, septicemia, and/or an infectious focus.

Infectious focus on admission was determined by reviewing the admission note and any note (by the admitting service or consulting service) in the first 24 hours after admission. If a blood stream infection and another focus were noted, the case was considered a blood stream infection. Similarly, we determined the focus of infection at discharge by review of the discharge summary, as well as the discharge billing codes. Here again, if a blood stream infection and another focus were noted, the case was included as a blood stream infection. If a patient had a positive culture result prior to admission, treatment aimed at this specific infection was deemed appropriate based on the susceptibility of the organism(s). Neither infiltrate on chest radiograph nor signs and symptoms suggestive of soft-tissue infection in the absence of a culture positive for growth were deemed sufficient to narrow the antibiotic spectrum.

Whenever it was unclear whether the antibiotic regimen met national guidelines, the senior author, an infectious disease specialist, reviewed the medical record and determined appropriateness of other antibiotics based on characteristics of the pathogen. Because single-agent antibiotic therapy with a 4th-generation cephalosporin or meropenem meets guidelines, more medical records were examined from the first 2 eras than from the latter. Other regimens deemed to meet national guidelines included regimens with broad-spectrum antibiotics with antipseudomonas coverage. When appropriate for site and by susceptibility testing, such regimens included piperacillin-tazobactam, ciprofloxa-

cin, and an antipseudomonal beta lactam and gentamicin. A few cases with multiple allergies received unconventional antibiotic regimens; these patients were categorized as appropriately treated only after review by the infectious disease specialist.

Statistical analyses included descriptive statistics, analysis of variance (ANOVA) for comparison of continuous variables, and the Mantel-Haenszel test for linear trend for comparison of discrete variables. The statistical analysis was completed using SAS version 9.3 (SAS Institute, Cary, North Carolina), and *P* values <.05 were considered significant.

RESULTS

Three hundred ninety-nine hospitalized patient records were reviewed, of which 184 were excluded (Table 1), most commonly for transient neutropenia, that is, only 1 measurement of ANC <500/μL (.5 × 10^9/L) or lack of neutropenia on admission (36%), lack of fever on admission (30%), admission for chemotherapy only (18%), drug induced (4%), and other causes (12%). The remaining 215 cases were included in the study.

Median age was 69 years. Median length of stay was 4 days. ANC on admission ranged from 0/μL to 490/μL (0–.49 × 10^9/L), with a median ANC of 70/μL (.07 × 10^9/L). ANC on discharge ranged from 0/μL to 192 000/μL (0–192 × 10^9/L), with a median of 1220/μL.

Over the 3 eras, solid tumor patients comprised most of the frequent FN cases (34%). Underlying causes of neutropenia over the 3 eras are listed in Table 2. Patients had received recent (within 1 month) chemotherapy in 60% of all included cases, most frequently in patients with solid tumors (89%) and non-Hodgkin lymphomas (80%). Eight cases had drug-induced neutropenia (not including myelosuppresive chemotherapy). The drugs responsible were methotrexate (2 cases), rituximab, sulfasalazine, vancomycin, trazodone, azathioprine, and amiodarone.

In the Prehospitalist, Transitional, and Hospitalist eras, hospitalists admitted <10%, approximately 65%, and >90% of patients with FN, respectively. A few patients in the Prehospitalist era were admitted by primary care internal medicine. In all 3 eras, and with very few exceptions, patients with neutropenic fever who were not admitted by hospitalists were admitted by either the hematology or oncology service.

The infectious focus identified on admission and discharge over the 3 eras is listed in Table 3. Although respiratory source was identified as the most common source of infection in all 3 eras, no identifiable focus of infection was more common at discharge during the Prehospitalist era compared with the Hospitalist era (*P*=.003).

Antibiotic regimens were defined as *primary antibiotics* (antibiotics instituted within 24 hours of admission) or *secondary antibiotics* (antibiotics added after 24 hours). We examined the use of an antipseudomonas 4th-generation cephalosporin and/or carbapenems, compared with other regimens, usually based on fluoroquinolones or broad-spectrum penicillins/1st- to 3rd-generation cephalosporins. Over time, regimens containing 4th-generation cephalosporins and/or carbapenems were used more frequently. The percentages of patients treated appropriately in the 3 eras were 84.9, 85.5, and 98.2, respectively (*P*=.019), including 4th-generation cephalosporins and/or carbapenems (Figure 1).

During the study period, there was no significant change in the La Crosse area antibiotic susceptibility patterns. For instance, the susceptibility ranges of the major pathogens—*Staphylococcus aureus,* 65% to 68% to oxacillin, *Klebsiella sp*, 96% to 100% to ceftriaxone, *Pseudomonas aeruginosa* 82% to 85% to quinolones, and 98% to 99% to piperacillin—were remarkably stable.

The infectious disease service was consulted in 33% of cases overall. Over the 3 eras, the service was consulted in 20%, 34.6%, and 45.1% of cases, respectively. This trend over time was statistically significant (*P*=.005).

Median length of stay was 4 days (range 1–44 days). The median ANC on admission was 70/μL, range 0–490/μL, (.07 × 109/L, range 0–.49 × 10^9/L) and 1200/μL, range 0–192,000/μL (1.2 × 10^9/L, range 0–192 × 10^9/L) at discharge. Mean length of stay declined slightly over the 3 eras (6.7, 5.9, and 5.7 days, respectively), although this was not statistically significant (*P*=.724).

Table 1. Reasons for Exclusion of Patients from a Study of Comparison of Treatment of Neutropenic Fever by Hospitalists and Hematologists/Oncologists (N=184)

Reason for Exclusion	No. of Patients Excluded (%)
Transient neutropenia	66 (36)
No fever	55 (30)
Admitted for chemotherapy only	33 (18)
Drug-induced	8 (4)
Other[a]	22 (12)

[a]Other includes neutropenia secondary to severe, nonhematologic illness (n=13); patient on hospice care (n=3); autoimmune diseases (n=3); human immunodeficiency virus infection (n=1); infectious mononucleosis (n=1); and transfer from rehabilitation unit, that is, admission analyzed previously (n=1).

Table 2. Underlying Cause of Neutropenic Fever in Study Patients Admitted to Hospital by Era[a]

Underlying cause	Prehospitalist n=60	Transitional n=104	Hospitalist n=51	Total N=215
Solid tumors	23 (38.3)	36 (34.6)	15 (29.4)	74 (34.4)
Leukemia	13 (21.7)	31 (29.8)	19 (37.3)	63 (29.3)
Lymphoma	21 (35.0)	22 (21.2)	2 (3.9)	45 (20.9)
Myelodysplastic syndrome	3 (5.0)	12 (11.5)	9 (17.7)	24 (11.2)
Other[b]	0 (0.0)	3 (2.9)	6 (11.8)	9 (4.2)

[a] All data are presented as number of patients (%).
[b] Other includes aplastic anemia (n = 3), multiple myeloma (n = 4), and Waldenström (n = 2).

Table 3. Infectious Focus of Inpatients with Neutropenic Fever upon Admission and at Discharge by Era[a]

	Prehospitalist n=60		Transitional n=104		Hospitalist n=51	
Infectious focus	**Admission**	**Discharge**	**Admission**	**Discharge**	**Admission**	**Discharge**
Respiratory	16.7	25.0	18.3	23.1	11.8	33.3
Skin, nose, mouth	15.0	13.3	9.6	6.7	7.8	15.7
Abdominal	3.3	10.0	12.5	8.7	7.8	11.8
Blood stream[b]	1.7	16.7	3.8	25.0	2.0	15.7
Urologic	1.7	0.0	2.9	6.7	0.0	9.8
Other	3.3	1.7	1.0	1.0	0.0	2.0
No focus	61.7	45.0	56.7	36.5	70.6	17.6

[a]Some patients had more than 1 infectious focus noted, so totals do not equal 100%.
[b]Including intravenous catheters.

Figure 1. Percentage of Antibiotic Regimens Deemed Appropriate for the Treatment of Neutropenic Fever by Era

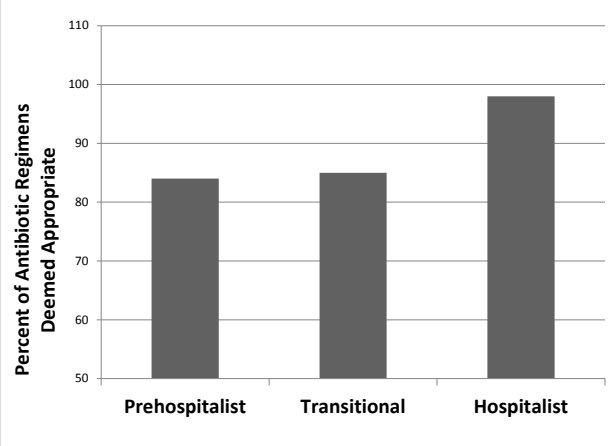
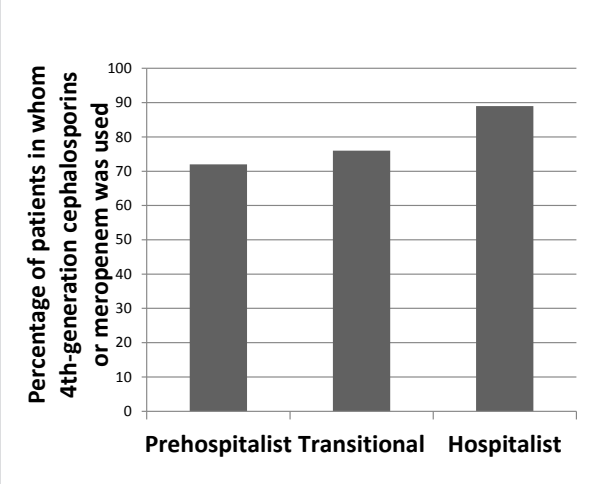


Figure 2. Use of 4th-generation Cephalosporins or Meropenem in Percentage of Patients by Era ($P<.027$).



Overall, 15.3% of study patients either died in hospital or were discharged to hospice. Analysis by era demonstrated that 26.7% of patients died or were discharged to hospice in the Prehospitalist era, compared with 7.8% in the Hospitalist era ($P=.05$). Both inpatient and overall 30-day mortality fell significantly from the Prehospitalist (17% and 35%, respectively), to the Transitional (8% and 17%, respectively), and to the Hospitalist eras (2% and 12%, respectively) ($P=.006$ and $P=.002$). Additionally, in-hospital death from inappropriately treated sepsis occurred in only a few cases during the entire study, precluding statistical analysis.

In the Prehospitalist era, 81.9% of patients received chemotherapy with curative (vs palliative) intent, compared with 72.5% in the Hospitalist era, although this difference was not significant ($P=.248$). The percentage of patients receiving chemotherapy with curative intent for solid tumors in the Prehospitalist and Hospitalist eras was similar (34% and 37.9%, respectively), but there was a shift in diagnosis pattern of cases receiving chemotherapy with curative intent only. Whereas in the Prehospitalist era 24% of cases had leukemia and 42% had lymphoma, in the Hospitalist era 55% had leukemia and 6.9% had lymphoma ($P=.007$).

DISCUSSION

Although it appears that hospitalists will eventually replace primary care internists in most large hospitals, the degree to which hospitalists will admit patients with subspecialty diagnoses remains to be determined. In recent times, hospitalist as a subspecialty is an evolving practice group.[6] The medical center examined in this study has been at the forefront of the hospitalist movement. By 2010, not only were all patients with general medical illnesses admitted to hospitalist services, but also virtually all patients with subspecialty illnesses were cared for by hospitalists, with the exception of some with cardiology or pulmonology diagnoses. Over the 5 1/2 years this study reviewed, the internal medicine hospitalist service essentially assumed care of all patients with neutropenic fever (from <10% in 2003 to >90% in 2007 and 2008). No study that we could identify has documented such a transfer of care from specialists to hospitalists.

Our study shows that over the period of 5 1/2 years analyzed, the transfer of care from hematologists and oncologists to internal medicine–trained hospitalists resulted in significant management changes. Hospitalists were more likely to pursue aggressive antibacterial treatment (more often starting with a 4th-generation cephalosporin, typically cefepime), whereas specialists, despite knowledge of the national guidelines, more frequently used alter-

native regimens. Several factors could explain this. For instance, although the 2002 IDSA guidelines approve the use of cefepime or an antipseudomonal carbapenem in high-risk patients with neutropenic fever, we found that such a unitherapy beta lactam recommendation was not uniformly used in the Prehospitalist era, when 76.1% patients received only a 4th-generation cephalosporin or carbapenem, compared with the Hospitalist era, in which 94.1% of patients received such approved treatments, although the difference was not statistically significant ($P = .101$). Familiarity of the hematologists/oncologists with their patients prior to admission, including their past morbidities and prior response to different antibiotics, appeared to explain this difference because they were more likely to "aim" for a relapse of a prior infectious focus. Conversely, hospitalists often meet patients for the first time on the day of admission and were more likely to opt for single broad-spectrum beta-lactam antibiotic until more information becomes available.

The hospitalists in our study knew the national guidelines for the treatment of neutropenic fever. However, the treatment of patients with FN offered in the most recent era, managed primarily by hospitalists, was deemed "appropriate" more frequently than was treatment offered in the earliest era, in which their treatment was managed by hematology/oncology specialists. Whether this finding is true in other hospital settings is unknown.

The same pattern was true for infectious disease consults. The frequency of infectious disease consultation nearly doubled in the 5 1/2 year period we examined. It is perhaps not surprising that hospitalists, who are generalists by training, seek more advice in treating this very sick patient population.

The observed change in treatment patterns is at least partly unrelated to the hospitalist movement. The study period spanned 5 1/2 years. In this time, myelosuppresive chemotherapeutics and national (but not local) microbial resistance patterns had changed.[7] Arguably, these changes led to a sicker patient population and/or to physicians' belief in the need for broader-spectrum antibiotics and more frequent infectious disease consultation. While data support the use of available guidelines for treatment of patients hospitalized with FN, non–guideline-based therapy has also been increasingly used, as we saw in the Prehospitalist era, in this high-risk population.[8]

It is interesting to note that the number of patients receiving chemotherapy for curative intent admitted for neutropenic fever fell over the course of years, from 50 in the Prehospitalist era to 29 in the Hospitalist era. This is likely due to the change in pattern of chemotherapy regimens over time and, possibly, to the use of granulocyte colony–stimulating factor (G-CSF) support in patients receiving aggressive high-dose chemotherapy with curative intent.

A marked change in the admission diagnoses was noted over the 3 eras. Although lymphoma represented 26.9% of admissions in the Prehospitalist era, it represented only 6.9% in the Hospitalist era, with leukemia constituting 55.2% of admissions in this era. This is likely due to adherence to National Comprehensive Cancer Network (NCCN) guidelines in our facility for recommended use of G-CSF in high-risk patients with lymphoma and, thus, a trend toward lower rate and shorter duration of neutropenic fever.[9]

Overall, the 30-day case mortality rate fell drastically, from nearly a third of patients in the Prehospitalist era to approximately 10% of patients in the Hospitalist era (26.7% vs 7.8%, $P = .005$). Changes in antibiotic treatment alone cannot account for this shift. A low septic death rate did not change through these years; rather, the majority of the shift in mortality can be explained by the fact that more terminal patients were treated at home in the Hospitalist era. In addition, inpatients treated by our palliative care service, which expanded significantly from 2003 to 2008, usually did not have blood tests done. Thus, they did not meet inclusion criteria for this study, artificially lowering the case mortality in the Transitional and Hospitalist eras.

To determine whether intention of treatment could attribute to change in pattern of mortality, we compared patients receiving curative and palliative intent chemotherapy. In this subgroup analysis, patients receiving chemotherapy with curative intent did not demonstrate change in 30-day mortality pattern or discharge to hospice rate over the 3 eras ($P = .151$). Involvement of our palliative care team with most patients with incurable malignancies at the outset was done in the outpatient setting, and when these patients with incurable malignancies required hospitalization, they often opted for nonaggressive measures of therapy and comfort-based options. Furthermore, a more active involvement of our palliative care team in the inpatient setting developed, thus accounting for more discharges to hospice.

There are limitations to our study. Although we conducted a retrospective analysis of a unique period of transition from subspecialists to hospitalists, the outcomes listed are likely more reflective of case mix or changes in practice that occurred over time, rather than to the treatments provided by particular groups of physicians. A prospective study with a larger patient population would be ideal to assess whether the difference in outcome was, in fact, due to the transition to another type of physician service. Secondly, we do not have specific microbiology on every patient. However, a review of the documented infections did not show a change in the pattern of infection or a significant resistant pattern that could be attributed to application of broader-spectrum antibiotics in the Hospitalist era.

This is the first study to examine the treatment of neutropenic fever by hospitalists in the United States. It is one of few studies comparing treatment and outcomes of hospitalists with those of medical subspecialists, despite the fact that hospitalists in the United States admit increasing numbers of subspecialty

patients. This is remarkable when one considers the number of studies dedicated to the comparison of primary care physicians with hospitalists.

In conclusion, this study focused on a finite and unusual period in health care in America. It shows that as the care of neutropenic fevers transitioned to hospitalist providers, therapy became more guideline-based and used infectious disease consultation more frequently; however, it was not possible to prove a higher value for this change. Equal or better outcomes due to the rapidly changing therapies and approaches to neutropenia/cancer were apparent, even in this single medical center over a short 5 1/2 year period. But as the landscape of inpatient medicine continues to change, careful studies should be dedicated to the transfer of care from specialists to hospitalists, and possibly to subspecialty hospitalists, if this transition is to justify claims of lower resource utilization or better outcomes. More likely this change will continue, driven by other medical system needs, without true value of care measurements.

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An Investigation of Antibiotic Susceptibility to Empiric Therapy for Community-associated Methicillin-resistant *Staphylococcus aureus*

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ABSTRACT

Objective: To analyze antibiotic susceptibility patterns of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) isolates obtained from skin and soft tissue infections among Wisconsin outpatients.

Design: Retrospective genotype testing.

Setting: Isolates were forwarded to the Wisconsin State Laboratory of Hygiene and Marshfield Labs from clinical laboratories throughout Wisconsin.

Methods: MRSA isolates submitted during April, 2010–February, 2012 underwent genotype analysis using pulsed-field gel electrophoresis. Antibiotic susceptibility patterns were determined for all isolates identified by electrophoresis subtyping as strain type USA300, and pattern comparisons were made by public health region.

Results: Among 835 MRSA isolates submitted, 217 (26%) were genotyped. Of these, 152 (70%) were USA300 MRSA. Among the 152 USA300 isolates, 95% were susceptible to clindamycin and 99% were susceptible to tetracycline and trimethoprim-sulfamethoxazole. The proportion of clindamycin-susceptible isolates from the southern region was significantly lower when compared to the other 4 regions combined ($P = 0.03$). One southern region clindamycin-resistant isolate was also resistant to trimethoprim-sulfamethoxazole.

Conclusions: USA300 MRSA was the predominant strain isolated from outpatient skin and soft tissue sites. Antibiotic susceptibility patterns among Wisconsin USA300 MRSA isolates are similar to patterns found in national studies. Local providers should continue to follow national practice guidelines for treatment of outpatient skin infections. A cluster of 4 clindamycin-resistant isolates and 1 trimethoprim-sulfamethoxazole resistant isolate was detected in the southern region, warranting continued surveillance for antibiotic resistance among community-associated MRSA isolates.

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INTRODUCTION

Staphylococcus aureus causes myriad of infections ranging from superficial skin and soft tissue infections to more invasive infections such as pneumonia, septicemia, and endocarditis.[1]

During the 1960s methicillin-resistant *S aureus* (MRSA) emerged among people with health care-associated risk factors. Health care-associated MRSA is typically resistant to all antibiotics except vancomycin and newer agents such as linezolid and daptomycin. These infections classically occur among older patients, recently hospitalized patients, nursing home residents and people exposed to invasive devices or procedures. Health care-associated MRSA is commonly associated with serious invasive infections such as pneumonia and bacteremia.[1,2]

Community-associated MRSA emerged during the 1990s among people with no health care-associated risk factors. This strain of MRSA typically is resistant only to the beta-lactam antibiotics and is most commonly associated with superficial skin and soft tissue infections.[1] Community-associated MRSA infections of the skin tend to be more purulent in nature compared to beta-hemolytic streptococcal infections, which generally lack purulence and exudates.[3] Community-associated MRSA infections usually occur among younger individuals compared to persons typically infected with health care-associated MRSA.

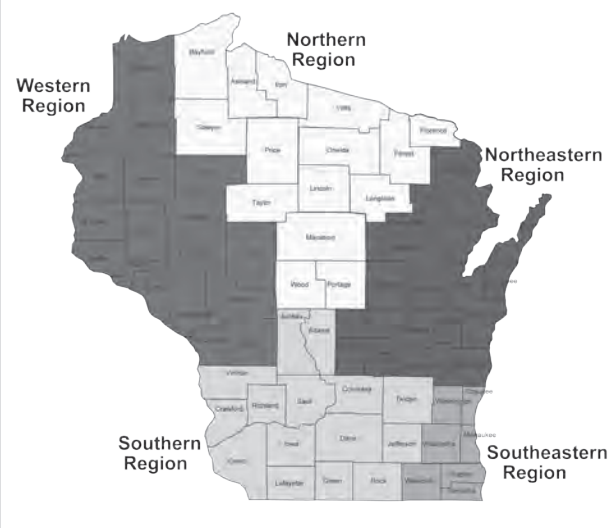
Evidence-based recommendations to guide antibiotic treatment of community-associated MRSA infections were lacking until recently. In 2011 the Infectious Disease Society of America published evidence-based clinical practice guidelines for

Table 1. Empiric Oral Antibiotic Treatment of Purulent SSTIs[3]

Treatment	Adult Dose	Strength of Recommendation
Clindamycin	300-450mg TID	A-II
TMP-SMX	1-2 DS tab BID	A-II
Doxycycline	100mg BID	A-II
Minocycline	200mg x1, then 100mg BID	A-II
Linezolid	600mg BID	A-II

Abbreviations = SSTIs, skin and soft tissue infections; TID, three times daily; BID, twice daily; DS, double strength; TMP-SMX= Trimethoprim-Sulfamethoxazole.

Figure 1. Wisconsin Division of Public Health Regions



treatment of a variety of MRSA infections. Incision and drainage continues to be the recommended primary treatment in simple boils and abscesses.[3] In settings where incision and drainage alone are not adequate such as severe or extensive disease, patient comorbidities, or failed incision and drainage, the recommendations include first line oral antibiotic options for empiric coverage of community-associated MRSA among outpatients with superficial skin infections.

The Centers for Disease Control and Prevention reports strain type USA300 MRSA as the predominantly circulating community strain in the United States. This strain is the major cause of skin and soft tissue infections in community settings such as daycare centers and correctional facilities.[1,4] USA300 MRSA is considered susceptible to all of the first-line oral antibiotic empiric therapies outlined in the 2011 evidence-based practice guidelines. Table 1 includes a brief summary of these empiric antibiotics for purulent lesions. Clindamycin is among the first-line options for empiric coverage, but the national guideline authors acknowledge that clindamycin susceptibility may vary by region.[3] Subsequently, the Wisconsin Division of Public Health initiated a statewide study to determine the proportion of USA300 MRSA isolates from skin infections that were susceptible to the empiric therapies outlined in these 2011 national practice guidelines. The results of that study are included in this report.

METHODS

We conducted a retrospective study of 217 MRSA isolates examined at 2 laboratory facilities in Wisconsin. The specimens were collected from superficial infections of skin and soft tissue among outpatients during April, 2010–February, 2012. Isolates were either referred to the Wisconsin State Laboratory of Hygiene (state lab) from clinical laboratories for confirmatory testing or were recovered from clinical samples submitted to Marshfield Labs. The isolates were obtained from patients in all 5 state public health regions (Figure 1).

All 99 outpatient MRSA isolates submitted to the state lab from the northeastern, southeastern and southern regions underwent genotype analysis using pulsed field gel electrophoresis. Among 736 outpatient MRSA isolates submitted to Marshfield Labs from the western, northern, northeastern and southern regions, 118 (16%) randomly selected isolates underwent electrophoresis genotype analysis. The number of genotyped isolates among each public health region ranged from 27 to 37.

Preparation of chromosomal DNA for electrophoresis analysis was performed using previously described methods[5,6] with slight modifications. Agarose plugs were made by mixing a standardized turbid bacterial suspension, molten agarose and lysostaphin. Cells were lysed by incubating plugs in Staphylococcus Lysis Buffer at 54°C for 2 hours (state lab) or in EC buffer at 37°C for 4 hours (Marshfield Labs). Lysis buffer was removed by washing twice in Millipore water and 4 times in TE Buffer. Plugs were restricted with 30 units of SmaI enzyme (New England Bio Labs, Inc, Ipswich, Massachusetts) for 2 hours at 25°C. DNA fragments were resolved in 1.0% agarose at 14°C for 18 hours (state lab) or 20 hours (Marshfield Labs). Switch times of 5.0 to 40.0 seconds and voltage of 6.0v/cm were applied using a CHEF Mapper XA Chiller System (Bio-Rad, Life Science Research, Hercules, California). Methods were validated by both laboratories using USA-series reference strains including USA300-0114 to assure inter-laboratory reproducibility. Analysis was performed using BioNumerics software (Applied Maths, Austin, Texas) with the Dice coefficient at 1.25% tolerance and the unweighted pair group of arithmetic averages algorithm. Genetic similarity was interpreted according to the criteria of Tenover et al.[7]

Antibiotic susceptibility testing was conducted on all MRSA isolates identified as USA300 MRSA. Susceptibility testing at Marshfield Labs was performed using the Phoenix System (BD Diagnostic Systems, Sparks, Maryland) PMIC panels according to the Clinical and Laboratory Standards Institute guidelines.[8]

Susceptibility testing at state lab was performed using a Kirby Bauer disk diffusion and the D Zone test, also according to the same established guidelines.[8] Antibiotic agents tested included erythromycin, clindamycin, levofloxacin, rifampin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin.

The proportion of USA300 MRSA isolates susceptible to selected antibiotic agents was determined statewide. Additionally, the proportion of isolates susceptible to clindamycin, trimethoprim-sulfamethoxazole, and tetracycline was determined by public health region and statistically significant differences among regional antibiotic susceptibility patterns were determined using the Fisher's exact test.

Table 2. Proportion of strain type (ST) USA300 MRSA Isolates Susceptible to Select Antibiotic Agents, by Wisconsin Public Health Region, April 2010–February 2012

Public Health Region	Western	Northern	Northeastern	Southeastern	Southern
Number of specimens	27	29	29	37	30
Clindamycin % susceptible	96	96	96	100	87
95% CI	(81–99)	(82–99)	(81–99)	(90–100)	(69–96)
P-value[a]	1.00	1.00	1.00	0.20	0.03[b]
TMP-SMX % susceptible	100	100	100	100	97
95% CI	(87–100)	(88–100)	(88–100)	(90–100)	(83–99)
P-value[a]	1.00	1.00	1.00	1.00	0.20
Tetracycline % susceptible	100	100	100	100	97
95% CI	(87–100)	(88–100)	(88–100)	(90–100)	(83–99)
P-value[a]	1.00	1.00	1.00	1.00	0.20

[a]*P*-value is for Fisher's exact test comparing the proportion of susceptible isolates in a single region to the proportion of susceptible isolates in the remaining 4 regions.
[b]statistically significant
Abbreviation: TMP-SMX, trimethoprim-sulfamethoxazole

Table 3. Proportion of Susceptible Wisconsin strain type (ST) USA300 MRSA Isolates Compared to EMERGEncy ID NET Isolates, by Antibiotic Agent

Agent	2010–2012 Wisconsin Number Susceptible/ Number Tested (% Susceptible) Isolates	2008 EMERGEncy ID Net[12] Number Susceptible/Number Tested (% Susceptible) Isolates	2004 EMERGEncy ID Net[2] Number Susceptible/Number Tested (% Susceptible) Isolates
Clindamycin	145/152 (95%)	344/366 (94%)	215/226 (95%)
Erythromycin	8/151 (5%)	34/350 (10%)	13/226 (6%)
Fluoroquinolones	50/82 (61%)	155/346 (45%)	111/176 (63%)
TMP/SMX	150/151 (99%)	366/367 (99%)	217/217 (100%)
Tetracycline	146/147 (99%)	343/350 (98%)	207/226 (92%)
Rifampin	151/151 (100%)	323/326 (99%)	186/186 (100%)
Vancomycin	151/151 (100%)	326/326 (100%)	No data

Abbreviation: TMP-SMX, trimethoprim-sulfamethoxazole

RESULTS

Among 217 outpatient MRSA isolates tested, 152 (70%) were identified as USA300 and 4 (2%) were identified as USA400. These represent community-associated strains. The remaining 61 (28%) isolates were identified as USA100, USA500, and USA800, all of which represent health care-associated strains.[9] The age distribution of 165 patients with USA300 isolates was: age 0 - 4 years, 28; 5 - 17 years, 28; 18 - 44 years, 64; 45 - 64 years, 35; and ≥ 65 years, 10. The median age was 38 years. Among 103 patients for which information was available, 44% were males.

The proportion of USA300 isolates susceptible to selected antibiotic agents is provided by public health region in Table 2. The antibiotic susceptibility pattern was similar in all regions except for clindamycin susceptibility among southern region isolates when compared to isolates obtained from the remainder of the state (87% vs 98%, $P = 0.03$). The 4 southern region isolates that were nonsusceptible to clindamycin were obtained from 4 unique patients treated at 2 different outpatient clinics in the region. One of the 4 isolates, cultured from an eye specimen, is also the only isolate that was nonsusceptible to trimethoprim-sulfamethoxazole.

The overall statewide USA300 antibiotic susceptibility pattern is provided in Table 3, along with findings from national studies conducted among emergency department patients during 2004 and 2008. Among the antibiotics used for empiric treatment of community-associated MRSA, virtually no differences were noted between the Wisconsin and the national susceptibility.

DISCUSSION

The USA300 MRSA strain is becoming synonymous with community-associated staphylococcal disease in the United States. Outbreaks of community-associated MRSA infections among athletes, children attending daycare, and inmates of correctional facilities during the early 2000s demonstrate the dominance of a single electrophoresis pattern designated as strain type USA300-0114.[10,11] This strain continues to be a major cause of superficial skin infections among young healthy individuals.[11]

Two prospective prevalence studies were conducted during 2004 and 2008 among outpatients with acute, purulent skin infections seeking care at 1 of 11 EMERGEncy ID NET sites, a network of university-affiliated emergency departments in the United States. MRSA was isolated from 59% of approximately 1000 patients with superficial infections during the 2 studies, and USA300 comprised 97% of the MRSA isolates. USA300-0114 remained the dominant MRSA strain and its antibiotic susceptibility pattern was remarkably stable during 2004–2008.[12,13]

Table 4. Empiric Oral Antibiotic Treatment of Non-purulent SSTIs[3]

Treatment	Adult Dose	Strength of Recommendation
Beta-lactam (eg, cephalexin and dicloxacillin)	500mg QID	A-II
Clindamycin	300-450mg TID	A-II
Beta-lactam (eg, amoxicillin) and/or TMP-SMX	Amoxicillin: 500mg TID, TMP-SMX: 1-2 DS tab BID	
or a tetracycline	Doxycycline: 100mg BID	A-II
Linezolid	600mg BID	A-II

Abbreviations = SSTIs, skin and soft tissue infections; TID, three times daily; BID, twice daily; DS, Double Strength; TMP-SMX= Trimethoprim-Sulfamethoxazole; QID, four times daily.

The evidence-based practice guidelines for empiric treatment of skin and soft tissue infections released during 2011 were based heavily on the 2 aforementioned EMERGEncy ID NET studies and were founded on the premise that the majority of outpatient skin infections were caused by USA300 MRSA. Our findings in Wisconsin are similar to those of both national studies. Although USA300 MRSA isolates comprise a substantially smaller proportion of total MRSA isolates in Wisconsin compared to the EMERGEncy ID NET studies (70% vs 97%, $p < 0.01$), USA300 MRSA remains the predominant community-associated MRSA strain in Wisconsin and all isolates demonstrate the characteristic 0114 strain type pattern. Importantly, antibiotic susceptibility among Wisconsin USA300 isolates is remarkably similar to susceptibility patterns among USA300 isolates from the 2 national studies. In general, USA300 MRSA is considered susceptible to clindamycin, tetracycline, trimethoprim-sulfamethoxazole, rifampin, and vancomycin, with at least 90% of isolates susceptible to these antibiotics.

USA300 MRSA was resistant only to beta-lactam and macrolide antibiotic agents when initially isolated during 2000. During the past 5 years, clusters of clindamycin and tetracycline resistance among USA300 MRSA isolates have demonstrated broadening antibiotic resistance of this strain. Resistance is largely plasmid-mediated, highly transmissible and varies among patient populations.[14] For example, during a San Francisco General Hospital study, 16% of USA300 MRSA isolates among patients in a small outpatient HIV clinic were clindamycin resistant compared to 2% clindamycin resistance among a random sample of USA300 MRSA isolates obtained from the entire hospital-affiliated system.[3,15] Additionally, 48% clindamycin resistance was noted among USA300 isolates at the Fenway Community Health Center in Boston compared to only 7% clindamycin resistance among similar strains associated with a nearby health network.[16] Although overall susceptibility to clindamycin determined by national studies remains high, clusters of clindamycin resistance are evident. These clusters are acknowledged in the 2011empiric treatment guidelines, but clindamycin is still considered a first-line empiric therapy for USA300 MRSA skin infections, given the high levels of clindamycin susceptibility nationally.

Likewise, in our study of Wisconsin isolates clindamycin susceptibility was high (95%), but when stratified by public health region, a relatively high level of clindamycin resistance was observed in the southern region (13% vs 2% among the remaining 4 regions). In the context of the noted clusters, these regional differences in susceptibility among USA300 MRSA strains demonstrate the need for ongoing surveillance to more accurately describe variations in antibiotic susceptibility patterns among localities over time.

Beta-lactam antibiotic resistance among USA300 MRSA isolates is chromosomally encoded, but clindamycin resistance is mediated by the pSK41-like conjugative plasmid.[14] The pSK41-like plasmid previously was identified only in limited geographic areas such as the aforementioned San Francisco and Boston areas where clusters of clindamycin-resistant USA300 MRSA strains were detected. However, a 2010 analysis of national surveillance databases determined the pSK41 plasmid was present in 5 of the 8 states where surveillance was conducted. This plasmid is an important mechanism for the dissemination of clindamycin resistance among USA300 MRSA isolates. Prior to this 2010 study, it was believed the plasmid mediator for USA300 MRSA resistance was limited to a small number of rare clusters, but its proven presence in the surveillance database indicates the plasmid is more widespread than previously believed. This finding bolsters the case to continue monitoring community MRSA strains for emerging antibiotic resistance.[17]

Of note, 1 Wisconsin clindamycin-resistant USA300 MRSA isolate was also resistant to trimethoprim-sulfamethoxazole. Among approximately 1000 superficial infection samples enrolled in the EMERGEncy ID NET studies during 2004 and 2008, only 1 USA300 MRSA isolate was resistant to trimethoprim-sulfamethoxazole.[2,13] The mechanism conferring trimethoprim-sulfamethoxazole resistance in *S aureus* is linked to a gene carried on the same pSK41-like plasmid associated with clindamycin resistance, hence emergence of trimethoprim-sulfamethoxazole resistance via the same plasmid-mediated mechanism is of concern.

The authors of the 2011 practice guidelines recognized that treating outpatient skin infections with agents active against both community-associated MRSA and beta-hemolytic streptococci is controversial. Beyond clinical interpretations of purulent vs nonpurulent lesions as discussed previously, the need for broader coverage may depend on local epidemiologic features. Trimethoprim-sulfamethoxazole, doxycycline, and minocycline have demonstrated good in vitro activity against community-

associated MRSA, but their activity against beta-hemolytic streptococci is not well studied. Clindamycin is active against both community-associated MRSA and beta-hemolytic streptococci, but variable MRSA clindamycin susceptibility levels and emerging resistance must be considered when choosing an empiric treatment for outpatient skin infections, particularly among pediatric patients.[3] The 2011 Infectious Disease Society of America practice guideline recommendations for nonpurulent superficial skin infections are summarized in Table 4.

Our study has at least 3 noteworthy limitations. The retrospective design limited the availability of patient demographics, risk factors for MRSA acquisition, and clinical presentation (purulent vs nonpurulent lesions). Additionally, the number of isolates tested when stratified by region was small. Because clindamycin and trimethoprim-sulfamethoxazole resistance are relatively rare events, the small sample size may have reduced the ability to identify additional differences in regional antibiotic susceptibility patterns. Although the mechanism of resistance among Wisconsin clindamycin-resistant USA300 MRSA isolates is likely associated with the presence of the pSK41-like plasmid, this was not confirmed by laboratory analysis.

CONCLUSION

Consistent with national published data, USA300 MRSA is the predominately circulating MRSA strain associated with skin and soft tissue infections among Wisconsin outpatients. A small cluster of clindamycin-resistant isolates and 1 isolate determined to be resistant to both clindamycin and trimethoprim-sulfamethoxazole in 1 Wisconsin region demonstrate an antibiotic susceptibility pattern that is rare among community-associated MRSA isolates in national studies.

Overall resistance to non–beta-lactam antibiotics among Wisconsin USA300 MRSA isolates remains low and is comparable to findings in the national studies contributing to the 2011 practice guidelines. Local providers should continue to follow the 2011 practice guidelines released by the Infectious Disease Society of America for treatment of outpatient skin and soft tissue infections, but the emergence of resistance to these agents in at least 1 area of the state warrants further study. If history is a predictor, community-associated strains of MRSA will continue acquiring antibiotic resistance traits in its epidemic spread across the United States. Regional variation in antibiotic susceptibility must be monitored carefully through collaboration among private laboratory and public health partners.

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A Pilot Study of Herbal Medicine Use in a Midwest Latino Population

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ABSTRACT

Background: Herbal medicine use is common in the United States, especially in immigrant populations. Understanding of this plant use is incomplete, with significant gaps in the literature for people living in the Midwest, about the plant species used, and about how home herbal medicine use interacts with allopathic medicine.

Methods: This pilot project used a qualitative research approach (interviews and focus groups, convenience sampling) to explore this topic for Latin America immigrants living in Madison, Wisconsin.

Results: Eight interviews and focus groups consisting of 42 people yielded 199 minutes of audio recordings and the mention of 57 medicinal plants. These plants were obtained from gardens, relatives and friends (abroad and local), mail order, and local retail establishments. Retail sites sold fresh plants, dried plants, spices, foods, and packaged products, ranging from 20 to over 150 plant products per site. A preponderance of plants, especially in Latino-focused stores, was food that also served a medicinal purpose. Participants mentioned 35 distinct health and disease categories for which herbal medicines were used, and sometimes, but not always, discussed plant use with their health care provider. When compared with likely Latin binomial taxonomic names, clinically relevant confusions with the use of common plant names also were identified.

Discussion: Overall, the findings presented illustrate the complexities surrounding herbal medicine use and create a case for future work to involve other demographics, and focus on botanical identification, the quantification of disclosure rates, and the development of educational interventions for physicians and patients.

INTRODUCTION

Herbal medicine, variously defined as "herbs," "plant medicines," or "botanical medicines"[1] is a common treatment throughout the world. It is estimated that 80% of people rely on traditional medicine, which is mostly herbal medicine, to meet their primary health care needs.[2,3] In the United States, the use of complementary and alternative medicine (CAM), one component of which is herbal medicine, is common. For example, recent estimates are that approximately 20% of the US population regularly uses herbal medicine.[4,5] The prevalence of herbal medicine use by some ethnic and cultural groups in the US may be even higher; one meta-analysis found that 4% to 100% (mean 30%) of Latinos living in the United States regularly used herbal medicine.[6] A possible explanation for the wide prevalence range in that meta-analysis is a diversity of research methodologies, including geographic location, study size, and demographics of study participants.

In addition to the challenges of interpreting the pooled Hispanic herbal use data as mentioned above, the published literature has omissions that compromise the applicability and relevance of the research for clinicians, patients, and researchers. For example, Latino herbal medicine use in the Midwest is a relative unknown; of the articles in 2 recent reviews,[6,7] only 4 originated from the Midwest (3 in Illinois, 1 in Ohio). In addition, although several nationwide surveys have yielded data about the use of herbal medicines by Latinos that may be relevant to the Midwest, the authors of one of these reviews found significant regional variation in prevalence data and difficulties in extrapolating between regions;[6] their recommendation was for more regional surveys in order to more accurately understand this topic. Furthermore, herbal surveys may or may not address the source of plants, relevant to safety concerns given some recent reports of herbal adulterations from suspect sources; the source of herbal knowledge; or a complete list of plants being used in a given community. With respect to the latter, commonly only a subset of herbal remedies is reported by researchers (for example, "most common herbal remedies"[8]), though a complete list may be the most informative for clinicians and patients.

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Table 1. Focus Group Questions in English and Spanish

Questions in English	Questions in Spanish
Which plants, herbs, etc do you use for medicinal purposes?	¿Usan Uds cuales plantas (hierbas, etc) para curarse?
For which medical problems?	¿Para cuales enfermedades?
How often?	¿Las usan a menudo, raramente, de vez en cuando…?
Who taught you? (no names, just "friend," "mother," "herbalist," etc)	¿Quién les enseñó a Uds. como usar las plantas? (sin nombres, sólo "amigo," "madre," "curandero," etc"
Where do you obtain the plants?	¿Dónde las consiguen?
Do you tell your physician about this use?	¿Si las usan, le informan a su médico que las están usando?

This study was designed to begin the process of addressing some of the shortcomings mentioned above in the Latino herbal medicine literature by studying 1 Midwestern community (Madison, Wisconsin). The primary aims were: (1) to compile a comprehensive list of plants used for medicines (common names), (2) determine the diagnoses for which plants were being used, and (3) document the sources of plants (including retail sites) and plant knowledge. As a pilot study, the data collected is part of a larger research project meant to improve on the communication about and the safe and effective use of traditional herbal medicines in the context of the allopathic medical system.

METHODS

This was a qualitative research project, utilizing individual interviews and focus groups, as well as a visual survey of herbal medicine retail outlets in Madison, Wis. Madison has an estimated population of 239,901, with 6.8% of the population self-designated as Hispanic or Latino, most commonly from Mexico or Puerto Rico.[9] There are several Latino-focused community organizations which, combined with knowledge of the Latino community by 2 of the authors (PTG, DK), were used initially to identify study participants for the interviews and focus groups.

Individual interviews and multi-person focus groups

Individual interviews and focus groups were held between August, 2012, and February, 2013. Inclusion criteria for participation in this research project were any adult (age 18 and older) Latino community members interested in or using (past or present) herbal medicine for personal or professional purposes. Gender, race, health concern, or treatment status were not considered when selecting participants for this study. A convenience sampling of individuals with interest and experience in herbal medicine was used to locate initial study participants; this approach was in line with other herbal medicine use surveys. As mentioned above, the initial identification of research participants occurred through Latino community organizations and Latino community members. Additional participants were identified through "snowballing," a reference to the query of participants if they might be able to suggest other potential research participants.

Interviews and focus groups were conducted in Spanish by one of the authors (DK) who is fluent in both Spanish and English. An attempt was made to schedule numerous people for a few set focus group times, though sometimes only 1 person would attend the session (a de facto individual interview) or a study participant requested a time and place that suited their availability but no one else's. The introduction to both the interviews and focus groups included a statement of the project's purpose, which was to explore the use of any and all plants for healing, and that the discussion would focus on the individual's own herbal medicine use. In addition, it was requested that neither sensitive personal information nor any secret "family recipes" relevant to herbal medicine preparation be shared. These safeguards were put in place to protect the individuals and their intellectual property. Furthermore, if the conversation veered onto the topic of plants used while living abroad (by the participant or their families), the discussion was redirected to a US focus; plants used while living in other countries or knowledge about plants used abroad were not included in the summaries for this project. A list of the questions and topics for the focus groups in English and Spanish is provided in Table 1.

With permission, audio recordings were made of the focus groups, although in 1 case, due to the large group size and deemed difficulty in transcribing the recording, only written notes were taken. None of the individual interviews were recorded. In accordance with the University of Wisconsin Institutional Review Board exemption granted this project, participants remained anonymous and an extensive series of steps were taken to maintain strict confidentiality and human subjects protection. The audio recordings were heard only by the lead researcher (DK) and a professional transcription service used previously by the University of Wisconsin Department of Family Medicine. After transcription, the audio recordings were destroyed, and were not used for any presentations or professional meetings.

Focus groups and interviews continued to be scheduled until it became clear to the lead researcher (DK) that saturation was reached. Saturation of the data collected for this project was apparent by failure of subsequent meetings to yield new plant species, new retail outlets, novel herbal medicine uses, or a unique approach to learning about herbal medicines.

Transcriptions and written notes were reviewed to identify

Table 2. Summary of 3 Aspects of Herbal Medicine Use From 8 Focus Groups in Madison, Wisconsin

Number of Attendees	Number of Plants Mentioned	Source(s) of Plants	Source(s) of Information
4	11	Grocery stores, sent from abroad, pharmacies, mail order from US companies, *tiendas*	Internet; family
1	6	Sent from abroad, plant nurseries, grocery stores	Herbalist abroad
4	19	Sent from abroad, mail order from US companies, natural areas	Family, television
1	4	Pharmacies	General knowledge from home country
1	4	Home gardens; mail order from US companies	General knowledge
5	14	Gardens	General knowledge, HCPs, family,
3	25	Sent from abroad, grocery stores, *tiendas*	Herbalists, internet, books
23	27	Grocery stores, *tiendas,* home gardens	Family, reading, friends

any plant used by study participants while living in the United States and mentioned as having medicinal use. Herbal medicine and medical literature[10-14] were used to find a likely English common name and a Latin binomial name for some of the highly mentioned plants and their Spanish common names. When there was ambiguity in the literature about the identification of a plant based on its Spanish common name, alternative possible Latin binomial names were noted. Transcriptions and written notes also were reviewed for sources of herbal medicine information and plant material, as well as health conditions for which the plants were used. The latter information included any symptom, health condition, or mechanism of action. When the herbal medicine use was vague, an attempt was made during the focus groups to clarify the use to a more specific symptom or medical condition. Any mention of a health care provider (HCP) in the transcripts or written notes was explored for themes about disclosure of herbal medicine use, including how that decision was made, as well as when disclosure did or did not happen.

Survey of retail outlets

During preliminary community discussions in preparation for this project, the researchers realized that retail outlets served an important purpose with respect to procuring medicinal plants for personal consumption. For this reason, retail sites that stocked plants of medicinal importance to the Latino community were surveyed. Such outlets were located through several methods: mention by community members or study participants, local clinicians' knowledge about the Madison area, and internet searches using the terms "Madison, Wisconsin," "herbal medicines," "Latino," "Hispanic," or any combination thereof. These sites were visited in person between July, 2012, and January, 2013. Each site was visited by at least 1 member of the research team. The researcher(s) introduced themselves to the store owner(s) or employee(s), distributed business cards and a description of the project in English and Spanish, and asked for permission to inspect any plant products as well as take pictures or revisit the site should future questions surface. Retail products were inventoried based on their potential uses as medicines, including foods with medicinal uses in the Latino community, dietary supplements, and topical treatments. The "food as medicine" products included any ingested fresh or dried spices, herbs, fruits or vegetables used for cooking or food consumption. "Dietary supplements" included both non-culinary herbs that are ingested whole, powdered, or as teas, tablets, or capsules, and purified compounds used as supplements. "Topical treatments" consist of any product that is applied to the skin. The total number of products in each of the categories for each of the retail sites was recorded.

RESULTS

Three individual interviews and 5 focus groups were held, comprising a total of 42 study participants and 199 minutes of audio recordings. Table 2 summarizes the total plant species mentioned during each meeting; depending on the meeting, 4 to 27 plants were listed by study participants. These plants were procured most often from grocery stores, mail order from US companies, pharmacies, home gardens, and specialized grocery stores selling Latin American foods and other products (*tiendas*). Family members were the most common source of information for study participants.

A compilation of plants mentioned by study participants is presented in Table 3. Only the Spanish common plant name is listed, the direct form of the information from focus group and interview transcriptions and written notes. Fifty-seven different plants were mentioned in the 8 meetings. As is evident in the table, some plants, such as *manzanilla* or *hierba buena* were mentioned in most, if not all, meetings. Other plants, such as *árnica, maca* or *uña de gato* were discussed in only 1 meeting.

Study participants mentioned many symptoms and health conditions for which they used herbal medicine, which is detailed in Table 4 for those symptoms or conditions with more than 1 plant treatment. The symptoms or conditions for which the most herbal medicines were used were diabetes, gastritis, hyperlipidemia, hypertension, indigestion, pain, stomachache, and upper respiratory tract infections. Medicinal plants mentioned but only used abroad were excluded from Table 4, as were plants mentioned as being "medicinal," but without specified use(s) (*borraja, malva, estafiate, hierba mora, jamaica,* and *té verde*). For the symptoms or conditions mentioned in Table 4, plants were used in some cases for both prevention and treatment, the distinction of

which is not made in the presentation of the data. Also excluded from Table 4 were the few medical conditions with only 1 herbal treatment. These were usually mentioned by just 1 study participant and included alphabetically by Spanish common names (English) *alpiste* (canary seed) for obesity, *calendula* (calendula) for bruises, *jengibre* (ginger) for depression, *linaza* (flax) to "*limpiar el sangre*" (clean the blood), *llantén* (plantain) for fractures, *manzanilla* (chamomile) to foster childbirth, *orégano* (oregano) for menstrual cramps, *ruda* (rue) for lice, *sábila* (aloe vera) for good luck, *sábila* (aloe vera) for hair loss, *uña de gato* (cat's claw) for cancer, and *yuca* (cassava) for alcoholism.

The results of extrapolation from Spanish common names to likely English common name(s) and Latin binomial name(s) is found in Table 5. This analysis was done for only a few of the plants, those with concrete botanical taxonomic information in the literature, in order to illustrate a range of the published data that exists for herbal medicine nomenclature. For some plants (ie, garlic, ginger, green tea), there is only 1 species corresponding to a given common name, negating the chance for obfuscation. In other cases, a Spanish common name could refer to 1 of several different plants (*árnica, canela, estafiate*), or there might be 2 Spanish common names for 1 plant (*paico* and *epazote* both likely refer to *Dysphania ambrosioides*). The possible clinical significance of this is discussed below.

The disclosure of herbal medicine use by study participants to their HCPs was complex. Rather than a simple "yes" or "no," participants discussed some treatments with their HCP, but then decided to withhold disclosure about other herbal therapies, at times due to the HCP's lack of knowledge or respect about the topic in an earlier encounter. In addition, participants of 1 focus group mentioned that disclosure depends on the perceived medical condition; colds and flus, for instance, were treated at home with herbal medicines, primarily because the allopathic options available were deemed ineffective.

The retail outlet survey of the city of Madison located 10 establishments with herbal medicine products or raw materials for sale (designated at A-J in Figure 1). This number included grocery stores mentioned by study participants as having foods that they purchased and used as medicines. An example of one such food mentioned is *nopal* (prickly pear cactus, *Opuntia* spp), a typical food in Latino culture, but also a plant that serves to lower serum glucose[15] (Figure 2). Eight of the retail outlets (A-H) clearly had a Latino focus with most or all signage in Spanish, and were referred to by study participants as *tiendas*. Two retail outlets (I and J in Figure 1) could be considered as specialty herbal medicine stores, with a significant portion of their space dedicated to herbal medicines and dietary supplements. The product offering of these 2 stores included hundreds of products, but, for the purpose of comparison with the other retail outlets, was arbitrarily designated as 150 in Figure 1. These 2 sites were mentioned by

Table 3. Medicinal Plants Mentioned by Study Participants as Compiled From Focus Group and Interview Results

Plant	Focus Group or Interview Number							
Spanish name	1	2	3	4	5	6	7	8
Ajo	X					X	X	X
Albahaca								X
Alpiste			X					X
Anís							X	X
Apio			X				X	X
Árnica					X			
Avena			X				X	
Berenjena							X	
Borraja				X				
Calendula								X
Canela	X		X					
Cebolla			X					X
Chia								
Clavo			X				X	X
Cola de caballo						X	X	
Echinacea			X					
Elote						X		X
Epazote			X					
Espino blanco	X							
Estafiate	X							
Eucaliptus		X		X			X	X
Flor de azahár						X		
Gordolobo	X		X					
Guisazo de caballo						X		
Hierba buena	X	X	X		X	X	X	X
Hierba de perro								X
Hierba de sapo	X	X						
Hierba luisa						X	X	
Hierba mora								X
Hoja de la suerte						X		
Jamaica								X
Jengibre								X
Jugo menonita	X							
Laurel								
Limón		X	X					
Linaza							X	X
Llantén							X	X
Maca							X	
Malva				X				
Manzanilla	X	X	X	X	X	X	X	X
Mastuerzo							X	
Menta	X		X			X		
Nopal		X	X		X			
Orégano	X					X	X	X
Paico								X
Papa							X	
Papaya								X
Pepino								X
Piña			X					
Remolacha							X	
Ruda			X					X
Sábila			X			X	X	X
Té verde							X	
Tilo						X		
Uña de gato								X
Uva			X					
Yuca							X	

The 57 medicinal plants mentioned by study participants are listed in alphabetical order by common name. ("X" indicates a mention of that plant in a given focus group).

Table 4. Herbal Medicine Used for Symptoms or Health Problems, as Reported by Focus Group Participants

Use (Alphabetical by Symptom or Health Problem)	Common Spanish Plant Names (and English, if Easily Identifiable)
Anxiety (for "nerves")	tilo (linden), valeriana (valerian)
Cardiovascular disease prevention (for "circulation," for "heart")	ajo (garlic), apio (celery), espino blanco
Colic (childhood)	anís (anise seed), manzanilla (chamomile), orégano (oregano)
Cough	ajo (garlic), cebolla (onion), echinacea (echinacea), eucalipto (eucalyptus), hierba buena (peppermint)
Dermatitis (including "skin problems" and sunburn)	llantén (plantain), mastuerzo, sábila (aloe vera)
Diabetes	albahaca (basil), alpiste, apio (celery), berenjena (eggplant), hierba del sapo, jugo meninito, nopal (prickly pear)
Earache	ajo (garlic), ruda (rue)
Edema and swelling	llantén (plantain)
Gastritis (including *H pylori* and "ulcers")	ajo (garlic), hierba buena (peppermint), jengibre (ginger), limón (lemon or lime), menta (spearmint), nopal (prickly pear cactus), sábila (aloe vera)
Headache (including migraine)	hierba buena (peppermint), papa (potato)
Heartburn	hierba buena (peppermint), menta (spearmint)
Hepatitis	hierba del sapo, sábila (aloe vera)
High blood pressure (including hypertension, and a diuretic action)	ajo (garlic), alpiste, apio (celery), espino blanco, hierba del sapo, pepino (cucumber), remolacha (beets), sábila (aloe vera)
High cholesterol	alpiste, berenjena (eggplant), chia (chia), hierba del sapo, linaza (flax)
Indigestion (or to help with digestion, including gas)	anís (anise seed), hierba buena (peppermint), jengibre (ginger), manzanilla (chamomile), boldo, menta (spearmint), nopal (prickly pear), orégano (oregano), papaya (papaya), sábila (aloe vera)
Insomnia	manzanilla (chamomile), menta (spearmint), orégano (oregano)
Kidney stones	cola de caballo (horsetail), pelo de elote (corn silk), sábila (aloe vera)
Pain (including joint pain, rheumatism)	ajo (garlic), camphor (camphor), llantén (plantain), maca, ruda (rue), uva (grapeseed oil)
Sore throat	eucaliptus (eucalyptus), limón (lemon juice), miel de abeja (honey)
Stomachache	anís (anise seed), epazote (wormseed), gordolobo (mullein), hierba buena (peppermint), hierba del perro, manzanilla (chamomile), orégano (oregano), paico (wormseed)
Toothache	calendula (calendula), canela (cinnamon), clavo (clove)
Upper respiratory tract infections (including sinusitis, colds, flu, bronchitis, phlegm)	ajo (garlic), canela (cinnamon), eucalipto (eucalyptus), ganoderma (reishi), laurel (laurel), orégano (oregano), sábila (aloe vera)
Wounds	arnica (arnica), calendula (calendula), cebolla (onion)

Table 5. Selected Herbal Medicines Mentioned by Study Participants

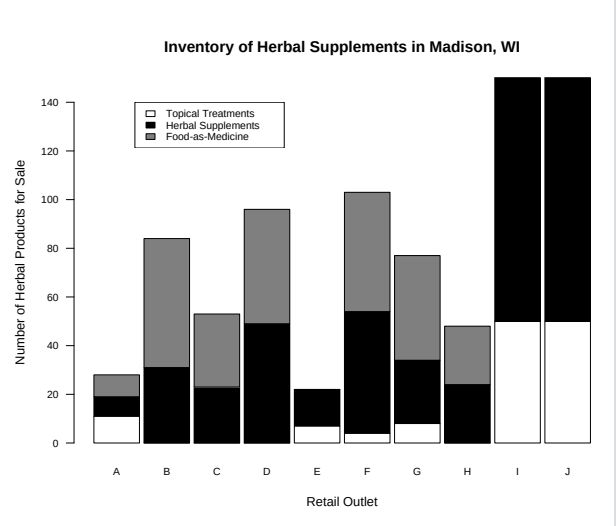
Spanish Name	English Name	Latin Binomial Name for Likely Plant	Alternative Plants (as Latin Binomial Names) for a Given Spanish Name
Ajo	Garlic	*Allium sativum*	N/A
Árnica	Arnica	*Arnica montana*	*A fulgens, A chamissonis*
Canela	Cinnamon	*Cinnamomum cassia*	*Cinnamomum verum*
Echinacea	Purple coneflower	*Echinacea purpurea*	*E angustifolia, E pallida*
Epazote	Wormseed, wormwood	*Dysphania ambrosioides*	*Chenopodium ambrosioides*
Estafiate	Wormwood	*Artemesia spp*	*A absinthium, A annua, A maritima, A pontica*
Jengibre	Ginger	*Zingiber officinale*	N/A
Hierba buena	Peppermint	*Mentha x piperita*	*Mentha spicata*
Manzanilla	Chamomile	*Matricaria recutita*	*Chamaemelum nobile*
Menta	Spearmint	*Mentha spicata*	*Mentha x piperita*
Paico	Wormwood	*Dysphania ambrosioides*	*Chenopodium ambrosioides*
Sábila	Aloe	*Aloe vera*	*Aloe barbadensis* (synonym)
Té verde	Green tea	*Camellia sinensis*	N/A
Uña de gato	Cat's claw	*Uncaria tomentosa*	*U guianensis*

Herbal medicines listed alphabetically by Spanish common names, with corresponding likely English and Latin binomial names. The last column lists alternative plant species (listed by Latin binomial names) corresponding to a given Spanish common name.

study participants, but did not appear to have a Latino focus; rather, they are important sources of herbal medicines for the Madison community as a whole and offer little, if any, literature or advertising in Spanish. Another clarification necessary is about retail outlet "E." This was a nationwide pharmacy with 1 branch in Madison that stocked herbal products clearly marketed toward Latinos; these products were located in a separate section and were labeled in Spanish. For "E", the herbal products in the separate section were the products counted and included in Figure 1, not the multitude of dietary supplements, nor the herbal lotions, creams, or shampoos that are also found in such large, conventional pharmacies.

In addition to a range in number of herbal products offered for sale, Figure 1 shows that each retail outlet sells a unique proportion of topical treatments, herbal supplements, and food-as-medicine plants. For the Latino-focused sites (A-H), an average of 4.7% of products sold were topical treatments, 43.1% were herbal medicines, and 52.1% were food-as-medicine plants (Figure 3).

Figure 1. Number and Category of Herbal Products Sold for Latino Herbal Medicine Retail Outlets in Madison



DISCUSSION

A complete description of the factors involved in herbal medicine use is complex, as evidenced by some of the findings of this pilot research study. With respect to the diversity of plants being used for medicinal properties, Latinos in Madison mentioned 57 plants as being useful for 35 distinct health conditions. Some of those plants are foods, some are spices, and some are plants used only for their specialized healing properties. It was beyond the scope of this pilot project to identify the plants to their established Latin scientific name, but that is an important next step in eliminating the confusion that exists, and which was illustrated in the results present here, in communication about herbal medicine that is based solely on common names.[16] Few studies have used dried plant specimens deposited in an herbarium to definitively identify plants from their common name;[17,18] this could be a model for future research efforts on this topic. Nonetheless, the large number of plants mentioned by study participants in this project is an important addition to the literature; most other Latino herbal surveys provide detail on only 10 to 20 plants.[6,7]

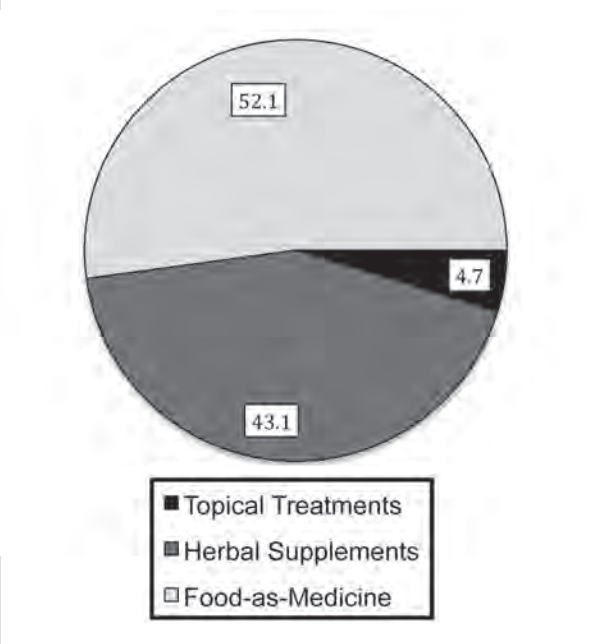
Comparison to Other Studies

Expanding on the 4 prior Midwestern Latino herbal surveys,[19-22] this study provides information about Wisconsin, offers information about more plants, and takes a broader view of herbal medicine use in a given community. As a comparison, one of the prior Midwestern studies interviewed 26 customers of an herbal store in Chicago, documenting the use of 12 medicinal plants, some of which overlapped with the results from this project.[19] Two of the other herbal use studies were surveys of women living in Chicago, 30 in "midlife,"[20] and 56 who were peri- or postmenopausal.[21] Again, these 2 studies documented plants similar

Figure 2: Prickly Pear Cactus

Prickly pear cactus pads, called nopal in Spanish, are from the genus *Opuntia spp.* This typical food in Latino culture is used to treat diabetes; some studies do show that it helps to lower serum glucose. *(Photo credit: David Kiefer)*

Figure 3. Average Percentage of Products in the 3 Herbal Medicine Categories for 8 Latino-focused Stores (*tiendas*) in Madison, Wisconsin



to those in the current study, while the latter also found a reliance on herbal information from friends and family, in agreement with these Madison results. Finally, an Ohio study in 20 people with diabetes found that 8 were using herbal medicines.[22] That diagnosis-specific survey was a different approach than this study's attempt to more broadly survey a community about herbal use. Some experts posit that a local focus on herbal medicine use research has scientific merit.[6] Their assertion is that such research, rather than large, national surveys, provides a more accurate view of herbal medicine use, with more specifics about sourcing and preparation, and provides "qualitative insight into herb use trends." As much as this Madison project accomplishes that goal, the small, pilot nature of this study and some of the study limitations detailed below prohibit drawing concrete conclusions or comparisons between other regions or survey results.

Herbal Medicine Sources

With respect to herbal medicine sourcing, the results of this community survey found that, in addition to gardens, sources abroad, and mail order, retail sites are one of the places where Latinos obtain herbal medicines in Madison. Several types of retail outlets exist, offering a variety of herbal products, and dozens of plant products are available for sale, demonstrating a robust herbal medicine culture in Madison. It was outside the scope of this project to do a comprehensive survey of home or community gardening, though these were mentioned by study participants as important sources of herbal medicines, especially during the summer months. A collaboration with community gardens to explore this aspect of plant use would a valuable offshoot of these research results.

Plant Identification

Another finding is that the reliance on common plant names causes the possibility of confusion in the use of some herbal medicines. Without collection of plants in an adequate form for taxonomic identification in an herbarium, it is difficult to know definitively that *epazote*, for instance, is a specific species of *Artemesia*; the several species of *Artemsia* listed in Table 4 have unique physiological effects that could have clinical significance.[11] Another example is cinnamon, or canela, commonly used for diabetes. It could be 1 of 2 species, though the most studied and likely to have hypoglycemic effects is Cassia cinnamon (*Cinamomum cassia*).[23] Although there is conflicting research about Cassia cinnamon's effects, some studies show additive effects with a patient's hypoglycemic pharmaceuticals; a HCP would want to know which and how much of a particular cinnamon product their patient with diabetes might be taking and provide appropriate counseling. Several other plants listed in Table 4 could have this clinically relevant confusion, making a case for a Latin binomial focus of HCP plant discussions and product labeling. Along these lines, future projects should attempt to identify, through herbarium specimens if possible, the plants listed in Table 3.

Food as Medicine

A final element of this study that carries significant clinical relevance is the prevalence of "medicinal" food plants. Though this was not one of the original primary aims of this study, the preponderance of medicinal plants that are also foods or spices further supports the importance of dietary discussions between clinicians and patients. Given that over half of the plants sold by Latino *tiendas* in Madison are food plants (Figure 3) and the physiological significance of many foods and spices (as referenced above), this study underscores the clinical relevance of food-as-medicine discussions with Latino patients.

Study Limitations

There are several limitations to this study that limit the generalizability and internal validity of the results, much of which is due to the fact that this is a small pilot research study using a convenience sampling methodology. One avenue of future exploration that would allow calculation of prevalence of herbal medicine use and more definitive comparison with other surveys would be an expansion of data collection through community-wide surveys. Another limitation is that this study relied on self-reported herbal use, leading to data unreliability. For example, although the physician conducting the interviews and focus groups was not the personal physician of any of the study participants, an

inherent distrust of allopathic HCPs for a variety of reasons, a reluctance to share personal information about herbal use, or simply forgetting some of the plants used recently could have affected the data collected. The selection bias of herbal users to be interviewed further limits the generalizability of these results; again, an argument for follow-up surveys to accurately determine herbal use prevalence and expand on the project's other data.

Nondisclosure

Some of the study participants mentioned when they do or do not disclosure their herbal medicine use to their HCP. The limitations of the study methodology prohibit drawing firm conclusions from these reports, but lack of disclosure is concordant with some important published work that documents significant nondisclosure rates of herbal use to primary care providers.[24,25] Future research efforts to further understand this nondisclosure may lead to safer herbal use; if patients and HCPs communicate about herbal medicines, perhaps adverse plant-pharmaceutical interactions or the use of unsafe plants or dosages can be avoided.

Summary

Overall, the results of this pilot study, even with its methodological limitations, illustrate an extensive culture of herbal medicine use amongst Latinos in Madison. This culture involves a broad network of information and plant sources, and plants that include foods and spices. Several extensions of this data for future research projects are suggested to provide the herbal medicine detail necessary to further advance clinical applicability.

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A Case of Late-onset Segmental Neurofibromatosis

Heather McLimore, MS; Cort McCaughey, MD; Erin Vanness, MD

ABSTRACT

Segmental neurofibromatosis (NF5) is a rare variant of neurofibromatosis. To our knowledge, there have been few reports of cases presenting later in life. The recognition of NF5 is important, as there have been reports of paraneoplastic manifestations and transmission to offspring. Here we present the case of a patient who presented with NF5 first appearing in her mid-50s. This case illustrates the subtle nature of NF5, which often leads to misdiagnosis.

INTRODUCTION

Segmental neurofibromatosis (NF5) is a rare variant of neurofibromatosis (NF) with cutaneous lesions typically limited to one body region, and an absence of systemic complications in the majority of patients.[1,2] The median age of onset is 28 years in men and 27 years in women.[2] The clinical findings can be subtle, and therefore NF5 is often under- or misdiagnosed. This is an important clinical variant of NF to recognize, since offspring of patients with this condition are at risk of developing NF1, with the possibility of developing oculocutaneous lesions, bony abnormalities, seizures, and learning difficulties.[1-4]

CASE PRESENTATION

A 59-year-old white woman was seen in dermatology clinic for evaluation of small skin-colored bumps on her right shoulder that had been present for approximately 4 years (Figure A,B). The lesions were completely asymptomatic, but she was bothered by their cosmetic appearance. She had no family history of similar lesions and reported no history of skin lesions in her children.

A skin exam revealed firm, grouped skin-colored papules 3-10 mm in size, with a positive buttonhole sign (easy manual invagination of lesion) in a dermatomal distribution on the right shoulder. She did not have any other ocular, bony, or cutaneous features of type I neurofibromatosis, including Lisch nodules, kyphoscoliosis, diffuse or plexiform neurofibromas, café au lait macules or axillary/inguinal freckling.

There is a fairly narrow differential diagnosis for segmental cutaneous neoplasms (Table), and given the clinical appearance of her lesions, our clinical suspicion for segmental NF was high. Despite this, a biopsy of one of the lesions on the shoulder was obtained. Histologic examination of the tissue by a dermatopathologist demonstrated spindle and s-shaped cells within a delicate stroma. There was no significant atypia or melanocytic proliferation identified. These findings were consistent with a neurofibroma.

DISCUSSION

Segmental neurofibromatosis most commonly presents as isolated and unilateral neurofibromas occurring in a cervical distribution, although there are other rare variants.[2,4] It is considered a non-inherited form of NF caused by a post-zygotic mutation resulting in mosaicism. If mosaicism is present within gonadal cells, it is possible that a person with NF5 can have offspring with generalized NF.[4,5]

This disease is interesting in that the clinical picture can provide insight into which particular somatic cell lines harbor the mutation. For example, patients with manifestations limited to only neurofibromas are thought to have the mutation in Schwann cells, explaining why neurofibromas occur in a dermatomal distribution. Patients with only pigmentary manifestations are thought to have the mutation in fibroblasts, explaining the blaschkoid distribution of café au lait macules in NF5.[6]

In contrast to NF, systemic complications including ophthal-

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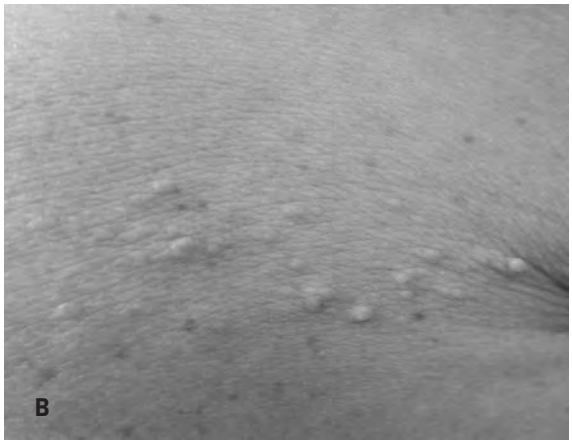
Figure. Dermatomal Distribution



Lesions on right shoulder (A); close-up examination of segmental neurofibromas (B).

mologic involvement and neurological complications are rare in NF5.[1,4,7,8] Recently there has been speculation that the incidence of malignancy in patients with NF5 may be comparable to those with NF1, and therefore, age-appropriate malignancy screening is indicated.[7-9]

CONCLUSION

Segmental neurofibromas or café au lait macules should prompt further evaluation with complete history and physical examination and dermatology consultation to ensure that patients do not have more generalized disease consistent with NF1. Genetic counseling and evaluation of offspring for NF skin lesions or cognitive impairment is also advisable given the small risk of transmission to offspring. Patients should be followed-up to monitor for disease progression and to screen for systemic complications seen in NF1.

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Table. Clinical Differential Diagnosis of Dermatomally Distributed Nodules[a]

Infection	
	Syphilis
Neoplasm	
	Benign: Syringocystadenoma papillerferum, Trichoepithelioma Malignant: Basal cell carcinoma, squamous cell carcinoma, lymphoma, plasmacytoma, cutaneous metastases
Other	
	Granuloma annulare, neurofibromatosis type I, pseudolymphoma, rheumatoid nodules, sarcoidosis, xanthomas

[a]Adapted from Hager et al.[2]

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Neurocysticercosis in Wisconsin: 3 Cases and a Review of the Literature

Elie Naddaf, MD; Susanne K. Seeger, MD; Carl E. Stafstrom, MD, PhD

ABSTRACT

Neurocysticercosis is the most common parasitic infection of the brain. Endemic in many regions of the world, neurocysticercosis is now showing up in nonendemic areas such as Wisconsin. We present 3 patients that illustrate features typical for neurocysticercosis in a non-endemic area, including immigrant/travel status, presentation with focal seizures, classic magnetic resonance imaging features of single enhancing lesions, and good response to treatment with anticonvulsants, anti-inflammatory agents, and cysticidal drugs. It behooves physicians involved in the care of at-risk populations to be aware of the clinical features, radiographic signs, diagnostic tests, and general principles for treating neurocysticercosis.

INTRODUCTION

Neurocysticercosis (NCC), the most common parasitic infection of the brain, is caused by ingestion of eggs the tapeworm *Taenia solium.*[1,2] NCC is endemic in the developing countries of Central America, South America, and parts of Africa and Asia, including India. NCC is a major cause of epilepsy in these endemic areas, where 25% to 40% of patients with new-onset epilepsy have evidence of NCC. At the same time, reported cases of NCC are increasing in the United States (especially in southwestern states) and other developed countries, especially among immigrants from endemic areas.[3] Here we report 3 cases of NCC that presented to our institution over the past few years, and review the epidemiology, life cycle, clinical presentation, diagnosis and treatment of NCC, to increase awareness of this disease among clinicians in nonendemic areas.

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CME available. See page 79 for more information.

CASE PRESENTATION

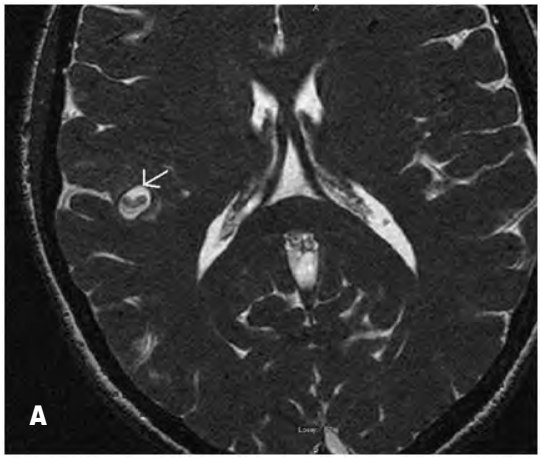
Patient 1

A 25-year-old woman presented with 3 focal seizures consisting of episodes of left jaw deviation and left eyelid and tongue twitching, plus chronic right-sided headache. She moved to Wisconsin from the Philippines 2 months prior to presentation. On examination, she had no focal neurological deficits. Brain magnetic resonance imaging (MRI) scan showed a 6 mm ring-enhancing lesion located superficially in the right frontal lobe adjacent to the motor strip. Electroencephalography (EEG) was unremarkable. Serum and cerebrospinal fluid (CSF) cysticercosis IgGs were negative by western blot of CSF and enzyme-linked immunosorbent assay (ELISA) of serum. The clinical diagnosis of NCC was highly suspected. The patient was given dexamethasone for 15 days followed by albendazole for 15 days. She also was started on levetiracetam for seizure prophylaxis. Two years later, she had an episode of left lip twitching after missing a few doses of levetiracetam. Otherwise, she has remained healthy and seizure free for the past 4 years. A follow-up MRI scan could not be obtained due to loss of insurance coverage.

Patient 2

A 38-year-old woman presented with intermittent left face, arm and leg dysesthesias, followed by a generalized tonic clonic seizure. She had moved from Mexico 14 years previously. On examination, there was decreased sharp perception on the left limbs with allodynia to cold and warm temperatures. At another facility, brain MRI scan showed a 16 x 8 mm ring-enhancing lesion in the right inferior frontal parietal area (Figure 1A). At the outside facility, a high suspicion for tumor resulted in 2 brain biopsies: one showed normal brain tissue and the second showed a mixed chronic inflammatory infiltrate with lymphocytes and eosinophils. When evaluated at our

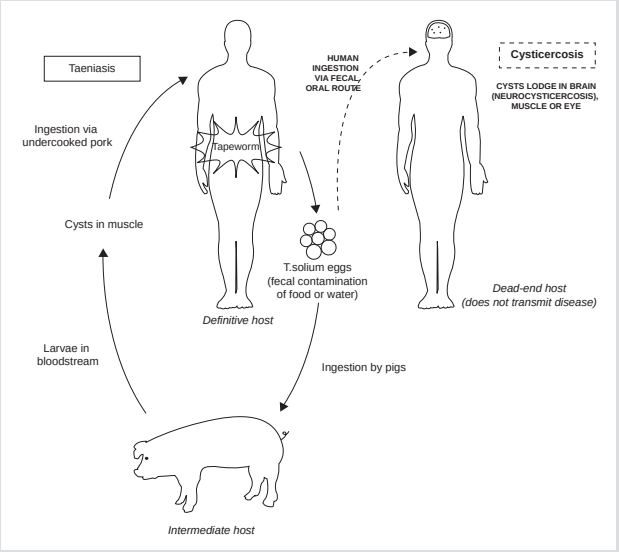
Figure 1. Brain Magnetic Resonance Imaging Scans of Patients 2 and 3



(A) Axial Sheath T1 with contrast of patient 2 showing ring-enhancing lesion with central T1 hypointensity in the right inferior frontal lobe. (B) Fast imaging employing steady state acquisition or FIESTA sequence of patient 3, showing sharply circumscribed cyst with complex internal structures (scolex).

hospital, NCC was suspected. Serum cysticercosis IgG was negative by ELISA. Per recommendation of an infectious disease consultant, she received a course of prednisone and 30 days of albendazole. Her dysesthesias were controlled by gabapentin and her seizures remain well controlled on lamotrigine 4 years after presentation. Follow-up brain MRI scan showed decreased size of the enhancing lesion.

Figure 2. Life Cycle of Pork Tapeworm, *Taenia solium*



Humans (definitive hosts) with adult tapeworm infection (taeniasis) excrete proglottids/eggs, which are ingested by pigs. Pigs (intermediate hosts) ingest tapeworm eggs or gravid proglottids from infected soil or vegetation. In pig intestine, eggs (oncospheres) hatch into larvae. Larvae invade intestinal mucosa, spread hematogenously to reach tissues such as muscle, brain, or eye, where they encyst as mature cysticerci. If eggs are ingested by humans via undercooked pork, they will get taeniasis – active tapeworm infection – completing the life cycle. Alternatively, humans can incur cysticercosis if they ingest tapeworm embryonated eggs via fecal-oral route. Oncospheres hatch in intestine, circulate to muscle, brain, or eye. In brain, larvae become cysts (cysterici), and the disease is called neurocysticercosis.

Patient 3

A 23-year-old woman presented with episodes of left arm dysesthesias described as "thousands of raindrops rushing up and down my left arm," sometimes ascending into her left neck and face, associated with numbness of the left arm and mild difficulty speaking and hearing. She also described chronic dull bilateral headaches for the year prior to presentation. She had traveled to Mexico multiple times, most recently 2 years prior. Her neurological examination was normal. Brain MRI scan showed a 9 x 12 mm ring-enhancing lesion in the right parietal lobe near the distal sylvian fissure with an internal soft tissue component within the cyst consistent with a scolex (Figure 1B). Cysticercosis serum IgG level by ELISA was 0.61 OD (>0.5 OD is considered positive). She was treated with prednisone and a 10-day course of albendazole, and was put on levetiracetam for seizure prophylaxis. She is doing well 8 years after initial presentation.

DISCUSSION

Epidemiology

In many areas of the world, NCC is endemic. In the United States, cases of NCC are increasing,[3,4] with estimates of about 1000 new cases annually.[5] NCC is not well known in Wisconsin,

Table 1. Diagnostic Criteria for Neurocystercosis[14]

Absolute Criteria
Histologic demonstration of parasite from biopsy of brain or spinal cord lesion
Cystic lesions showing scolex on CT or MRI
Direct visualization of subretinal parasites by fundoscopy
Major Criteria
Lesions highly suggestive of NCC by neuroimaging
Positive serum immunoblot for anticysticercal antibodies
Resolution of cystic lesions after therapy with albendazole or praziquantel
Spontaneous resolution of small single enhancing lesions
Minor Criteria
Lesions compatible with NCC by neuroimaging
Clinical manifestations suggestive of NCC
Positive CSF ELISA for anticysticercal antibodies or cysticercal antigens
Cysticercosis outside of CNS
Epidemiologic Criteria
Evidence of household contact with *T solium* infection
Individuals from areas where cysticercosis is endemic
History of frequent travel to disease-endemic areas

A definitive diagnosis requires 1 absolute or 2 major plus 1 minor and 1 epidemiologic criterion. A probable diagnosis requires 1 major plus 2 minor criteria, or 1 major plus 1 minor and 1 epidemiologic criterion, or 3 minor plus 1 epidemiologic criterion.
Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; NCC, neurocysticercosis; CSF, cerebrospinal fluid; ELISA, enzyme-linked immunosorbent assay; CNS, central nervous system; *T, Taenia*.

but as emphasized by our cases, health care professionals should be aware of this disorder. Of the 3 cases presented here, 2 patients are immigrants while the third patient is a Wisconsin native who traveled widely in endemic areas. A case of spinal intramedullary cysticercosis of the conus medullaris in an immigrant from Mexico previously was reported from our institution.[6]

Life cycle

The life cycle of the pork tapeworm *T. solium* is illustrated in Figure 2. Adult tapeworms consist of a scolex and numerous body segments called proglottids. The terminal proglottid contains thousands of eggs that are shed in carriers' stools. Cysticercosis is transmitted by the ingestion of *T. solium* eggs shed in the stools of a human tapeworm carrier (definitive host). Oncospheres (larvae or embryos) hatch in intestine of a pig or human that ingests them (intermediate hosts); the larvae invade the intestinal wall and disseminate hematogenously to other organs such as muscle and brain, where they mature into cysts (cysticerci) over several weeks. Cysticerci consist of a membranous wall filled with fluid and an invaginated scolex (head).

Humans who eat undercooked pork containing cysticerci can develop a tapeworm infection (taeniasis) but do not necessarily develop NCC. However, these individuals are at very high risk of autoinfection and resultant cysticercosis if they ingest tapeworm eggs through the fecal-oral route. Therefore, NCC is not acquired through eating undercooked pork but rather from oral-fecal transmission from definitive hosts shedding eggs in their stools. For example, an outbreak of NCC occurred in a non-endemic area of New York City when the parasite was transmitted by food workers (immigrants from endemic regions) infected with the tapeworm via the fecal-oral route.[7] Close contacts of a definitive host (who has taeniasis) are at risk for NCC. Humans with NCC (neurocysticercosis) are dead-end hosts and do not transmit the disease.

Clinical presentation

Clinical presentation of NCC varies depending on cyst localization, number, size, and stage. The most common presentation of NCC is seizures (75%),[8] followed by headaches (38%), focal deficits (16%), and signs of increased intracranial pressure (11%).[9] Up to 40% of new onset seizures in endemic regions are thought to be caused by NCC.[10] Seizures are typically focal but can secondarily generalize. The latency to presentation with seizures or other symptoms can be years. Focal seizures and dysesthesias were present in all of our patients.

NCC can be divided into 5 forms, according to the location of the lesion: parenchymatous, subarachnoid, intraventricular, spinal, and ophthalmic. Here we focus on the parenchymatous form, which is most common and affected each of our patients.

In the parenchymatous form of NCC, single or multiple cysticerci lodge in brain parenchyma as cysts or enhancing lesions. Three developmental stages of the cyst correspond to radiologic findings. First, the viable cyst stage consists of an invaginated scolex surrounded by translucent fluid and a membranous wall. There is little or no inflammation due to lack of host immune response, so minimal or no enhancement is observed on CT scan. The cyst may exist in asymptomatic form for months to years. The radiographic finding of a scolex within the cyst is pathognomonic for NCC.[11] In the degenerating cyst stage, fluid leaking from the cyst elicits an inflammatory response with enhancement on CT and MRI scans. Subsequently, further degeneration consists of larval decay, vesicle involution, and thickening of the vesicle wall. Finally, the calcified cyst stage comprises punctuate calcifications on CT scan and represents dead parasites.

Seizures are most likely to occur in the degenerating cyst stage, due to local direct pressure, inflammation, or edema, possibly exacerbated by a secreted substance such as cytokines that might alter ion channel function or network excitability.[12] Flares of edema surrounding otherwise inactive calcified lesions can also lead to seizures.[13]

Diagnosis

Diagnosis of NCC can be challenging, especially in nonendemic areas. History should emphasize residence in or travel to endemic areas in patients with an appropriate clinical presentation. Diagnostic guidelines for NCC are summarized in Table 1.[14]

Head CT scan is usually the first step in a diagnostic work-up.

The presence of a single enhancing lesion less than 20 mm, with a regular outline and no midline shift, is highly suspicious for NCC. CT findings change with developmental stage, as described above. MRI scans have higher resolution and can pick up small lesions, inflammation, and lesions adjacent to bone. Differential diagnosis of a single small enhancing lesion includes a primary or metastatic tumor, pyogenic or fungal brain abscess, toxoplasmosis, or tuberculoma.[15] It is critical to know the immune status of the patient in considering these possible etiologies. All of our patients were immunocompetent, human immunodeficiency virus (HIV) negative, and had not received a transplant.

Serology might be helpful when neuroimaging is nondiagnostic. Enzyme-linked immunoelectrotransfer blot (EITB) on serum is now the preferred laboratory method,[16] with a specificity of 100% and a sensitivity of 98% in patients with more than 1 cyst, though these values are lower in individuals with a single lesion; patients with only calcified lesions are often seronegative.[17] EITB is less widely available than ELISA, which has a lower diagnostic yield. Two of our patients were seronegative by ELISA and the diagnosis was suspected from clinical and radiologic findings. CSF studies are not helpful in most cases, though nonspecific abnormalities such as pleocytosis, elevated protein, and hypoglycorrachia have been reported.[18] Brain biopsy may offer a definite diagnosis but is not usually necessary. Of note, patient #2 underwent 2 brain biopsies searching for tumor, delaying the NCC diagnosis. This patient underscores the importance of recognizing the clinical signs and symptoms of NCC.

A reasonable diagnostic work-up for a patient presenting with a ring-enhancing lesion and seizures would include neuroimaging, EITB, toxoplasmosis serology, CSF gram stain and culture, HIV antibody testing, and tuberculosis testing. By the diagnostic criteria in Table 1, our patients #1 and #2 have probable NCC, while patient #3 has a definitive diagnosis. It is important to emphasize that although all of our cases had relatively good outcomes, NCC is not always benign, especially when multiple lesions are present.[2]

Treatment

The overall goals of NCC treatment are to prevent seizures, reduce inflammation, and reduce active cysts. A primary care provider can initiate an anticonvulsant drug and a neurologist can advise about subsequent treatment and drug discontinuation. The decision about cysticidal therapy is best made in consultation with an infectious diseases specialist.

Antiepileptic drugs

A patient with symptomatic NCC should be started promptly on an anticonvulsant. Seizures are usually controlled with a single agent. Phenytoin or carbamazepine is chosen most often, especially in developing countries, due to availability and low cost. Newer drugs such as levetiracetam or lamotrigine can be effective, as in our cases. Before tapering, some authorities recommend treatment for 2 years seizure-free or 6 to 12 months after radiographic resolution of viable/enhancing cysts. For children with a single small enhancing lesion, 1 year may be sufficient.[19] An abnormal CT scan with persistence of calcified lesions and an abnormal EEG are the most reliable predictors of seizure recurrence and should inform decisions about anticonvulsant tapering.

Anti-inflammatory treatment

Corticosteroids are used to decrease inflammation and edema, but a positive response is not pathognomonic as several etiologies of ring-enhancing cerebral lesion (see differential diagnosis above) may respond to steroids. Given the risk of exacerbating the host response after initiation of cysticidal therapy, corticosteroids are usually used as adjunctive therapy and should be given whenever cysticidal agents are used.[20] Steroids alone do not significantly improve outcome.[20,21] Treatment duration depends on disease burden.

Cysticidal agents

Accumulating data supports the use of cysticidal agents, especially in parenchymatous NCC, with the goal of treatment being elimination of active cysts. Recent evidence-based guidelines suggest that albendazole plus dexamethasone or prednisolone should be considered for patients with NCC, to reduce long-term seizure frequency and decrease the number of active lesions.[20,22] Concerns about the use of cysticidal agents include exacerbation of the inflammatory reaction causing more scarring and calcification, as well as uncertainty as to whether cysticidal agents alter the disease course. Of the two cysticidal agents most often used, albendazole and praziquantel, albendazole is better tolerated and interacts less with anticonvulsants.[23,24] There is no clear consensus about the duration of therapy, with 7 to 14 days vs 28 days shown to be equally effective. Patients with a large number of viable parenchymal lesions should be treated for a longer period. Treating single small enhancing lesions is controversial. Cysticidal drugs should not be used in patients with calcified lesions because the parasite is already dead. Again, consultation with an infectious diseases specialist is advised.

Prevention

As yet, there is no vaccine available for humans. Vaccination of pigs to control human *T solium* infection might be feasible. The mainstays of prevention are public awareness and education, careful hand hygiene, appropriate sanitation, and avoidance of undercooked pork and vegetables to reduce the prevalence of definitive hosts.[2]

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CME

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Quiz: Neurocysticercosis in Wisconsin: 3 Cases and a Review of the Literature

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be able to:

1. Raise awareness and index of suspicion of signs and symptoms of neurocysticercosis particularly in nonendemic areas.
2. Review the lifecycle of *Taenia solium* (tapeworm) with implications for preventive strategies.
3. Outline the components of a diagnostic workup for neurocysticercosis including absolute, major and minor criteria.
4. Summarize treatment strategies including the use of antiepileptic, anti-inflammatory and cysticidal agents.

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QUESTIONS

1. Which of the following is true?

   A. The most common presentation of neurocoystercosis (NCC) is seizures.

   B. Up to 40% of new onset seizures in endemic areas are due to NCC.

   C. Seizures are typically focal but can generalize.

   - ❑ A and B
   - ❑ A and C
   - ❑ All of the above

2. Which of these 3 diagnostic criteria fits the **absolute** criteria for neurocystercosis?
   - ❑ Positive serum immunoblot for anticysticercal antibodies.
   - ❑ Lesions highly suggestive of NCC by neuroimaging.
   - ❑ Cystic lesions showing scolex on CT or MRI.

3. Which is the preferred laboratory method for serum testing in suspected neurocystercosis?
   - ❑ EITB (enzyme-linked immunoelectrotransfer blot).
   - ❑ ELISA (enzyme-linked immunosorbent assay).

4. Humans who eat undercooked pork containing tapeworm cysts (cysticerci) can develop a tapeworm infection (taeniasis) but the ingestion of tapeworm eggs through the fecal-oral ingestion route is required to develop neurocysticercosis.
   - ❑ True
   - ❑ False

5. Of the two cysticdal agents used in treatment of neurocysticercosis which is better tolerated and interacts less with anticonvulsants?
   - ❑ Albendazole
   - ❑ Praziquantel

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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 E. Lakeside St, Madison, WI 53715 or fax to 608.442.3802. You must include your name, address, telephone number and e-mail address. You will receive an e-mail from wmj@wismed.org with instructions to complete an online evaluation. Your certificate will be delivered electronically.

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Michael C. Fiore, MD, MPH, MBA

Robert N. Golden, MD

The 50th Anniversary of the Surgeon General's Report on Smoking and Health

Robert N. Golden, MD; Michael C. Fiore, MD, MPH, MBA

Reflections and lessons to be learned for other public health challenges

January 11, 2014, marked the 50th anniversary of the first Surgeon General's Report on the Health Consequences of Smoking. That report represents one of the seminal public health events of the 20th century, documenting—for the first time—smoking as a cause of cancer, and concluding that this serious public health risk warranted "appropriate remedial action."

The release in January 1964 by Surgeon General Luther Terry is legendary. His team chose to distribute the report on a Saturday to minimize its impact on financial markets and maximize its dissemination potential—it was front-page news in virtually every Sunday paper in our country the next day. The government invited a limited number of reporters into a locked conference room for the press briefing and distributed the report in sealed brown paper packages.

For many Americans, January 11, 1964, marked the first time they became aware that smoking was harmful. Countless Baby Boomers cite that release as the impetus for their decision to quit smoking.

The public health and clinical response since 1964 also has been legendary. Smoking, which was ubiquitous and socially acceptable then, is now dramatically less common. Smoking rates have fallen from about 43% of all adults in 1964 to about 18% today. In the 1960s, people could smoke in planes, classrooms, restaurants and even doctor's offices. Now, smoking is prohibited in the indoor environments of 30 states, including Wisconsin. What was referred to as a "habit" then is now recognized as an addiction so powerful that former Surgeon General C. Everett Koop famously equated it to heroin and cocaine.

Yet despite the enormous progress over the past 50 years, tobacco use remains responsible for almost half a million annual deaths in America (about 8000 each year in Wisconsin). Tobacco use is now concentrated among the least advantaged members of our society, with smoking rates double the overall average among the poor, the least educated, and individuals with mental health and/or substance abuse diagnoses.

The University of Wisconsin School of Medicine and Public Health, partnering with the United States Public Health Service, has played a pivotal role in confronting tobacco dependence in America. For the past 25 years, the UW Center for Tobacco Research and Intervention (UW-CTRI) has been among the nation's leading centers devoted to reducing tobacco use.

UW-CTRI's contributions to tobacco control include:

- Helping more than 200,000 Wisconsin smokers quit, using the Wisconsin Tobacco Quit Line—a service funded by the Wisconsin Department of Health—that provides free counseling and medications to any smoker in our state via 1-800-QUIT NOW.
- Advocating for the establishment of tobacco use as one of the vital signs collected on all patients at every clinic visit. This simple, low-cost intervention is now the standard of care across America, with more than 80% of smokers reporting that they were asked about tobacco use at their last clinic visit.
- Assisting the US Department of Health and Human Services in creating the National Action Plan for Tobacco Cessation, which outlined the key public policy approaches for eliminating tobacco use, including a $2 per pack increase in the price of cigarettes.
- Chairing the 3 US Public Health Service Clinical Practice Guideline Panels that produced *Treating Tobacco Use and Dependence* (1996, 2000, and 2008), the evidence-based gold standard for the clinical treatment of smokers.
- Assisting with the passage of both the

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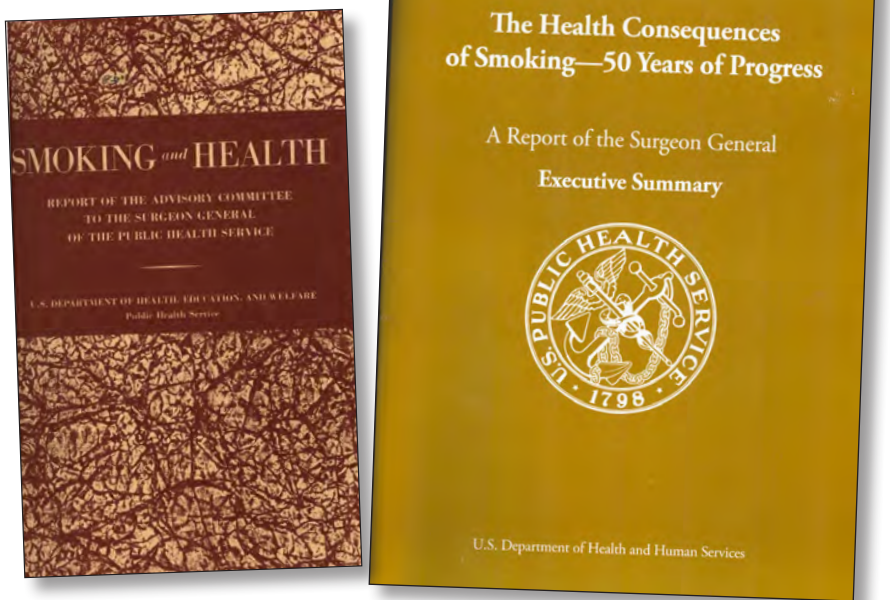
Dr Golden is dean, University of Wisconsin School of Medicine and Public Health (UWSMPH), vice chancellor for medical affairs, UW-Madison; Dr Fiore is professor, UWSMPH Department of Medicine, and director, UW Center for Tobacco Research and Intervention.



The 1964 and 2014 Surgeon General Reports

Michael Fiore, MD, with Timothy McAfee, MD, director of the US Office on Smoking and Health, at the January 16, 2014, White House release of the Report of the Surgeon General.

Madison and Wisconsin clean, indoor air ordinances.

- Publishing more than 300 research articles on tobacco dependence and successful intervention strategies.
- Creating the website www.ctri.wisc.edu, which recently ranked as number 1 by Google for tobacco research and serves as a resource for smokers and clinicians.
- Working with Wisconsin smokers from disadvantaged populations to help them quit.
- Generating more than $100 million in external grant funding to support its research and outreach missions.

We believe several lessons can be learned from the successful approach to the tobacco epidemic that may help guide efforts to combat current and emerging public health challenges in Wisconsin, including childhood obesity and binge drinking. What insights from the "tobacco wars" can be applied to other public health imperatives?

Recognize the Disease

Our perceptions of smoking changed markedly once tobacco use was recognized as an addiction rather than a "free choice" and "just a bad habit." This recognition led the US Public Health Service to designate tobacco dependence as a chronic disease that warrants medical attention. It drove the National Institutes of Health and other agencies to support research that provided a scientific basis for treatment. Thus the recognition of obesity and binge drinking as serious public health crises can serve as a cornerstone for the development of effective diagnoses and treatments.

Know the Enemy

A critical turning point in the war against tobacco was the recognition that the tobacco industry was the primary agent responsible for enlisting new generations of children as lifelong tobacco addicts. Each year the tobacco industry spends about $10 billion on advertising and promotion, with much of this activity directed at enticing children to serve as replacement smokers. Just as the tobacco industry was forced to alter its behavior (television advertising bans, the Master Settlement Agreement that provided more than $250 billion to states), entities that target children to engage in underage drinking and pursue unhealthy diets must be held accountable.

Get the Word Out

With the tobacco industry spending $10 billion annually in advertising and promotion, a vocal public counterweight was needed. Dr. C. Everett Koop served effectively in this role, using the bully pulpit as US Surgeon General. More recently, the US Centers for Disease Control and Prevention, through its "Tips from Former Smokers" media campaign (http://www.cdc.gov/tobacco/campaign/tips/) has highlighted the real health costs to smokers. In a similar way, First Lady Michelle Obama has shined a powerful light on childhood obesity. Getting the word out regarding the human and societal costs of childhood obesity and binge drinking will be essential in reducing these public health dangers.

In January 2014, the tobacco-control community came together at the White House for the release of the 50th Anniversary Surgeon General's Report on the Health Consequences of Smoking (www.surgeongeneral.gov/library/reports/50-years-of-progress/index.html). It was not sealed in brown paper packages. For the first time, that report detailed an "end-game" plan for fully eliminating the harms of tobacco use in our society. While far from complete, the promise of achieving this goal in Wisconsin and America will save half a million lives per year, and provide a blueprint for confronting other public health scourges of our time.

External Peer Review Services Available Through MetaStar

Jay A. Gold, MD, JD, MPH; Conni Brandt, RN, BSN, CPHQ

Health systems and hospitals are challenged to evaluate the quality of care provided to their patients by reviewing the gap between recommended and actual practice. Internal quality efforts usually include medical peer review processes. Internal peer review may assess a health care professional's overall practice patterns or a specific case review with an adverse outcome. A hospital's internal peer review policy also may include the option for external peer review.

External peer review may be indicated under the following circumstances:

- In the event of an adverse outcome, a hospital or health system wants to determine that appropriate care was provided.
- There are concerns about a practitioner's pattern of care; for example, where a practitioner has a disproportionate number of adverse outcomes.
- A hospital or health system does not have a same-specialty peer to provide a peer review.
- There are concerns that the relationship of available peers with the physician under review could impair those peers' objectivity.
- A hospital or health system wishes to validate its internal peer review process and findings.

Organizations like MetaStar provide board-certified peer reviewers from a broad range of specialties to match the health care professional being reviewed. The peer reviewer attests that no conflict of interest exists with regard to the hospital, the patient, or the practitioner. The hospital provides the medical record(s) for review. The external peer reviewer applies professionally recognized standards of care and guidelines to evaluate the quality of the care provided.

In addition, a utilization review may be performed to determine whether the services provided to a patient were, or proposed services are, medically necessary and provided at the appropriate level of care.

For both quality and utilization reviews, a report is submitted to the hospital, including a case summary and a summary of the expert opinion addressing the appropriateness of the care provided.

An objective, external peer review is a cost-effective tool available to health systems and hospitals to evaluate and to ensure the quality of care provided to their patients.

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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 U.S. Department of Health and Human Services. The contents presented do not necessarily reflect CMS policy. 10SOW-WI-CRSP-14-02. Dr Gold is senior vice president and chief medical officer for MetaStar; Ms. Brandt is MetaStar's vice president of review services and performance measurement.

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