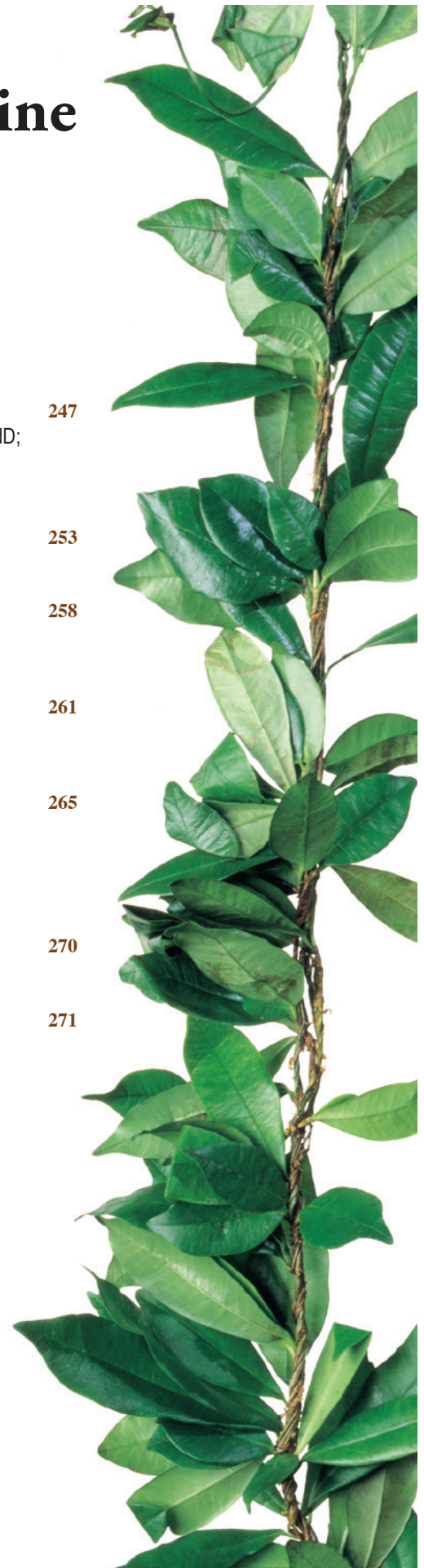


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Factors Inhibiting Physical Activity as Treatment for Diabetic Chuukese in Chuuk and Hawai'i

Nia Aitaoto PhD; Shelly L. Campo PhD; Linda G. Snetselaar PhD; Kathleen F. Janz EdD; Edith Parker DrPh; Tayna Belyeu-Camacho BS; and Father Ryan P. Jimenez MDiv

Abstract

Type 2 diabetes is epidemic in the US Pacific. Developing culturally sensitive physical activities and anti-sedentary interventions may reduce morbidity and mortality associated with type 2 diabetes. The purpose of the study was to identify sedentary and physical activity factors related to diabetes prevention and control among Chuukese living in Chuuk and Hawai'i. This study utilized grounded theory to identify socio-cultural influences that hinder or facilitate adherence to physical activity recommendations. Data was gathered through focus group discussions with individuals with diabetes and their caretakers. Findings include in-depth and detailed information on five different types of sedentary behaviors (purposeful sitting, lazy sitting, wasting time, resting and recreation sitting, and no-can move) and environmental factors that influenced participants' sedentary behaviors and physical activity. These findings underscore the need for physical activity and anti-sedentary interventions that are purposeful, collectivistic, age and gender appropriate and church based.

Keywords

Physical Activity; Diabetes; Pacific Islanders; Chuukese; Community Based Participatory Research

Acronyms

T2DM (type 2 diabetes); FARRA (Faith in Action Research and Resource Alliance); UI (University of Iowa); CBPR (Community Based Participatory Research); CWC (Chuuk Women's Council); MU (Micronesians United); FSM DHSA (Federated States of Micronesia's Department of Health and Social Affairs)

Introduction

Type 2 diabetes is epidemic in the US Affiliated Pacific Islands.^{1,2} In the Federated State of Micronesia's State of Chuuk, the prevalence of type 2 diabetes (T2DM) is 35.4%,³ four times higher than the United States prevalence of 9.3%.⁴ Diabetes is also the leading cause of death, with 40% of all deaths being attributed to diabetes and its related co-morbidities (septicemia, myocardial infarction, cerebrovascular disease, and hypertension).⁵ Research shows that physical activity and anti-sedentary interventions can reduce morbidity and mortality associated with T2DM.⁶⁻¹¹ In 2012, the Federated States of Micronesia's Department of Health and Social Affairs (FSMDHSA) released physical activity data collected in 2009 and found that the Chuukese have low rates of physical activity. Among Chuukese adults, 63% reported low, 18% moderate, and 26% high physical activity levels as compared to 16% low, 22% moderate and 65% high in the United States.^{12,13} There is limited data on the burden of diabetes and lack of physical activity among Chuukese living in Hawai'i, however anecdotal evidence suggests that there are significant problems of obesity, diabetes, and cardiovascular

diseases.¹⁴ There is also a lack of information about differences in physical activity levels among Chuukese residing in Chuuk compared to those living in Hawai'i. Furthermore, little data is available on cultural and social determinants of physical activity and the Chuukese could benefit from a further understanding of the culture and context (geographic location, social and political environment) of T2DM risk factors.

The scientific study of sedentary behavior is relatively new. In an effort to determine how this emergent knowledge base can be used for health promotion and disease prevention, we applied the *Sedentary Behavior Epidemiology Research Framework*, which consists of five main research phases: (1) establish the link between sedentary behavior and health; (2) develop methods for accurately assessing sedentary behavior; (3) identify factors that influence levels of sedentary behaviors; (4) evaluate interventions to reduce levels of sedentary behavior; and (5) translate sedentary behavior research into practice.⁹ The purpose of the study was to (1) identify sedentary and physical activity factors related to diabetes prevention and control among Chuukese living in Chuuk and Hawai'i, and (2) evaluate how this emergent knowledge base can be used for health promotion and disease prevention.

Methods

To explore the contributions of culture and local context on risk factors related to T2DM, including sedentary behaviors, the Faith in Action Research and Resource Alliance (FARRA), a group of health advocates in the Pacific, partnered with the University of Iowa (UI), the Chuuk Women's Council (Chuuk), and Micronesians United (Hawai'i). Community-based participatory research (CBPR) principles were followed, which dictated community members' approval of methods, research topics, and study subjects.

The Chuuk Women's Council (CWC) and Micronesians United (MU) participated in the identification of subjects, recruitment, and logistics during data collection. Participant identification and recruitment involved presentations during CWC and MU meetings, at church events, and community gatherings to explain the purpose and requirements of the study in Chuuk and Hawai'i. A total of 120 individuals were interested in participating, and all 120 were formally invited to join the study via email and telephone. A total of 102 adults agreed to participate (43 from Chuuk and 59 from Hawai'i). Sixteen focus groups were held (8 in Chuuk and 8 in Hawai'i). Per cultural

protocols, all focus groups were divided by gender.¹⁵ The female focus groups were facilitated by a female staff member (also a church leader) and the male focus groups were facilitated by a male staff member (also a priest). Group facilitators were Pacific Islanders but did not reside on the same island as the participants. Staff were trained in qualitative methods, including focus group facilitation. Focus groups were conducted in English and sessions lasted 2 hrs 25 min to 2 hrs 75 min hours and were recorded. The audiotapes were reviewed after each session to guide probing questions for the next session. Participants also completed a one-page demographic questionnaire that includes age, sex, religion/denomination, and diabetes status. The University of Iowa's Institutional Review Board approved the study protocol and all participants provided written, informed consent.

A grounded theory approach was used to guide the analysis process.¹⁶ The grounded theory method involves the discovery of theory through the analysis of data rather than beginning with a hypothesis. This study began with focus groups and questions that included: (1) What is the role of family, religion (church), and community in controlling diabetes? (including decreasing sedentary behavior and increasing physical activity); and (2) What are some cultural attitudes and beliefs regarding sedentary and physical activity? From the collected data, segments were coded with a label that concurrently categorizes, summarizes, and accounts for each piece of data.⁷ The coding team, which included members of the Pacific Community, worked through the transcripts looking for coding incidences and paying attention to *In Vivo* codes or words/phrases that compress meanings or consist of widely-used terms from the participants themselves. The team then sorted the initial codes and grouped them into common themes. These groupings were then used to develop major categories and subcategories with links between them. These grouping and results were also validated via member checking through our community partners.

Results

The average age of participants was 46 years (43 years in Chuuk and 47 in Hawai'i); 55% were female, 53% had T2DM, and 90% had a primary healthcare provider (Table 1). Focus group responses revealed five different types of sedentary behaviors including personal factors (Table 2) and environmental factors that influenced participants' sedentary behaviors and physical activity. There were no differences in responses from female and male participants. Similar responses were also observed across all themes between Hawai'i and Chuuk study participants.

Personal Factors and Types of Sedentary Behaviors

The following five sedentary behaviors were described by participants in each focus group and were differentiated by narrating (1) purpose or actions, (2) reasons or motives, and (3) rewards or consequences.

Purposeful Sitting. Purposeful Sitting is sitting while engaging in activities that meet the needs of the individual, family, church,

and/or community. During sitting, there may be movements (eg, sewing, weeding grass, or weaving baskets) or there may not be movements (eg, participating in meetings or watching the house). Motivations behind engaging in these activities included a desire to conform to cultural expectations, kindness, and fulfilling family roles (eg, mother, caregiver, and provider). Participants reported feelings of satisfaction, fulfillment, and pride in engaging in these activities, which can also be a reward for continuing the behavior. Furthermore, these activities are approved and encouraged by the community. As one of the male participants narrated:

We have a consensus culture so we encourage a lot of discussions—long discussions. That means we have a lot of meetings that require us to sit, listen, and discuss - so not a lot of moving around. A lot of people outside of our culture think that we have too many meetings, and we sit too much or too long, but these meaningful discussions are very critical in our culture.

Another participant added:

We also sit for other good reasons like weaving mats and weeding grass. Sitting in this case is not bad because we are doing something useful.

Lazy Sitting. Lazy sitting is when there are needs to be met and individuals are physically able to meet those needs, but they choose not to take part. Participants reported sitting without actions (eg, watching television and talking story) and the most reported feelings were of hopelessness, indifference, and sadness. As a result of lazy sitting, participants reported feeling angry and frustrated. A female from Chuuk recounted:

I know I have to participate in our women's group church clean-up every Saturday, but sometimes, like last week, I just didn't feel up to it. There is absolutely nothing wrong with me physically, and I was not busy, but I just give up sometimes.

Wasting Time. Wasting time is similar to lazy sitting or sitting when there are needs to be met, but the difference is the emotions behind the inaction, as wasting time, was due to feeling angry and frustrated with family and others versus "just being lazy." Furthermore, although some participants narrated feeling guilty or ashamed (similar to lazy sitting), most reported feeling satisfied and delighted. They felt justified in their actions and do not feel shame, but the community as a whole frowns upon wasting time because wasting time does not serve the needs of the community. A participant from Hawai'i explained:

There are times when I deliberately did not do what I was supposed to do and not because I was tired or not motivated, I was just angry with somebody or something. Call it passive-aggressive, but to me it is one of the few ways I can show my frustration.

Resting and Recreational Sitting. Resting and recreational sitting was described as sitting to give the body needed rest or to reward oneself for engaging in purposeful activities. Although

actions are similar to lazy sitting and wasting time, participants reported being fulfilled and satisfied, as one participant from Chuuk explained:

The body needs rest, and in our culture a break from doing work for your family, church, and community is encouraged. Resting is necessary so it is just not sitting there to be lazy or wasting time.

No-can Move. No-can move is sitting and not engaging in purposeful activities due to an illness or injury. Depending on the illness or injury, individuals engaged in action and/or non-action activities. Although the community approved of this type of sedentary behavior, those who no-can move reported feeling guilty or sad that they cannot participate. Others feel blessed that they have a family and community who can do work. As one amputee said:

As you can see I can't walk or even stand by myself, so I just sit. I feel bad that my family members have to take care of many of my needs on top of everything else. In our culture this is acceptable, and I'm grateful. I wish I could do more, but I just can't.

Environmental and Cultural Factors

Environmental factors influenced participants' sedentary behaviors and physical activity. Participants identified: (1) access to facilities and culturally- or contextually-appropriate programs; (2) deeply engrained cultural practices and norms related to physical activity/inactivity; and (3) lack of support from healthcare providers, faith leaders, their church, and the community.

Access. The discussions of socio-cultural influences began with poverty and living in low-income communities where streets are not safe for walking and facilities are lacking. These themes were present across all focus groups in Chuuk and Hawai'i. Chuuk participants cited a lack of sidewalks, no streetlights, stray dogs, and teens throwing stones at pedestrians as barriers to walking (main type of purposeful physical activity). They also reported the lack of physical activity facilities such as gyms, playgrounds, soccer/football fields, and running tracks as barriers to recreational physical activity. Hawai'i participants reported the availability of sidewalks, but safety was a barrier as the rate of crime and gang activity was high in their neighborhoods. Moreover, there were facilities (gyms, playgrounds, and fields) near the housing areas, but participants reported bullying and safety issues, so they were not utilizing them.

Chuukese Cultural Practices and Norms. Prominent topics discussed by participants were (1) collectivistic practices; (2) age-appropriate physical activities; and (3) gender-specific physical activities. The most mentioned culture-related topic was the collectivistic practices of engaging in activities as a

group and putting great value on group consensus and approval. This results in more sedentary behaviors, as participants have to sit for long periods of time at lengthy community meetings. A faith and community leader explained,

We do a lot of group discussions as part of our cultural practice of making decisions, so we sit through those meetings. We also attend church services and events that last two to five hours, so more sitting.

The second most mentioned cultural practice was age-appropriate activities. The discussion centered on the practice of the young serving elders. A caregiver from Chuuk gave this explanation:

Our culture fully respects our elders; they contributed a lot to our community and when they are older they deserve to be served. You see many of the old folks sit and the younger folks fetch drinks, serve food, massage, and stuff like that. This is how we show respect, and if we don't do it then other people will think that we are bad people. Our culture frowned on not following these practices.

An elder woman from Chuuk added:

It is not regal for older folks to do all the running around, so we normally sit and play the role of advisor.

Finally, participants discussed gender-specific cultural roles, and their relationship with physical activity. Culture dictates the separation of males and females in many situations including chores and recreational activities. A focus group participant from Hawai'i observed:

We moved here [Hawai'i] from Chuuk about eight years ago, and I know the culture here is different—men and women can do stuff together. I saw men and women doing exercise dancing in the same room, but none of us joined in because it just doesn't feel right.

Healthcare Provider Support. People with diabetes and caregivers reported a lack of support in the form of encouragement and accountability from healthcare providers. People with diabetes recalled their doctor or nurse telling them to "exercise," but they did not provide physical activity education, referrals, or encouragement. The majority of the patients reported tuning out the "exercise" advice because they have heard it many times and felt that providers are required to say that for all other conditions. They also felt that there was no sense of urgency or importance in the doctors' and nurses' voices or actions. One diabetes patient from Hawai'i recalled his last visit to the doctor:

I was only in there less than 10 minutes, he went over my test results, spent most of the time explaining my medication, and at the end he told me to watch what I eat, exercise, and take care.

Table 1. Participants' Demographic Characteristic		
	n	Years
Mean Age		
Overall		46
Chuuk	43	43
Hawai'i	59	47
Mean Residency		
Chuuk	43	43
Hawai'i	59	47
Gender		
Male	46	45
Female	56	55
T2DM Status		
Present	54	53
Not present	48	47
Do you have a primary healthcare provider?		
Yes	92	90
No	10	10

Table 2. Sedentary and Sitting Behaviors, Actions and Reasons				
Sedentary Behavior	Purpose/No purpose	Actions/No-Actions	Personal Factors	Rewards and Consequences
Purposeful Sitting	Engaging in activities that have purpose or meet the needs of the individual, family, church and community.	Sitting with actions (eg, sewing, gardening and weaving baskets). Sitting without actions (eg, participating in meetings and watching the house).	Conform to cultural expectations, kindness, and fulfilling family roles.	Personal: Fulfillment, Pride, and Satisfaction Community: Approves
Lazy Sitting	Not engaging in purposeful activities when there is a need and individual has the capacity to engage.	Sitting without actions (eg, watching television, talking story and people watching).	Lack of motivation due to hopelessness, indifference, sadness, and emotional pain.	Personal: Guilt and Shame Community: Disapproves
Wasting Time	Not engaging in purposeful activities when there is a need and individual has the capacity to engage.	Sitting with actions (eg, playing games). Sitting without actions (eg, watching television, talking story, and people watching).	Expression of anger, frustration, and discontentment	Personal: Satisfaction, Pleasure, Enjoyment, Guilt and Shame Community: Disapproves
Resting	Resting from purposeful activities	Sitting with actions (eg, playing games). Sitting without actions (eg, watching television, talking story, and people watching)	Taking a break from or reward for purposeful activities	Personal: Fulfilling, Proud, and Satisfaction Community: Approves
No can move	Not engaging in purposeful activities with actions but individual does not have the physical capacity to engage	Sitting without actions (eg, watching television, talking story, and people watching)	Illness or injuries	Personal: Guilty, Sad, Grateful, Blessed Community: Approves

Discussion

This was the first study that investigated socio-cultural influences that hinder or facilitate adherence to physical activity recommendations for Chuukese in Chuuk and Hawai'i. Participants elucidated five sedentary behaviors that emphasized the importance of purpose, motivation, and attitudes. They also expressed the need for anti-sedentary and physical activity interventions that are purposeful, collectivistic, age and gender appropriate, and church-based. These findings can be used to inform future programs and research.

At the core of sedentary and physical activity behavior discourses was the idea of purpose and meeting the needs of individuals, family, church, and community. Participants unpacked cultural influences (eg, collectivistic, age-appropriate behaviors, role of faith leaders and churches, and gender-appropriate activities). Collectivistic practices of engaging in activities as a group and putting great value on group approval were central in individuals' motivation to engage in physical activity. Culture dictates the division of activities according to age. Participants reported that, "the older you get, the fewer activities you are expected to do" and the bulk of work especially "heavy work" is required of younger adults who have "strength" and "skills." Surveillance results showed this pattern as the percentage of younger adults (age 44 and younger) engage in higher levels of physical activity than older adults (age 55-64).¹² Data for individuals over the age of 65 years showed even lower levels of physical activity. Study participants reported that it is not regal for elders to engage in physical activity and they are expected to sit and play the role of advisor. Culture also dictates the separation of activities by gender. Males were expected to engage in more rigorous, arduous, and dangerous purposeful and recreational physical activities. FSM DHSA surveillance data showed that the percentage of males were also engaging in higher levels of physical activity than women. Finally, the roles of churches and faith leaders are key to successful interventions. Participants regarded faith leaders as highly respected and influential and they serve as role models in addition to providing education and motivation through one-on-one counseling, group sessions, and sermons. They would like to see physical activity reminders and tips in the Sunday bulletins and on bulletin boards. Participants also would like their church to sponsor exercise programs such as standing during service, physically intensive community cleaning, and implement policies such as walking to church. A comprehensive review of faith-based physical activity interventions shows significant promise for improving physical activity participation and related health outcomes.¹⁷

Participants also mentioned the following environmental and cultural factors and norms that influenced the types and levels of sedentary behaviors: safe places to engage in non-sedentary activities, cultural practices and norms that promote sedentary activities, and support in the form of motivation and encouragement from healthcare providers. It is critical to understand and address these influencers in order to develop an environment that is conducive to promoting physical activity and anti-sedentary behaviors.

The limitations of this study include the use of the English language as those who are not fluent in English might have different experiences and perspectives. Having a priest as a focus group facilitator might have prompted participants to give socially desirable replies among the men. To minimize this, the priest and a female church leader were from another Pacific Island. Another limitation is that responses from participants are not separated by geographic location. Since Chuuk and Hawai'i differ, studies looking at these populations separately may be needed.

Conclusion

This study identified sedentary and physical activity factors related to diabetes prevention and control among Chuukese living in Chuuk and Hawai'i. Researchers, health practitioners, and policy makers can use these findings to inform future research interventions that are purposeful, collectivistic, age and gender specific, and church based. This is the first study to elucidate sedentary behaviors of the Chuukese and the cultural influences on sedentary behavior that are specific to this population. It is a first step in developing culturally-sensitive interventions for a nation with a significant need to reduce morbidity and mortality associated with T2DM.

Conflict of Interest

None of the authors identify a conflict of interest.

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A Case Report of a Left Atrial Mass: The Importance of a Detailed Physical Exam

Corey J. Lum DO; Thuan V. Nguyen MD; and Zia Khan MD

Abstract

Cardiac myxomas are rare clinical findings. They are frequently found in the left atrium and more commonly affect women. Clinical presentation can vary widely and symptoms can be vague and non-specific. We present a case of a 67-year-old woman presenting with 3 weeks of progressive heart failure symptoms that failed to respond to oral diuretic therapy. On physical exam, she was found to have a diastolic murmur, rumble and an early diastolic plop. Transthoracic echocardiogram revealed a 5.6 cm x 2.5 cm x 4.3 cm left atrial mass attached to the mitral valve causing left atrial outflow obstruction. The patient subsequently underwent surgical resection of the mass with resolution of symptoms immediately thereafter. Lack of recognition of this pathologic process as a cause of heart failure symptoms and lack of a quality physical exam can lead to a delay in diagnosis and treatment.

Introduction

Primary cardiac tumors are rare with a reported incidence approximately 200 per 1,000,000.¹ Among primary cardiac tumors, approximately 75% are benign.² Of the benign tumors, nearly half are cardiac myxomas, which predominantly arise from or near the interatrial septum and extend into the left atrium.¹ Cardiac myxomas more commonly affect women and can arise in all age groups but present with a mean age of 62 years old \pm 13 years.³

Clinical presentation can vary widely. Most commonly, patients present with symptoms of obstructive heart failure but other presenting symptoms may be vague and non-specific such as arrhythmia, systemic embolization, or constitutional symptoms (ie, fever, night sweats and weight loss).⁴ In one fifth of the cases, a myxoma can be asymptomatic and discovered as an incidental finding.⁵

Case Presentation

A 67-year-old woman presented to her primary care physician with progressive worsening dyspnea on exertion, orthopnea and bilateral lower extremity edema. She was treated empirically for presumed congestive heart failure with oral diuretic therapy and a non-urgent transthoracic echocardiogram was ordered. Her symptoms initially improved with oral diuretic therapy, but after approximately a week, her symptoms progressively worsened and prompted her to come to the emergency department for further evaluation and treatment.

Upon evaluation in the emergency department, she had normal vitals but a diastolic murmur, rumble and early diastolic plop were heard on cardiac auscultation. She did not have jugular venous distension, hepatomegaly, hepatjugular reflux or any lower extremity edema. Her baseline labs revealed normal electrolytes, renal function, hepatic function, and complete blood count. A troponin I was <0.02 ng/mL (reference <0.05

ng/mL) and N-terminal pro-brain natriuretic peptide was slightly elevated at 397 pg/mL (reference <125 pg/mL). A chest X-ray showed cardiomegaly but otherwise without any acute cardiopulmonary pathologic process (Figure 1). Twelve-lead electrocardiogram showed an ectopic atrial rhythm with an incomplete right bundle branch block and non-specific T-wave changes. A transthoracic echocardiogram revealed a 5.6 cm x 2.5 cm x 4.3 cm multi-lobulated, gelatinous left atrial mass attached to the lower portion of the interatrial septum that prolapsed through the mitral valve causing moderate obstruction with a 10 mm transvalvular gradient (Figure 2). A coronary angiogram was performed demonstrating only mild, diffuse atherosclerotic coronary disease. She was then referred to a cardiothoracic surgeon for surgical removal of the tumor. Intraoperative transesophageal echocardiogram images (Figures 3 and 4) and gross anatomic specimens (Figures 5 and 6) were obtained. The mass was sent to the pathology department for histological analysis, which confirmed the diagnosis of a cardiac myxoma. Her postoperative course was uneventful and she was discharged on post-operative day 4 without any oral diuretic therapy. She has been followed in the clinic with serial transthoracic echocardiograms demonstrating no recurrence of the left atrial mass.

Discussion

Cardiac neoplasms may present as obstructive, embolic, and constitutional symptoms such as fever, weight loss, or systemic symptoms thought to be due to tumor-induced interleukin-6.⁶ Left-sided cardiac tumors can obstruct blood flow through the mitral valve mimicking signs and symptoms of mitral stenosis, including dyspnea, orthopnea, syncope, and paroxysmal nocturnal dyspnea.⁶ In addition, it may induce valvular damage and impair myocardial contractility.⁶ Some tumors can invade into local myocardium to cause conduction disturbances, which can lead to arrhythmias such as supraventricular tachycardia or ventricular tachycardia.⁶ Cardioembolic features of left-sided cardiac masses can manifest as stroke, visceral infarction, myocardial infarction or peripheral emboli.⁶

Our patient initially presented with heart failure symptoms to her primary care physician. During that initial presentation, a diastolic murmur, rumble and plop were likely missed on physical examination. An outpatient transthoracic echocardiogram was ordered, but unfortunately the patient was not able to get it done in time before her symptoms worsened, which brought her to the emergency department for evaluation. It ultimately led to a delay in her diagnosis and treatment of a left atrial myxoma.

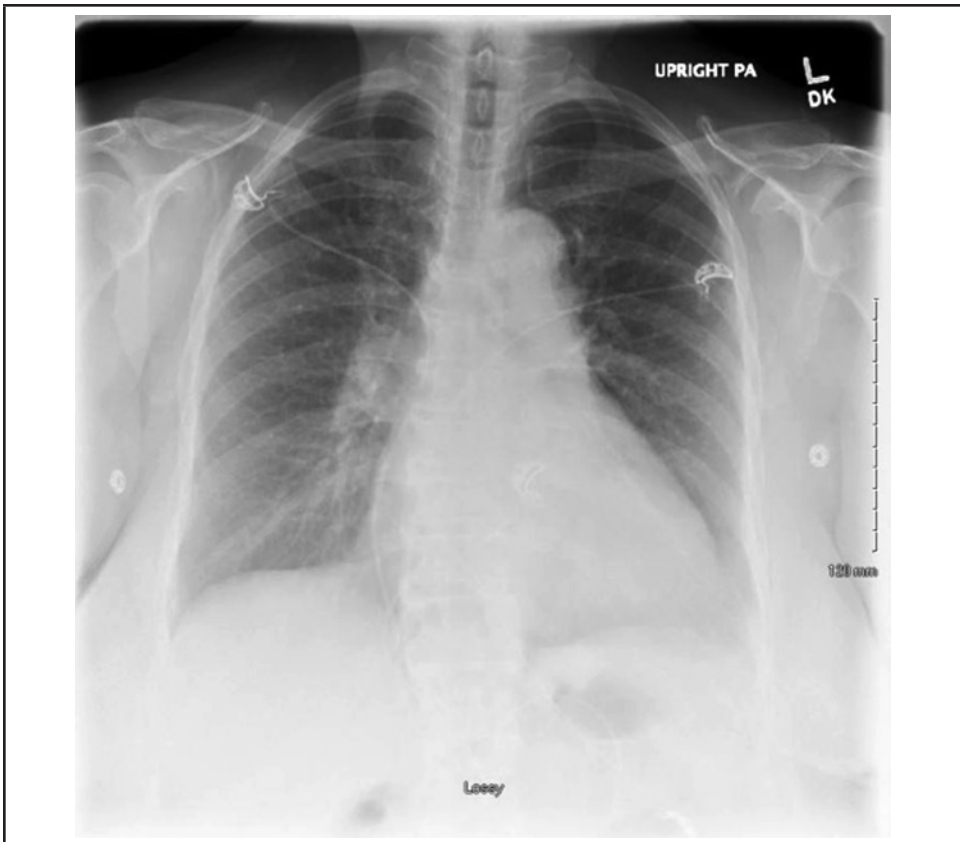


Figure 1. Chest X-ray with mild cardiomegaly but no acute cardiopulmonary pathologic process.

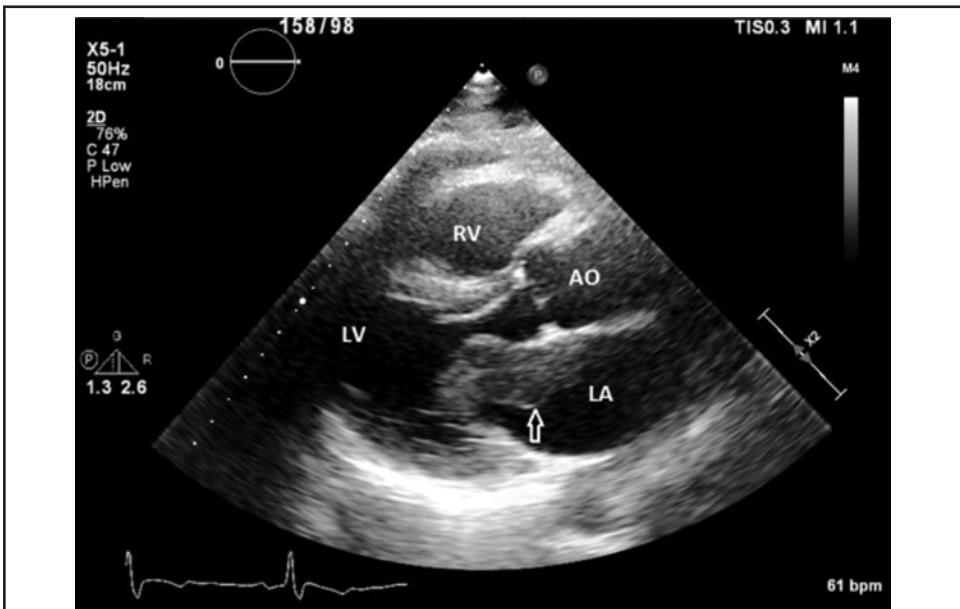


Figure 2. Transthoracic two-dimensional echocardiogram, parasternal long axis view. LA = left atrium, LV = left ventricle, RV = right ventricle, AO = aorta, arrow = tumor.

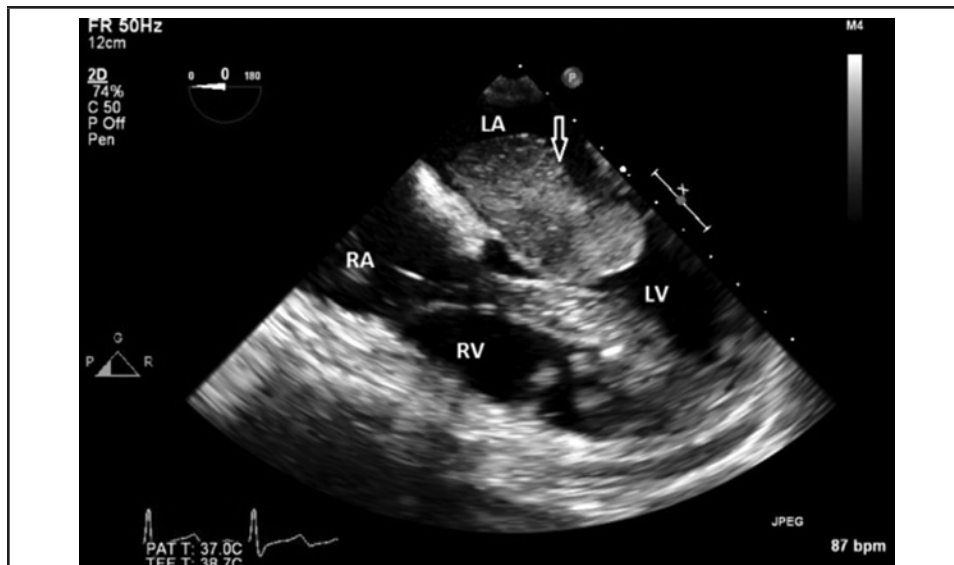


Figure 3. Intraoperative transesophageal echocardiogram, mid-epigastric four-chamber view. RV = right ventricle, RA = right atrium, LA = left atrium, LV = left ventricle, arrow = tumor.

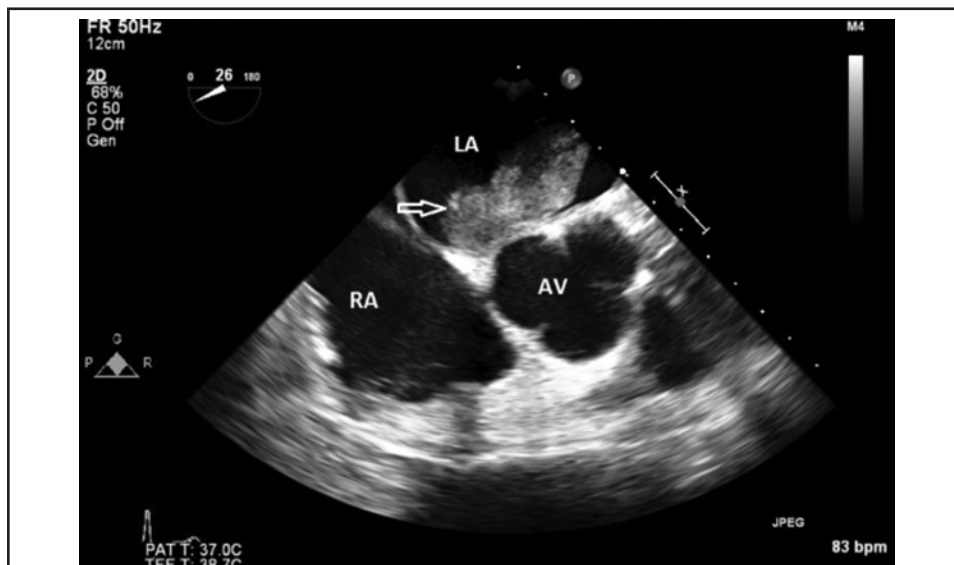


Figure 4. Intraoperative transesophageal echocardiogram, mid-epigastric aortic valve short-axis view. AV = aortic valve, RA = right atrium, LA = left atrium, arrow = tumor.

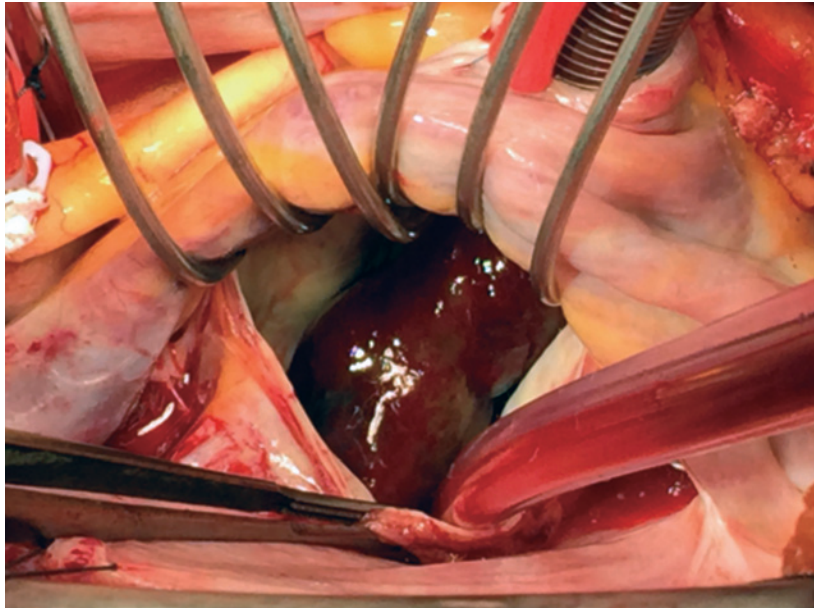


Figure 5. Intraoperative picture of the left atrial mass.



Figure 6. Left atrial mass following excision.

This case stresses the importance of a detailed and thorough physical examination. In addition, the pathologic importance of a diastolic murmur was missed during her initial encounter, resulting in a delay in diagnosis and treatment. On physical examination, a diastolic murmur is pathologic until proven otherwise and should always warrant a provider to promptly perform further diagnostic studies.⁶ The differential diagnoses of a diastolic murmur include aortic insufficiency, pulmonic regurgitation, mitral stenosis, tricuspid stenosis, atrial myxoma, Austin Flint murmur, and left-to-right shunts.⁷

The murmur of a left and right atrial myxoma can have similar auscultatory findings as mitral and tricuspid stenosis, respectively.⁷ It is typically a mid-diastolic, crescendo diastolic murmur.⁷ The diastolic murmur occurs as the atrial myxoma causes atrioventricular valve obstruction. The murmur from a left atrial myxoma can be difficult to distinguish from mitral stenosis but the character and intensity of the murmur from an atrial myxoma may change with position.⁸ Auscultatory abnormalities were found in 64% of patients with atrial myxomas.⁶ In addition, a “tumor plop” may be heard in only 15% of patients, which is suspected to represent either sudden tensing of the tumor stalk or impact of the tumor against the septum.⁹

Even though a thorough physical examination can be suggestive of a cardiac tumor, initial diagnostic tool is typically a transthoracic two-dimensional echocardiogram. It can provide information including location, size, mobility, and potential consequences.⁶ Depending on the location, a transesophageal echocardiogram can provide greater spatial resolution of the tumor and provide further details with regards to the site of attachment.¹⁰ Other diagnostic modalities include cardiac magnetic resonance imaging (MRI) or cardiac computed tomography (CT). Both modalities can provide greater detailed images to better characterize the tumor beyond echocardiography, if needed.

This case reminds us of the significance of a detailed and thorough physical examination and pursuing early diagnostic testing for new heart failure findings. Although diastolic murmurs are often missed on physical exam, any patient presenting with a new clinical syndrome of heart failure should urge a provider to obtain urgent transthoracic echocardiogram. Reluctance to proceed to higher level of diagnostic testing can result in a delay in the patient’s diagnosis and treatment.

Conflict of interest

None of the authors report a conflict of interest.

Comment

Personal identifiers were excluded to maintain the patient’s confidentiality. Informed consent was not obtained for this case report.

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MEDICAL SCHOOL HOTLINE

Connecting with Patients through Humanism and Humility

Kamal Masaki MD and William L.T. Fong MD

The Medical School Hotline is a monthly column from the University of Hawai'i John A. Burns School of Medicine and is edited by Satoru Izutsu PhD and Kathleen Kihmm Connolly PhD; HJMPH Contributing Editors. Dr. Izutsu is the vice-dean of the University of Hawai'i John A. Burns School of Medicine and has been the Medical School Hotline editor since 1993.

The following two speeches were delivered to John A. Burns School of Medicine (JABSOM) students and alumni in 2017. The first, by Dr. Kamal Masaki, was given at the White Coat Ceremony. This ceremony is when JABSOM's first year students receive their first white coat, also called "cloaks of compassion." The ceremony emphasizes the importance of the doctor-patient relationship and encourages acceptance of the obligations inherent in the practice of medicine: to be excellent in science; compassionate; and lead lives of uprightness and honor. The second speech, by Dr. William L.T. Fong, was delivered at JABSOM's Gold Humanism Honor Society reception, which recognizes students who exemplify humanism in medicine as demonstrated by qualities of integrity, excellence, compassion, altruism, respect, and empathy towards patients.

Balancing the Art and Science of Medicine – White Coat Ceremony Keynote Address, July 14, 2017

Kamal Masaki MD

Dr. Izutsu, Dr. Blanchette, Dr. Nakamura, Faculty, the Burns Family, Guests, and Students of the Class of 2021, I'm honored to be speaking to you this evening. Congratulations to our new medical students! You made it through the very competitive admissions process and are on your way to becoming a doctor. Congratulations also to the parents, family and friends of our new students, because they couldn't have made it this far without your love and support. Dr. Izutsu asked me to make this speech inspirational and brief. I will certainly make it brief, although I can't promise inspirational.

I'd like to start with a story. Like most of you, I was lucky to be pretty healthy, and I was 40 years old before I first needed to be admitted to the hospital. It wasn't a serious illness but I did require major abdominal surgery. I remember the day after the surgery feeling like I had been run over by a truck — parts of my body ached that I didn't even know I had. But the second morning, I woke up feeling great and my pain was controlled, so I assumed that I was going to be discharged home. When the surgeon came to see me, he said I had a fever overnight and had to stay one more day. I was so disappointed that I cried after he

left the room, and I remember thinking how many times I had said these same words to patients and not understood why they were so upset. Experiencing illness helps us understand firsthand what our patients go through and makes us better doctors. Some of the students are looking anxious — don't worry, I'm not going to suggest that all of you get hospitalized tonight, but I do want you to learn to put yourself in your patient's shoes.

It's so important that we provide patient centered care. Listen to your patients and find out what's important to them — it may surprise you. Nowhere is this more important than in my chosen specialty of geriatrics, where we care for the most vulnerable, frail patients. Geriatric Medicine is the best field — of course, I'm not biased at all. I love hearing my patients' life stories and learning from the wisdom that they have accumulated through their lives. Nowadays, most of medicine is the continuing care of chronic diseases. There are few things we can actually cure. Understand your patients for who they are as human beings, not just their collective medical problems. Providing small acts of compassion, with a touch or with your words, can make a huge difference to your patients and their families. The doctor-patient relationship is a sacred trust that you must honor and respect.

You have embarked on an exciting journey, but it will also be an arduous one. All of us start out very idealistic, wanting to help people. Unfortunately, the difficult journey itself makes some lose their compassion and kindness. Please be kind to your patients, and also to each other. Support each other through the difficult times. You will stumble sometimes, as I have done many times, and that's okay, but please learn from every mistake that you make. The demands of technology and documentation have increased tremendously in medicine. How many times have you visited a doctor, and had the doctor stare at the computer the entire time, rather than looking at you and talking directly to you? Technology should not prevent us from actively listening to our patients. Patients won't remember your board exam scores, but they will remember how you made them feel.

I have now been on the faculty at JABSOM for 26 years. I consider my best students and fellows to be the ones who had the biggest hearts, who had the most humanism and empathy. I have been blessed with wonderful colleagues among our faculty. These great people will be your role models and will help inspire

you to become the best that you can be in your chosen fields. They will teach you the importance of the art of medicine, in addition to the science. You will be successful if you treat all your patients in the same way that you want to be treated, and that you want your family and friends to be treated.

You have joined the John A. Burns School of Medicine, named after Governor Burns. He championed this school and it was named after him because he knew that without it, many of Hawai'i's children would not have the opportunity to become doctors. I never met him, because he passed away long before I moved to Hawai'i. However, I had the honor to meet and get to know his son, Judge Jim Burns, who passed away a few months ago. Judge Burns continued his dad's legacy and became a strong supporter of the school. He was one of the kindest people I met and exemplified the principles of humanism. He was always present at events like this one, and all of us miss him deeply. I'm so happy to see his family here tonight, and that his kids are continuing the Burns family legacy – thank you for your continued support!

I'd like to recommend a book entitled *Being Mortal: Medicine and What Matters in the End*, by Dr. Atul Gawande, an American surgeon and writer. He wrote, "In the end, people don't view their life as merely the average of all its moments — which, after all, is mostly nothing much plus some sleep. For human beings, life is meaningful because it is a story. A story has a sense of a whole, and its arc is determined by the significant moments, the ones where something happens. We have purposes larger than ourselves." "Sometimes we can offer a cure, sometimes only a salve, sometimes not even that. But whatever we can offer, our interventions, and the risks and sacrifices they entail, are justified only if they serve the larger aims of a person's life. When we forget that, the suffering we inflict can be barbaric. When we remember it, the good we do can be breathtaking." Now that's inspirational — I wish I could write like that.

For the Class of 2021, congratulations again on your acceptance to JABSOM. Wear your white coat proudly! I leave you with 3 charges. First, as you gain in knowledge and skills, don't lose your humanism, kindness and compassion. Second, learn how to always put yourself in your patient's shoes, they will appreciate your efforts. And lastly, after you finish your training, come home to Hawai'i, we need you here! Welcome to the JABSOM Ohana and good luck to all of you!

**It's Not About You –
JABSOM Gold Humanism Honor Society
Induction Ceremony, April 7, 2017**

William L.T. Fong MD

First of all, let me say how much I appreciate the invitation to join this esteemed honor society. For seven or eight years now I have given a talk on Professionalism to every 3rd year student as they rotate through Ob Gyn and I always mention the Gold Foundation. So to be included as a member is such a privilege. Thank you so much. And I am doubly honored that

I have the opportunity to share a few words with you as well.

This room is filled with high-achievers. After all, most of you are either in medical school or have been through medical school. Some of you just a couple of weeks ago, after all these years of incredible effort, opened your white envelopes and with both excitement and maybe a little bit of relief, were finally able to utter those two words, "I matched!" And now you're on your way to becoming the family doc or pediatrician or surgeon that you always wanted to be. For all of you going forward, and maybe to some extent it's already happened, doors will open and opportunities of all varieties, offered to very few people in this world, will arise, simply because you're a physician. So what I'm about to say to you might sound a bit bizarre but I hope it's fitting on this occasion. Despite all that you've accomplished so far and will accomplish in the days ahead, I hope you will carry around in your heart and mind this one little thought, just four little words..."It's not about you."

It's not about you...my goodness! Here you've worked your tail off for the last three or four years; endured unbelievable stress; sacrificed sleep and other forms of physical well-being; amassed huge debt; literally put the rest of your life on hold. And then you hear me say, "It's not about you"? OK...so then, who or what IS it all about?

Well, the first thing that comes to mind is somewhat obvious...you didn't grow up in a vacuum. You are a product of your upbringing and your surroundings. No doubt, many of the influences in your life up until now speak of just how fortunate you have been; but truth is, many of these influences were not of your own doing. Whether you had the benefit of belonging to a supportive family, inheriting good genes, stumbling upon great role models along the way, or simply being in the right place at the right time, you personally had little hand in creating many if not most of the circumstances under which you prospered and thrived. You are simply the fortunate beneficiary of these circumstances. Did you ever stop to think, "How is it that I, out of all the deserving people out there, could end up being the one so blessed?" It's both wondrous and overwhelming to take a moment to ponder this and let it sink in. At the same time, there may also have been some hardships along the way, maybe some pain, some sad, confusing or even dark moments in the journey that finally got you here. Don't deny these times either, even embrace them because when it's not only about you, you begin to realize that even these traumatic experiences have helped to shape you and provided invaluable lessons on resilience and perseverance and character. So this is the place in my talk that I'm supposed to tell you how I almost dropped out of medical school way back when. You see, I was not a very good student. But it's a long story and I'll save it for another occasion.

When you remember that it's not about you, you also begin to notice how many people there are these days who are so much needier and less fortunate than you...and as you practice medicine you will come upon these individuals all the time. Do not forget them, neglect them or ignore them. Just the other day I read an article and the headline said, "Mayo Clinic will

prioritize private insurance patients over Medicare and Medicaid.” Now, it’s not as though this isn’t common practice all over the place. It’s just that no one ever said it out loud before, definitely no one of the stature of the CEO of the Mayo Clinic. But there will be days when your time, energy or resources will be stretched so thin that it will come down to having to choose between seeing the patient who has insurance, is nicely dressed, speaks your language, and will help pay the bills...or the patient who fits none of the above. I’ve been there. It’s not an easy decision to make. But if you ever are in a position of having to make or influence such a choice--whether you’re the CEO of a big medical group or a community doc just doing your own thing, I hope that at that moment you will be conflicted; that you will struggle with your conscience; and that your sense of justice and compassion will be in total upheaval over this kind of dilemma. Because when it’s not about you, I hate to tell you, that’s what ends up happening.

I was on a panel at JABSOM last year and the topic was teaching and evaluating professionalism in a medical education environment. Let me interject here that while in medical school we often use the term “professionalism” I think the Gold Society’s use of the term “humanism” is more meaningful. So someone in the audience asked the panel, “When interviewing applicants for residency, is there a good way to identify someone who possesses a high level of professionalism (or humanism, if you will)? My reply was this, I wish I could come up with one key question that I could ask any applicant interested in our program that would reveal not his or her IQ (intelligence quotient) or even their EQ (emotional quotient). I wish I had one key question I could ask that, depending on how they answer, would unequivocally measure their HQ or “humility quotient.” You see, those that have a high HQ have

no problem understanding that it’s not necessary to be right all the time; that they’re not above making mistakes if they can learn from them; that asking for advice is not a sign of weakness; that their rights are not more important than the rights of others; that they are not God’s gift to medicine; and that caring for patients does not mean you’re doing them a favor but is indeed a sacred privilege. This is the kind of resident I would rather recruit for my program over one who is simply brilliant or a great surgeon. Give me a bunch of residents like this and life in a residency program will be so enjoyable and drama-free.

When it’s not about you, it’s often about responding to a call, a voice, a spirit, a virtue within you that’s of a higher nature than can come from you alone; one that drives you to make decisions and choices that are way loftier than your degrees, your publications, even your own common sense and logic. Be quiet and listen intently to that voice, that spirit, that call. That is a call that is saying “be different; don’t get sucked in to popularity or social positions or comfort zones; follow your conscience more than the crowd; if you don’t take the high road, who will; the easy way is not always the best way; give until it hurts; always find the good.

A wise person once said, “Of those to whom much is given, of him or her much will be expected.” You have been called, now you have a duty. Serve well. Care deeply. Live abundantly. My best wishes to each and every one of you. Aloha.

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INSIGHTS IN PUBLIC HEALTH

Improving Reproductive Life Planning in Hawai'i: One Key Question®

Sarah Hipp BA; Alyssa Carlson MPH; and Elizabeth McFarlane PhD, MPH

Insights in Public Health is a monthly solicited column from the public health community and is coordinated by HJMPH Contributing Editors Tetine L. Sentell PhD from the Office of Public Health Studies at the University of Hawai'i at Manoa and Donald Hayes MD, MPH from the Hawai'i Department of Health in collaboration with HJMPH Associate Editors Lance K. Ching PhD, MPH and Ranjani R. Starr MPH from the Hawai'i Department of Health.

Background

Nearly half of all pregnancies in the United States are unintended despite federal, state, and community driven pregnancy prevention efforts.¹ Additionally, recent data reflects a plateau in maternal and infant mortality rates in the United States despite the continuing advances of medicine over the past century.² In 2010, 56% of all pregnancies in Hawai'i were unintended.³ The state also has an average infant mortality rate of 5.9 per 1,000 live births over the years 2000 to 2015.⁴ Unintended pregnancy disproportionately affects low income and minority women with lower educational attainment and these disadvantaged groups are more likely to suffer from increased maternal and infant mortality rates.^{1,5} Unintended pregnancies can lead to poor birth outcomes and risky maternal health behaviors during pregnancy, including inadequate prenatal care, developmental delay in children, poor parent-child attachment, and higher rates of long term poverty.⁶⁻⁸ Given Hawai'i's racially and ethnically diverse population as well as its sizeable percentage of persons living below the federal poverty level, it is critically important that healthcare providers across the state employ comprehensive and evidence-informed primary prevention programs that improve contraception provision and preconception health promotion to Hawai'i's vulnerable populations. The same standards apply to community-based organizations delivering reproductive health education and health promotion services to these populations. Indeed, the American Public Health Association (APHA) highlights the effectiveness of community-based reproductive health services and asserts that the same standards apply to these organizations.⁹

In recent years, researchers and healthcare providers alike have advocated for more comprehensive and effective reproductive healthcare services that target influential maternal health factors prior to conception¹⁰ and attenuate the social and individual determinants of health that place individuals at higher risk of unintended pregnancy.¹¹ Additionally, as the broader life course perspective continues to gain more support within research and clinical practice, expert health organizations, community health agencies, and direct service providers have recognized the need for health interventions that focus on the full spectrum of reproductive healthcare services with an emphasis on

maternal health promotion. One concept that seeks to fill this gap is Reproductive Life Planning (RLP). Home visiting, an evidence-based strategy that strives to address a multitude of health determinants and mitigate the intergenerational transmission of risk, has recently adopted RLP into their service model in Hawai'i to bolster support of vulnerable families and mothers.

Reproductive Life Planning

RLP is a collaborative process between the patient and provider that involves exploring and identifying a patient's reproductive goals and with provider support, acting appropriately to achieve these goals.¹² RLP is designed to help women identify reproductive goals in the context of other life goals and personal values such as future education, professional and career development, personal and family health, and healthy relationships with others.^{12,13} Its core components include desire to have children, number of children desired, spacing of children, and timing of children.¹⁴ Both contraceptive counseling and preconception care are elements within the larger RLP conversation, depending on pregnancy desire. Women are encouraged to create a personalized and dynamic reproductive plan with input from both their partner and provider that focuses on health promotion and allows for change as a woman's goals and life situation evolve.¹² Importantly, RLP is intended to motivate women to reflect on their health status and any high risk behaviors, regardless of desire for pregnancy. RLP strategies have the capacity to normalize ambivalence towards pregnancy and seek to provide a woman with the key knowledge and tools needed to reach a healthier state of being so that in the event that she becomes pregnant, both she and her child are in optimal health. Grounded in this framework of acknowledgement, validation, and support as well as a greater life course perspective, RLP can empower women, their partners, and their families by helping to create a positive, prepared vision for the future.

RLP, a primary prevention strategy with ample potential, encourages the integration of women's primary care and reproductive care to treat the whole woman at once, including social determinants of her health.^{10,15} This allows for a continuous, seamless approach to care that views a woman's health holistically rather than dichotomizing her as a pregnant or

nonpregnant individual.¹⁶ By discussing reproductive health at every healthcare encounter and encouraging women to establish a reproductive life plan, clinicians help patients achieve their life and reproductive goals by providing informed, nonjudgmental support and by connecting them to adequate and appropriate preconception or contraception health services. Several prominent medical and health policy organizations, including the American Public Health Association (APHA), the American College of Obstetricians and Gynecologists (ACOG), and the Centers for Disease Control and Prevention (CDC) advocate for a shift towards and adoption of comprehensive, culturally appropriate RLP strategies in health promotion and clinical practice to fully educate, support, and facilitate women's and men's reproductive goals.^{9,17,18}

RLP not only aims to reduce unintended pregnancies but also serves as a platform to improve birth outcomes by addressing chronic maternal health conditions and health behaviors prior to conception. Even when pregnancies are planned, many women do not receive prenatal care until after the critical period of fetal development, thus already negatively impacting fetal and infant health. As discussed previously, evidence supports that when pregnancies are not planned, both mother and child are at increased risk of poor health consequences. Research shows theoretical evidence linking the key concepts and constructs of RLP with improved maternal and child health indicators. Reducing unintended pregnancies and ameliorating underlying factors contributing to increased risk of infant mortality such as preterm birth, low and very low birth weight, and neural tube defects all fall within the scope of RLP.^{15,19} Given the magnitude and gravity of adverse repercussions that RLP has the potential to mitigate, attending to reproductive healthcare needs consistently and routinely through RLP can spur positive changes in the state of maternal and child health. By modifying knowledge, attitudes, and behaviors surrounding reproductive health to welcome healthier births and delay pregnancy until desired through RLP, Hawai'i can more comprehensively allay maternal and child health risks and promote greater autonomy over pregnancy and birth outcomes.

Adoption of One Key Question® in Community Practice

On a local level, community providers and advocacy agencies across Hawai'i have begun adopting and implementing a RLP strategy into practice to strengthen efforts to reduce Hawai'i's high unintended pregnancy rate and to promote preconception care. Spearheading this effort is the Hawai'i Maternal and Infant Health Collaborative (HMIHC), a cohesive group of public and private partners as well as community stakeholders with the shared mission of coordinating efforts and working to minimize gaps and needs in maternal and infant health at the policy, delivery system, clinical practice, and payer system levels.²⁰ As part of its vital initiatives, the Collaborative selected the RLP strategy One Key Question® to pilot in targeted community agencies that deliver both clinical and nonclinical services statewide, including home visiting agencies, managed care

organizations, and designated health clinics serving Hawai'i's marginalized populations.

Developed by the Oregon Foundation for Reproductive Health, One Key Question® is an evidence-informed RLP intervention that assists women in identifying and clarifying their reproductive desires and goals, with a specific emphasis on promoting highly effective birth control methods for women who do not desire pregnancy.²¹ One Key Question® is not only a tool to reduce unintended pregnancy but also a mechanism to address underlying maternal health conditions and risky health behaviors that have a detrimental impact on both mother and baby's health before, during, and after pregnancy by asking the simple question "Would you like to become pregnant in the next year?" This strategy focuses on what women desire rather than what they plan, as research indicates that pregnancy planning is not a phenomenon that resonates with all ages, cultures, and backgrounds.^{22,23} Additionally, One Key Question® has the potential to circumvent stigma associated with pregnancy planning in low-income populations.²² The One Key Question® algorithm includes four response categories, "Yes," "No," "I'm Not Sure," and "I'm OK Either Way." Since this question does not require a binary answer, this intervention further has the potential to navigate ambivalence and fatalism surrounding pregnancy desire and intention that anecdotally is common in Hawai'i's diverse communities. Focusing on the desire of the individual woman, it is a non-judgmental, non-confrontational algorithm that opens the reproductive healthcare dialogue with the goal of connecting women to the most effective contraceptive and preconception healthcare services.²⁴ Consistent with RLP research, One Key Question® developers advocate for screening in every healthcare encounter in order to evolve with a woman's changing desires and goals and achieve optimal results.²⁴ As part of the One Key Question® rollout, the Collaborative has hosted trainings on intervention delivery, contraception, and preconception care for partner agencies and community stakeholders as well as established formal data collection and tracking mechanisms. The Collaborative plans to expand the adoption and implementation of One Key Question® following its pilot implementation in select settings across the islands.

A Unique Pilot Setting

The Home Visiting Services Unit (HVSU) within the Maternal and Child Health Branch of the Hawai'i Department of Health has recognized its distinctive opportunity to support the mission and goals of the Collaborative in conjunction with its own priorities and initiatives. In 2010, the Maternal and Child Health Branch established Your 'Ohana (formerly the Hawai'i Home Visiting Network), a formal partnership of diverse community agencies delivering evidence-based home visiting services to specific priority populations across the islands. Mirroring populations that experience higher disparities in unintended pregnancy rates and maternal and birth outcomes, priority populations for home visiting services include families in communities with high levels of poverty, unemployment, receiving high rates of government assistance, low educational achievement,

and high rates of child abuse and neglect.²⁵ Shared goals of the HVSU and the Collaborative include improving maternal and newborn health, facilitating strong parent-child relationships, and coordinating referrals to community resources and support systems. Recognizing this alignment of priorities and goals, the HVSU has partnered with the Collaborative to implement One Key Question® within a novel setting- home visits between a trained paraprofessional and new mothers.

In November 2016, the HVSU began piloting One Key Question® within three Your ‘Ohana agencies that provide home visiting services in four service areas on Hawai‘i Island, Moloka‘i, and O‘ahu. Home visitors are uniquely poised to provide a seamless integration of One Key Question® into existing service delivery, weaving together the complementary goals of evidence-based home visiting and RLP. The role of a home visitor is one of support, reflective listening, and exploratory counseling with the ultimate goal of supporting the health and happiness of mother and baby. Home visitors can speak with mothers about optimal preconception health and highly effective contraception options while also discussing core tenets of home visiting curriculum such as achieving financial and economic self-sufficiency, pursuing education or job training, and creating Family Goal Plans. Response to the implementation of One Key Question® in home visiting has largely been positive, with many home visitors and mothers reporting feelings of empowerment and increased knowledge of reproductive health. The HVSU recently launched its soft rollout of One Key Question® in July 2017 to all six home visiting agencies at ten home visiting sites within Your ‘Ohana and anticipates full implementation by October 2017. Both the HVSU and the Collaborative are confident that this specialized setting with abundant opportunity to align goals will ultimately promote the best outcomes, both short term and long term, for mothers and babies.

The investment of the HMIHC and the HVSU to advance RLP in primary and community care settings is an important first step. To fully realize the intentions of these investments, evaluation of implementation across settings as well as rigorous evaluation of process and outcomes must follow. Several evaluations of One Key Question® pilot sites are underway or planned. We anticipate that future publications will describe these efforts.

Summary

Research to date has shown positive reception and endorsement of RLP by both providers and patients.^{26,27} Several prominent health policy organizations, including the APHA and ACOG, support One Key Question® as an appropriate and effective RLP strategy.^{17,28} As prevention research has asserted, utilizing and implementing evidence-based prevention strategies and interventions to effect change is of the utmost importance.²⁹ In piloting the One Key Question® intervention, the Hawai‘i Maternal and Infant Health Collaborative is using research and data to inform implementation and program monitoring efforts statewide to reduce infant mortality and improve birth outcomes as well as continue to build the evidence base for the RLP intervention One Key Question® in various health clinics, social service community agencies, and prevention organizations. Through its partnership with the Collaborative, the Hawai‘i Home Visiting Services Unit has expanded and enhanced their mechanisms to improve primary and reproductive care coordination and further support the overall health and wellbeing of vulnerable mothers, children, and families in Hawai‘i.

Disclaimer

The discussions in this article are those of the authors and do not necessarily represent the official position of the Hawai‘i Department of Health or the Hawai‘i Maternal and Infant Health Collaborative.

Conflict of Interest

None of the authors identify a conflict of interest.

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Precision Medicine Through the Use of Pharmacogenomics: Current Status and Barriers to Implementation

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Abstract

The precision medicine initiative brought forth by President Barack Obama in 2015 is an important step on the journey to truly personalized medicine. A broad knowledge and understanding of the implications of the pharmacogenomic literature will be critical to the achievement of this goal. While a great amount of data has been published in the areas of pharmacogenomics and pharmacogenetics, there are still relatively few instances in which the need for clinical intervention can be stated without doubt, and which are widely accepted and practiced by the medical community. As our knowledge base rapidly expands, issues such as insurance reimbursement for genetic testing and education of the health care workforce will be paramount to achieving the goal of precision medicine for all patients.

Keywords

pharmacogenomics, pharmacogenetics, precision medicine

Introduction

The term “precision medicine” has become very popular in the news in recent years, particularly after the State of the Union address given by President Barack Obama in January of 2015. In this address, the president announced the “Precision Medicine Initiative,” which is a long-term research endeavor between the National Institutes of Health (NIH) and many other research centers, that aims to “understand how a person’s genetics, environment and lifestyle can help determine how best to prevent or treat disease.”¹ A very important component of precision medicine is “pharmacogenomics,” which is the study of how the entire genome affects the response to drugs. The term “pharmacogenetics,” is often used interchangeably but incorrectly with pharmacogenomics. Pharmacogenetics, is the study of how a particular gene is involved in the response to a particular drug. In the dream of personalized medicine we aspire to discard the “one size fits all” approach to medicine and group patients into manageable and treatment-tailored groups. Many practitioners recognize this concept termed in the literature as “disease-state management.”² This article will examine the possibilities as well as the potential road blocks to using pharmacogenomics to make precision medicine a reality.

Why focus on pharmacogenomics/ pharmacogenetics?

The full sequence of the human genome was reported in Nature in April of 2003.³ Since then, the scientific literature related to genome analysis has exploded and many excellent correlations between genomic variations and clinical effects of drugs have been elucidated. However, there are many difficulties inherent in this analysis that make things far from straightforward, and while it is an amazing accomplishment, sequencing the genome was a bit like coming upon a highly evolved alien speaking a language for which we had only the alphabet. Many brilliant scientists have spent the majority of their careers helping those of us who are not geneticists begin to babble our first words. We have learned for instance, that genetics influences all of the processes that involve the disposition of drugs (absorption, distribution, metabolism and elimination). Single nucleotide variations may have profound effects on how a drug is handled among individuals. This makes perfect sense when a group of physically comparable patients receive the same drug and dose but exhibit differences in clinical response and occurrence of adverse events.

Yet there are many DNA sequence variations that have no known clinical consequence. The latest estimates indicate that the number of protein-coding genes carried by humans is about 20,000.⁴ Variations in our DNA sequence are what make each of us unique individuals. The burden of clinical genetics and more specifically pharmacogenetics is not only to identify common variations in the genome, but also to determine to what degree these variations occur and their clinical significance. The reason for the recent focus on pharmacogenomics is readily apparent when we look at the major causes of morbidity and mortality in our country. In the FDA’s online learning module “Preventable Adverse Drug Reactions,” it is stated that adverse drug reactions cause over 100,000 deaths in the United States, making them the 4th leading cause of death, with an associated cost of over 136 billion US dollars per year.⁵ Any tool that could help us predict and potentially avoid these events would not only help us tailor drug therapy to individuals but would save many lives and significantly affect the cost of health care.

Impact of pharmacogenomics on safe medication prescribing and adverse effects

One of the areas in which pharmacogenomics is well utilized is in oncology. Ongoing research has elucidated that tumors with certain genetic mutations have a better response to certain antineoplastic drugs or monoclonal antibodies. This knowledge allows oncologists and oncology pharmacists to choose effective cancer chemotherapy in a much more selective manner and helps them avoid toxicities from unnecessary therapy. Consider the traditional first-line chemotherapy treatment of non-small cell lung cancer (NSCLC), which usually involves the use of the two agents cisplatin and vinorelbine. Both of these agents can cause severe nausea and vomiting, bone marrow suppression, and other significant adverse effects. Unfortunately, most patients who undergo this therapy will eventually have disease progression. Patients in this situation who have tumors that carry the PD-L1 or PD-L2 genetic marker have been shown to respond to the drug nivolumab (Opdivo™) which blocks the interaction of cancer cells with PD-1 receptors on T-lymphocytes, which then allows the immune system to recognize and attack the cancer cells. Nivolumab is generally much better tolerated than other second-line agents like docetaxel and offers many of these patients the opportunity to prolong their life.⁶

An increase in the amount of information in the area of genetic influence on drug metabolism has also occurred. The cytochrome P450 enzyme family is involved in the metabolism and potential effects of most drugs. Numerous studies have shown that genetic variations that determine the activity of these enzymes are clinically relevant not only to the efficacy but also the toxicity of drugs. A striking example of this may be seen with the commonly used opioid pain medication codeine. One of the most practice-changing events occurred after a 2013 FDA drug safety communication regarding the use of codeine in children after tonsillectomy and adenoidectomy surgeries.⁷ Effective pain relief involves the conversion of codeine to morphine via the liver's cytochrome P450 2D6 system. Activity of this enzyme system is genetically determined and individuals may be divided into four groups of enzyme activity: ultra-rapid metabolizers, extensive metabolizers, intermediate metabolizers, and poor metabolizers. Poor metabolizers do not convert codeine to morphine well and thus get very little pain relief. Extensive and ultra-rapid metabolizers have much higher blood levels of morphine than intermediate metabolizers. However, this inherent enhanced metabolism may lead to greater toxicity. Children who are ultra-rapid metabolizers of codeine can therefore develop life-threatening amounts of morphine in the body sometimes leading to death.⁸ Prior to this FDA warning, codeine was commonly used in children not only following tonsillectomy but also as a cough suppressant. As a result of this pharmacogenomics research, usage of codeine in children has declined sharply.

Pharmacogenetics can also help us predict which patients are most likely to suffer life-threatening adverse reactions to drugs and thus avoid their use. HLA markers on our cells help us determine whether tissues or blood from one person will

match immunologically with another person. This concept is used in medicine daily to determine which persons might be compatible blood donors or organ donors. Recently it has been determined that patients of Han Chinese descent who carry the genetic marker HLA-B*1502, have an increased risk of the potentially fatal dermatological toxicities of Stevens-Johnson syndrome, and toxic epidermal necrolysis when exposed to the anti-epileptic drug carbamazepine. Genotyping patients before using this drug allows us to predict who might have these events, and to avoid the use of this drug in those patients.⁹

Challenges to Widespread Implementation of Pharmacogenomics Guidelines

Over 140 drugs include pharmacogenetic-related information in their labelling. The PharmGKB website (<http://pharmgkb.org>), a pharmacogenomics knowledge resource, provides links to the Clinical Pharmacogenetics Information Consortium (CPIC) guidelines (<http://cpicpx.org/guidelines>), with prescribing recommendations based on genotype/phenotype for thirty-three commonly used medications. There are however stumbling blocks that exist to widespread implementation and use of this type of information. A perfect example occurs with the very commonly used drug clopidogrel (Plavix™). The CPIC Guideline on CYP2C19 genotype and clopidogrel therapy was originally released in 2011¹⁰ and updated in 2013¹¹ with the FDA mandated label change for clopidogrel occurring in 2016.¹² Clopidogrel (Plavix®) is an anti-platelet drug used in patients with heart disease, recent stroke, and peripheral vascular disease to prevent future events. The activity of clopidogrel is dependent on its conversion in the liver to an active metabolite carried out in part by the cytochrome P450 enzyme CYP2C19. Similar to the information mentioned above regarding the cytochrome P450 2D6 system, patients may be divided into a range of ultra-rapid, extensive, intermediate, and poor metabolizers. Studies have linked clinical response in patients taking clopidogrel for acute coronary syndrome (ACS) and in patients taking it after percutaneous coronary intervention (PCI) to CYP2C19 metabolizer status.¹³ Poor metabolizers would convert less clopidogrel to its active metabolite and could therefore get less anti-platelet activity. The black-box warning for clopidogrel states that other platelet P2Y12 inhibitors should be considered in patients identified as CYP2C19 poor metabolizers. The pharmacogenomics section of the Plavix package insert goes on to state that the prevalence of poor metabolizers is higher in Asian patients and cites a crossover study in which poor metabolizers showed diminished platelet aggregation.¹⁴ Additionally, in a meta-analysis examining the association of CYP2C19 genotype (ie, what group of metabolizers a patient belongs in) and clinical outcomes in 9685 patients treated with clopidogrel primarily for percutaneous coronary intervention (PCI),¹⁵ the authors found that patients undergoing PCI treated with standard doses of clopidogrel who have either one or two reduced-function CYP2C19 alleles (forms of the gene) were at increased risk for major adverse cardiovascular events. Both the CPIC Guidelines and the FDA black box warning however stop

short of recommending genetic testing for ACS/PCI patients, leaving many physicians unsure how to proceed in this situation. This situation became even more complex when in 2015 Bhopalwala and colleagues published a complete review of the literature relating to CYP2C19 polymorphisms and clopidogrel¹⁶ published from January 2009 to June 2014. In their conclusion of the review, the authors did not support routine screening for CYP2C19 polymorphisms in patients treated with clopidogrel. Since that time however, additional data on clinical outcomes has been collected and multiple papers both for and against CYP2C19 genetic testing have been published, again leaving practitioners somewhat confused on choosing a proper course of action. At present these issues remain unresolved.¹⁷⁻²⁰ One criticism of CYP2C19 genetic testing is a lack of randomized controlled trial data as well as cost-effectiveness data to support genotype-guided therapy. The IGNITE Pharmacogenetics Working Group (**Implementing Genomics in Practice**), was formed in 2015 to tackle some of these issues. Six NIH-funded institutions and nine affiliate members will share data and outcomes on a CYP2C19-clopidogrel project which will examine genotype-guided therapy after PCI.²¹ This clinical outcomes trial which could provide more solid guidance is expected to be completed in 2020.

A pharmacogenomics issue of particular concern in Hawai'i is the lack of clarity on ethnicity and race in much of the clinical pharmacogenomics literature. Unfortunately, in most studies, participants are asked to self-identify race and/or ethnicity. In an interesting comment in the *Lancet* in 2007, Alain Li Wan Po of the National Genetics Education and Development Centre in the United Kingdom addressed the question: "Who is an Asian?"²² and noted some of the pitfalls of inferring drug-response phenotype from ethnicity. This problem becomes especially acute in Hawai'i where 23.6% of residents define themselves as "2 or more races."²³ Upon reading the pharmacogenomics literature it becomes readily apparent that grouping people as "Chinese" or "Pacific Islanders" can lead to misinterpretation of outcomes. For instance, in a review of CYP2C19 and CYP2D6 genotypes in Pacific peoples, Nuala A. Helsby²⁴ reported that "the CYP2C19*3 allele appears to be relatively uncommon in Polynesians compared with Melanesians, with an allele frequency of 0.04 vs. 0.19. A recently published study on genetic variation in CYP450 genes among ethnic groups in Singapore showed distinctive differences in polymorphisms for CYP450 enzymes between the Indian, Chinese, and Malay subjects.²⁵ A better, more specific way of sorting pharmacogenetics data is certainly needed if we want a clear picture of drug-genotype relationships.

Economic Reimbursement for Ordering Pharmacogenetic Testing

An added problem for practitioners who would like to order genetic testing lies in the patient's reimbursement program. Coverage for genetic testing varies widely among insurers. Most insurers will cover only the few tests that are required by FDA, such as HLA-B*57:01 testing prior to abacavir use,²⁶

HLAB*15:02 testing for carbamazepine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis,²⁷ and tests relating to the treatment of certain cancers such as BRCA testing in the treatment of breast cancer.²⁸ Table 1 provides a list of drugs for which FDA requires genetic testing for insurance reimbursement. Coverage of "recommended" tests varies. The Centers for Medicare and Medicaid Services (CMS) allows its local contractors to decide these issues, and in a small non-scientific survey conducted via the Internet by this author, most testing was considered by contractors to be "experimental" or "investigational."^{29,30}

Next Steps — National Recommendations, Reimbursements, and Education

Recently a 15 member congressional panel sent a letter to the Secretary of the Department of Health and Human Services, Thomas E. Price, and the Chairman of the Medicare Payment Advisory Commission, Francis J. Crosson, requesting that the federal government examine how improvements can be made in patient access to genetic testing.³¹ In this letter, the members of Congress requested that studies be conducted to:

- Examine how genetic testing can improve preventative care measures and precision medicine initiatives;
- Make recommendations on how the federal government can encourage the expansion of health insurance coverage of genetic testing, support the development of evidence for the clinical utility of genetic tests and strengthen related workforce training efforts;
- Analyze how the utilization of genetic testing can reduce health care expenditures

The letter further requested that the Medicare Payment Advisory Commission initiate a study to:

- Review how the current Medicare and Medicaid coverage determination framework may restrain the use of genetic tests;
- Develop recommendations on how the Centers for Medicare and Medicaid Services can make coverage determinations that better suit a precision medicine approach to treatment and;
- Analyze how the utilization of genetic testing can reduce expenditure.

Medication Reimbursement With Genetic Testing

Some insurers require pharmacists to submit genetic testing information with a prescription prior to providing coverage for that prescription. This seems common in cases where a drug benefits only patients with a specific genotype. For example, patients with cystic fibrosis must show evidence of the gene mutation F508del (a mutation of the CFTR gene encoding the chloride channel) before most insurance companies will cover their prescription for Orkambi™, (ivacaftor/lumacaftor), a medication that is efficacious in cystic fibrosis patients with this particular mutation. In fact, the FDA mandates that genetic

testing be performed before this drug is prescribed.³² This becomes a problem for the pharmacist attempting to fill the prescription if the pharmacist does not have direct access to this type of information, relying on communication between prescriber and/or patient, and a potential delay in timely start or maintenance of therapy. Even if an insurer would cover the prescription without the genetic testing, the pharmacist's check of appropriate medical indication (through the use of the diagnosis code) for a drug must still be considered since Orkambi is FDA approved only for patients with the previously mentioned specific genotype.

As the number of prescription medications with pharmacogenetic verified indications increases, policies and procedures and education processes must be developed to appropriate professional responsibility.

Most currently practicing health care professionals have had little if any training in the area of pharmacogenomics. Recent health professional graduates may have received limited didactic or experiential training. The Accreditation Council for Pharmacy Education (ACPE) 2016 standards have included a statement on essentials for pharmacists to master in the area of pharmacogenomics/genetics that include the "genetic basis for disease and individual differences in metabolizing enzymes, transporters, and other biochemical impacting drug disposition and action that underpin the practice of personalized medicine."³³ In accordance, the Daniel K. Inouye College of Pharmacy offered an elective course in Pharmacogenomics in the fall of 2016, which will become a three credit required core course in fall 2017. Many professional schools are now offering continuing

education courses or seminars in pharmacogenomics/genetics. Access to education is vital and may be assisted by the integration of clinical decision pathways for appropriate testing and test interpretation into the electronic medical record. Pharmacists and physicians who are well versed in pharmacogenomics/genetics and informatics will help to streamline this process.

Conclusion

The explosion of data in the field of pharmacogenomics/genetics has allowed the idea of truly personalized medicine to come closer to realization. There are however many issues that need to be investigated and resolved before we can fully integrate this knowledge into our everyday practice. Progress in this field will require (1) continued interpretation and evaluation of the pharmacogenomics research literature to determine clinically relevant issues; (2) working with providers, researchers, and insurance plans to resolve coverage issues; (3) timely and efficient education of the health care workforce on pharmacogenomics issues; and (4) development of patient education tools to help patients understand these complex issues. Lagging attention to these issues will limit widespread use of pharmacogenetics testing in the mainstream clinical practice even with the growing body of research advocating application to improve patient care.

Conflict of Interest

The author identifies no conflict of interest.

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Abacavir	Cobimetinib	Exemestane	Olaparib	Rucaparib
Afatinib	Crizotinib	Fulvestrant	Osimertinib	Sodium benzoate
Alectinib	Dabrafenib	Gefitinib	Palbociclib	Phenylbutyrate
Anastrozole	Dasatinib	Ibrutinib	Panitumumab	Tetrabenazine
Arsenic trioxide	Denileukin difitox	Imatinib	Pegloticase	Trametinib
Bosutinib	Divalproex sodium	Ivacaftor	Pembrolizumab	Trastuzumab
Carbamazepine	Eliglustat	Ivacaftor/lumacaftor	Pertuzmab	Trastuzumab emtansine
Carglumic acid	Elosulfase alfa	Lapatinib	Phenylacetic acid	Tretinoin
Ceritinib	Erlotinib	Letrozole	Pimozide	Velaglycerase alfa
Cetuximab	Eteplirsen	Maraviroc	Primaquine	Vemurafenib
Cholic acid	Everolimus	Nilotinib	Rasburicase	Venetoclax

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Gold Humanism Honor Society Application Essay – On Humanist Medicine

Ryder Onopa MD

Editors' Note: This short essay, the work of the late Ryder Onopa MD, (JABSOM 2013) is a uniquely mature, accurate and perceptive statement of the role of the student of medicine in today's educational structure. We publish it as a reminder to us all that our first task is to strive to improve the mental and physical health of our patients with the tools we have, the most important of which is informed compassion.

Humanism is the perspective through which I understand my desire to help others feel secure as persons, while under duress, in otherwise dehumanizing circumstances. It is an outlook regarding medicine, rather than a skill set within it; a set of priorities that refocus care around the patient as an individual, beyond the scope of their immediate medical predicament.

The practice of medicine is rife with de-humanization, from issues of autonomy to concepts of wellbeing in general. In most cases, expedience and limitations of circumstance set the priorities of care. When emergent treatment allows for only superficially informed consent, or when time constraints and language barriers force a patient to accept a care plan without adequate understanding, human connection is sacrificed for systematic efficiency. Whatever its origin, however ubiquitous its practice or beneficent its intent, this failure to fully engage as humans can only degrade the basis of trust underlying the patient-physician interaction.

In this regard, the hospital experience stands out. From admission to discharge, the inpatient experience immerses the patient in a rigid and alien culture of medicine. The routines of daily life are disrupted, the social order and environment unknown, forcing a patient to abruptly reconstruct their own identity within the bounds of illness. A patient's hospitalization risks becoming an existential threat, and demands they reshape their sense of self in response to pathology they may neither understand nor accept.

Throughout my brief time on rotations this year, I've met many patients grappling with this phenomenon. Across ages, genders, cultures; these people find themselves stranded in illness, unable to explain exactly how they came to be here in the care of strangers, awaiting some vague and jargon-shrouded cure. Some react with anger, others with resignation, some small few with relief, but most share a sense of frustration at their inability to alter their own state of affairs.

With most of these patients, I—as a medical student—can do very little to influence their care plan, or shift the course of their physical illness. Rounding on my patients, recording their complaints and physical findings, generally serves a useful but minimal role in their routine care. In many cases, the protections that buffer me from liability wind up insulating me from meaningful patient care. As frustrating as these limitations can be, they provide me with an environment of otherwise stunning potential for interpersonal empowerment.

If my role as a medical student renders me impotent as a practitioner, it leaves me all the more empowered as a human actor within the healthcare system. I am uniquely entrusted with access into the lives of those undergoing profound stress, which allows me to address gaps in care and barriers to meaningful communication that might otherwise be invisible to healthcare providers. The most useful I've felt has been in simply talking story with my patients and their families, encouraging them to remember and engage with their lives, to set goals and priorities beyond the walls of their hospital room.

These conversations, these moments of semi-contrived normalcy, do not relate to the treatment of physical illness *per se*. They represent an effort in parallel with treatment, with complementary goals. Acting to empower a patient's sense of autonomy or self-value does not serve toward curing a pathology, but functions to aid a patient's transition away from a perspective of illness. This psychological transition, however abstract, is absolutely essential to the individual healing process. This focus on the subject, the patient, rather than the science of medicine, is Humanism at work.

THE WEATHERVANE

RUSSELL T. STODD MD; CONTRIBUTING EDITOR

THE PATIENT DIED FROM A GASTRIC ULCER – NOT!

We like to think of a hospital as a place of refuge where problems are solved, or at least defined and alleviated. It is increasingly evident that hospitals in fact are very dangerous places and should be avoided whenever possible. In Manhattan Beach, California, a 71 year-old woman was admitted for surgical treatment of a stomach ulcer. Shortly after, she was fighting for her life, and a doctor had underlined “CRKP” on the chart an ominous abbreviation for an infection with a superbug, carbapenem-resistant *Klebsiella pneumoniae*. After five weeks of intensive care she expired from her infection, and the doctor signed the death certificate as death due to respiratory failure and septic shock caused by her ulcer. No mention was made of her hospital acquired CRKP. The doctor explained that had she not had an ulcer she would not have been in the hospital. Her daughter was angry and challenged the hospital administration to no avail. The case is hardly unique. An epidemic of hospital-acquired infections is going unreported, according to medical experts. Researchers at the University of Michigan found in 2014 that patient’s billing record shows much more closely what the patient was being treated for rather than the death certificate. The Centers for Disease Control and Prevention (CDC) call CRKP one of the nation’s most urgent health threats. Bottom Line – stay away from the hospital whenever possible.

INTERNATIONAL SCHOOLS ARE ANSWERING THE CALL, AND WE DO NOT CARE ABOUT IMMIGRATION.

Medical schools in the United States (U.S.) are struggling to educate enough doctors to meet the needs in rural and other underserved areas of this country. Still, there is a shortage and the Association of American Medical colleges forecasts a worsening picture with between 40,800 and 104,900 physician deficit by 2030. International medical schools are stepping in to provide help. In 2016, 3,298 U.S. citizens from foreign schools were certified to enter American residency and fellowship programs. A few of the schools outperform when it comes to getting students into residency programs at U.S. teaching hospitals. Ross University Medical School of Medicine in Dominica, American University of the Caribbean School of Medicine in St. Maarten, along with a handful of others, regularly post match rates of 85%. Of aspiring doctors who applied for residency matches in 2016, 15% were U.S. citizens who attended foreign schools. At this time it appears obvious that the USA will benefit from the influx of foreign medical school graduates without an impact on quality of care. Go for it.

SPARKS MAY BRIGHTEN THE SKY FOR RPE 65.

Spark Therapeutics Inc. is a startup biotechnology company using gene therapy to improve vision. Gene therapy involves injecting genetic material to treat or prevent disease. Initial efforts in the 1990s were sidetracked when some study participants died or developed cancer. Gene therapy is gaining ground again following the successful treatment of patients with a rare enzyme deficiency in a study done in Europe. Sparks study tested 19 patients with a copy of a functional RPE 65 gene where the original gene failure caused loss of night vision, loss of peripheral vision, reduction in acuity, and eventually progresses to complete blindness. The Sparks gene is encapsulated in a virus that acts as a delivery vessel and is injected into the eye. Patients receiving therapy had improved “functional” eyesight compared with the control group. Debra Thompson, professor of ophthalmology at Michigan’s Kellogg Eye Center, not involved in the study, stated, “We’ve all been hoping that gene therapy will be approved for these retinal diseases. Getting this close is very exciting.

“THE SHOT GIVES YOU THE BREAK YOU NEED.” ARMY GENERAL BOLDUC, COMBAT PTSD PATIENT.

Terms for the condition, Shell Shock, Combat Stress Reaction, Battle

Fatigue, or Post Traumatic Stress Disorder the condition is roughly the same with various symptoms but no specific therapy. Sufferers are often irritable, edgy, depressed, and quick to anger. The most common psychological treatments, called exposure therapies, where the sufferer repeatedly revisits the traumatic event to weaken its effect, will prove useful in about 60% of PTSD. In recent years some military physicians have begun treating PTSD patients, especially Army Green Berets and Navy SEALs with stellate ganglion blocks. The theory is that the block locks down the autonomic nervous system and the reaction to stress hormones. Doctors inject ropivacaine in the right side of the neck, using ultra-sound to guide the needle to the ganglion. The Army has an ongoing \$2 million study, but finds it hard to get volunteers. Word of mouth has caused many subjects to refuse for fear of being in a control group. They all want therapy, and they know they can get it free from military hospitals without signing up for the program. Treatment is further confused since Green Berets and SEALs want to get back to their unit, while others have an incentive to stay sick. The VA pays benefits to those suffering from combat-induced PTSD, but has no specific policy regarding the use of stellate blocks. Physician advocates of the stellate block say it improves the effectiveness of traditional treatments. Another case of “go figure.”

HEY, DOC. I’VE HEARD OF BLOWING SMOKE UP MY—BUT STEAM?

About half of the male population over the age of 50 has some degree of prostate enlargement. Symptoms are frequent urination at night and urinary urgency during the day. Sufferers are offered two choices, surgery or medication, both of which may cause sexual dysfunction. Now a minimally invasive procedure called Rezum (resume) developed by NxThera Inc has become widely available in the United States in the second half of 2016. Rezum uses thermal energy in the form of steam applied to the prostate with a needle. As it cools it releases heat energy into the tissue killing cells and shrinking the gland. It leaves sexual function intact. The procedure costs about \$2,000, generally covered by insurance, and can be performed in the doctor’s office in just a few minutes. The downside is that the duration of effectiveness is unknown.

SKIN PIGMENT VARIATIONS ARE DISAPPEARING.

Fifty years ago the Supreme Court recognized the right of racial intermarriage. In 2015 one in six American newlyweds crossed the racial line. Asian and Hispanic newlys are by far the most likely to have intermarried with nearly three in ten choosing someone of a different race. The biggest percentage increase is in African-Americans, though black men are much more likely than black women to intermarry. Negative attitudes among nonblacks toward marrying black people have taken a particularly steep drop, according to Pew analysis of data from the General Social Survey conducted by NORC at the University of Chicago. In 1990, 63% of nonblacks said they would be opposed to a close relative marrying someone who is black. By 2016, that figure had fallen to 14%. Color and culture are freely mixed in the 50th state, and no one notices or cares.

ADDENDA

- Ernest Hemingway rewrote the final page of “A Farewell to Arms” 39 times.
- The technical term for goosebumps (chicken skin) is horripilation.
- Dezi’s mother was one of the heirs to the Bacardi Rum Foundation.
- Where there’s smoke there’s toast.
- In biblical times a man had as many wives as he could afford. Just like today.
- Help! I’m being held captive by my heredity and environment.
- Schick has a new four blade razor. The first three are to cut your beard, and the fourth one ask your wife not to use it to shave her legs or other body parts.

ALOHA AND KEEP THE FAITH *rts*

(Editorial comment is strictly that of the writer.)

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