



advancing the art & science of medicine in the midwest

**WMJ**

volume 114 • no. 1 • february 2015

**Can social marketing  
increase childhood  
immunizations in  
vulnerable populations?**

# HEALTHCARE REMIX

redefining the culture of medicine

## Wisconsin Medical Society Foundation Fundraising Dinner & Silent Auction

Friday, April 24, 2015

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7 p.m. Dinner

8 p.m. Program

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This activity has been approved by the American Board of Family Medicine as an external provider of Maintenance of Certification for Family Physicians Part IV credit. This activity has been renewed from October 22, 2014, to October 22, 2015.

This activity is approved through the American Board of Internal Medicine's (ABIM) Approved Quality Improvement (AQI) pathway and is eligible for 20 points towards the Self-Evaluation of Practice Performance requirement of Maintenance of Certification (MOC).

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**COVER THEME**  
**Can social marketing  
increase childhood  
immunizations in  
vulnerable populations?**

Although immunizations have been a public health success, vaccine-preventable diseases continue to occur disproportionately within vulnerable populations. A study in this issue of *WMJ* explores the efficacy of using targeted social marketing to increase parental awareness and intention to immunize.

Cover design by  
Mary Kay Adams-Edgette

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

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# WMJ

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# A Long Way Off

Karl H. Doege, Medical Editor; Mr. J.G. Crownhart, Managing Editor; Miss Dorothy Cirdland, Assistant Editor

*Editor's note: The following editorial was published in WMJ, Volume 39, p. 113, February 1940.*

In her weekly column in *The Progressive* of December 30, 1939, Mrs. Philip F. La Follette, wife of our former governor, was discussing unemployment ills, the federal efforts and expenditures when she said:

"I can't help feeling that Washington is always a long way off, not only by geography but also in thought, from the mass of the people. All too often when I talk to extremely able people down there I get the sense that they are living in a vacuum with their blueprints and plans; that they are sincerely trying very hard to find a solution to our difficulties but somehow they need to get out into the countryside and re-see nature and the mass of their fellow human-beings."

It was the truth of this statement that led our Society two years ago to make a first hand study of health needs in Wisconsin, not from statistical tables but after across-the-table-talks with people from all walks of life and in thirty-nine of Wisconsin's seventy-one counties. Disease occurs in people and not in cartons. The physician must treat disease where it occurs and his efforts in the field of prevention must encompass the whole welfare of the thousands of individuals that go to make up Wisconsin's population.

In all of our health plans and planning, if we for one moment lose sight of the individual physician and his individual patient, we are not apt to think that if we just do this or just do that, a whole problem will be solved. And, in that type of plan, too frequently there is failure on the part of those who are removed from the day-by-day experience with life itself to realize that education has a great role to play, now and forever in the future.

In the field of health, too often the ignorance of a person or parent,

the unreasoned or illogical fear of a surgical procedure, the upkeep of the car but neglect of the human machine, the unwillingness to admit that something is probably "out-of-gear," the acceptance of health and reluctance to think of disease except when something happens, superstition itself, these and many other factors are all basic facts that charts fail to reveal. And plans and blueprints made without the basis of medical knowledge and experience are even more apt to lead to failure and actual retreat than battle-maps made without knowledge of the terrain.

Mrs. La Follette has put her finger upon the reason why medicine constantly emphasizes that plans must be made to meet existing local conditions; why funds must be administered under local direction by those who know the local needs and problems.

The writer's father once made the point in a different fashion when he pointed out that complaints as to a local condition could be voiced by the complainant in person to the official in charge; that complaints as to a condition governed by state officers too often required aid from an attorney at Madison, and complaints as to conditions governed by federal authorities had best be forgotten if the official in charge did not act upon the basis of the first letter.

Funds are needed oftentimes in the battle to improve health conditions of our people who were described by the Surgeon General of the U.S. Public Health Service on January 1 as the healthiest generation in the healthiest country in the world. But, if we are not to enter upon a state of confusion resulting in retreat or disaster, those funds must be applied in the amount required to meet local conditions and administered under plans made by those who understand the health terrain on which the battle is to be fought. We cannot afford to have the plans made by sincere people who live in a vacuum of unrealities.

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# A Summer House Call in Wisconsin

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Justin Yamanuha, MD

On a cool, sunny, summer Wisconsin day  
I made a house call  
Landline to landline, no text messages exchanged

I followed the verbal directions, no fancy navigation system utilized  
For the instructions were clearly outlined on notebook paper:  
“Turn right out of the parking lot, left at the dentist’s office and proceed to the end of the street”

I parked under the oak tree with its newly green leaves  
Just around the corner from the patient and her longtime abode  
I knocked on the door and her kindness welcomed me

An old fashioned patient-doctor encounter  
My modern day eye pressure checker completed the designated task  
We talked about her medications and the home routine  
Of applying the eye drops, and marking a box on her notebook paper once completed

We walked past the family photos  
and the refrigerator covered with magnets  
I exited her home and concluded the house call

In an age in which time and distance can instantly connect IP addresses  
There will always be a place for a caring hello, a gentle smile, and a warm hug  
Basic human interactions, at a patient’s street address

House calls are an anachronism in the most modern of ages  
A trip back to the period when physicians made house calls regularly  
And carried black bags of equipment instead of laptops or tablets

House calls can still have a place in Western health care  
A privilege now typically granted to community and home health nurses  
Humble interactions that mean so much more  
Than any meaningful use metric

A house call validates health care and welfare  
Without a code to match its true value or a modifier to capture its significance  
It is an extension of the delivery of services and rounds out the sphere of care

• • •

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# Education Saves Lives

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John J. Frey, III, MD, *WMJ* Medical Editor

An article from the November 28 issue of *Science* may be one of the most important articles about health and society in decades, linking education worldwide to survival rates from natural disasters.<sup>1</sup> The authors make the case that more lives are saved by expanding education—particularly for young women and girls who are often family decision makers—than by large engineering projects seeking to mitigate the effects of rising seas and increased severity of storms. The more literate and educated the population, the fewer people die in hurricanes, tsunamis, tornadoes, floods, and natural disasters of all sorts. While the linkages are not apparent at first, the article discusses research that shows that education increases adaptive choices and decreases vulnerability. Education increases income and enables families to live in less high-risk locations. Lutz and colleagues use 30 years of data from around the world to show that increasing education would dramatically shift the population curve, not merely through the inverse relationship between education and birth rate, but by helping people make better personal choices of all kinds, including their geographic and built environments, which will save lives.

On a local rather than global level, we know that our patients who have less education and therefore lower incomes often engage in a disproportionate number of poor choices (eg, smoking and/or drug use) that lead to worse health outcomes such as mental health issues and obesity. They also suf-

fer complications of chronic illness at higher rates than patients who have more education.<sup>2</sup> Office-based approaches to these problems can work around the edges, and health education constructed with ethnic and cultural input can have some positive effects.

selves and to influence public policy relating to social needs. Doing so in a respectful and open-minded way is also an important part of clinicians' education about the challenges their patients face.<sup>4</sup>

The article by Ngui and colleagues<sup>5</sup> in this

Education is an investment that pays off  
in many ways, some more evident than others,  
and disinvestment or neglect leads to long-term  
health outcomes that burden society.

But all the research on social determinants of health shows that education and culture almost always trump medical care. Practice redesign only goes so far—and often not that far with the people who need it most—without entering into systems in communities, such as schools, safe housing, and transportation, that need improvement as well. Education is an investment that pays off in many ways, some more evident than others, and disinvestment or neglect leads to long-term health outcomes that burden society.<sup>3</sup> Perhaps the best activity physicians could participate in is to be civically engaged in active ways in schools and communities where patients live their lives on a daily basis. Clinicians also need to be engaged in schools, from pre-K through college, to both educate students and them-

issue of *WMJ* describe a community-based social marketing and education campaign created in an attempt to increase immunization rates in vulnerable populations. The authors used interviews to assess how and what neighbors need to know about immunization practices and then developed a series of posters on basic themes directed toward a number of health habits. Some of these messages appeared on billboards, flyers, and other mediums, and the results are encouraging. People remembered the ads and signs, they understood their value, and they intended to act on the messages they contain. A strategy that engages citizens in their community's own health issues works. Neighbors' voices are essential to be effective.

While not comparing public marketing

strategies with office-based ones, one can't help thinking that catchy ads on buses may have more value to the population in Ngui's study than the reams of paper generated in offices for "meaningful use," which quickly find their way into the recycle bins just outside of clinic buildings.

One of the most important messages for clinicians from Ngui and colleagues' study is in its conclusions: "The long-term sustainability and effectiveness of a social marketing campaign in increasing immunization coverage for children will depend on continuing community-academic collaboration and engagement of the larger health care systems." Clinicians cannot sit in hospitals and clinics and hope to change the quality of health in the communities where their patients live.<sup>6</sup> Public health professionals and academic researchers cannot sit in front of computers to find the solution to complex societal problems. Joining the academic, practicing, public health, and large health systems together in Wisconsin has not been easy for a number of reasons to this point in time. For care to be effective, we need to join forces in serious efforts that require focusing on what there is to win for our state rather than what we have to lose by adjusting long-held positions and behaviors that have impeded collaborations from happening.

This issue of *WMJ* also contains an important study that explains the challenges that make the care of targeted populations—in the case of Garvey and Evenson,<sup>7</sup> women with abnormal Pap tests—effective. Physician adherence to complex and changing protocols, effective communication with patients, and office systems that lack agreement among various staff all make what should be straightforward plans not achieve the desired results. There is much to learn from this study and its honesty about barriers to overcome.

Finally, there is nothing like reading a scholarly review that affirms that our current methods of managing a ubiquitous problem—in this case beginning and stopping warfarin—

and finding it to be based on solid science. Burmester and colleagues<sup>8</sup> look at the extensive literature on genetic factors that might influence the slope of discontinuing warfarin and, happily, they found none. Warfarin management may be one of the most effective protocols in chronic clinical care and office systems, and patients are well served by following current protocols.

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Kim, diagnosed in 2000

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# Evaluation of a Social Marketing Campaign to Increase Awareness of Immunizations for Urban Low-Income Children

Emmanuel M. Ngui, DrPH, MSc; Chelsea Hamilton, MA; Melodee Nugent, MS; Pippa Simpson, PhD; Earnestine Willis, MD, MPH

## ABSTRACT

**Objective:** To assess community awareness of childhood immunizations and intent to immunize children after a social marketing immunization campaign.

**Methods:** We used 2 interviewer-assisted street-intercept surveys to evaluate awareness of childhood immunizations and intent to immunize low-income children. The “Take Control! Immunize” social marketing campaign was developed using a community-based participatory research approach and used billboards, flyers, and various “walking billboard” (eg, backpacks, pens) to deliver immunization messages in the community settings.

**Results:** Over 85% of community members recalled the “Take Control! Immunize” message. Almost half of those who saw the immunization message indicated that the message motivated them to act, including getting their children immunized or calling their physician to inquire about their children’s immunizations status. All respondents indicated that immunizations were important for children and that they were likely or very likely to immunize their children. Respondents who reported that “Take Control!” messages motivated them to act in the first intercept survey were significantly more likely than those in the second intercept to report being likely or very likely to immunize their children.

**Conclusion:** Culturally appropriate social marketing immunization messages in targeted urban settings can increase parental awareness and behavioral intention to immunize children.

## INTRODUCTION

Racial and ethnic disparities in immunization coverage exist in the United States,<sup>1-3</sup> with racial/ethnic children of color less likely than white children to be up-to-date on their immunizations.<sup>3,4</sup>

• • •

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Under-vaccinated children are more likely to be black, have a young mother, reside in urban, central city settings, and live in poverty.<sup>5</sup> The burden of under vaccination is evident in inner city Milwaukee, Wisconsin neighborhoods, where immunization coverage for low-income children 19-35 months is estimated at 35% to 40% compared to over 75% in the state. According to the United States Census Bureau, Milwaukee is the second most segregated and the fourth most impoverished city in the nation, with almost half of the children and 20.9% of residents (compared to 12.5% in the state) living in poverty. These demographic characteristics further complicate efforts to increase childhood immunization in the city. Research shows that poverty accounts for almost all the racial/ethnic disparities for childhood immunization rates<sup>6</sup> and contributes significantly to other immuni-

zation barriers including limited access to transportation, lack of insurance coverage, and inadequate availability of health care providers and vaccines.<sup>7</sup> Traditional approaches to increase immunization coverage, however, have had limited effectiveness in reaching the most marginalized and vulnerable populations, especially low-income, inner city and rural populations of children. Reducing racial/ethnic disparities in childhood immunizations coverage is, therefore, an important social and public health goal.

Almost one-third (28%) of parents report they are unsure, delayed, or refused vaccines.<sup>8</sup> Although the underlying reasons for parental hesitancy to immunize children<sup>9,10</sup> are not clear, a number of factors, including poverty; cultural or religious objections; media misinformation of risk, benefits, and effectiveness of vaccines; and historical racism and mistrust of state and national agencies that formulate immunization guidelines and regulations play a role.<sup>11-15</sup>

**Figure.** Community Health Improvement for Milwaukee's Children Social Marketing Campaign Evaluation Poster with Mock Messages



The American Academy of Pediatrics (AAP) policy statement on increasing immunization coverage advocates for mounting a vigorous "...public relations campaign to inform the public and counter the influence of misinformation spread by celebrities and others who participate in the antivaccination movement to minimize the negative impact of this false information on the health of children. The public must be educated with regard to the risks associated with vaccine-preventable diseases and the impact of immunizations on their prevalence by using culturally tailored materials in English and other languages."<sup>16</sup> The use of social marketing approaches is an effective strategy to accomplish this AAP social and public health education immunization goal. As a behavioral change model, social marketing "applies traditional marketing principles and techniques to influence targeted audience behaviors to benefit the individual and society, such an example would be tobacco control and prevention programs."<sup>17</sup> As a behavior change strategy, social marketing uses a "marketing mix" consisting of 4 Ps of marketing (place, price, product, and promotion) to develop effective strategies to achieve a desired behavior change.<sup>17</sup> The application of social marketing in a community-based participatory research (CBPR) context is an innovative approach of increasing community input and participation in the design, content, and application of immunization messages in under-resourced communities.

The main objective of this study was to examine the efficacy

of a social marketing campaign aimed at increasing awareness and behavioral intent to immunize children in low-income urban setting. We examined whether: (1) there were significant differences between "billboard" and "billboard-enhanced" social marketing approaches in increasing awareness and intent to immunize African-American children in urban, low-income communities; and (2) the overall social marketing campaign was associated with increased awareness and intent to immunize children.

## METHODS

The social marketing campaign was implemented in 2 phases as part of the Community Health Improvement for Milwaukee's Children (CHIMC) Save Lives-Immunize project. Since 2005, this CBPR project was funded by the National Center for Minority Health and Health Disparities (NCMHD) to improve immunization coverage in select predominantly African American low-income urban neighborhoods in Milwaukee. The Milwaukee neighborhoods targeted by the program had low immunization coverage of about 35% at baseline for children 19-35 months compared to 73.6% in Milwaukee County, 77.7% in Wisconsin, and 76.1% in the United States.

The first phase (billboards only) included the use of project and community health plan cobranded billboards located in a minimum of 3 locations within targeted Milwaukee ZIP codes and immediate adjacent areas. The project staff distributed fliers

**Table 1.** Social Marketing Campaign Intercept Participant Demographic

Characteristics	Intercept 1 (n=202)	Intercept 2 (n=206)	All (n=408)
Not a participant of the CHIMC project (%)	99.5	97.6	98.5
Willing to participate in the intercept survey (%)	100	100	100
<b>Residence ZIP codes (%)</b>			
53206	18.5	15.2	16.4
53208	11.8	14.7	13.0
53209	6.7	12.3	9.3
53210	13.8	6.4	9.8
53212	4.1	10.3	7.1
53216	12.0	7.4	9.3
53218	6.2	7.8	6.9
All other ZIP codes combined (%)	26.9	25.9	28.2
Abbreviation = CHIMC, Community Health Improvement for Milwaukee's Children.			

at community events during the social marketing implementation phase. The second phase (billboard enhanced) was more comprehensive and included Phase 1 activities along with a variety of “walking billboard” marketing materials including backpacks, pens, pencils, magnets, hand sanitizers, band-aid holders, door hangers, t-shirts, stickers, and fliers that contained the social marketing message to children and families throughout the targeted areas. The staff handed out these items at community events, posted fliers at community locations (eg, community agencies, grocery stores, retail sites), and dropped off backpacks (for back-to-school events) filled with the project’s products at community sites to be distributed to residents. This study compared a “billboard” (Phase 1) and “billboard-enhanced” (Phase 2) campaign using 2 intercept surveys corresponding to each phase.

### Messages

The development of the social marketing campaign messages began in January 2010. Cluster analysis was used to identify and place respondents into categories based on their attitudes toward immunizations: health advocate, immunization advocate, fence-sitter, go along to get along, and skeptic, as described by Gust and colleagues.<sup>18</sup> To develop the social marketing messages, the project team conducted 2 focus groups in March and April of 2010 among respondents categorized as advocates (health advocates and immunization advocates) and fence-sitters (undecided). In these sessions, respondents engaged in brainstorm activities to identify culturally appropriate marketing messages for the campaign that were utilized to inform and guide the development of the social marketing intervention messages. Options for the final messages were presented to the project’s steering committee for deliberation and a vote to identify the final message for use in the social marketing campaign. The steering committee chose the message “Take control! Protect your child with immunizations” along with 3 additional mock messages (Figure). The social marketing campaign intervention began in May 2010 and consisted

of posting positive messages about keeping children up-to-date with their immunizations. Marketing of the campaign message “Take control! Protect your child with immunizations” was conducted in collaboration with a community health plan using billboards, fliers, and posters placed in strategic community locations.

### Intercept Surveys

The project team evaluated the social marketing campaign using 2 interviewer-assisted street-intercept surveys applying a stratified convenience sampling technique of community members in Milwaukee aged 18 and over. The first intercept was planned to occur 2 months after the billboards were posted in communities. The intercept survey consisted of 6 questions administered by trained community outreach workers and community members who were part of the project and were trained as part of the CBPR colearning process. The survey assessed awareness of the immunization message and its influence on motivating them to take any subsequent actions to address their children’s immunizations.

Phase 1 intercept surveys were conducted between August and September, 2010 and Phase 2 between February and April 2011 in targeted ZIP codes in Milwaukee. Respondents were asked to recall any health messages about children that they had read, heard, or seen within the last 3 months, first without prompts and second with visual prompts (Figure). The intercept surveys were conducted in various community settings including outside community grocery stores, neighborhood streets and bus stops, community health centers and other community sites (eg, area malls). The Children’s Hospital of Wisconsin Institutional Review Board approved this study.

### Data Analysis

We assessed the efficacy of the social marketing campaign by conducting an impact evaluation to directly measure the short-term effects of the campaign. To address our first objective, we compared Phase 1 and Phase 2 intercept categorical responses using chi-square or Fisher exact tests, with  $P < 0.05$  considered statistically significant. Overall awareness of immunization and behavioral intent to immunize was assessed using the combined data from intercept 1 and 2. Data analysis was conducted using SPSS 20 (IBM, Armonk, New York).

## RESULTS

### Respondents

As shown in Table 1, intercept 1 and 2 surveys consisted of 202 and 206 respondents, respectively. All of the respondents resided in the targeted city neighborhood, with the majority living in ZIP codes 53206, 53208, 53209, 53210, 53212, and 53216. About half of the respondents had at least 1 child (range: 0 to 8 children). Consistent with the project’s target population, almost all of the intercept respondents (>97%) self-reported their race as African



American. All the respondents were not associated with the CHIMC project. No significant differences were found between the use of billboards only and billboard-enhanced social marketing approaches.

### Message Recall

As shown in Table 2, about half of respondents in intercept 1 and 2 recalled reading, hearing, or seeing any health messages in the past 3 months without prompting. When respondents were shown visual prompts (Figure) that included the project's social marketing campaign message with 3 additional mock messages, over two-thirds of respondents in both intercepts reported that they recalled seeing any health messages.

Among respondents who recalled any health messages, many indicated that they recalled the "Take control! Protect your child with immunizations" messages when given a visual prompt that included mock messages. Significant differences were identified in the proportion of respondents who recalled the mock nutrition message "Good Nutrition Saves Lives," with 25% in intercept 1 and 14% in intercept 2 reporting that they recalled the message ( $P=0.015$ ). No significant differences were found between the 2-intercept surveys with regard to the other messages including the social marketing campaign message. We note, however, that the recall for the mock "Good nutrition saves lives" and "Choose water not soda," messages decreased between the 2 intercept periods, whereas the recall for the mock "Pick on fruit, not on children! Stop bullying" and the project's "Take control! Protect your child with immunizations" message increased.

### Motivation to Act on Messages

The survey also measured whether respondents who recalled the immunization message reported that the message motivated them to do anything. Almost twice as many respondents in intercept 1 reported that they got their child immunized compared to those in intercept 2 (17%). The proportion of respondents who reported that they called their doctor because of the social marketing message doubled, from about 6% in intercept 1 to 13% in intercept 2. A statistically significant difference—an 8-fold increase—between the 2 intercepts in the proportion of respondents who reported that they asked their doctor about immunizations in intercept 1 (2%) and intercept 2 (16%,  $P=0.010$ ) was identified.

The proportion of respondents who reported that they had

**Table 2.** Social Marketing Intercept Results: Childhood Immunization Awareness and Intent to Immunize

Characteristics	Billboard Intercept 1 % Yes (n)	Billboard-enhanced Intercept 2 % Yes (n)	Combined Intercepts <sup>a</sup> % Yes (n)	Change <sup>b</sup>	P value <sup>c</sup>
Recalled any public health messages (without prompting)	48 (202)	54 (206)	51 (408)	+	0.278
Saw any public health messages (with visual prompt)	69 (202)	73 (206)	71 (408)	+	0.317
<i>If Yes, Which Messages Have You Seen:</i>					
CHIMC take control message	84 (139)	85 (151)	84.5 (290)	+	0.765
Mock nutrition message	25 (139)	14 (151)	19.5 (290)	-	0.015
Mock water soda message	16 (139)	13 (151)	14.5 (290)	-	0.428
Mock stop bullying message	17 (139)	24 (151)	20.5 (290)	+	0.131
<i>If Yes to CHIMC "Take Control" Message, Did it Motivate You to Do Anything</i>	47 (116)	49 (129)	48 (245)	+	0.721
<i>If Yes, What Did it Motivate You to Do:</i>					
Get child immunized	30 (54)	17 (64)	23.5 (118)	-	0.109
Call doctor	6 (54)	13 (64)	9.5 (70)	+	0.196
Ask doctor about immunization	2 (54)	16 (64)	9 (118)	+	0.010
Review immunization records	15 (54)	13 (61)	14 (115)	-	0.793
Tell someone	9 (54)	6 (64)	12 (118)	-	0.540
Believe immunizations are important for children	96 (198)	97 (203)	96.5 (401)	+	0.755

<sup>a</sup> Combined intercept shows the total combined sample (n) with the average percentage of the 2 intercepts.

<sup>b</sup> + and - Indicates either a positive (increase) or negative (decrease) change between intercept 1 and 2

<sup>c</sup> P values based on Pearson chi-square or Fisher exact test comparisons between intercept 1 and intercept 2.

reviewed their children's immunization records or told someone decreased slightly between the 2 intercept surveys. Comparing both intercepts, the proportion of respondents who reported that they checked the state's immunization registry increased slightly, while those who reported telling someone about immunizations decreased. Among those who selected "other" actions, those mentioned most frequently actions included checking with their clinic or health care provider, scheduling appointments, making sure a child was up-to-date, and trying to get their children enrolled into health plans.

### Location of Messages

The most frequently mentioned locations of the project's messages included buses (35%), billboards (15%), TV/newspapers (15%), children's hospital sites (10%), and doctors' offices (10%), among other locations.

### Immunization Importance and Behavioral Intentions

Almost all (96%) of the respondents reported that they believed immunizations are important for children and that they are "very likely" to immunize their children. Overall, respondents who reported that "Take Control!" messages motivated them to act were significantly more likely to report that they were likely or very likely to immunize their children ( $\chi^2=6.19$ ,  $P=0.028$ ) in intercept 1 but not intercept 2 ( $\chi^2=1.60$ ,  $P=0.281$ ). Moreover, significant association was found between the perceived likeli-

hood of immunizing children and respondents' belief that immunizations were important for children. Among respondents who reported that immunizations were important for children (about 97% in both intercepts) indicated that they were likely or very likely to immunize their children in intercept 1 ( $\chi^2=23.37$ ,  $P=0.001$ ) and intercept 2 ( $\chi^2=72.1$ ,  $P<0.0001$ ).

## DISCUSSION

Except for 2 measures, this study found no significant differences between the "billboard" and "billboard-enhanced" social marketing approaches used. The finding suggests that the use of strategically located billboards with culturally appropriate immunization messages in targeted low-income African American urban communities can be an effective way of increasing community awareness of childhood immunizations in those neighborhoods.

Our findings also indicate that the social marketing campaign message penetrated the targeted community as indicated by the high percentage of people who heard the message, almost all of whom were not affiliated with the project. A large proportion of respondents recalled the social marketing campaign "Take Control!" message, with almost half (46%) of those who recalled the message indicating that they were motivated to act, including almost one-third who mentioned getting their children immunized. We note that many of the people who selected "other" actions did mention things related to immunization services such as making sure their child's immunizations were up-to-date. The proportion reporting that they called a doctor doubled between the 2 periods. Similarly, we found an 8-fold increase between the 2 intercepts in the number of respondents who reported that they asked their doctor about immunizations because of the project message, suggesting that the immunization message was motivating some behavioral changes and intentions to immunize children among the respondents.

The finding that almost all the respondents perceived immunizations as important for children suggests the need for more community immunization outreach similar to those of the project. The findings suggest that the social marketing message penetrated the targeted community as indicated by the high percentage of people not affiliated with the project who identified the "Take control. Immunize!" message.

Social media campaigns such as the "ask 5" model build on this type of deliberate effort to prime patients to come prepared to ask questions about their health.<sup>19</sup> Many patients, even those with higher education levels, often are less likely to ask their provider questions and are more likely to go home with unanswered questions. It is possible that the importance and urgency of the flu outbreak provided a natural way of discussing flu immunizations and logically a discussion of children's immunization status for other immunizations. Prompting about immunizations could therefore have originated from either the provider or the parents.

This study has several limitations. First, although we tried to reduce recall bias by using a short (2 months) recall period in the questions, differences in recall of the messages may still exist. Second, findings of this study may be generalizable to similar African American communities but not to other racial/ethnic communities. Additional research with a more generalizable sample is needed. Third, the drop in the number of parents reporting that they had their child(ren) immunized may depend on the timing of the interviews. Intercept 1 occurred at a time when many other immunization messages from various health agencies were encouraging people to get flu shots. The public health urgency of the flu may have increased awareness of the value of immunizations throughout the community and prompted parents to get their children immunized during the first intercept survey. As such, it is possible that the same urgency may not have been present during the second intercept surveys. Indeed, more respondents in the second intercept reported that they asked their doctor about immunizations than during intercept 1. Prior research shows that when prompted to ask about immunizations or other health concerns for their child(ren), parents are more likely to ask than when they are not prompted.<sup>20</sup>

Although mock messages were used in the study, they were designed to contain positive messages—on healthy nutrition, choosing water over soda, and stopping bullying—that were consistent with other public health priorities for children. Many of the respondents reported seeing these messages. Parents may have been more inclined to agree with the messages regardless of whether or not they had seen or heard them because these messages were positive and consistent with other public health messages to which the community had been exposed during the same period. The significant drop in the proportion of those reporting seeing the nutrition message is interesting. A drop in the other mock messages also exists—except for bullying—which suggests a differentiation of the immunization message from other types of messages in the community.

The increase in the proportion of respondents reporting seeing the "Stop Bullying" message is perhaps a reflection of antibullying messages in the local media<sup>21,22</sup> during the second intercept after a couple of serious bullying incidents received widespread coverage and responses from public health and policy makers. These incidents may have heightened awareness of bullying as a community problem, thereby making more respondents likely to identify this mock message as one they had heard or seen.

## CONCLUSION

Although immunizations have been a public health success, vaccine-preventable diseases continue to occur disproportionately within low-income, racial/ethnic populations. These conditions and their associated health consequences are preventable given that community awareness is elevated and the vaccines are made

available through the health care delivery system. This study finding suggest that the use of a CBPR approach in designing the messages and identifying community placement for the billboards may have been effective in reaching the targeted communities. Culturally appropriate immunization billboards that are strategically located in targeted community sites can be an effective approach to increasing awareness and intent to immunize children in low-income urban minority neighborhoods. The social marketing campaign “Take Control!” messages initiated by the project continued in Milwaukee after the study ended, allowing for a continual influence. In addition, many of the health care delivery systems in the city have adopted immunizations as one of their health priority areas, which will allow synergy among partners to increase immunization coverage rates. The long-term sustainability and effectiveness of a social marketing campaign in increasing immunization coverage for children will depend on continuing community-academic collaboration and engagement of the larger health care systems.

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# Factors That Affect Rate of INR Decline After Warfarin Discontinuation

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## ABSTRACT

**Background:** Despite vast literature on warfarin, optimal strategies for temporarily discontinuing and restarting warfarin have not been established. To improve warfarin discontinuation processes, we investigated known medical and genetic factors that influence stable warfarin dose to determine how well they predict the time until patients become subtherapeutic after discontinuing warfarin.

**Methods:** This was a retrospective cohort study of patients who temporarily discontinued warfarin before an elective procedure and had at least 2 international normalized ratio (INR) values available during the discontinuation period. Data abstracted included date of discontinuation, warfarin dose, INR values, body surface area, gender, age, indication for warfarin, current medications, eGFR, and presence of bridging therapy with heparin. DNA variants were tested in CYP2C9, VKORC1, and CYP4F2 genes. Subjects were excluded if they received vitamin K, fresh frozen plasma, or prothrombin complexes to reverse anticoagulation. Asymptotic regression models were used to approximate decline in INR during warfarin clearance. Spearman correlations and Kruskal-Wallis tests were used to characterize associations of model estimates with quantitative variables and for group comparisons, respectively.

**Results:** Other than the expected association with baseline INR, correlations of model parameter estimates with clinical variables were generally weak and not statistically significant. The strongest associations with slope were with serum creatinine and eGFR. There were no significant associations with CYP2C9, VKORC1, or CYP4F2 DNA variants, but there were few subjects combined in the nonwild groups for CYP2C9. Estimated slope showed moderate correlation with observed dose.

**Conclusion:** Known clinical and genetic predictors of therapeutic dose were not found to be strongly associated with the slope of INR decline after warfarin discontinuation.

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## INTRODUCTION

Warfarin is a commonly prescribed anticoagulant used in the prevention and treatment of arterial and venous thrombosis.<sup>1-3</sup> Patients on long-term anticoagulation therapy with warfarin may require temporary discontinuation to attain partial or complete reversal of anticoagulation before undergoing elective surgical and/or non-surgical procedures.<sup>4-6</sup> Decisions regarding discontinuation are based on the risk of intraoperative and postoperative bleeding weighed against the probability of a thromboembolic event.<sup>7</sup> For patients at low risk for arterial or recurrent venous thromboembolic events, standard practice involves withholding 3 to 5 daily doses of warfarin before the procedure, usually resulting in an international normalized ratio (INR)  $\leq 1.5$  by the procedure day, providing an acceptably low risk of postoperative bleeding. Warfarin is then typically restarted sometime after the procedure. Patients at high risk for arterial or recurrent venous thromboembolic events (VTE) (eg, mechanical heart valve, VTE event within past 3 months, or arterial embolism in the previous 30 days) receive bridging therapy

with unfractionated or low molecular weight heparin that is initiated when INR becomes subtherapeutic (generally  $<2.0$ ), and continued postoperatively until a therapeutic INR is achieved.<sup>8-10</sup>

Despite vast literature on warfarin, including its initiation, management, and genetic factors that affect therapeutic dose, optimal strategies for temporarily discontinuing and restarting warfarin have not been adequately assessed.<sup>4,6</sup> Current clinical management on temporary warfarin discontinuation is based on a single case series reported in 1995 using data from 22 patients who achieved therapeutic anticoagulation levels but subsequently

discontinued warfarin therapy.<sup>11</sup> For patients with an INR of 2.0 to 3.0, an exponential, but widely variable rate of decline in INR was noted. By day 5 most patients achieved INR values <1.5. The wide variability in rate of decrease in INR was attributed to age, with a 7% decrease in rate of INR decline for each 10-year increase in age. Age has been recognized as a factor associated with warfarin dosing, with older patients generally requiring a smaller dose compared to younger patients. Thus, older patients reportedly not only require smaller doses, but also take longer to eliminate this drug after discontinuation.

Phenotypic and genetic factors have been identified that systematically influence the therapeutic dose of warfarin.<sup>12-14</sup> In addition to age, these factors include body surface area (BSA), gender, diabetes mellitus, heart valve replacement, medications, and genetic polymorphisms (cytochrome p450 [CYP] 2C9, vitamin K epoxide reductase 1 [VKORC1], and CYP4F2). The influence exerted by these factors on warfarin during discontinuation for patients who were previously stable, and the time to achieve normal or near normal INR value in subjects who temporarily discontinue warfarin is currently unknown. Such knowledge is valuable since improved estimates of time to normal INR following warfarin discontinuation can lower patients' risks for thromboembolic events by reducing the amount of time that patients are without anticoagulants. For high-risk patients, it may be possible to reduce the number of preprocedural days required for successful bridging, thus reducing health care costs, especially those associated with unnecessary utilization of low molecular weight heparin. Furthermore, patients would benefit from an enhanced ability to schedule surgery and procedures with an improved degree of certainty that acceptable INR levels would be attained by the scheduled intervention date.

The goal of this study was to measure the decline in INR over time among subjects who had attained a therapeutic warfarin dose, examine the potential effects of the spectrum of known clinical and genetic factors that influence therapeutic warfarin dose on INR decline, and model when warfarin can be safely discontinued before elective and invasive surgical or medical procedures.

### METHODS

The retrospective cohort included patients on a therapeutic dose of warfarin who temporarily discontinued before an elective procedure. Subjects were required to have at least 2 INR values available during the period of discontinuation, although not necessarily on consecutive days. Subjects were excluded if they received vitamin K, fresh frozen plasma, or prothrombin complexes to reverse anticoagulation, or had moderate to severe hepatic insufficiency based on a serum aspartate aminotransferase or alanine aminotransferase more than 2 times the upper limit of normal.

**Table 1.** Baseline Patient Clinical Characteristics (N=91)

Clinical Characteristic	Number (%)
Male	51 (56%)
Diabetes mellitus	18 (20%)
Liver disease (mild)	2 (2%)
Bridging therapy	49 (54%)
Heart failure	13 (14%)
<b>Indication for warfarin discontinuation</b>	
Surgery	16 (18%)
Endoscopy	7 (8%)
Coronary catheterization	42 (46%)
Other	26 (29%)
Acetaminophen	20 (22%)
Aspirin	46 (51%)
Fluconazole	2 (2%)
Levofloxacin	4 (4%)
Simvastatin	2 (2%)

**Table 2.** Baseline Quantitative Characteristics

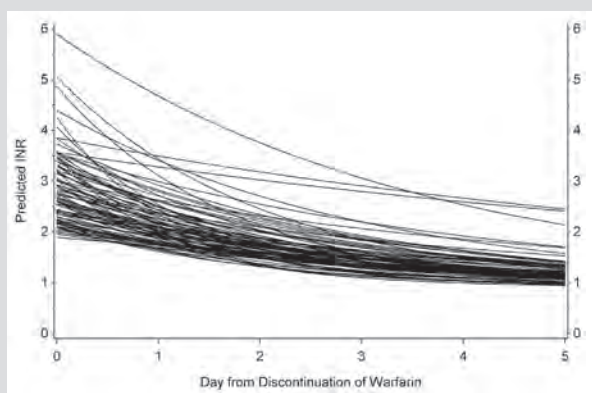
	Patients	Mean	Minimum	Median	Maximum
Age (years)	91	71.2	25	73.9	92
BMI (kg/m <sup>2</sup> )	90	29.7	21.4	28.7	50.3
Serum creatinine (mg/dL)	83	1.1	0.6	1.1	4.0
Dose (mg/day)	91	4.7	1.0	4.3	24.3

Abbreviation = BMI, body mass index.

A provisional study cohort of 285 subjects was identified using electronic data. Application of manually abstracted inclusion and exclusion trimmed the final study cohort to 91 subjects. The most limiting factors in cohort development were inadequate data to establish prediscontinuation therapeutic warfarin dose, fewer than 2 INRs during the discontinuation period, and direct clinical intervention to decrease anticoagulation level. The study cohort included 89 subjects with genotype data; genotypes were available both from previous studies<sup>12,15</sup> and from genotyping conducted specifically for this study using samples from Marshfield Clinic's Personalized Medicine Research Project DNA bank.<sup>16</sup> Clinical data were abstracted manually from subjects' electronic medical records, including date of discontinuation, warfarin dose, INR values, gender, age, indication for warfarin therapy, current medications, and the presence of "bridging therapy" with heparin or low molecular weight heparin.

CYP2C9, VKORC1, and Cyp4F2 genetic testing was performed using assays purchased from Applied Biosystems (ABI) (Foster City, California). ABI assays for CYP2C9 were C\_25625805\_10 and C\_27104892\_10. The ABI assay for VKORC1 was C\_2847860\_10. ABI assay C\_16179493\_10 was used to test the CYP4F2 polymorphism.

**Figure.** Clearance of Warfarin



Predicted international normalized ratio (INR) by subject based on a linear model. The model was fit to all subjects using a linear INR scale and shows predicted INR for each subject.

**Table 3.** Spearman Correlation Coefficients (91 Total Patients)

	Slope r P-value	Day 2 INR r P-value
Intercept	-0.244 0.020	0.654 <0.001
Slope		0.474 <0.001

Abbreviations = r, estimated correlation; INR, international normalized ratio.

### Statistical Analysis

For subjects meeting the eligibility criteria, INR data were graphically reviewed as a quality assurance measure, and outliers were investigated and updated as necessary. Statistical models were fitted to obtain an estimate of the rate of decline in INR (slope) after discontinuation of warfarin for each subject. In previous work,<sup>17</sup> we used a sigmoidal dose-response curve to model the INR response upon initiating warfarin, and we attempted to fit this model to the discontinuation data. However, due to limitations on the frequency of available INR measures, the full model could be fit on only 30% of the subjects. We developed a linear approximation model as an alternative so data for the entire cohort could be used.<sup>11</sup> This approximation assumes that INR after warfarin discontinuation will show an approximately exponential decline asymptotically over time to a warfarin-free value of about 1.0. Under this assumption, transforming INR by taking the logarithm after subtracting the asymptote results in a linear model. The primary estimates of interest from this model were the intercept (baseline INR, Day 0) and slope (rate of INR decline). To help illustrate the clinical results, we also analyzed model estimates of the expected INR at a specified time after discontinuation, arbitrarily choosing Day 2 as the reference time. The predicted INRs on Day 2 from the full logistic model were quite similar to the results from the linear approxi-

mation for the 29 subjects that could be fit with both models (Spearman correlation = 0.73,  $P < 0.001$ ).

These estimated slopes were summarized to provide information on the overall variability in time to become subtherapeutic. Clinical and genetic factors were evaluated for possible association with the estimated slopes. The Spearman correlation was used to characterize the association with quantitative variables (eg, age), and the Kruskal-Wallis test was used for comparisons among groups (eg, by genotype).

### RESULTS

Baseline clinical characteristics for study subjects are summarized in Tables 1 and 2. Subjects ranged in age from 25 to 92 years (mean 71), and 56% were male. Median warfarin dose was 4.3 mg/day, which is consistent with our previous studies (Table 2). One in 5 in the study cohort had diabetes mellitus and 1 in 7 had heart failure. Over 50% of the cohort used aspirin and over 20% used acetaminophen. Antibiotic, antifungal, and statin use at time of discontinuation was infrequent (Table 1). Common invasive procedures were the principal indication for discontinuation; surgery, endoscopy, and coronary catheterization represented over 70% study discontinuations. Bridging therapy was used to manage clinical risks in 54% of patients in the cohort.

The number of INRs modeled per subject ranged from 2 to 10 (median 4). Plots showing the model fit for all subjects using a linear INR scale are shown in the Figure. The model estimates were correlated to varying degrees (Table 3); higher starting INR (intercept) was associated with faster rates of decline in INR (more negative slope), and both higher starting INR and slower decline were associated with higher Day 2 INR.

The correlations of the model parameter estimates with clinical variables tended to be weak and not statistically significant. The strongest associations with slope were shown by age and estimated glomerular filtration rate (GFR) (Table 4). There were no significant associations with the genetic variants in CYP2C9, VKORC1, or CYP4F2 (data not shown); however, there were only 4 subjects combined in the \*2/\*2, \*2/\*3, and \*3/\*3 groups of CYP2C9.

### DISCUSSION

Although warfarin is commonly used for the prevention and treatment of a variety of acute and chronic venothromboembolic conditions, there is a paucity of evidence regarding the best way to discontinue warfarin before elective surgical or medical procedures.<sup>8-10</sup> We sought to increase the evidence base for warfarin discontinuation by investigating factors known to affect metabolism and therefore therapeutic dose. These included medications, disease and clinical conditions (eg, liver disease), and genetic factors (CYP2C9, VKORC1, CYP4F2).



**Table 4.** Spearman Correlation Coefficients

	n	Intercept		Slope		Day 2 INR	
		r	P-value	r	P-value	r	P-value
Male gender	91	0.00	0.987	-0.07	0.500	-0.12	0.258
Body surface area	90	0.02	0.837	-0.07	0.536	-0.06	0.545
Body mass index	90	-0.06	0.565	-0.06	0.558	-0.13	0.221
Age	91	-0.12	0.255	0.19	0.066	0.05	0.640
Serum creatinine	83	0.09	0.424	0.16	0.151	0.24	0.026
Estimated GFR	83	-0.04	0.747	-0.21	0.053	-0.27	0.013

Abbreviations = r, estimated correlation; INR, international normalized ratio; GFR, glomerular filtration rate.

Our principal analysis modeled the decline in INR after warfarin discontinuation using a constrained logistic function based on a published model previously used for warfarin initiation.<sup>17</sup> The model was constrained to the assumption that the INR measurement for subjects free of warfarin is approximately 1.1, since this was the median from our cohort. Imposing this constraint allowed us to fit this initiation model to a higher percentage of the cohort, even though many subjects had limited numbers of INRs in the time period of interest. Given limits on the INRs available, lack of precise INR times and some imprecision in the INR measurement itself, we expected reasonable simplifications to the models to be helpful. Our approach involved perhaps sacrificing a small amount of information in a few subjects with the most INR measurements; however, it allowed us to include many other subjects who had adequate data to fit with a simplified model but not enough for a more complex model.

Contrary to our a priori expectations, our study did not reveal strong correlations between genetic or clinical predictors of therapeutic dose and the slope of INR decline after warfarin discontinuation. We found no genetic or weak associations between clinical factors known to relate to warfarin therapeutic dose and the time needed for INR to decline to subtherapeutic levels.

Genetic factors may well have asymmetric effects on warfarin initiation and maintenance compared to discontinuation among individuals who achieve a stable dose. During initiation, person-level genetic differences matter and contribute to the well-known variability in dose-response patterns during this clinical period. However, eventually these interperson genetic differences and other patient factors are revealed and become reflected in a stable dose. When stable-dose patients discontinue warfarin, the rate of INR decline per unit of time may be expected to be more consistent across individuals precisely because those factors that affect daily warfarin clearance are embedded in daily dose. Variation in rate of INR decline during discontinuation is more likely to be related to changing patient conditions and clinical response than to genetics.

Our results on clinical factor effects generally are consistent with the observations previously reported.<sup>10,11</sup> In both studies, the rate of INR decline was not affected by height, weight (body

mass index), or gender. However, advanced age, decompensated heart failure, active malignancy, and extreme elevations in INR were factors that accounted for sustained elevation of INRs >4.0 in patients with supratherapeutic INRs at entry into the study. Our study did not confirm the relatively weak age effect noted by White et al.<sup>11</sup>

Our study has weaknesses that temper our findings and limit comparison of our results with other investigations. The retrospective nature of our study limited both the quantity of INR measures available for analyses and increased the variability of time intervals between INR measures across study subjects. Our preferred approach would have been to model hours from discontinuation; instead, we had to model days from discontinuation. Despite these limitations, our model results generally are consistent with the rate of INR decline as a function of time reported in White et al.<sup>11</sup>

Another limitation was the small number (N=4) of non-wild CYP2C9 genotypes in the study cohort. Because our study cohort did not include larger numbers of rarer genotypes known to impact warfarin dose, we cannot rule out the possibility of genetic effects on INR decline following discontinuation. Additional studies with larger numbers of rare genotypes will be needed to make this determination. However, as we noted earlier, to the extent that therapeutic warfarin dose has been established, it reflects underlying genetic variation among individuals. Therefore, we hypothesize that the effects of rare genotypes known to affect therapeutic warfarin dose would be similar to those of wild types on rate of INR decline following discontinuation.

## CONCLUSION

Contrary to our hypothesis, our study did not identify strong clinical or genetic predictors of therapeutic dose and the slope of INR decline after warfarin discontinuation. Further, we found no evidence to suggest that the current general clinical management guidelines for warfarin discontinuation should be amended. Generally, these include a recommendation to withhold warfarin for 4 to 5 doses (days) for patients with stable INRs in the range of 2.0-3.0 in order to achieve an INR ≤ 1.5 on

procedure day. For elderly patients and patients with INRs > 3.0, more time is generally required to reach a subtherapeutic target INR of < 1.5.<sup>9</sup>

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# Increased Patient Communication Using a Process Supplementing an Electronic Medical Record

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## ABSTRACT

**Background.** Importance: Patients with cervical cytology abnormalities may require surveillance for many years, which increases the risk of management error, especially in clinics with multiple managing clinicians. National Committee for Quality Assurance (NCQA) Patient-Centered Medical Home (PCMH) certification requires tracking of abnormal results and communicating effectively with patients.

**Objectives:** The purpose of this study was to determine whether a computer-based tracking system that is not embedded in the electronic medical record improves (1) accurate and timely communication of results and (2) patient adherence to follow-up recommendations.

**Methods.** *Design:* Pre/post study using data from 2005-2012. Intervention implemented in 2008. Data collected via chart review for at least 18 months after index result. *Participants:* *Pre-intervention:* all women (N=72) with first abnormal cytology result from 2005-2007. *Post-intervention:* all women (N=128) with first abnormal cytology result from 2008-2010. Patients were seen at a suburban, university-affiliated, family medicine residency clinic. *Intervention:* Tracking spreadsheet reviewed monthly with reminders generated for patients not in compliance with recommendations. *Main Outcome and Measures:* (1) rates of accurate and timely communication of results and (2) rates of patient adherence to follow-up recommendations.

**Results:** Intervention decreased absent or erroneous communication from clinician to patient (6.4% pre- vs 1.6% post-intervention [ $P=0.04$ ]), but did not increase patient adherence to follow-up recommendations (76.1% pre- vs 78.0% post-intervention [ $P=0.78$ ]).

**Conclusions:** Use of a spreadsheet tracking system improved communication of abnormal results to patients, but did not significantly improve patient adherence to recommended care. Although the tracking system complies with NCQA PCMH requirements, it was insufficient to make meaningful improvements in patient-oriented outcomes.

## BACKGROUND

Although the incidence of cervical cancer is declining over time, cervical cancer and dysplasia still occur and require clinical vigilance, sometimes tracking abnormalities over several years.<sup>1</sup> Inadequate follow-up could result in failure to diagnose cancer or delay treat-

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ment of cancer, two of the most common reasons for litigation in the United States.<sup>2</sup>

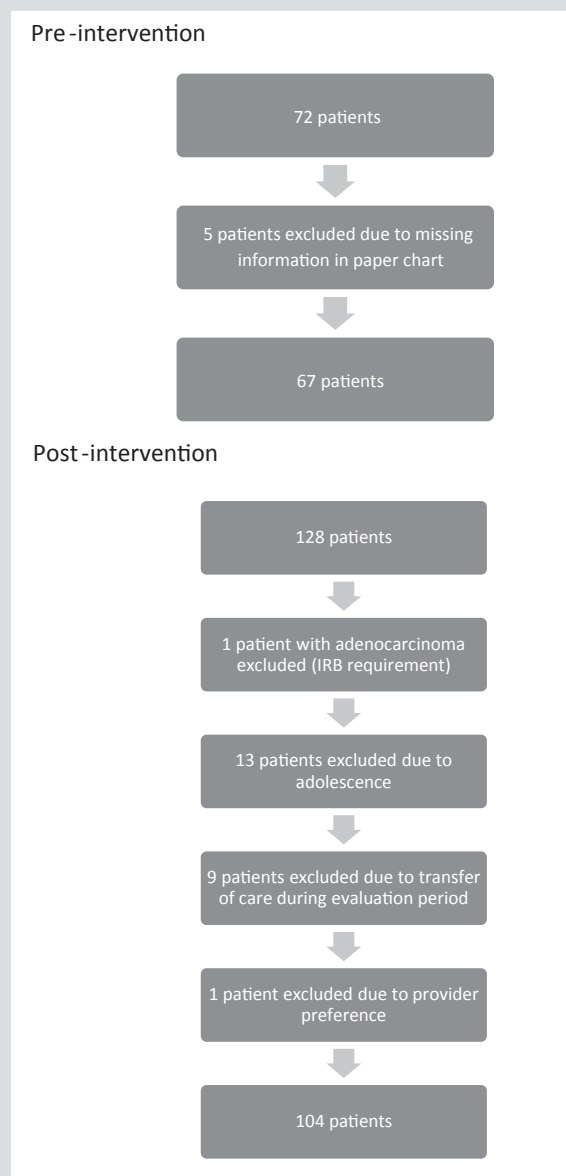
Ten percent to 40% of patients do not receive adequate follow-up care for cervical screening abnormalities.<sup>3,4</sup> Thirteen percent of invasive cervical carcinomas are attributable to failure to follow-up an abnormal cervical screening result.<sup>5</sup> Appropriate surveillance of abnormal cervical cytology results may be more difficult in a residency clinic and in other clinics with multiple clinicians due to attrition, clinic expansion, part-time employment status, or patient choice of a new primary physician.<sup>6,7</sup> In addition, resident physicians may lack experience with cervical cancer surveillance algorithms.

Many programs have been evaluated to increase patient adherence to cervical cancer screening follow-up recommendations including, interventions intended for patients (eg, transportation incentives or telephone counseling), clinicians (eg, increased discussion of monitoring and treatment options with patients), and systems (eg, use of reminder letters from cytopathologists to clinicians or the presence of

on-site colposcopy).<sup>3,4,8-13</sup> Based on these studies and others, the use of tracking systems is recommended by the American College of Obstetricians and Gynecologists to reduce medical errors in the screening and evaluation of laboratory and radiology abnormalities.<sup>14</sup> However, the effective use of tracking systems in clinics with large numbers of clinicians and/or clinician turnover has not been adequately studied. Swanson et al studied a tracking system in a residency clinic population, but the patients were those who had cervical cryotherapy, suggesting a population open to procedures and compliant with follow-up. With this study we evaluated the real-world effectiveness of a tracking system based in a residency clinic and included all clinic patients with an abnormal cervical cytology result.



**Figure.** Flow Diagram of Pre- and Post-intervention Patient Exclusions



## METHODS

This research was granted an exemption from further review by the university institutional review board (IRB); no informed consent was required. This was a pre- and post-intervention study evaluating a process to identify and track patients with abnormal cervical cytology cases. The pre-intervention group was all patients (N=72) from a university-affiliated, suburban, family medicine residency clinic with a first abnormal cytology result between November 2005 and November 2007. The post-intervention group was all patients (N=128) from the same clinic with a first abnormal cervical cytology result between November 2008 and November 2010. Identification of cases was possible through review of an aggregate monthly abnormal cytology report from

our pathology laboratory. Study data was collected via paper and electronic medical record review. Five patients were excluded from the pre-intervention group because of difficulties with their paper chart review, such as difficulty establishing the existence of prior Papanicolaou (Pap) smears or cervical intraepithelial neoplasia treatment (Figure). One patient was excluded from the post-intervention group at her primary physician's request. Thirteen patients were excluded from the post-intervention group because they were less than 21 years of age, and screening was no longer indicated in this age group.<sup>15</sup> Nine patients were excluded because they transferred care out of our clinic system prior to the need for follow-up. In compliance with the requirements of our IRB, one patient was excluded due to the presence of adenocarcinoma.

An Excel spreadsheet was created and included patient identifiers, cytology results, and recommended and actual management steps (see addendum online at [www.wisconsinmedicalsociety.org/publications/wmj/pdf/114/1/114no1\\_evensen\\_addendum.pdf](http://www.wisconsinmedicalsociety.org/publications/wmj/pdf/114/1/114no1_evensen_addendum.pdf)). The tracking process was implemented in November 2008 and reviewed monthly until May 2012. Cytology and pathology data was entered manually into the tracking spreadsheet. If a patient did not follow up as recommended, a reminder was sent first to the managing clinician and, if patient did not respond, she was sent a certified letter. Monthly spreadsheet reviews initially were done by a physician (AE); later the task was transitioned to a nurse. Data entry and reminder letters for all actively managed patients typically required 1 to 2 hours per month.

This study used care steps as a unit of measurement. A care step was defined as an action recommended by the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines such as "perform colposcopy" or "repeat cytology." If the recommended care step occurred within 3 months of the interval recommended by the ASCCP, it was scored as "appropriate." If the recommended step was not done or was delayed more than 3 months, the step was scored as "inappropriate." More frequent or vigilant follow-up (such as recommending colposcopy where only repeat cytology was indicated) was scored as "appropriate" because: (1) the 2001 ASCCP guidelines recommended more aggressive testing, and (2) colposcopy is indicated not only for abnormal Pap results, but also clinical concern regarding patient history or appearance of the cervix. Referrals to a gynecologist and transfer of care to another clinician were considered "appropriate." Scoring continued for at least 18 months after the index abnormal cervical cytology result and was halted when an inappropriate step occurred.

If a patient did not have a care step completed after appropriate clinician communication it was scored as "patient error." If communication was inappropriate it was scored as "clinician error." For all steps that were inappropriate, chart review was performed seeking documentation of communication (telephone call, letter, or office visit) from clinician to patient regarding the need for follow-up. Both a recommended next care step and a time frame

in which to complete this care step were required to be present and in accordance with the ASCCP algorithms for the communication to be considered “adequate.” When communication was not adequate, the communication error was categorized as either an absent or delayed communication or as a clinician misinterpretation of the ASCCP algorithms. The management context of the error also was documented (ie, whether it occurred after a colposcopy or cytology care step).

One author (TG) performed unblinded chart reviews of all patients in the pre- and post-intervention groups. The clinical steps performed were compared to the care recommended in the 2001 ASCCP guidelines<sup>16</sup> for the pre-intervention group and the 2006 ASCCP guidelines<sup>7</sup> for the post-intervention group. In general, the 2006 guidelines recommend less aggressive management of atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesion (LSIL) cytology results as compared to the 2001 guidelines. One author (AE) reviewed a random selection of patient medical records (20 of 171, 11.7%). Inter-rater reliability was 0.95 (agreement in 19 out of 20 reviewed medical records).

The percentage of care steps that were appropriate was calculated. For care steps that were inappropriate, the percentage that had adequate clinician-patient communication (ie, correct step and correct time frame communicated to patient) was determined. For care steps that had inadequate communication, the percentage that had absent/delayed preceding communication and the percentage that had documented communication that was erroneous (clinician misinterpretation of results) were determined. In addition, for steps with inadequate communication, those that followed a colposcopy or cytology care step were tallied. These analyses were repeated using patients instead of care steps as the unit of analysis. Results were analyzed with Fischer’s test to determine significance and two-tailed *P*-values were recorded.

### RESULTS

There were 109 care steps recommended for 67 patients in the pre-intervention group and 191 care steps recommended for 104 patients in the post-intervention group. The most common index cytology result in both groups was ASCUS (68% to 69%) followed by LSIL (22% to 26%). High grade cytology results were found in 6% to 9% of patients in both groups. The frequency of abnormal results was not statistically different between the 2 groups.

Use of the tracking and reminder system did not significantly increase the number of appropriately completed care steps (pre-intervention 83/109 [76.1%] and post-intervention 149/191

**Table.** Comparison of Care Steps Pre- and Post-intervention

		Pre-intervention	Post-intervention
<b>Appropriately completed care steps</b>		<b>83 (76.1%)</b>	<b>149 (78.0%)</b>
<b>Inappropriately completed care steps</b>			
Care steps with <i>clinician</i> error	No or late communication	7 (6.4%)	3 (1.6%)
	Erroneous communication due to misinterpretation of results/management algorithms	4 (3.7%)	9 (4.7%)
Care steps with <i>patient</i> error		15 (13.8%)	30 (15.7%)
<b>Total care steps</b>		<b>109</b>	<b>191</b>

[78.0%], *P*=0.78) or the number of care steps with adequate provider communication (pre-intervention 98/109 [90.0%] and post-intervention 179/191 [93.7%], *P*=0.26). Use of the tracking and reminder system, however, significantly reduced the number of care steps with no or late communication (pre-intervention 7/109 [6.4%] and post-intervention 3/191 [1.6%]; *P*=0.04). These data are summarized (Table).

In the pre- and post-intervention groups there were 11 and 12 steps with clinician errors respectively. In the pre-intervention group, 3 of the clinician care errors followed a colposcopy care step and 8 followed a cytology care step. In the post-intervention group, 11 of the clinician care errors followed a colposcopy care step and 1 followed a cytology care step. A common error in guideline interpretation was the return to routine screening for a patient with an index cytology result of ASCUS/HPV negative after a single negative cytology rather than waiting for negative cytology tests at both 6 and 12 months or 1 negative HPV test at 12 months. Another example of an error in guideline interpretation was the return to routine screening for a patient with an index cytology of LSIL followed by a negative colposcopy and then an ASCUS cytology result. These patients should have a repeat colposcopy instead of return to routine screening. In other cases, communication of abnormal results occurred late, not at all, or incorrectly (eg, patient was erroneously told that abnormal results were normal).

The data also was analyzed using patients instead of care steps as the unit of analysis. Use of the tracking system did not significantly increase the number of patients with appropriate care (pre-intervention 40/67 [59.7%] and post-intervention 60/104 [57.7%]; *P*=0.87).

### DISCUSSION

Use of a tracking and reminder system improved communication of abnormal results to patients, but did not improve patient adherence with recommended follow-up of abnormal cervical cytology. These results are in contrast to a previous randomized controlled trial of a cytopathology laboratory-based tracking system<sup>8</sup> and 2 pre/post studies<sup>9,11</sup> of clinic-based tracking systems that showed modest improvements in follow-up of abnormal cer-

vical cytology results. However, the study design of these trials differed from this design. The Hermens study<sup>8</sup> was done in a setting with universal health care coverage (the Netherlands), which may have made tracking patients easier and could have reduced the potential patient-level barrier of medical costs. The Swanson study<sup>11</sup> included only those patients who had cervical cryotherapy, suggesting a population open to intervention and compliant with follow-up. The Dupuis<sup>9</sup> study had no improvements in patients lost to follow-up, but the patients had fewer days to follow-up. Other studies of complex interventions that include tracking systems have been completed with mixed results.<sup>12,13</sup> Two of these studies evaluated clinician reminder systems<sup>8,9</sup> and 3 studies evaluated patient reminder systems.<sup>11-13</sup> By including all clinic patients with an abnormal cervical cytology result, this study contributes new, clinically relevant information to the growing body of knowledge regarding abnormal result tracking and patient compliance.

The rates of patient adherence to follow-up recommendations in both pre- and post-intervention groups are frustratingly low. There are potential patient-, clinician-, and system-level barriers that may explain these results. We attempted to address some of these barriers with the design of the tracking system. For example, the tracking system was designed to overcome the potential patient- and clinician-level barriers of forgetfulness and misinformation. With reminder letters or phone calls, patients and clinicians were prompted when follow-up appointments were overdue. This study's supervising physician was available on-site to review case management decisions and assist with ASCCP algorithm interpretation. We addressed some systems-level barriers as well. Prior to the introduction of the Excel spreadsheet used in this study, any tracking of abnormal cytology results in our clinic was the responsibility of individual clinicians. Clinicians were not formally surveyed regarding the use of individual tracking systems prior to 2008, but anecdotally this was not being done. Thus, simply introducing this process has helped our clinic create the foundation for further improvements in case management and meets some abnormal laboratory tracking and communication requirements for National Committee for Quality Assurance (NCQA) Patient Centered Medical Home (PCMH) certification.<sup>17</sup> Our system incorporated several features known to improve patient adherence with abnormal cervical cancer screening follow-up recommendations: the use of a patient reminder system, the use of a reminder system from cytopathology lab to clinician, increased communication between clinicians and patients, and the use of on-site colposcopy.<sup>3</sup>

Nonetheless, the system as designed was not sufficient to change patient adherence to follow-up recommendations. Our system was based on the assumption that clinicians would interpret the ASCCP guidelines correctly. This was often the case, but during data analysis management errors were discovered. Frequent misinterpretation of algorithms previously has been documented

in a study of family physicians, obstetricians, and internists in which only 12% of clinicians made recommendations consistent with ASCCP guidelines for ASCUS.<sup>18</sup> We suspect that these management errors occur because clinicians may incorrectly perceive ASCUS as a "low-risk" result.<sup>19</sup>

Frequent updates and evolution of guidelines for management may have been challenging for clinicians.<sup>7,18,19</sup> One author suggests decreasing the complexity of the cytology management algorithms, but new ASCCP algorithms for managing abnormal cytology results were published in 2013.<sup>18,20</sup> Although the new algorithms recommend less aggressive management of low-grade changes, especially in patients under 24 years of age, the algorithms are more complex (now 20 pages in length) and the recommended surveillance time periods have increased in length, creating potential barriers to use by clinicians. Several mobile devices have applications for navigating the algorithms, but they are neither available for desktop computers nor integrated into our electronic medical record (EMR).<sup>21</sup> It is unclear how the introduction of the human papilloma virus vaccination (2006) during the course of this study may have changed physician awareness of algorithms and potentially confounded the results.

Overcoming additional clinician-, system-, and patient-level barriers may improve patient adherence to follow-up. One clinician-level change that already has been implemented is to give clinicians patient-specific feedback (eg, "since Ms Jones had an ASCUS result following CIN 1 on colposcopy, she should have a repeat colposcopy rather than repeat cytology"). Several additional system-level changes have been suggested by Berkowitz et al. These include increasing ease with which patients can schedule appointment, increasing continuing education, using reimbursement strategies that support guideline-adherent practices, and developing web-based decision and risk analysis tools.<sup>18</sup> Nurse-based, protocol-driven management has been successful in improving immunization rates and could be considered in the setting of cervical cancer screening follow-up.<sup>22</sup> Currently the tracking spreadsheet is electronic but not integrated into the EMR. Our EMR lacks automated scheduling and patient recall functionalities, so a separate tracking system was needed. It would be ideal to have the patient registry embedded in an EMR that could receive and log abnormal results and generate automated reminders for patients or clinicians at the point-of-care.<sup>14,23</sup> Other improvements in patient adherence to recommendations may be achieved by identifying additional patient-level barriers such as lack of transportation, cost of care, or fears associated with diagnosis and treatment.<sup>3,4,6</sup>

## LIMITATIONS

Interpretation of our data is limited by the pre/post study design, the publication of more lenient ASCCP guidelines in 2006 (during the post-intervention evaluation period), and a gradual implementation of an EMR at the residency clinic over the course of the

project. We expected that because the 2006 ASCCP algorithms are more lenient than the 2001 algorithms, we would see improvement in patient adherence to follow-up, but this did not occur. The stepwise implementation of the EMR confounds interpretation of results, because it is unclear whether clinicians were more or less likely to document their conversations and recommendations with patients in the paper or electronic medical record. It was also impossible to determine if cancelled patient encounters had been intended to address abnormal cytology or complete the next listed care step.

## CONCLUSION

The use of a computer-based tracking system consistent with NCQA PCMH requirements for abnormal laboratory result tracking and communication improved timely communication of abnormal cervical cytology results to patients. The development of an abnormal lab result tracking process was an important first step for our clinic even though this iteration did not improve patient adherence to follow-up recommendations. As recommended abnormal cytology follow-up intervals increase and patient-clinician continuity decreases, it will be increasingly important to have a patient registry fully integrated in the EMR. Many potential patient-, clinician-, and system-level barriers should be examined to create a system that does more than simply meet PCMH requirements and truly improves patient-oriented outcomes.

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# Coronary Dissection in a Patient with Essential Thrombocytosis

Padmavathi Mali, MD; Sudheer Muduganti, MD; Kamilla J. Buddemeier, MD

## ABSTRACT

A 50-year-old man was admitted to the hospital with left shoulder and arm discomfort. He had no recent history of change in his energy level, limitations to activity, exertional chest pain, or shortness of breath. He had cardiac risk factors, including a strong family history of premature coronary artery disease and dyslipidemia. He had a syncopal episode in 2003 with a positive troponin I, but had a negative cardiac workup, including cardiac catheterization that showed luminal irregularities and no significant coronary artery disease. An echocardiogram was performed to rule out potential cardiac causes for shoulder pain and showed regional wall motion abnormalities. Follow-up cardiac catheterization revealed left anterior descending artery proximal and mid dissection and a long area of dissection in the first diagonal branch. Laboratory evaluation showed significant platelet elevation and positive *JAK2* study. Ultrasound of the abdomen revealed moderate splenomegaly. The enlarged spleen, positive *JAK2* study, and persistently elevated platelet count confirmed the diagnosis of essential thrombocythemia. Essential thrombocythemia can predispose individuals to vascular dysfunction and damage, which may contribute to coronary artery dissection. With this case, we propose that essential thrombocythemia should be excluded in the presence of coronary dissection and thrombocytosis.

## INTRODUCTION

Coronary dissection is a rare, potentially fatal condition that usually affects women.<sup>1</sup> The etiology of spontaneous coronary dissection (SCD) is unknown, but reports suggest a potential association with certain myeloproliferative disorders, such as polycythemia vera.<sup>2</sup> We report a case of coronary dissection of the left anterior descending artery and first diagonal branch in a male patient with essential thrombocythemia. This is the first report demonstrating an association between essential thrombocythemia and SCD. The patient was treated conservatively and continues to be asymptomatic.

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## CASE PRESENTATION

A 50-year-old man was admitted to the hospital with left shoulder and arm discomfort in 2013. The discomfort was not associated with any chest pain or shortness of breath. The pain was worse in the elbow area, and he had tenderness to palpation in the posterior shoulder. The pain showed no sign of improvement over a period of 3 days, and the patient was admitted to rule out acute coronary syndrome. He had no recent history of change in his energy level, limitations to activity, exertional chest pain, or shortness of breath.

The patient had cardiac risk factors, including a strong family history of premature coronary artery disease and dyslipidemia. No other familial risk factors for

acute coronary syndrome were noted. He did not smoke and denied any history of hypertension or diabetes. The patient had no history of drug abuse and reported medications included only naproxen, multivitamin, omeprazole, and *Lactobacillus* supplements. Of note, he had a syncopal episode in 2003 with a positive troponin I, but had a negative cardiac workup, including cardiac catheterization that showed luminal irregularities and no significant coronary artery disease.

Upon admission, the patient's troponin I was negative. An electrocardiogram revealed poor anterior R-wave progression. An echocardiogram showed mildly decreased global left ventricular systolic function with an ejection fraction of 40% with akinetic apex and hypokinetic apical septal, apical lateral, apical anterior, and apical inferior segments. Baseline regional wall motion abnormalities indicated cardiac catheterization rather than stress echocardiogram.

Cardiac catheterization showed a normal left main artery, but the left anterior descending artery had ostial and very complex proximal and mid dissection with the appearance of multiple lumens (Figure). A large first diagonal branch also had a long area of dissection. The circumflex artery was free of significant

disease. The dominant right coronary artery provided collaterals to the distal left anterior descending. No significant lesions were noted in the right coronary artery. Left ventriculography revealed apical akinesia with low normal to mildly decreased overall left ventricular function. Left ventricular end-diastolic pressure was 15 mmHg.

Cardiothoracic surgery was consulted to evaluate for coronary artery bypass graft surgery. However, it was felt that the angiographic findings were chronic, and that the patient would not benefit from bypass grafting. Therefore, he was treated medically with a betablocker, clopidogrel bisulfate, nitrates, and aspirin.

Laboratory results showed elevated hemoglobin (18.2 g/dL, normal 12.9–17.3 g/dL), hematocrit (52.4%, normal 38–51%), white blood cell count (WBC) (11,000/ $\mu$ L, normal 4,100–10,900/ $\mu$ L), and platelets (581,000/ $\mu$ L, normal 175,000–450,000/ $\mu$ L). Platelet levels increased further, reaching 696,000/ $\mu$ L 2 days later. Previous laboratory results from 2003 showed a hemoglobin of 17.3 g/dL, hematocrit of 48.8%, WBC of 10,300/ $\mu$ L, and platelets of 681,000/ $\mu$ L. Lipoprotein(a) was normal at <3 mg/dL. LDL cholesterol was normal at 81 mg/dL, HDL was low at 31 mg/dL (normal 35–80 mg/dL), and total cholesterol was 137 mg/dL. Other common causes for SCD, such as Marfan's syndrome, were ruled out by genetic testing.

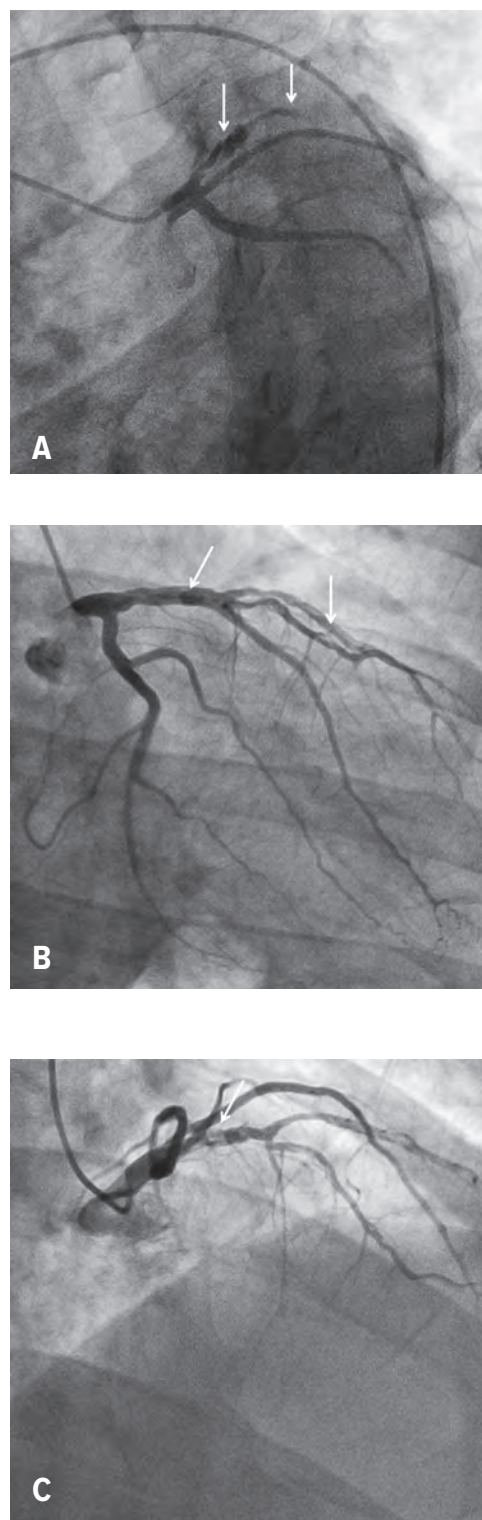
Further workup for thrombocytosis came back negative by polymerase chain reaction for *BCR-ABL* mutation, ruling out chronic myeloid leukemia, and positive for *JAK2* mutation. The patient also had a normal erythropoietin level at 4 mU/mL (normal 4–24 mU/mL). Ultrasound of the abdomen revealed moderate splenomegaly with slightly increased size since 2003. Platelet count 5 days later was persistently elevated at 482,000/ $\mu$ L.

The enlarged spleen, positive *JAK2* study, and persistently elevated platelet count confirmed the diagnosis of essential thrombocythemia. The patient was continued on aspirin and began hydroxyurea to lower platelet count. Following administration of hydroxyurea, the patient's platelet count came down to 458,000/ $\mu$ L in 6 months and to within the normal range at 348,000/ $\mu$ L in the following 6 months. The patient continues to be followed by hematology for monitoring of platelet counts.

## DISCUSSION

The pathogenesis of SCD remains controversial. It traditionally has been associated with young, predominantly female patients without cardiovascular risk factors, especially in the peripartum period.<sup>1</sup> SCD also has been associated with connective tissue disease, vasculopathies, and chronic inflammatory processes.<sup>3</sup> SCD is a rare cause of myocardial infarction, accounting for less than 1% of cases,<sup>4</sup> and lack of available data makes optimal treatment unclear.<sup>1</sup> In the context of acute coronary syndrome, management depends on the location, accessibility and extent of dissection, and the patient's clinical status.<sup>1</sup> Conservative treatment

**Figure.** Cardiac Catheterization



Shows a normal left main artery, but (A) left anterior descending artery with ostial and (B) very complex proximal and mid dissection and the (C) appearance of multiple lumens.

is preferred when SCD involves small vessels,<sup>1,4</sup> and percutaneous angioplasty or coronary bypass surgery is recommended in multivessel lesions, proximal lesions, or in patients with persistent ischemia, as they generally have the worst prognosis.

Essential thrombocythemia is a myeloproliferative disorder characterized by a high platelet count, originating from a pluripotent stem cell and is more commonly found in females, with an average age at diagnosis of 50 to 60 years.<sup>1</sup> Previous reports in the literature describe asymptomatic, chronic cases of SCD as well as an association with polycythemia.<sup>2,5</sup> Others have reported an association between essential thrombocythemia and internal carotid artery dissection and coronary occlusion,<sup>6,7</sup> but no association between SCD and essential thrombocythemia has been previously reported.

Myeloproliferative disorders are categorized broadly into 2 groups, including classic and atypical myeloproliferative neoplasias. For a complete discussion of these disorders, please see the World Health Organization (WHO) classification system described in 2009 by Tefferi and colleagues.<sup>8</sup> The group of classic myeloproliferative disorders includes polycythemia vera, essential thrombocythemia, primary myelofibrosis, and chronic myelogenous leukemia, all of which are associated with hypercoagulability. The incidence of thrombosis in patients with myeloproliferative neoplasms is significantly elevated with a higher incidence of arterial, rather than venous, thrombosis. Strokes are also frequent, followed by myocardial infarction, and peripheral arterial occlusion. Approximately 50% of patients with essential thrombocythemia are asymptomatic, while the other 50% have vasomotor, thrombotic, or hemorrhagic symptoms. Typical essential thrombocythemia is a Philadelphia *BCR-ABL* mutation-negative (Ph1-), chronic myeloproliferative disorder with a good prognosis for overall survival.<sup>9</sup>

The Polycythemia Vera Study Group (PVSG) originally defined diagnostic criteria for essential thrombocythemia in the 1980s, including a platelet count >600,000/ $\mu$ L, megakaryocytic hyperplasia on bone marrow aspiration and biopsy, absence of the Philadelphia chromosome, absence of infection, inflammation, or other causes for reactive thrombocytosis, normal red blood cell mass or a hemoglobin concentration of <13 g/dL, and the presence of stainable iron in a bone marrow aspiration or  $\leq 1$  g/dL increase in hemoglobin concentration after a 1-month trial of oral iron therapy.<sup>10</sup> Notably, the PVSG criteria did not include histopathological data. In 2001, the WHO developed a classification for chronic myeloproliferative disorders, incorporating clinical, laboratory, and morphologic data.<sup>11</sup> These classifications were further updated in 2008 with availability of additional genetic data.<sup>8</sup> The original PVSG criteria proposed a sustained platelet count of >600,000/ $\mu$ L, but the WHO lowered the threshold to 450,000/ $\mu$ L since the 95th percentile for normal platelet count, adjusted for gender and race, is below

400,000/ $\mu$ L and the PVSG criteria were thought to potentially compromise the detection of early phase essential thrombocythemia. The demonstration of *JAK2* mutation is present in 50% to 55% of patients with essential thrombocythemia, and demonstration of this marker or another clonal in its absence is included in the WHO criteria. Since the *JAK2* mutation is absent in approximately half of essential thrombocythemia patients, bone marrow biopsy is still required for diagnosis according to WHO criteria. Importantly, the *JAK2* mutation is absent in patients with reactive thrombocytosis.<sup>8,9</sup>

There is no consensus as to which set of criteria should be followed for diagnosis of essential thrombocythemia and some hematologists continue to use the PVSG criteria. Ultimately, the diagnosis of essential thrombocythemia is made by sustained platelet elevations of 450,000/ $\mu$ L without signs of reactive thrombocytosis and the presence of the *JAK2* mutation, or in its absence, a bone marrow exam excluding the presence of other myeloproliferative disorders, such as polycythemia vera, primary myelofibrosis, or chronic myeloid leukemia.

The management of thrombocytosis in patients with myeloproliferative neoplasms currently entails the use of antiplatelet and cytoreductive therapies. In a randomized trial, aspirin was found to reduce the risk of thrombosis in patients with polycythemia, but it did not reduce mortality.<sup>9</sup> Cytoreductive therapies, such as hydroxyurea, phlebotomy, and interferon- $\alpha$ , are considered for patients at high risk for thrombosis or bleeding, including those older than 60 years of age, those with a history of major thrombosis or hemorrhage, and those with platelet counts greater than 1.5 million/ $\mu$ L. Hydroxyurea effectively reduces elevated cell counts, spleen size, and thrombotic risk.<sup>9</sup> In the case presented here, the patient was treated conservatively with aspirin and hydroxyurea, and continues to be asymptomatic.

## CONCLUSION

Essential thrombocythemia can predispose individuals to vascular dysfunction and damage, which may contribute to coronary artery dissection. With this case, we propose that essential thrombocythemia should be excluded in the presence of coronary dissection and thrombocytosis.

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# Proceedings from the 2013 Annual Meeting of the American College of Physicians, Wisconsin Chapter

The following abstracts were presented during the 58th Annual Meeting of the Wisconsin Chapter of the American College of Physicians in 2013. Internal medicine residents from each of Wisconsin's 5 residency programs presented their research and/or unusual clinical experience via case- and research-based vignettes and posters. All of the vignettes as well as the winning posters are published here. Additional poster presentations are available online and can be accessed at [www.wisconsinmedicalsociety.org/professional/wmj/WPAC\\_abstracts\\_2013.pdf](http://www.wisconsinmedicalsociety.org/professional/wmj/WPAC_abstracts_2013.pdf).

## CASE-BASED VIGNETTES

### 1st place

#### Adderall-induced Bilateral Blindness

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**Introduction:** Pseudotumor cerebri (PTC) is a rare disorder of unknown etiology, most commonly seen in obese females of child bearing age, that usually has a self-limited disease course. Although certain medications (tetracycline, retinoids, etc) have been associated with PTC, there have only been 6 case reports of adderall-associated PTC. We describe the case of a 35-year-old man on Adderall who developed PTC with bilateral vision loss.

**Case:** A 35-year-old man on Adderall with a history of attention deficit hyperactivity disorder (ADHD) presented with 6 days history of rapid bilateral complete vision loss. He also complained of headache but no diplopia. Physical exam revealed no perception of hand movements or light, normal intraocular pressure on eye exam. Fundoscopy revealed bilateral papilledema with retinal hemorrhages. The rest of his neurological exam was normal. Complete blood cell count (CBC), comprehensive metabolic panel (CMP), erythrocyte sedimentation rate (ESR), angiotensin-converting enzyme

(ACE) levels, magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) were all normal. Lumbar puncture (LP) demonstrated an opening pressure of 330 mm H<sub>2</sub>O with significant relief of his headache and improvement of vision. Cerebrospinal fluid (CSF) analysis including protein, glucose, cell count, Venereal Disease Research Laboratory test (VDRL), herpes simplex virus (HSV), varicella-zoster (VZ) polymerase chain reaction (PCR) test, *Toxoplasma*, cryptococcal antigen, West Nile Virus, *B burgdorferi*, Gram stain, bacterial, viral, and fungal cultures, and cytology were all normal. Work-up for multiple sclerosis (MS) was negative. He was diagnosed with Pseudotumor cerebri. Adderall was stopped. He was treated with acetazolamide and steroids. A lumboperitoneal (LP) shunt was placed with continuous gradual improvement in vision. Post discharge he regained his vision completely and, as a result, optic nerve fenestration procedure was felt unnecessary.

**Discussion:** PTC is a rare disorder with an incidence of 1/100,000. More than 90% of cases are seen in women of child bearing age. It is extremely rare in a young male like our patient. It is characterized by headache, vision loss, and papilledema, normal MRI, MRV, and an elevated opening pressure on

LP. Optic neuritis, MS and glaucoma all were ruled out in our patient. PTC also has been associated with other diseases such as hypoparathyroidism, anemia, and systemic lupus erythematosus (SLE), which were ruled out in our patient. Medications have been associated with PTC. Growth hormone, tetracycline, and retinoids have well-defined association. Others with more anecdotal evidence include lithium and steroid withdrawal. There have been only been 6 reports of PTC in patients on Adderall. Our patient's only home medication at presentation was Adderall. Treatment options include acetazolamide, steroids (short term) and surgical options like optic nerve sheath fenestration (ONSF) and CSF shunt. Our patient was started on acetazolamide and had a CSF shunt placed with dramatic improvement in his vision.

#### Airway Compression Resulting from Mediastinitis

Istiaq Mian, University of Wisconsin School of Medicine and Public Health, Madison, Wis

**Introduction:** Fibrosing mediastinitis is described as excessive fibrotic reaction in the mediastinum. It can result in the compromise of airways and great vessels. It is thought to be a sequel of histoplasmosis, though it can be idiopathic or autoimmune. Less than 1% of 500,000 annual cases of histoplasmosis develop fibrosing mediastinitis, making it a rare diagnosis.

**Case:** An 81-year-old retired man with a history of deep vein thrombosis (DVT) presented to the emergency department (ED) for a tender right neck mass of 1 day duration. He reported that he was hospitalized twice in the past 6 months for this type of transient mass. Chest x-ray showed no acute cardiopulmonary findings. Computed

tomographic (CT) scan of his neck showed findings compatible with a myositis vs parotitis. The patient was diagnosed with parotitis and discharged on augmentin, just in time to make his granddaughter's wedding.

The patient returned 3 days later presenting with the same complaint. Exam was significant for a 6 x 4-cm rubbery, warm pink mass over the right sternocleidomastoid (SCM) muscle. ESR was elevated at 104. CT scan of his neck compared to 3 days prior showed enlargement of SCM and the right-sided strap muscle overlying the thyroid cartilage, increasing 3-fold in thickness compared to the contralateral side. The larynx was displaced in a leftward direction and there was subtotal fibrous occlusion of the superior vena cava. Ultrasound-guided biopsy of the right SCM muscle showed dense fibrosis.

Though there is no curative therapy for fibrosing mediastinitis, a case report on SCM enlargement suggested treatment with prednisone. To treat airway compression resulting from his neck mass, the patient was given 60 mg prednisone and the patient's neck mass dissolved over the next 2 days. At follow-up 1 week later, the patient did not report symptoms.

*Discussion:* This case illustrates a rare diagnosis resulting in airway compression. Though it is reported that glucocorticoids do not appear to be beneficial in treatment of fibrosing mediastinitis, controlled trials have not been performed. In this case, when airway compression presented, glucocorticoids proved to alleviate symptoms.

### **Bleomycin-induced Pulmonary Fibrosis**

Chris Lowry, DO, Rachel Hawker, MD, FACP, Gundersen Health System, La Crosse, Wis

*Case:* A 43-year-old woman presented to the ED of our institution with the chief complaint of cough and minimal shortness of breath for 5 days duration. She denied fevers, chills, sweats, malaise, and/or any other global symptoms. Chest radiograph revealed a suspected right lower lobe infiltrate and her vitals were significant only for mild tachycardia. She was started on treatment for community-acquired pneumonia with Levaquin, supplemental oxygen, and intravenous (IV) fluids and admitted to the floor.

The patient's medical history was significant for hypertension, recurrent cystitis, and a granulosa cell tumor, for which she had undergone surgery and completed chemotherapy 3 months prior. Within the first 24 hours, the patient's clinical picture remained unchanged. She never mounted an increased leukocytosis and had no improvement in her tachycardia with fluid resuscitation. Echocardiogram was obtained showing normal ejection fraction (EF) and no global ischemia or impaired cardiac function. Due to failure to improve, a chest CT and pulmonary consult were ordered. Her CT showed diffuse ground glass opacities concerning for diffuse infection vs diffuse alveolar damage. An infectious disease consult was placed for further guidance and the patient was started on anti-fungals as well as additional antibiotics for broader coverage. She also was started on steroids for *Pneumocystis jirovecii* pneumonia (PCP) coverage and suspected bleomycin-induced lung injury. A bronchoscopy with bronchial-alveolar lavage was performed, which yielded no findings on Gram stain and all cultures had no growth. All rheumatological assays also remained negative and the patient was diagnosed with bleomycin-induced lung injury. During an 18-day hospital course, the patient developed acute respiratory failure that was refractory to all treatments and therapies available and attempted. Care was withdrawn on day 18, as her prognosis had been determined as terminal and futile and family chose not to pursue further care/treatment.

*Discussion:* This case represents the known complication of pulmonary fibrosis secondary to bleomycin toxicity. Although rare, this complication is often fatal and should be considered in patients with prior therapy presenting with respiratory complaints.

### **Cutaneous Findings as a Clue for Occult Metastatic Prostate Cancer**

Jesse Jacobs, Benjamin Ekstrom MD, David Wagner MD, Department of Medicine, Medical College of Wisconsin, Milwaukee, Wis

*Introduction:* While prostate cancer is among the most common cancers in men, cutaneous findings indicative of metastatic disease are exceedingly rare. Here we present a case of cutaneous metastasis from prostate cancer

in a gentleman presenting with neurological findings.

*Case:* An 83-year-old-man with a history of congestive heart failure (CHF), pacemaker-dependent atrial fibrillation, and prostate cancer (status post transurethral resection of the prostate [TURP] in 2012) presented from an outside hospital for recurrent falls, progressive weakness, and dizziness over 4 months. Head CT 3 months prior was concerning for acute posterior circulation ischemic stroke, but a recent head CT revealed multiple hypodense, contrast-enhancing lesions more consistent with metastatic malignancy. On admission, further imaging showed widespread lung, mediastinal, pelvic, and prostate involvement. Findings on exam revealed a 4 x 4-cm hard, mobile nodule on the left central chest that had been present for "roughly 10 years," but previously had been deemed a benign cyst by an outside provider. Skin biopsy showed an invasive, poorly differentiated tumor deep within the dermis with positive prostate-specific antigen (PSA), prosaposin (PSAP) and CD56 immunostaining. PSA was noted to be 27.1 during admission, and was 14.9 four months prior. The patient was stable throughout his stay and offered radiation and chemotherapy treatment, but elected for hospice care closer to home. Per the patient's request, his cardiac defibrillator was deactivated, and he subsequently passed away 5 days after discharge.

*Discussion:* This case begs the question if earlier identification of a PSA-positive cutaneous nodule might have allowed earlier intervention, which could have altered this patient's outcome. While cutaneous presentation is indeed a rare finding in metastatic prostate cancer, care should be taken to investigate any unusual skin finding in the setting of a known malignancy. Furthermore, we submit that metastatic lesions should be included in the differential for a hypodense lesion in the brain, even when ischemic stroke is the primary concern.

### **A Heart in Trouble**

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*Background:* Pulmonary embolism (PE) ranges from asymptomatic, incidentally dis-

covered emboli to massive, fatal embolism. Acute PE can occur unpredictably and may be difficult to diagnose. We describe a highly unusual initial presentation of PE involving syncope, Torsade de pointes, rapidly progressive heart failure, and pulmonary hypertension.

**Case:** A 19-year-old morbidly obese man was hospitalized after presenting with micturitional syncope. While hospitalized, he had 2 additional episodes of unresponsiveness requiring cardiopulmonary resuscitation (CPR), during which he was noted to be in polymorphic ventricular tachycardia (Torsade de pointes). He had return of spontaneous circulation following defibrillation and was transferred to our tertiary care center. On admission, he denied dyspnea or chest pain and had normal vital signs. He was found to have a prolonged corrected QT interval of >630 ms and a mild troponin leak. A transthoracic echocardiogram (TTE) revealed biventricular failure with an EF of 40%, moderate right ventricular dysfunction, moderate tricuspid regurgitation (TR) and pulmonary hypertension. A cardiac catheterization revealed elevated right-sided filling pressures, normal left-sided filling pressures, pre-capillary pulmonary hypertension, and decreased cardiac output. A repeat TTE 2 days later showed stable left ventricular function but worsened right ventricular function and pulmonary hypertension, and severe TR that had acutely worsened. A chest CT angiogram revealed a massive, saddle PE with signs of right heart strain and bilateral pulmonary infarction of the lower lobes. He was treated with systemic thrombolytic therapy and heparin bridging to long-term warfarin. An ultrasound with Doppler imaging of his lower extremities confirmed a large acute deep vein thrombosis in the left lower extremity, for which an inferior vena cava filter was placed. He remained without recurrence of any syncopal events or arrhythmias, and a repeat TTE prior to discharge showed modest improvement in his right ventricular systolic function.

**Discussion:** This patient had no provocative factors for venous thromboembolism (VTE), and clinical prediction scores indicated a low probability of PE. The clinical presentation

of tachyarrhythmia-induced syncope, rapidly progressive heart failure in the absence of dyspnea, chest pain, hypoxia, or hypotension makes this case an unusual presentation for PE. Additionally, the unprovoked nature of this event means strong consideration for lifelong anticoagulation should be given.

### **A Heart-smelting Case of Chest Pain and Dyspnea Following Zinc Oxide Exposure**

Daniel Harland, Jeff Gehl, Mohan Dhariwal, Medical College of Wisconsin Affiliated Hospitals, Milwaukee, Wis

**Background:** Metal Fume Fever, otherwise known as Smelter's Fever, is a well-documented constellation of symptoms that follow inhalational exposure to certain metal fumes.

**Case:** A 48-year-old man auto parts manufacturer with no past medical history presented with complaints of chest tightness and difficulty breathing. One day prior, the patient was at work during a "meltdown" wherein molten zinc was accidentally mixed with hydraulic fluid, producing a thick white smoke that the patient breathed in for approximately 2 to 3 minutes. The patient stated that shortly thereafter he developed a cough. He woke up the next day with difficulty breathing, pleuritic pain, and a sensation like his chest "had concrete on it." He denied hemoptysis or palpitations. On admission he was febrile to 101.2 but defervesced quickly. Chest x-ray showed no acute lung pathology but demonstrated a heart size at the upper limits of normal. He underwent CT PE-protocol that showed no PE but demonstrated a possible pericardial effusion with no other lung involvement. The patient was started on ibuprofen for pericarditis and given PRN nebulizers for shortness of breath. Overnight the patient improved markedly with supportive care and reported resolution of his dyspnea and improvement in his cough, although he had some lingering chest discomfort. He was discharged home with a prescription for 14 days of ibuprofen therapy three times a day and a short course of inhaled steroids and albuterol. Based off of his presumed exposure to zinc oxide fumes and presentation with delayed onset chest pain, shortness of breath, and fever, the patient was likely experiencing Metal Fume Fever.

**Discussion:** Metal Fume Fever is an acute, self-limited illness that is tied almost exclusively to inhalational exposure of heavy metal oxides and is a common occupational hazard among welders and smelters. The diagnosis is made largely by constellation of symptoms and recent inhalational exposure to metal oxides. Typical presentation is 24 to 48 hours after exposure and patients often complain of chest pain, fevers, and chills. Symptoms rarely last longer than 24 hours and the care is supportive. It is important to distinguish this illness from other common respiratory conditions that may require more aggressive medical therapy.

### **Hypoxemia, Heart Failure, and Recurrent Stroke Associated With a Giant Pulmonary AVM**

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**Background:** Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder of the vasculature characterized by telangiectasias and arteriovenous malformations (AVMs) of the skin, mucous membranes, lung, brain, and gastrointestinal (GI) tract. Patients with HHT experience a wide range of symptoms depending on the location of vascular abnormalities. We present a patient with HHT admitted with a massive pulmonary AVM (pAVM), hypoxemia, and heart failure. This pAVM is among the largest in the literature successfully treated with embolization; previously reported massive pAVMs have been treated with resection.

**Case:** A 70-year-old woman with a long-standing history of HHT, atrial fibrillation, and recurrent cerebrovascular accidents was admitted with confusion, hypoxia, and generalized weakness. On arrival, she was tachypneic and hypoxic. She had an irregularly irregular heartbeat, clear lungs, 3+ lower extremity edema, and lip telangiectasias. Labs were significant for elevated brain natriuretic peptide (BNP) and hypoxemia. Her P/F ratio was 52. Chest imaging showed cardiomegaly, a large right lower lobe pAVM, and no pulmonary embolism. Transthoracic echo revealed an apical thrombus in the left ventricle, EF 30%, and severely dilated cham-



bers. Shunt study demonstrated a fraction of 25%. The patient's pAVM measured 3.6 x 7 cm and the feeding artery measured 14 mm. Her pAVM was successfully embolized with a 22 mm Amplatzer upon which her P/ F ratio improved to 263.

*Discussion:* AVMs are direct connections between arteries and veins with resultant bypass of capillary beds. In the lungs, capillaries facilitate gas exchange, but also filter emboli and bacteria from the bloodstream. Loss of capillary bed filtration and right-to-left shunting from pAVMs allow passage of emboli into the cerebral circulation. Patients can develop brain abscesses, transient ischemic attacks, or ischemic strokes; unfortunately, these are often the first manifestations of a pAVM. Because of these potentially catastrophic initial presentations, routine screening for pAVMs is recommended for all patients with HHT. Guidelines suggest embolization of pAVMs with feeding arteries >1 mm.

*Conclusion:* HHT can be associated with dysfunction of multiple organs; screening for involvement of brain and lung vasculature is important because early intervention can significantly decrease morbidity and mortality.

### **Inferior Vena Cava Syndrome in a Patient With Giant Hepatic Hemangiomas**

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*Background:* Inferior vena cava (IVC) syndrome is caused by compression of the IVC. This syndrome is characterized by abdominal discomfort, anasarca below the level of the diaphragm, abdominal ascites, hepatomegaly, shortness of breath, and increased risk for infection and thrombosis. IVC syndrome most commonly occurs in the setting of thrombosis. IVC syndrome also can occur in patients with neoplastic hepatic masses and has been reported in association with biloma.

*Case:* We present a 60-year-old woman who developed IVC syndrome in the setting of multiple giant hepatic hemangiomas. She had recently been hospitalized for management of bleeding from the hepatic hemangiomas and had undergone chemical and coil embolizations of the superior right hepatic artery and the right hepatic segmental arter-

ies. Presenting symptoms included fatigue, increasing difficulty with activities of daily living, insomnia, right upper quadrant pain, back pain, and redness and weeping of right thigh. Pertinent findings on examination included shallow respirations with clear lung fields, prominent abdominal ascites, anasarca up through the abdomen, and weeping ulcers on right thigh and groin. Laboratory abnormalities included anemia, elevated liver function tests and international normalized ratio (INR), hypoalbuminemia, hyponatremia, and hypochloremia. She was re-admitted to the hospital. Abdominal ultrasound and subsequent abdominal CT scan imaging demonstrated multiple giant hepatic hemangiomas causing mechanical compression of the IVC. Initial attempts at volume reduction using diuretics and paracentesis were unsuccessful with persistence of hyponatremia and slight worsening of renal function. Subsequent fluid challenge improved sodium but increased dyspnea and anasarca. Despite evidence for anasarca and ascites, she appeared to be intravascularly volume depleted. Hyponatremia only responded to IV fluids, which caused worsening of her other symptoms. The patient was ultimately transferred to another medical center for stenting of the IVC, a procedure that has been successful in patients with IVC syndrome associated with hepatic neoplasms. Unfortunately, the patient died from complications of the IVC stenting procedure.

### **Nasal Type Extranodal NK/T-cell Lymphoma: A Diagnostic Challenge**

B. Yeneneh, MD, MS, L. Boujelbane, MD, MPH, Aurora Health Care, Milwaukee, Wis

*Introduction:* Extranodal NK/T-cell Lymphoma (ENKTL) is an aggressive non-Hodgkin's lymphoma (NHL), rare in the United States. It is common in Asia and Latin America. It primarily involves the nose and upper aerodigestive tract. It is invariably associated with Epstein-Barr virus (EBV) infection. This case illustrates the potential challenge in the diagnosis of ENKTL.

*Case:* A 49-year-old Hispanic woman presented with progressively worsening headaches for 2 months, low-grade fever, foul-smelling nasal discharge, and left periorbital

swelling. She was treated previously for bacterial sinusitis. Physical exam noted blood mixed purulent drainage from nares and tender sinuses bilaterally. Labs showed anemia and microscopic hematuria. CT scan showed soft tissue mass in the right nasal cavity extending into the left orbit. Bilateral nasal endoscopy showed advanced necrosis, highly suspicious for Wegener's granulomatosis. Biopsy showed extensive bone and soft tissue necrosis. Though serologic markers were negative, patient was started on treatment for Wegener's granulomatosis. Due to lack of improvement after 14 days, patient had additional biopsies. Pathology this time revealed ENKTL. Patient was started on chemoradiation. She did well initially, but passed away 6 weeks later from disseminated disease.

*Discussion:* ENKTL is a rare malignant disorder (1.5% of all lymphomas in the United States), presenting in adults in their 5th decade with 3:1 male predominance. Most present with nasal obstruction, sinusitis, ulcer, or epistaxis. ENKTL is characterized by an extensive vascular destruction and tissue necrosis, aggressive clinical course, and poor clinical outcome. Accurate diagnosis is prolonged and very challenging due to insufficient tissue samples, extensive necrosis, and limited clinician experience. A meticulous examination by otorhinolaryngologist is mandatory. Nasal endoscopy should be performed and multiple biopsies obtained from involved and suspicious areas. Tissue samples should be fresh and forwarded to an experienced pathologist. Combined chemoradiation may be effective for localized disease if diagnosed early.

### **Orofacial Dystonia as a Manifestation of Globus Pallidus Lesions**

Suma Singh, MD, Reena Kunreddy, MD, Lori Remeika, MD; Marshfield Clinic, Marshfield, Wis

*Background:* Basal ganglia lesions are rare, generally reflecting global derangements such as toxic poisoning, metabolic abnormalities, vascular abnormalities, focal inflammatory and infectious conditions. These lesions usually manifest with movement disorders. We present the case of a patient who presented with new onset bruxism that coincided with bilateral signal intensity changes in her globi



pallidi believed to be secondary to decompensated liver disease.

**Case:** A 39-year-old woman with approximately 20 years of alcohol abuse and alcoholic liver disease presented to our facility for worsening abdominal pain. She also reported a 2-day history of speech changes. She previously had been at her baseline state of health, although she was chronically ill with alcoholic liver disease and its sequelae including jaundice, hepatic encephalopathy, cirrhosis, and ascites. Physical examination revealed jaundiced skin and sclerae, abdominal distension, and, perhaps most notably, a clenching of the teeth and jaw and slowed speech. She reported that her last drink was 9 months prior to presentation; blood alcohol levels were negative. She also denied using any other illicit drugs including cocaine or heroin. Urine drug screen was negative. MRI of her brain revealed focal, well-defined, symmetric areas of increased T1 and T2 in the globus pallidus bilaterally, which were not considered typical for alcoholism, nutritional abnormalities, or other metabolic factors. Workup for other heavy metals and carbon monoxide were negative.

After ruling out metallic, carbon monoxide poisoning and Wilson's disease, we think that the patient's presentation is most consistent with acute decompensation of alcoholic liver disease. We propose that her new onset diurnal bruxism was due to systemic metabolic derangement from chronic liver disease. Clinicians should look for systemic insults if bilateral lesions of the basal ganglia—especially the globus pallidus—are seen on brain imaging and may manifest as bruxism.

### **A Strikingly Unusual Skin Reaction to Vancomycin**

Sunitha Ittaman, MD, Chukwunyelu Enwezor, MD, John Melski, MD, Marshfield Clinic, Marshfield Wis

**Introduction:** Vancomycin has been in use for more than 50 years and has been associated with multiple dermatological adverse reactions such as morbilliform exanthem and red man syndrome with its more frequent use. In this report we document the joint occurrence of 2 rare hypersensitivity reactions sec-

ondary to vancomycin in the same patient.

**Case:** A 59-year-old Italian American man was admitted for the evaluation of vesiculobullous lesions. The patient was just discharged from the hospital after a 3-week stay for septic arthritis of the right shoulder and related *staphylococcus aureus* sepsis. During that period, the patient had received 1 dose of vancomycin with scheduled ampicillin/sulbactam. Ampicillin/sulbactam was subsequently discontinued because of the development of palpable purpura involving both lower limbs and left arm, proven to be leukocytoclastic vasculitis by histopathology. The patient also had splinter hemorrhages with no transesophageal echocardiogram (TEE) evidence for infective endocarditis. His serial blood cultures were negative and vancomycin was continued. The preexisting lesions, however, continued to worsen, turning to vesicles and bullae. Subsequent histopathology showed evidence of linear IgA Bullous dermatosis (LABD) without signs of vasculitis. Vancomycin was discontinued and the patient was started on low-dose dapsone that was advanced as tolerated to 100 mg daily and topical wound care. The lesions started getting better in 3 to 4 days.

**Discussion:** LABD is a very rare disease with an incidence of 0.5 to 2.3 per million people. A comprehensive literature search revealed only 2 case reports so far of leukocytoclastic vasculitis caused by vancomycin. LABD secondary to vancomycin has not yet been described as concurrent with vasculitis, which makes this a unique presentation. The treatment is always discontinuation of the offending drug.

### **Without a Target: Understanding Atypical Presentations of Lyme Disease**

B. Smeltzer, R. Krippendorf, K. Pfeifer, Medical College of Wisconsin, Milwaukee, Wis

**Introduction:** Lyme disease is the most common tick-borne disease in the United States and Europe. The most common clinical manifestation is the classic target lesion of erythema migrans. Patients also present without erythema migrans with nonspecific complaints such as headache, arthralgias, fatigue, cognitive slowing, and memory difficulty.

**Case:** A 75-year-old man presented with a 3-week history of weakness, low back pain, upper extremity tremors, and double vision. As a result of these symptoms, he reported having difficulty writing, dialing phone numbers, and reading. He also had a weight loss of 20 pounds over several weeks that he attributed to decreased appetite, dysphagia, and odynophagia. He denied possible ingestions of toxins, medication misuse, recent travel, and insect or tick bites. The patient's neurologic exam revealed decreased reflexes but normal muscle tone, bulk, and power. He had a positive Romberg test, intention tremor with finger-to-nose testing, delayed rapid alternating hand movements on his left side, and a wide-based gait. He also had vertical diplopia with leftward gaze and scored only 13 out of 30 on Montreal cognitive assessment. Brain MRI was significant for slightly prominent ventriculomegaly and global volume loss. He underwent lumbar puncture, and CSF analysis revealed elevated protein, elevated leukocyte count, normal glucose, negative cytology, and negative Gram stain and culture. Subsequent MRI of his lumbar spine revealed diffuse leptomeningeal enhancement along the visualized lower cord, conus, and cauda equina. Eventually, CSF Lyme serologies returned positive for IgG and were confirmed by western blot. The patient was treated with a 2-week course of ceftriaxone and was improved at the end of his therapy.

**Discussion:** The more serious clinical sequelae of Lyme disease develop as a consequence of the hematogenous spread of the spirochete. Approximately 10% of patients with erythema migrans who go untreated will have a neurologic manifestation such as trigeminal neuralgia, facial nerve palsy, meningitis, or encephalopathy. Lyme encephalomyelitis is a rare observation that occurs when inflammatory appearing parenchymal abnormalities appear in the brain or spinal cord. Randomized trials have shown that doxycycline, amoxicillin, and cefuroxime are effective oral treatments for Lyme disease. Those patients who have evidence of disseminated infection, including neurologic manifestations or Lyme carditis, might be considered for parenteral antibiotics.

## RESEARCH-BASED VIGNETTES

### 1st place

#### **RALYL Hypermethylation: A Potential Molecular Diagnostic Marker for Esophageal Squamous Cell Carcinoma**

J.W. Liu, MD, D. Sidransky, MD; Aurora Health Care Program, Milwaukee, Wis and Johns Hopkins University School of Medicine, Baltimore, Md

**Background:** Esophageal cancer is the third most common cancer of the human digestive tract. The most common types of esophageal cancer are squamous cell carcinoma and adenocarcinoma. Most esophageal cancer is diagnosed at advance stages, contributing to the high ratio of mortality to incidence. Therefore, it is important to discover novel molecular markers for esophageal cancer to augment current early detection approaches.

**Experimental Design:** Utilizing a pharmacologic unmasking and subsequent microarray analysis, we identified RALY-like protein (RALYL) as a novel cancer-specific methylated gene in esophageal squamous cell carcinoma (ESCC). A methylation-specific polymerase chain reaction (PCR) primer set was developed, methylation in RALYL promoter area was confirmed by DNA sequencing. We then performed real-time quantitative methylation-specific PCR (TaqMan-MSP) in primary cancer tissues to confirm hypermethylation of the RALYL promoter in tumor and analyzed its correlation with clinicopathological data.

**Results:** In this study, we found that RALYL was hypermethylated in human ESCC cell lines and primary tumor tissues but not in normal esophageal tissue. Quantitative MSP confirmed RALYL promoter hypermethylation in 61% (34/56) of the primary ESCC compared to 0% (0/17) in normal esophageal tissues with cutoff value of 10. RALYL methylation status was closely related to differentiation status of ESCC ( $P=0.016$ ). No significance was found between RALYL methylation and lymph node metastasis or tumor staging.

**Conclusion:** RALYL appears to represent a novel cancer-specific diagnostic DNA marker in esophageal squamous cell carcinoma, especially in well-differentiated ESCC.

#### **Endoscopic Protection From Left vs Right-sided Colon Cancer**

Y. Fotaria, S. Rathgaber, S. Pearson; Gundersen Health System, La Crosse, Wis

**Purpose:** We sought to determine if the protective effect of prior endoscopy was different for left- vs right-sided colon cancer within our integrated health system.

**Methods:** All patients diagnosed with primary colorectal-adenocarcinoma between January 2006 and March 2013 were reviewed retrospectively. Patients were excluded if they had a history of inflammatory bowel disease, an inherited cancer syndrome, or were less than 50 years at diagnosis. Patients with transverse colon tumors were excluded. Staging and location of tumors were confirmed by pathologic examination of surgical specimens. Patients were categorized by left- or right-sided cancer and by prior protective endoscopy within 6 months to 10 years before diagnosis or no prior protective endoscopy. Protective endoscopy was defined as colonoscopy completed to the cecum for right-sided cancer and colonoscopy or flexible sigmoidoscopy for left-sided cancer. Groups were analyzed for survival, stage, age, sex, and body mass index (BMI). Comparison of the prevalence of right- and left-sided cancers utilized the Mantel-Haenszel chi-square test. Survival curves were generated using the Kaplan-Meier method and survival times were compared using the log-rank test. Comparisons of BMI and age utilized the student's  $t$ -test.

**Results:** Three hundred fifty-seven patients were included. One hundred ninety-seven (55.2%) cancers were left-sided; 160 (44.8%) cancers were right-sided. One hundred thirty-three (31.6%) had a protective endoscopy. Fewer patients with left-sided cancer had prior endoscopy than right-sided cancer (25.4% vs 39.4%,  $P<0.005$ ). Cancer was diagnosed at an older age in patients with prior endoscopy (74.7 vs 70.2 years,  $P=0.0002$ ). Trends occurred in the prior endoscopy group toward earlier cancer stage ( $P<0.083$ ) and improved survival ( $P<0.074$ ). BMI had no effect on any category.

**Conclusion:** There is statistically significant difference in prior endoscopy rates between left- and right-sided colon cancer patients.

This suggests that endoscopy is more protective for left-sided colon cancer than right-sided colon cancer within this integrated health care system. A prior "protective" endoscopy may also result in earlier stage at diagnosis, improved survival, and older age at diagnosis.

#### **Provider Understanding and Utilization of Advance Directives**

Sharon Rikin, MD, Mark Repenshek, PhD, Adam King, MD, MS; Medical College of Wisconsin and Columbia-St. Mary's Hospital, Milwaukee, Wis

**Background:** Completion of advance directives (AD) can improve the quality of care for patients at the end of life and improve health care spending. AD allow patients to communicate health care preferences when they are no longer able to make these decisions. Despite many health system efforts, completion of AD ranges from 5% to 15% among hospitalized patients. The purpose of this study is to assess health care providers' knowledge, comfort level, implementation of, and barriers to use of AD in various health care settings.

**Methods:** We anonymously surveyed health care providers across all specialties within a tertiary care center in southeastern Wisconsin.

**Results:** Of 739 providers, 104 completed the survey. Respondents include physicians from internal medicine (60%), general surgery and surgical subspecialties (22%), family medicine (10%), and others. Approximately half of the providers work in acute care and half in an outpatient setting. The majority (70%) have over 8 years of experience. Most providers (69%) think AD are important in hospitalized patients and almost half (49%) think they are important for all patients over the age of 65. Many providers (41%) are unaware of how to access a patient AD stored in an electronic health record (EHR). The majority of providers (78%) feel knowledgeable or very knowledgeable about AD; similarly 85% felt comfortable or very comfortable with discussing AD. Providers are more likely to use AD to help determine Durable Powers of Attorney (DPOA) (68%), but only occasionally prior to hospitalization (30%) or to determine goals of care (48%). Significant barriers to utilizing AD include time constraints

(50%), not feeling a sense of responsibility to discuss AD (17%), not feeling knowledgeable about AD (13%), not feeling comfortable discussing AD (8%), not the right time (4%), patient factors (5%), and feeling that AD are unhelpful (2%).

*Discussion:* Although most physicians consider AD to be important and feel they have a good sense of knowledge and comfort with AD, many of them do not use AD in their clinical practice. Identified barriers are logistical (inability to access AD, time consuming) due to provider attitude or assumptions regarding AD (“not my responsibility as a provider,” “not the right time”) and relate to a need for patient education. The results reveal many areas for quality improvement to improve provider access to AD, to incorporate AD into the workflow, and for patient education.

### **Variability of Door-to-Device Times in Patients Presenting With STEMI at a Rural Tertiary Care Center**

Victor Abris, MD, Roxann Rokey, MD, FACC, FASE, Juan Mesa, MD, FACC; Marshfield Clinic – St. Joseph’s Hospital, Marshfield, Wis

*Background:* The goal door-to-device (DTD) time for ST-segment elevation myocardial infarction (STEMI) patients by the American College of Cardiology/American Heart Association has been 90 minutes, with no distinction between urban and rural hospitals. Compared to urban hospitals, rural hospitals have been reported to have longer DTD times for transferred patients. Longer DTD times have also been reported during after-hours. Seasonal variability has not been studied in this regard.

*Methods:* Four hundred twelve patients presenting with STEMI from 2006 to 2012 after initiation of the Rescue One program for their rapid triage and transfer were divided by season, method of arrival (ED, urgent care, field, and transfers), and time period (ON = Monday-Friday from 9AM to 5PM; OFF = after hours, weekends, and holidays). Median DTD times and proportions of patients achieving DTD times below and above 90 minutes in these subgroups were compared using statistical methods.

*Results:* Overall median DTD time was 85 minutes; 60% of patients achieved DTD

times below 90 minutes and 30-day mortality was 5.3%. A significant difference in median DTD time was observed between spring and fall, though this did not affect the proportions of patients achieving goal DTD times. Patients arriving by ED during OFF hours had a median DTD time 28 minutes longer than during ON hours, representing the time needed to call in the catheterization team; 21% fewer ED patients achieved goal DTD time during OFF hours. Other rural hospitals of similar size were found to have similar DTD times, proportions achieving goal DTD time, and mortality.

*Conclusions:* In a rural tertiary care center, seasonal variability in DTD time exists but does not affect achievement of goal DTD time. Transportation time needs to be taken into account in DTD times for transferred patients. Improving DTD times during OFF hours for patients arriving by ED may be warranted.

## **DISPLAYED POSTERS**

### **1st place**

#### **Re-emerging Cause of Acute Aseptic Meningoencephalitis**

Andrew P. Vreede, MD, Shery Youssef, MD, Meghan Brennan, MD; University of Wisconsin, Madison, Wis

*Introduction:* Determining the cause of acute aseptic meningoencephalitis requires a broad differential. In many cases, a specific cause remains elusive. We describe a 59-year-old woman presenting in April with fever, leukocytosis, rash, and altered mental status, who was found to have acute aseptic meningoencephalitis due to a re-emerging pathogen.

*Case:* The patient had no past medical history, lived in rural southern Wisconsin with healthy horses, had not traveled, and frequently cared for her young grandchildren. Two weeks prior to admission, a rash developed on her anterior thighs that spread to involve the remainder of her body, except her palms and soles. The week prior to admission, the patient noted fatigue, subjective fever, anorexia, sore throat, and congestion. On admission, the patient was febrile to 39°C, tachycardic to 110 with stable blood pressures. Physical exam was notable for a diffuse erythematous maculo-

popular rash. Laboratory analysis was notable for a leukocytosis of 18,400 (91% neutrophils), thrombocytopenia (118), and normal chemistry and liver enzymes. On hospital day 1, the patient acutely developed expressive aphasia and somnolence without headache or nuchal rigidity. Imaging demonstrated no evidence of stroke or focal process. A lumbar puncture demonstrated 121 nucleated cells (neutrophil predominance), protein of 95, and normal glucose. Empiric anti-infectives and dexamethasone were started. Ultimately, all CSF studies and serologic testing were negative, with the exception of a positive IgM at 2.25 (>1.21 positive) and IgG to mumps virus. On hospital day 4, the patient became afebrile with clinical improvement allowing discharge on hospital day 7.

*Discussion:* Although mumps is considered a disease of the pre-measles-mumps-rubella (MMR) vaccine era, frequent recent outbreaks have been described. Mumps has long been recognized to cause meningitis, which spontaneously resolves after several days. As only 50% of patients with mumps meningitis develop parotitis, the diagnosis requires a high index of suspicion.

### **2nd place**

#### **Nontyphoidal Salmonella Pericarditis**

Daniel Ortiz, MD, Aurora Health Care, Milwaukee, Wis

*Introduction:* Nontyphoidal salmonella (NTS) causes 1 million cases of foodborne disease in the United States annually. Bacteremia occurs in 3% to 8% of infections, and cardiovascular infections, including pericarditis, may develop in 1% to 5% of cases.

*Case:* A 62-year-old man with past medical history of systemic lupus erythematosus (SLE) presented after 3 days of rapid heart rate. He had a recent flare-up of drug-induced SLE treated with prednisone in addition to his maintenance mycophenolate. On presentation, his heart rate was 126 beats per minute, temperature was 98.5°F, and white blood cell (WBC) count was 14.8 K/mL. Electrocardiogram revealed atrial fibrillation with a nonspecific T-wave abnormality. Initial blood cultures were negative and there was no preceding history of GI symptoms. TEE revealed a 5.6 x 7.0-cm effusion with signifi-



cant mass effect on the right ventricle, which was believed to be inflammatory sequelae of SLE and treated conservatively, as he had a small chronic pericardial effusion. A few days after admission to the intensive care unit he became hemodynamically unstable and required emergent pericardiocentesis (PC), yielding 900 ml of purulent fluid. *S enteritidis* was isolated from the fluid. After antibiotic therapy with pericardiectomy for reaccumulation of the effusion, he fully recovered.

**Discussion:** Nontyphoidal salmonella pericarditis was reported 19 times in the last 20 years (1993-2013). Among them, 12 cases had an identifiable cause of immunosuppression, 6 were caused by medications, and 2 of these were on steroids for SLE, like this case. Although case immunosuppressive treatment and failure of opsonization has been attributed to salmonella infections in SLE, we postulate that the chronic pericardial effusions of SLE may increase susceptibility to pericarditis by serving as a nidus for infection; this being the first case with documented chronic pericardial effusion prior to infection. Like this case, 15/18 patients did not have GI symptoms reported prior to their pericarditis and only 60% had an elevated WBC. This is due to alterations in local intestinal mucosal immunity to mount an adequate response (including diarrhea), which increase rates of NTS

bacteremia. Lack of a GI prodrome adds to the diagnostic challenge that SLE NTS pericarditis presents of differentiating pericardial effusions intrinsic to the disease from those caused by infectious or other etiologies. As the population ages and more people receive immunomodulating drugs, it is possible that NTS bacteremia and cardiac infections will become more common. We believe empiric echocardiography should be considered for patients with NTS bacteremia who have risk factors for progression to pericarditis.

### 3rd place

#### **Gardner's Syndrome With Desmoid Tumor**

Nebiyu Biru, MD, Jason Haas, DO, Aurora Sinai Medical Center, Milwaukee, Wis

**Introduction:** Desmoid tumors account for 0.03% of all neoplasms, but may be seen in 10% to 20% of patients with Gardner's Syndrome (GS). GS is a variant of familial adenomatosis polyposis (FAP) characterized by the presence of benign and/or malignant extraintestinal lesions in association with colonic polyposis.

**Case:** A 21-year-old white woman was admitted to our institution for worsening fatigue and hematochezia. She reported having 5 to 6 episodes of bloody diarrhea daily for the past 5 years and a weight loss of 40 pounds over the past year. Her father underwent a total

colectomy at age 35 for unknown reasons. Her physical examination was significant for profound cachexia and palpable mid-abdominal masses. Laboratory findings revealed a hemoglobin of 5.7 g/dl. She underwent colonoscopy, which revealed hundreds of single and coalescing polypoid lesions throughout the colon with rectal sparing. Biopsies of the polypoid lesions revealed adenomatous tissue. Genetic testing confirmed FAP. She ultimately underwent a 2-stage total proctocolectomy with ileoanal anastomosis. A large mesenteric desmoids tumor was encountered during surgery and was resected. She is currently doing well.

**Discussion:** Desmoid tumors are locally aggressive tumors that do not metastasize. In patients with GS, the most commonly involved site is the intra-abdominal cavity (mesentery). These tumors are rarely symptomatic due to their indolent growth, but may present as intestinal obstruction or ischemia from local compression of surrounding organs. Desmoid tumors are responsible for death in up to 11% of patients with FAP. These tumors may be observed, but surgical resection is indicated when they become symptomatic. Unfortunately, these tumors have a high rate of recurrence after resection despite negative margins. Radiation therapy is effective in patients with high surgical risk.

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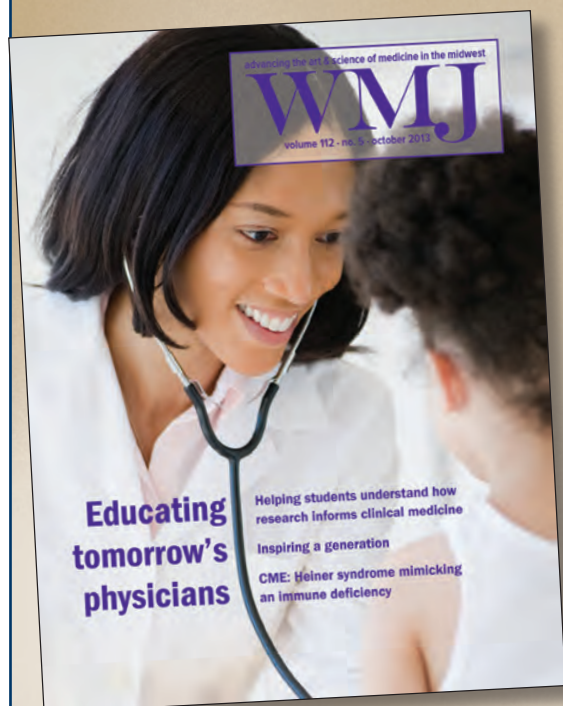




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