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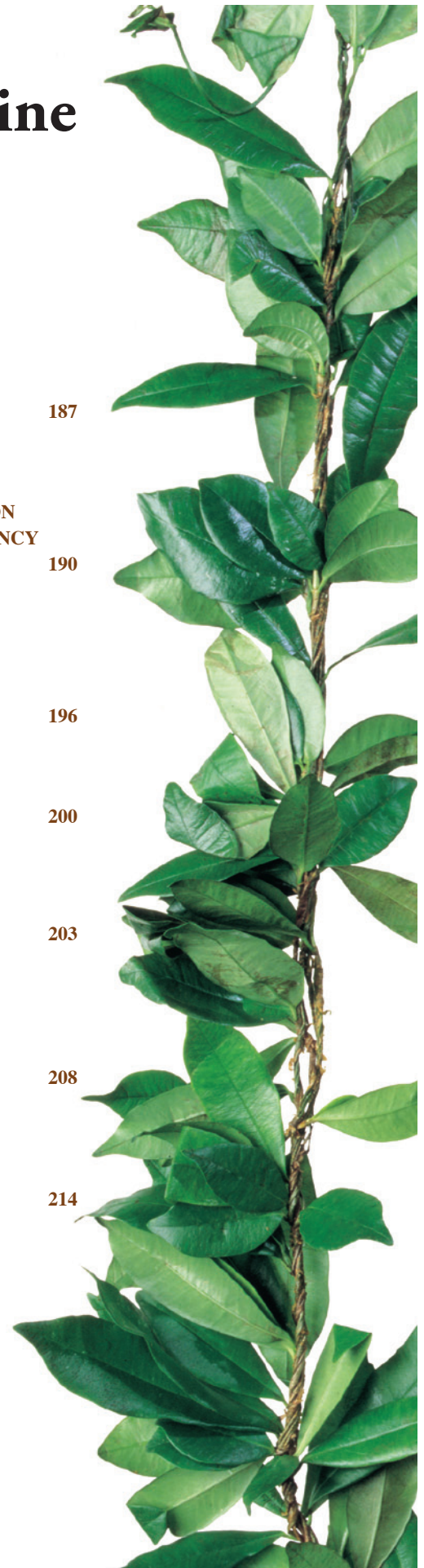
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Asymptomatic Giant Intraventricular Cysticercosis: A Case Report

Ornusa Teerasukjinda MD; Suwarat Wongjitraporn MD; Chawat Tongma MD; and Heath Chung MD

Abstract

Neurocysticercosis is a growing health problem in the United States and worldwide. Diagnosis and treatment is challenging especially if the physician is not familiar with this condition. The World Health Organization (WHO) estimates that neurocysticercosis affects 50 million people worldwide, especially in developing countries and causes approximately 50,000 deaths annually.¹ Neurocysticercosis is of emerging importance in the United States especially in Hawai'i because of immigration from disease-endemic regions.²

We present a case of a young Chinese immigrant male who presented with impressive imaging studies of a giant intraventricular neurocysticercosis. This case emphasizes the importance of recognizing neurocysticercosis, especially in the immigrant population.

Keywords

Case report, Neurocysticercosis, Cysticercosis, Intraventricular cystic brain lesion, *Taenia solium*

Introduction

Humans are definitive and intermediate hosts in the life cycle of *Taenia solium* (pork tapeworm). Humans become carriers of *Taenia solium* by ingesting undercooked pork which contains cysticerci in the muscle tissue. The scolex evaginates and attaches in the human intestines. Proglottids arise from the scolex and mature over a period of 2-4 months. Each proglottid segment contains 50,000 – 100,000 eggs which are shed in the stool. This condition is called taeniasis.

Cysticercosis is caused by ingestion of *Taenia solium* eggs shed in the stools of human tapeworm carriers. Humans can become accidental intermediate hosts by either ingesting food contaminated with eggs of adult tapeworms or by reverse peristalsis of eggs into the stomach in patients harboring tapeworms in their small intestine.^{3,4} The eggs hatch in the gastrointestinal tract and develop into the larval stage in 3-8 weeks. Thereafter, larvae disseminate to several body tissues with a strong tropism for the central nervous system, causing neurocysticercosis.⁵

Cysticercosis is endemic in many regions of Central and South America, sub-Saharan Africa, India, and Asia.⁶ The prevalence of cysticercosis is higher in rural areas with poor sanitation and where pigs are raised. In the United States, there is a high prevalence of cysticercosis among Latin American immigrants in locations such as Arizona, California, and Texas.⁷ Education about disease transmission and prevention should be emphasized especially in endemic areas to prevent fecal-oral transmission and to reduce *Taenia solium* carriers. Prevention strategies include improving sanitary conditions, encouraging good personal hygiene, and treating carriers.

Neurocysticercosis is characterized by its location. Parenchymal neurocysticercosis involves brain tissues while extraparenchymal neurocysticercosis involves other locations including the intraventricular space, subarachnoid space, and spinal cord.⁸ The intraventricular form of neurocysticercosis is seen in 7%-45% of cases.^{9,10} The fourth ventricle is the most common site of infestation (54%-64%), followed by the third ventricle (23%-27%), the lateral ventricles (11%-14%) and the aqueduct of Sylvius (9%).^{5,9,10}

Manifestations of neurocysticercosis are varied, ranging from asymptomatic to severe neurological symptoms. Presentations of neurocysticercosis depend on multiple factors including the number of lesions, location, type of cysticercus, its stage of development and involution, and intensity of the host immune response.¹¹ Parenchymal neurocysticercosis is usually associated with seizures and headaches. Often times, patients with extraparenchymal neurocysticercosis present with signs and symptoms of increased intracranial pressure secondary to hydrocephalus caused by mechanical obstruction of the cerebrospinal fluid (CSF) pathway or associated ependymitis or basal arachnoiditis, with resulting failure of CSF absorption.¹²

Usually, cysticerci do not cause inflammation of the surrounding tissue. Cysticerci have the ability to produce a variety of substances that inhibit host inflammatory responses. However, cysts could become degraded over time and cause edema and inflammation. Ultimately, the parasites transform into calcified nodules, presenting as calcified granulomatous lesions without associated edema or enhancement in imaging studies.

Gadolinium-enhanced magnetic resonance imaging (MRI) is the preferred imaging method for diagnosis of neurocysticercosis due to its superior contrast resolution and direct multiplanar capability.^{3,13-15} It is the most accurate technique to assess the degree of infection, location, and evolutionary stage of the parasite.¹

We present a case of asymptomatic large intraventricular neurocysticercosis treated with conservative management.

Case Presentation

A 37-year-old Chinese man who was previously healthy without significant past medical problems presented to our facility after sustaining a head injury from a car accident. He briefly lost consciousness during the incident and had a transient headache. He was admitted to the hospital for further investigation and close observation of neurological symptoms. Physical examination showed no significant neurological deficits. Non-contrast



Figure 1. A computed tomography of the brain without contrast shows a 7.4 x 5.7 x 6.2 cm right occipital intraventricular cystic lesion with a small partially calcified mural nodule and dilatation of the right lateral ventricle.

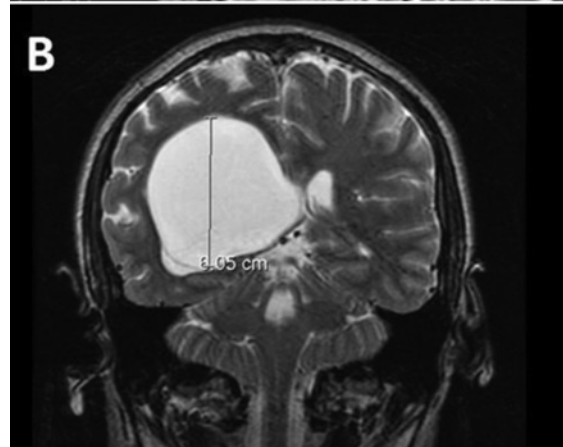
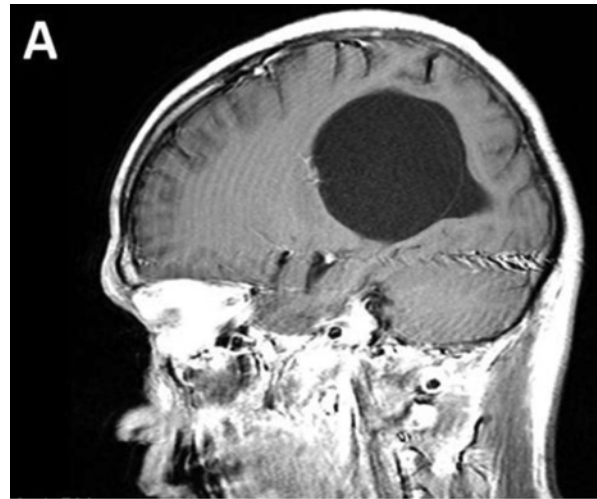


Figure 2. Magnetic resonance imaging of the brain with/without contrast (Panels A and B respectively) show a large solitary right ventricular cyst with partially calcified mural nodule. There is evidence of dysgenesis of the corpus callosum versus thinning of the posterior corpus callosum due to chronic mass effect.

head computerized tomography (CT) was obtained to rule out intracranial abnormality. The results showed a large cystic lesion measuring 5x6x7 cm in diameter in the right lateral ventricle, with a partially calcified lesion (Figure 1). Gadolinium-enhanced MRI of the brain (Figure 2) was obtained and revealed a large solitary right lateral ventricular cystic lesion containing a partially calcified mural nodule. There is evidence of dysgenesis of the corpus callosum versus thinning of the posterior corpus callosum due to chronic mass effect. No surrounding edema or inflammation was observed. The findings were highly suggestive of intraventricular cysticercosis. A complete blood count (CBC) revealed no evidence of eosinophilia and a stool sample for parasite confirmation was not obtained in this patient.

Further history revealed that he was born and raised in China, moved to Mexico, and then to Hawai'i three years prior to admission. He denied previous history of chronic headache, weakness, seizures, or visual impairment. He denied history

of tapeworm infection or household contact. The MRI result prompted neurosurgical evaluation. As the patient was asymptomatic and had no hydrocephalus, close outpatient follow-up without surgical intervention or treatment with medications was planned. After 6 months of follow up, the patient remained asymptomatic. Further MRI follow up revealed no change in the size of the cystic lesion or degree of surrounding inflammation.

Discussion

Neurocysticercosis is mostly diagnosed based on clinical presentation and imaging studies.^{16,17} Peripheral eosinophilia is usually absent. Stool examination for parasite is insensitive since most neurocysticercosis patients do not have a viable intestinal tapeworm at the time of diagnosis. Serology tests can be helpful but are not always necessary for diagnosis. Enzyme-linked immunoelectrotransfer blot assay (EITB) of either serum or CSF can be negative if the cyst is calcified.

Moreover, a positive test can persist for years even after death of parasites. Thus, a positive test does not necessarily indicate active disease. The presence of scolex through imaging is a pathognomonic feature for diagnosis of neurocysticercosis.¹⁷

This patient fits the definition of a “probable case” due to the absence of scolex in imaging studies. MRI of the brain revealed a calcified granuloma without surrounding edema. No viable parasite presented. Serologic tests were not performed in this case. The major differential diagnosis is an echinococcosis hydatid cyst which is mostly seen as a single cystic brain lesion. Cerebral hydatid cysts are extremely rare, comprising about 2% of all intracranial masses.^{18,19} Hydatid cysts are mostly located in intraparenchymal areas especially parietal areas or the middle cerebral artery (MCA) distribution.^{18,20} They are less likely in cases where the cyst is located intraventricularly.

Various modalities including cysticidal therapy, steroids, antiepileptic medications, neurosurgical removal and ventriculo-peritoneal shunt have been used to treat neurocysticercosis with the ultimate goal of eradicating the parasites, minimizing the inflammatory response, and releasing the obstruction or mass effect.^{1,14} Despite its high global health burden, the optimal treatment for intraventricular neurocysticercosis is still controversial.

The utility and safety of cysticidal therapy in conjunction with steroids in intraventricular neurocysticercosis is still unclear, as larvae are more recalcitrant to the treatment than in the parenchymal form and the treatment itself can trigger inflammation, causing ependymitis and arachnoiditis.^{1,21} Surgery, especially endoscopic, has shown encouraging results and is usually recommended for intraventricular cyst causing significant mass effect, hydrocephalus, or when the diagnosis is uncertain.^{4,14}

While surgery promises to be a fast and definitive method of cyst removal and eliminating risk of mechanical obstruction, chronic hydrocephalus related to inflammatory damage can still occur.^{3,22,23} Other potential life-threatening complications such as cerebral infarction and intraventricular bleeding have also been reported.^{1,23}

Treatment for neurocysticercosis should be tailored individually. This patient did not have signs of increased intracranial pressure, nor obstructive hydrocephalus that prompted an immediate intervention. If the cyst had been located in the fourth ventricle which is vulnerable to obstruction, surgical intervention would have been considered.²⁴ The patient’s brain MRI showed a non-obstructing intraventricular cystic lesion in a calcified stage without surrounding edema or inflammation. As a result, medical management with cysticidal therapy and steroid was of limited value in this circumstance. In this patient, deciding whether or not to perform endoscopic neurosurgery was challenging. As previously discussed, endoscopic surgery is an invasive procedure with multiple possible complications. In the end, surgery was not pursued because of concerns that removal of the large cyst might increase the risk of secondary hydrocephalus due to inflammatory damage.

Moreover, the patient was asymptomatic and the cystic lesion appeared to be in the calcific stage without evidence of inflammation or obstruction, providing further justification against

surgical intervention. However, since this cyst was relatively large, the patient will be closely monitored by clinical symptoms and MRI study which may prompt neurosurgical intervention in the future.

Summary

We present a case of an asymptomatic patient, with an atypically large intraventricular cysticercosis, who was managed by close observation. The conservative approach in a seemingly uncomplicated patient emphasizes the importance of tailoring the management of neurocysticercosis on an individual basis.

Conflict of Interest

None of the authors identify a conflict of interest.

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The Effect of Mobile Tablet Computer (iPad) Implementation on Graduate Medical Education at a Multi-specialty Residency Institution

John Dupaix MD; John J. Chen PhD; Maria B.J. Chun PhD; Gary F. Belcher MEd; Yongjun Cheng PhD; and Robert Atkinson MD

Abstract

Use of mobile tablet computers (MTCs) in residency education has grown. The objective of this study was to investigate the impact of MTCs on multiple specialties' residency training and identify MTC adoption impediments. To our knowledge, this current project is one of the first multispecialty studies of MTC implementation. A prospective cohort study was formulated. In June 2012 iPads were issued to all residents after completion of privacy/confidentiality agreements and a mandatory hard-copy pre-survey regarding four domains of usage (general, self-directed learning, clinical duties, and patient education). Residents who received iPads previously were excluded. A voluntary post-survey was conducted online in June 2013. One-hundred eighty-five subjects completed pre-survey and 107 completed post-survey (58% overall response rate). Eighty-six pre- and post-surveys were linked (response rate of 46%). There was a significant increase in residents accessing patient information/records and charting electronically (26.9% to 79.1%; $P < .001$), but a significant decrease in looking up drug and treatment reference material (97.0% to 82.1%; $P = .0039$). There was a significant increase in MTC use as a primary means of charting when conducting rounds (4.9% to 39.5%; $P < .001$) and a significant decrease in using paper charts (30.1% to 15.7%; $P = .0073$). There was also a significant increase in MTC use as a primary means for explaining a diagnosis (7.7% to 57.7%; $P < .001$). The use of MTC has an impact on how residents approach medical education, clinical practice, and patient education. The survey tool may be useful in collecting data on MTC use by other graduate medical education programs.

Keywords

mobile tablet computers, graduate medical training

Introduction

The adoption of mobile tablet computers (MTCs) among physicians has become increasingly common, particularly in the clinical setting. In a recent survey of 2,950 physicians, 72% reported owning a tablet computer and over half using these devices at point of care.¹ Recent studies described the benefits of MTC implementation in a variety of settings, including the emergency department and in rural locations.²⁻⁸ Interest regarding the utility of MTCs in graduate medical education (GME) has been noted from a variety of medical and surgical specialties.⁹⁻¹⁹

A number of specialties have evaluated the impact of MTC implementation on residents. The adoption of MTCs has been associated with increased perceived and actual resident efficiency in an internal medicine residency program, although enthusiasm was slightly diminished in a follow-up study.^{9,10} Other internal medicine programs have also found high integration and clinical use of MTCs following distribution.¹¹ Radiology residents have indicated that MTCs would be beneficial to them, particularly in studying, in addition to a change from printed to electronic

educational materials in this specialty after MTC distribution.¹²⁻¹⁵ Likewise, 81.6% of residents in an anesthesia program either agreed or strongly agreed that use of MTCs would improve their ability to learn their specialty.¹⁶ In a study of orthopaedic residents on an anesthesia rotation, it was similarly found that the residents' perception of the quality of the instruction was improved significantly following distribution of a syllabus, educational materials, and schedule on an iPad instead of a printed format.¹⁷ In neurosurgical training, the easy access to information through the MTC and its portability provided more opportunities and time for studying for 92% of residents polled and an improvement in both global scoring and on 16 of 18 individual scoring areas of the Congress of Neurological Surgeons Self-Assessment examination.¹⁸

More recently, a small multispecialty, resident pilot study found that there was a self-reported increase in clinical efficiency in addition to reported feelings that the universal adoption of iPads would have benefits in coordination of care and educational activities.¹⁹ To our knowledge, there are no studies on the impact of the implementation of mobile tablet computing on all residents in a multispecialty GME institution. This study seeks to delineate the impact of MTCs on various resident specialties regarding patient education: general, didactic, and clinical use, and to identify impediments to MTC adoption.

Methods

To evaluate the effect of MTCs on residents, a prospective cohort study was formulated. All residents were issued iPad 2s²⁰ at the start of the 2012-2013 academic year to support clinical and educational duties related to residency training. A mandatory completion of a hard-copy pre-survey and privacy/confidentiality agreement was required. The University of Hawai'i residency training programs total approximately 220 institutional residents and fellows from nine core programs and six subspecialty fellowship programs. The pre- and post-surveys were done upon the request of the residency program administration because they wanted to determine whether the introduction of the iPads had any impact on the residents' educational experiences/training. The overall hypothesis was: Use of the iPad would make residency training more efficient and effective by making educational materials more readily available to the residents.

The survey instrument was based on a previous assessment of residents from two programs (Orthopaedic Surgery and

Pathology) who had received iPads at the start of the prior academic year (2011-2012) as part of a pilot study. The survey items were developed largely based on the researchers' past experiences and perceptions of tablet use. In addition to the collection of demographic information, there were four primary domains of interest that were addressed: general computer usage, self-directed learning, usage in clinical duties, and usage in patient education activities. The voluntary post-survey was administered to all residents online (via SurveyMonkey®) immediately prior to the conclusion of the 2012-2013 academic year. The pre- and post-survey questions were identical, with the exception of utilizing past tense for the post-test survey.

A total of 185 residents were included in this study. Participants were allowed to install additional applications, and several specialties reimbursed residents for applications purchased during the study. Continual remote access to electronic medical libraries was provided in addition to wireless network access across the various training locations.

For questions with only a single selection out of a group, we dichotomized each variable based on the frequency distribution. For example, "time spent on study weekly" was coded into over 10 hours (10-13 hours, 14+ hours) vs less than 10 hours (0-3 hours, 4-7 hours, 7-10 hours). For questions where one could select multiple choices, we coded each choice into a binary variable: chosen vs not chosen. The University of Hawai'i's Institutional Review Board deemed this study as exempt (UH CHS #19371).

The survey data were summarized by descriptive statistics: frequencies, for categorical variables and for ordinal variables; means (standard deviations) of ranks of the data. Pre- and post-survey responses were compared using matched-pair McNemar's test for binary variables and non-parametric Wilcoxon signed rank test for ordinal variables, based on ranks of the data. All analyses were performed in SAS 9.3²¹ and a two-tailed *P*-value <.05 was considered statistically significant.

Results

One hundred eighty-five subjects completed the pre-survey and 107 completed the post-survey for a 58% overall response rate. Respondents had a mean age of 31±6 years and 52% were female (Table 1). Eighty-six pre- and post-surveys could be linked and merged for a response rate of 46%.

Comparing pre- and post-survey responses, a significantly lower proportion of residents reported using their MTC to look up drug and treatment reference material (97.0% to 82.1%; *P*=.0039) and a significantly higher proportion to access patient information and records (26.9% to 79.1%; *P*<.001) following implementation (Table 2). There was no significant difference in the other activities between the pre- and post- surveys. For types of MTC use, residents ranked patient education higher (rank difference: post-pre=-0.47, *P*=.0053) and studying lower in the post-survey (rank difference: post-pre=0.39, *P*=.039), while there was no difference in clinical use or entertainment (Table 2).

Age (year), Mean ± SD	31 ± 6	
Female, n (%)	96 (52%)	
Residency Programs	Sub-Specialty Fellowships	Pre-Survey Distribution by Program (n)
Family medicine		18
Internal medicine		40
	Cardiovascular disease	4
	Geriatric medicine	4
Obstetrics and gynecology		25
Orthopaedic surgery		2
Pathology-anatomic and clinical		4
Pediatrics		23
	Neonatal-perinatal medicine	1
Psychiatry		26
	Child and adolescent psychiatry	1
	Geriatric psychiatry	3
Surgery		21
	Surgical critical care	2
Transitional year		9
Unidentified		2
Total		185

SD = standard deviation

Table 2. Summary of Resident Use of Mobile Table Computer								
Survey Question	# Completed Surveys	Pre- / Post-Survey Status						P-value
		Yes / Yes: n	Yes / No: n	No / Yes: n	No / No: n	Pre-Survey Yes: n (%)	Post-Survey Yes: n (%)	
Activity with tablet computer								
Look up drug and treatment reference material	67	54	11	1	1	65 (97.0%)	55 (82.1%)	.0039
Access patient information/records	67	14	4	39	10	18 (26.9%)	53 (79.1%)	<.001
	# Completed Surveys	Pre-survey rank mean (SD)		Post-survey rank mean (SD)		Rank Difference (Post – Pre) mean (SD)		P-value
Type of use								
Studying	73	1.62 (0.79)		2.01 (1.34)		0.39 (1.60)		.039
Clinical use	73	1.88 (0.81)		2.12 (1.02)		0.24 (1.31)		.12
Patient education	73	3.15 (0.97)		2.68 (0.99)		-0.47 (1.42)		.0053
Personal entertainment	73	3.69 (1.02)		3.68 (0.92)		-0.01 (1.32)		.93
Other	73	5.59 (0.94)		4.51 (0.90)		-1.08 (1.37)		<.001

Note: Each respondent's answers to the pre- and post-distribution surveys were matched for McNemar Chi-square analysis for categorical variables and Wilcoxon signed rank test for ordinal variables. "# of completed surveys" is the number of respondents who provided responses to the same question in both the pre- and post- surveys. SD = standard deviation.

Impediments to MTC Adoption

There were no significant differences between the pre- and post- surveys in terms of residents' concerns about using mobile device to communicate between physicians (results not shown). For patient care activities, there was a significant increase in the concern that patients did not have the technology ($P=.018$) (results not shown).

Educational Use

Table 3 summarizes educational usage, clinical usage, and use in patient education of the MTCs. With regard to educational usage, there was a significant decrease in the percent of time spent studying from textbooks ($P<.001$). Similarly there was a significant decrease in the proportion of respondents studying over 10 hours weekly ($P=.033$). There was no difference in time spent studying from a computer. There was a significant decrease in use of print articles (59.0% to 42.2%; $P=.013$) as well as using a computer for assigned reading (47.0% to 31.3%; $P=.042$); conversely, there was a significant increase in the use of a MTC for assigned reading (14.5% to 66.3%; $P<.001$). Use of a phone for reading was rare in the pre and post-distribution analysis. Following distribution of the tablets, residents were significantly more likely to study at a hospital (rank difference: post-pre = -1.11, $P<.001$) or library (rank difference: post-pre=-1.90, $P<.001$) and less likely to study at home (rank difference: post-pre = 1.60, $P<.001$).

Clinical Use

There was a significant increase in the proportion of tablet use for logging procedures and cases (4.9% to 39.5%; $P<.001$) (Table 3). There was no difference in the use of a traditional computer for charting, however, there was a significant decrease in use of paper charts (30.1% to 15.7%; $P=.0073$) concomitant with a significant increase in use of a MTC for charting (6.0% to 27.7%; $P<.001$). There was a non-significant trend towards decreased use of Picture Archive and Communication System (PACS) (72.0% to 57.3%; $P=.052$) and a non-significant increased use of a tablet as the primary means for radiographic image viewing (2.4% to 8.5%; $P=.059$) (Table 3).

Patient Education

Regarding patient education, there were no significant differences in the use of media or an internet page and printouts or handouts as a primary means to explain a diagnosis in the pre and post-distribution survey. However, there was a significant increase in the use of a MTC as a primary means for explaining a diagnosis (7.7% to 57.7%; $P<.001$) (Table 3). There was no significant difference in the proportion of residents who felt that MTCs would reduce the patient's length of stay in the hospital or affect patient satisfaction.

Table 3. Medical Education, Clinical Practice and Patient Education Use of Mobile Tablet Computers								
Medical Education								
	# Completed Surveys	Pre-survey rank mean (SD)		Post-survey rank mean (SD)		Rank Difference (Post – Pre) mean (SD)		P-value
Preferred location to study								
Hospital study area	71	3.24 (1.51)		3.38 (1.24)		0.14 (1.75)		.50
Hospital work area	71	3.17 (1.46)		2.06 (1.16)		-1.11 (1.74)		<.001
Library	71	4.35 (1.43)		2.44 (1.34)		-1.90 (2.05)		<.001
Home	71	1.63 (0.98)		3.26 (1.28)		1.60 (1.61)		<.001
Coffee shop	71	3.75 (1.68)		3.85 (1.27)		0.10 (1.65)		.62
Survey Question	# Completed Surveys	Pre / Post Survey Status						P-value
		Yes / Yes: n	Yes / No: n	No / Yes: n	No / No: n	Pre-Survey Yes: n (%)	Post-Survey Yes: n (%)	
Percentage of time studying with tool								
Studying from textbooks: Yes: "≥50%" No: "<50%"	84	25	30	2	27	55 (65.5%)	27 (32.1%)	<.001
Weekly studying time: Yes: "10+ hrs" No: "<10 hrs"	83	6	16	6	54	22 (26.5%)	12 (14.5%)	.033
What was used to read assigned article								
Hard copy	83	26	23	9	25	49 (59.0%)	35 (42.2%)	.013
Computer	83	12	27	14	30	39 (47.0%)	26 (31.3%)	.042
Tablet Computer	83	10	2	45	26	12 (14.5%)	55 (66.3%)	<.001
Clinical Practice								
How were procedures/cases logged								
Tablet computer in addition to ACGME log:	81	3	1	29	48	4 (4.9%)	32 (39.5%)	<.001
How did you chart when conducting rounds?								
Paper Charts	83	9	16	4	54	25 (30.1%)	13 (15.7%)	.0073
Tablet Computer	83	1	4	22	56	5 (6.0%)	23 (27.7%)	<.001
Primary means by which you viewed radiographic images								
Dedicated PACS computer system (hospital)	82	34	25	13	10	59 (72.0%)	47 (57.3%)	.052
Tablet Computer	82	1	1	6	74	2 (2.4%)	7 (8.5%)	.059
Patient Education								
Print-out/hand-out	26	13	6	1	6	19 (73.1%)	14 (53.8%)	.059
Tablet Computer	26	2	0	13	11	2 (7.7%)	15 (57.7%)	<.001
Will the use of the tablet computer improve patient satisfaction? Yes: "Improve" No: "No effect"	82	31	19	10	22	50 (61.0%)	41 (50.0%)	.095

Note: Each respondent's answers to the pre- and post-distribution surveys were matched for McNemar Chi-square analysis for categorical variables and Wilcoxon signed rank test for ordinal variables. "# of completed surveys" is the number of respondents who provided responses to the same question in both the pre- and post- surveys. ACGME = Accreditation Council for Graduate Medical Education; HR = hour; PACS = Picture Archive and Communication System; SD = standard deviation.

Discussion

There has been recent interest in the literature in utilizing MTCs in GME. We sought to determine this effect across five domains: general use, impediments to use, educational use, clinical use, and use for patient education. There was a significant increase in the proportion of residents that used their iPad to access patient information and records with a small but significant decrease in use to find drug and treatment reference material in “general use.” These findings are consistent with other studies.^{9,11,19} Interestingly, the only significant change in pre- and post-distribution response concerning impediments to utilization of the device with physicians or patients was an increase in concern that patients did not have the technology.

In “educational use,” residents identified a significant increase in the use of hospital work areas and libraries as study locations with a commensurate decrease in the preference for studying at home. There was a significant shift from the use of print materials to the use of the tablet computer for access to textbooks and journal articles, as noted previously.¹³⁻¹⁵ There was also a significant decrease in the proportion of residents indicating that they studied for 10+ hours. This is in contrast to what was observed in other studies.^{13,14} However, this difference in findings may be a result of increased studying efficiency similar to the increased efficiency observed in internal medicine residents with iPads.⁹ Future studies could help determine if increased studying efficiency is present and if there is an improvement on objective outcomes such as in-training examination scores, as was demonstrated among orthopaedic residents in a previous pilot study.²²

Similar to the findings of MTC use in the general domain analysis, “clinical usage” residents indicated a significant increase in the use of their MTC for charting while conducting rounds. Over the same period there was a significant decrease in the proportion of residents reporting use of paper charting. This may highlight the advantages of access and portability of the MTC, but may also reflect a hospital/system requirement. This finding is similar to other studies where it was noted that iPads were heavily used for clinical work and were noted to have improvements on workflow.^{9,11}

Residents indicated an increase in their usage of their iPad as a primary means for explaining a diagnosis to a patient. There was also an increase in the proportion of residents who indicated that they felt use of iPads by residents would lead to improved patient satisfaction. This is similar in theme to the positive patient comments noted in studies of internal medicine residents.¹⁰

This study has a number of limitations. This is a single-institution study with a limited number of specialty residency programs, which may limit its generalizability. In both the pre- and post-distribution surveys the linked response rate was 46%, and indications of usage on the survey may have been affected by recall or participation bias. Also, the overall sample size does not allow for comparisons between specialties. Additionally, a few weeks prior to distribution of the second survey, policy was changed such that the iPads were available for purchase

at the end of residency at full price rather than a nominal fee. This may have led to negative associations with the study, and may have resulted in the lower response rate of the secondary survey. The lack of qualitative data limited our ability to explain the quantitative results. No educational outcome data, eg, in-training assessment data, were linked with the current study to formally evaluate the effectiveness of the MTC use. Lastly, this study did not specifically address potential concerns of patient privacy or data security. While a *small majority* indicated that concerns of patient privacy did not hold them back from pursuing physician-to-physician or physician-to-patient activities with their device, this was not explored further. However, the devices were secured with a password, and access to the EHR was through a password-protected secure server.

Conclusion

Since this study was initiated, the use of MTCs in GME has grown significantly. The use of MTC has a significant impact on how residents approach medical education, clinical practice, and patient education. The survey tool can be useful in collecting data on MTC use by other graduate medical education programs. However, formal evaluations of the effectiveness in improving educational outcomes are still needed. A more thorough assessment (quantitative and qualitative) needs to be conducted to determine the long-term impact of iPad use in residency education/training. A follow up study could be conducted across all specialties to identify commonalities in experience versus specialty-specific issues. If needed, this could aid efforts to better tailor MTC use, especially with regard to learning how to optimally care for patients.

Conflict of Interest

None of the authors identify any conflicts of interest.

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Miller Fisher Syndrome: A Case Report Highlighting Heterogeneity of Clinical Features and Focused Differential Diagnosis

Ilya V. Yepishin DO; Randall Z. Allison MSIV; David A. Kaminskas MD; Natalia M. Zagorski MD; and Kore K. Liow MD

Abstract

Miller Fisher Syndrome (MFS) is a rare variant of Guillain-Barré Syndrome (GBS) that has a geographically variable incidence. It is largely a clinical diagnosis based on the cardinal clinical features of ataxia, areflexia, and ophthalmoplegia, however, other neurological signs and symptoms may also be present. Serological confirmation with the anti-GQ1b antibody is available and allows for greater diagnostic certainty in the face of confounding symptoms. A self-limiting course is typical of MFS. The following case report is that of a patient who presented with generalized weakness, somatic pain, inability to walk, and diplopia following an upper respiratory illness. The patient exhibited the classic triad of ataxia, areflexia, and ophthalmoplegia characteristic of MFS, but also had less typical signs and symptoms making for a more challenging diagnostic workup. Our suspected diagnosis of MFS was serologically confirmed with positive anti-GQ1b antibody titer and the patient was successfully treated with Intravenous immune globulin (IVIG).

Introduction

The triad of ataxia, areflexia, and ophthalmoplegia was first described by James Collier in 1932. It was subsequently reported as a variant of Guillain-Barré Syndrome (GBS) by Charles Miller Fisher in three clinical cases in 1956.¹ Fisher recognized both the uniqueness of this cluster of clinical signs and its relationship to what is now considered a heterogeneous group of immune-mediated neuropathies classified under Guillain-Barré Syndrome.¹⁻³ Aptly named, Miller Fisher Syndrome (MFS) is a geographically variable variant of GBS observed in about 1% - 5% of all GBS cases in Western countries, yet up to 19% and 25% in Taiwan and Japan, respectively.⁴ There is an established male predominance at a ratio of 2:1 and a mean age of onset of 43.6 years, although cases of MFS have been reported in all age ranges.^{2,5} As in GBS, an antecedent infectious illness can be identified in the majority of MFS cases. *Campylobacter jejuni* and *Haemophilus influenza* have been the most commonly implicated pathogens; however, multiple others are also associated, including *Mycoplasma pneumonia*, and *cytomegalovirus*. Upper respiratory infection is the most commonly described prodromic entity, followed by gastrointestinal illness.^{2,4}

Unlike the classic ascending weakness or paralysis that is characteristic of the more typical types of GBS, neurological deficits follow a top down pattern in MFS, starting with diplopia in the eyes; caused by external ophthalmoplegia—the most common presenting symptoms.^{4,5} In a clinical series of 50 consecutive cases of MFS in Japan it was discovered that 78% of cases presented initially with diplopia, 46% with ataxia, and 34% with both. Other abnormalities reported, albeit less frequently, were limb dysesthesia; blepharoptosis; face, bulbar,

and pupillary palsies; mild (grade 4) motor weakness; and micturition disturbance.⁴

An acute onset is typical of MFS, beginning with neurologic symptoms approximately 8-10 days (range of 1-30) following the antecedent illness.²⁻⁴ The disease then progresses until a clinical nadir is reached approximately 6 days (range of 2-21) after the initial neurologic symptoms.⁴ The recovery period is marked by gradual improvement and often resolution of symptoms; although rarely, serious complications such as respiratory failure or cardiac arrhythmia (that are common in GBS, with 30% of cases requiring ventilator support) have been reported.² Ataxia and ophthalmoplegia resolve within 1-3 months after onset and near complete recovery is expected within 6 months.⁴ Areflexia may persist, but is not associated with functional disability.

Although self-limiting disease course is expected, disease modifying treatment options for MFS are no different than for GBS and include intravenous immune globulin (IVIG) and plasmapheresis. Benefits of treatment are not as clear in MFS, but a rationale for treatment is to encourage faster resolution of symptoms and perhaps decreased likelihood of complications.⁶

Despite its rarity, MFS has played an important role in understanding the pathogenesis of immune-mediated neuropathies, which is thought to involve molecular mimicry incited by antecedent infection.⁶⁻⁸ Chiba, et al, first reported the presence of anti-GQ1b antibodies in strong association with MFS in 1992.⁹ This serological marker, present in well over 90% of afflicted patients, has become an important diagnostic tool in MFS and has been implicated in other variants of GBS that involve ocular muscles.^{7,8} The following case presents key clinical features of MFS and offers a discussion of focused differential diagnoses, anti-GQ1b antibody test, prognosis, and available treatments. Familiarity with this rare syndrome will clue the clinician to consider MFS in patients presenting with areflexia, ataxia, and ophthalmic symptoms.

Case Report

A 50-year-old part-Hawaiian man presented to the emergency department (ED) with a principal complaint of generalized weakness. An emergency medical response unit had been summoned to the patient's home; upon arrival he was found lying on the couch, weak, and unable to ambulate. Recent history revealed that he had been to the ED earlier that day and was able to ambulate with some difficulty at that time. He had also been to another ED twice in the preceding three days. During those

visits he had complained of myalgias, weakness, and malaise. Further history revealed that the patient had been feeling ill with a tactile fever, sore throat, cough, and a runny nose three days prior to the onset of the presenting symptoms. The patient had not received a current influenza vaccination; however, he tested negative for rapid influenza A and B. Therefore, based on clinical evaluations, he was diagnosed with a viral syndrome and treated with analgesics and intravenous fluids.

A neurological consultation was conducted in the ED. The patient's additional complaints included diplopia that had started three days prior followed by a discomforting stiffness in his back, numbness in his mouth, and loss of taste. He then developed weakness in his arms, followed by his legs, and generalized achiness with movement. By the time of the evaluation he had progressed to generalized weakness and an inability to walk.

The patient's past medical, surgical, and family histories were largely non-contributory. He was residing in a group home and was a recovering methamphetamine and marijuana user with last use being 2-3 years prior to presentation. He worked in a restaurant kitchen.

Upon physical examination his vital signs were in the normal range. The patient was observed to be in a moderate level of discomfort, preferring to keep his eyes closed and occasionally moaning. Despite this, he was fully alert and oriented with an intact memory and no loss of his ability to communicate other than a delay in and mild slurring of his speech. Neurological examination revealed marked ophthalmoplegia with severe abduction palsy, prominent nystagmus on lateral gaze, and bilateral ptosis. His facial muscles were symmetrical without evidence of seventh cranial nerve deficit. There was marked pronator drift with the patient's arms bowing up and down in a pendulous fashion. He displayed significant dysmetria on finger-to-nose and alternating movements testing; this was less pronounced on heel-to-shin testing. A global areflexia was present, and muscle strengths testing revealed fairly symmetrical mild weakness of all extremities, at the grade of 4 out of 5. His sensory examination was normal. The patient was not able to walk.

Laboratory testing revealed normal complete blood count, comprehensive metabolic panel, thyroid stimulating hormone, and cardiac markers. Urine toxicology screens (collected on two separate ED visits) were negative for common substances of abuse. There was no elevation in erythrocyte sedimentation rate, C-reactive protein, or creatine kinase; HIV and RPR serologies were negative. Of note, laboratory investigations for some of the more commonly implicated pathogens in MFS (*Campylobacter jejuni*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, or *cytomegalovirus*) were not undertaken. A lumbar puncture was performed and revealed cytoalbuminologic dissociation in the CSF with normal cell counts and a mildly elevated protein count of 61.2 mg/dL.

Imaging studies were obtained of the patient's chest and brain. The chest radiograph showed no evidence of acute or chronic disease processes. Contrast enhanced brain magnetic resonance

imaging did reveal an incidental ectopic posterior pituitary gland that sat overlaying the anterior pituitary gland. It also revealed mildly thickened mucosal tissue in the left maxillary sinus indicating sinus disease; otherwise, the study appeared normal without areas of contrast enhancement or parenchymal abnormalities.

The patient was admitted to the telemetry unit for additional evaluation and treatment. His condition continued to worsen during the initial days of his hospitalization with more pronounced ophthalmoplegia, persistent weakness, and somatic discomfort. On the second hospital day the patient developed urinary retention requiring straight catheterization; this was indicative of dysautonomia in the presenting clinical scenario. Treatments for the likely conditions were initiated promptly. Because of the ataxia, areflexia, and history (albeit remote) of substance abuse, there was a concern for Wernicke's encephalopathy, and the patient was started on intravenous thiamine (500mg every 8 hours). One would expect a rapid response to treatment in this case; however, this was not observed. The other two main competing diagnoses at this time were an atypical presentation of Myasthenia Gravis (MG) or MFS. Tests were ordered to look for antibodies that would support or refute each of these diagnoses; meanwhile, decisions to start further treatment trials were made based on the patient's worsening symptoms. Continuing with the thiamine infusions, the patient was additionally given a cholinesterase inhibitor, Pyridostigmine, orally (60mg every 8 hours) to treat for possible MG; however, after three doses the patient did not show any clinical improvement. Lacking the expected clinical response in a case of MG, the Pyridostigmine was discontinued. The patient was subsequently treated with intravenous immune globulin (IVIG) for five days to treat for possible MFS. Serum antibody test results eventually refuted MG as a diagnosis, but were positive for GQ1b IgG—confirming the diagnosis of MFS.

While treatment with IVIG was initiated early in the patient's hospital course, the initial worsening of his condition prompted further workup looking for paraneoplastic maladies that may occasionally be the presenting symptoms of advanced cancer. A panel of paraneoplastic antibodies was negative, and a computed tomography scan of visceral organs failed to show suspicious lesions. The nadir of the patient's symptoms was reached by the sixth hospital day. Physical, occupational, and speech therapy specialists were working daily with the patient and he began to exhibit steady improvement. He was able to ambulate with assistance by the eighth hospital day, and on the ninth day he was discharged from the acute hospital to an inpatient rehabilitation facility.

Outpatient follow-up one month from the hospitalization revealed that the patient was doing very well with a nearly 80% improvement in his symptoms. He was ambulating with a cane and reported resolution of somatic discomfort. His ocular symptoms, which were the first symptoms to come on, had been the slowest to resolve.

Discussion

Miller-Fisher syndrome is known for the characteristic triad of ophthalmoplegia, ataxia, and areflexia without overt sensory deficits. It is considered a variant of GBS, which is also known as acute idiopathic neuritis. An increasing body of evidence suggests that a rather wide range of neurological features may be present and significant overlap exists in MFS and other forms of GBS. MFS seems to more notably affect the peripheral nervous system, yet evidence of central elements has also been reported. It is interesting to note that our patient exhibited many of the atypical abnormalities through the course of illness. Although the defining features of ataxia, ophthalmoplegia, and areflexia are generally required for the diagnosis of MFS, other symptoms and signs may be present and confound a clinician's diagnostic decision making.

The GQ1b ganglioside complex is most often associated with MFS, positive in over 90% of patients with MFS and is not present in unaffected individuals.³ The GQ1b autoantibodies, which target the epitopes that are abundant on cranial nerves III, IV, and VI are thought to give rise to the characteristic ophthalmoplegia of MFS. This antibody, however, is not unique to MFS and has been characterized in other conditions resulting in what some experts have designated as an "anti-GQ1b antibody syndrome" known for both central and peripheral nervous system deficits. Though not intended to be used as a clinical diagnosis, this syndrome is useful for recognizing the symptom cluster and perhaps providing rationale for using established treatments for GBS in other conditions.⁸

Differential Diagnosis of Ophthalmoplegia, Ataxia, and Areflexia

Other disease processes are known to cause ophthalmoplegia, ataxia, and areflexia, though often not in concert. Ophthalmoplegia caused by MFS is often rapid in onset compared to a more gradual course in chronic diseases such as myotonic dystrophy, thyroid eye disease, and myasthenia gravis. More than 50% of patients with MG present with ptosis and/or diplopia. The weakness of the ocular muscles may switch from one eye to another and improve or worsen over the course of a day, unlike MFS which progressively worsens until the nadir of symptoms has been reached before any recovery is seen.^{10,11}

Ataxia can be seen in many conditions, often affecting the cerebellum, the spinocerebellar tracts, or the proprioception channels in peripheral nerves and dorsal columns. Cerebellar ischemia occurs due to compromise of the posterior circulation and often presents with non-specific symptoms of unsteady gait, dizziness, headache, eye movement dysfunction, as well as nausea and vomiting.¹² As other authors have pointed out, presentation of MFS can be confused with an ischemic event.^{13,14} Though both MFS and vascular compromise are acute events, ataxic patients with MFS typically lack lateralization of ataxia which helps to differentiate MFS from the majority of cerebellar lesions.¹² Toxins and medications also have the capability of inducing acute onset ataxia.¹⁵ Sodium channel modulators such

as phenytoin and chemotherapeutic agents such as fluorouracil can precipitate ataxic episodes. Arguably the most frequent cause of ataxia, alcohol consumption, mostly affects the lower extremities and is also associated with poor fine motor control of the hands, slurred speech, and impaired vision. The natural history of MFS is progression of weakness in a "head down" fashion, whereas the initial symptom would not be weakness and ataxia in the lower extremities. Often alcohol consumption can be determined though the patient's history or urine toxicology screen.

Areflexia is indicative of a lower motor neuron deficit, which would not be seen in many of the conditions affecting the central nervous system. Paradoxically, patients with spinal shock—seen in transection or compression of the spinal cord—are areflexic or hyporeflexic in the subacute stage of the disease, which then progresses to hyperreflexia as the pathology evolves. Peripheral neuropathy, seen most often in diabetics and malnourished individuals, can lead to areflexia in severe cases. Anterior horn cell destruction, seen in polio and amyotrophic lateral sclerosis (ALS), will leave patients areflexic as well. Like MFS, spinal shock is an acute condition, while ALS typically has a gradual onset. Temporary paralysis and areflexia similar to that of MFS and Guillain-Barre can also be due to poliovirus infection, with functional recovery occurring 4-6 weeks after paralysis.⁸

Our case describes a patient who presented with diplopia and ataxia following an upper respiratory illness. He also had confounding symptoms of myalgias, dysesthesias, weakness, and bulbar muscle dysfunction. On examination he was dysdiadochokinetic, dysmetric, and severely ataxic, with prominent ophthalmoplegia. Autonomic dysfunction was also expressed in the form of transient urinary retention. Our top differential for this clinical scenario included Wernicke's encephalopathy, MG, and Miller Fisher variant of GBS. A high protein count in his CSF and anti-GQ1b antibodies were consistent with MFS, as was the favorable response with five days of IVIG treatment and his gradual recovery to improved function.

Conclusion

Although uncommon, MFS is an important diagnosis to make since the presenting symptoms of ataxia and ophthalmoplegia may confuse the clinician and suggest an upper motor neuron sign or central cause. The presence of additional neurological symptoms may make clinical evaluation more challenging. A keen clinician with a meticulous neurologic examination will stumble upon the findings of areflexia thus localizing the predominant lesion to the peripheral nervous system. This should trigger an evaluation for demyelinating disorders and lead to confirmation of MFS as the diagnosis with the presence of GQ1b autoantibodies. MFS should be included in the differential diagnosis of anyone presenting with central findings of ataxia, areflexia, and ophthalmoplegia.

Conflict of Interest

None of the authors identify a conflict of interest.

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MEDICAL SCHOOL HOTLINE

Liaison Committee on Medical Education Accreditation, Part VII: Diversity/Pipeline Programs and Partnerships

Winona K. Lee MD

The Medical School Hotline is a monthly column from the John A. Burns School of Medicine and is edited by Satoru Izutsu PhD; HJMPH Contributing Editor. 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.

This article is part of an ongoing series describing various components of the John A. Burns School of Medicine (JABSOM) medical education curricula, activities, and initiatives relevant to the Liaison Committee on Medical Education (LCME) accreditation standards.¹ JABSOM's LCME visit will take place in early 2017. This article provides an overview of JABSOM's diversity/pipeline programs and partnerships.

Introduction

Physicians must be prepared to care for Hawai'i and the nation's communities, whose patient populations are rapidly rising in the United States. In Hawai'i, Native Hawaiian and other Pacific Islanders (NHOPIs) compose 26.2% of the total population, but account for only 3.7% of the total physician workforce.² Diversity in medicine is important as the literature has demonstrated that minority physicians are more likely, than white physicians, to care for minority, poor, uninsured, rural, and Medicaid patients as well as practice in underserved areas.^{3,4} With the physician workforce shortage faced by Hawai'i, it is critical to produce local physicians who will be committed to practice in rural and underserved communities throughout Hawai'i.

The University of Hawai'i at Manoa (UHM) John A. Burns School of Medicine (JABSOM) continues to demonstrate a commitment to promote diversity in medicine. It is based in the Department of Native Hawaiian Health. This is the only clinical department in a U.S. medical school focused on improving the health of indigenous populations, through its longstanding diversity pipeline programs such as the Native Hawaiian Center of Excellence and the 'Imi Ho'ola Post-Baccalaureate Program.⁵ The following are examples of how JABSOM continues to address the following LCME requirement related to diversity.

Diversity/Pipeline Programs and Partnerships (LCME Element 3.3)

"A medical school has effective policies and practices in place, and engages in ongoing, systematic, and focused recruitment and retention activities, to achieve mission-appropriate diversity outcomes among its students, faculty, senior administrative staff, and other relevant members of its academic community. These activities include the use of programs and/or partnerships

aimed at achieving diversity among qualified applicants for medical school admission and the evaluation of program and partnership outcomes."

In 2015, JABSOM created its first institutional diversity policy. A Diversity Task Force Committee composed of clinical department chairs, faculty, students, and representatives from JABSOM Admissions, Human Resources, Medical Education, Office of Student Affairs, and representatives from the UHM Office of Student Equity, Excellence, and Diversity met for a year to create this guiding document for diversity-related activities at JABSOM. The policy, was approved by the JABSOM Executive Committee and JABSOM General faculty, and is used to monitor and evaluate the effectiveness of JABSOM's pipeline programs and other initiatives that support school-defined diversity among its student body and faculty.

JABSOM's Institutional Diversity Statement⁶

"The John A. Burns School of Medicine (JABSOM) embraces diversity and inclusion as part of our shared Hawaiian, Asian and Pacific values. These shared values are responsive to our unique location in the center of the Pacific. We uphold that an environment of inclusiveness, equal opportunity and respect for the similarities and differences in our communities advances our mission of education, research and innovation, community service and clinical healing."

JABSOM is committed to preparing a culturally competent health and science workforce that meets the needs of Hawai'i. We strive to reflect the demographics of Hawai'i, including representation of Native Hawaiians and Pacific Islanders, individuals from rural areas of Hawai'i, first generation college students, and those from economically, socially, and educationally disadvantaged backgrounds. JABSOM is cultivating a transformative teaching and learning environment that promotes the recruitment and retention of students, faculty, and staff, who represent the diverse population of Hawai'i.

A Diversity Dashboard Working Group, composed of leaders of JABSOM's diversity programs, Admissions Office, and Human Resources Office, insures that the Institutional Diversity Policy is upheld and diversity outcomes are monitored. This working group submitted the first annual JABSOM Employee

and Student Diversity Report to the JABSOM Executive Committee in October 2015. Highlights from this report are described below.

JABSOM's Student Diversity and Pipeline Programs

'Imi Ho'ola Post-Baccalaureate Program

'Imi Ho'ola's (Hawaiian meaning "those who seek to heal") goal is to support diversity of the physician workforce and produce physicians who demonstrate a strong commitment to practice in underserved communities in Hawai'i and the Pacific. Since 1973, 'Imi Ho'ola has upheld its mission to improve health care in Hawai'i and the Pacific by increasing the number of physicians through an educational program that addresses disadvantaged students' academic and professional needs. Up to twelve students from economically, socially, and/or educationally disadvantaged backgrounds are enrolled in the post-baccalaureate program each year.

Student recruitment is conducted quarterly on O'ahu as well as on the neighbor islands, which target middle school, high school, and college students from underserved communities. The curriculum prepares students for the rigors of medical school, with a student-centered, team-based teaching approach. Emphasis is the integration of concepts in the sciences and humanities and further development of students' communication, critical thinking, and learning skills. Throughout the program the students' community-based perspectives of health, medical professionalism and leadership is emphasized. Upon successful completion of the program, students matriculate into JABSOM as first-year medical students.

The program's retention activities for graduates enrolled at JABSOM include a formal student peer mentoring network, remediation services by program faculty, and the assignment of faculty advisors for each student. These activities are available throughout the students' four years of medical school.

Long-term Outcomes:

Of the total Native Hawaiians that graduated from JABSOM from 1978-2015, 38% (n=89/233) accessed JABSOM through 'Imi Ho'ola.

A retrospective analysis utilizing the program's centralized student database of program alumni (N=146) who matriculated

and/or graduated from JABSOM was conducted with the following outcomes:

- Majority of students originate from Hawai'i or the Pacific Basin (99.3%)
- 58.2% are females and 41.8% are males
- Of the 146 graduates, 32.2% were Native Hawaiian, 26.7% Filipino, and 24.0% are Asian
- 78.9% of students originate from rural communities
- 28.1% self-reported English as their second language

Native Hawaiian Center of Excellence (NHCOE)

The Native Hawaiian Center of Excellence seeks to improve the health of Native Hawaiians through education, research, and community partnership. NHCOE empowers Native Hawaiian students and faculty to succeed in medicine and other health professions.

NHCOE recruitment activities include the following: (1) health careers presentations and health fairs conducted statewide for K-12 and college students; (2) Native Hawaiian Pathways to Medicine Program, a workshop series for aspiring Native Hawaiian pre-medical students, created to improve the competitiveness for medical school admission utilizing cultural empowerment, mentorship, and social support networks; (3) Native Hawaiian Interdisciplinary Health Program, seminars that bring together Native Hawaiian pre-medical and Social Work students to learn about multi-disciplinary teamwork, inquiry-based learning, and importance of culture competency in caring for future patients/clients; (4) Nanakuli Pathways to Health, a program created to "grow our own healers" by partnering with a public middle and high school where 70% of students are Native Hawaiian, having medical students mentor these students.

NHCOE retention activities for Native Hawaiian students include the following: (1) preparing for Step 1 and 2 United States Medical Licensing Exam preparation support, (2) funding to support student health disparities research projects and presentations at national conferences, (3) advising and mentoring services for Native Hawaiian medical students, (4) functioning as lead unit for all cultural competency training for medical students at JABSOM.

Outcomes 2009-2015:

- Over 4,500 K-12 and college students exposed to the health professions
- 96 JABSOM students and graduates participated in the NHCOE pipeline
- 84 Native Hawaiians trained through the Pathway to Medicine Program and the Native Hawaiian Interdisciplinary Health Program
- Of the 84 Native Hawaiians students who participated in the NHCOE pipeline programs, 26% were successfully accepted to US medical schools to date, which include JABSOM, Cornell, Dartmouth, UC Davis, and UC San Diego
- 100% of JABSOM 1st and 2nd year medical students participated in cultural competency training

Ethnicity	Percentage of graduates that accessed JABSOM through the 'Imi Ho'ola Post-Baccalaureate Program (1978-2015)
Hawaiian	89/233 (38%)
Filipino	60/185 (32%)
Chamorro	19/34 (56%)
Samoan	14/17 (82%)
Micronesian	11/20 (55%)

'Imi Ho'ola Graduates = 242, JABSOM Graduates = 2,245 (1978 - 2015)

Area Health Education Center (AHEC)

The mission of the Hawai'i/Pacific Basin Area Health Education Center (AHEC) is to improve the health of the underserved through education. Areas of concentration include 4 areas of education: (1) educating and recruiting students to health professions (K-12), (2) educating health professions students in rural and underserved communities of Hawai'i, (3) recruiting health care professionals to rural communities and continuing medical education for health care providers, (4) providing community-based education for underserved communities.

Recruitment activities include the Health Professionals Speaker's Bureau, support for the Pre-Health Career Corps Program, Medical Student Mentorship Program, Teen Health Camp, Teen Mentorship Academy, and Pre-Health Advising Center.

Outcomes 2014-2015:

- Health careers recruitment activities for 3,433 students
- Inter-professional training for 300 students per year in Hawai'i and Pacific
- 8,000 hours of CME for over 2,000 providers
- Annual Health Workforce Summit
- State Loan Repayment Program
- Physician Workforce Assessment for State of Hawai'i

Health Careers Opportunity Program (HCOP)

The University of Hawai'i Health Careers Opportunity Program (HCOP) strives to build diversity in the health work force by providing students from socially, educationally, or economically disadvantaged backgrounds an opportunity to develop the skills needed to successfully enter and graduate from health professions schools. Established using federal funding in 2001, HCOP was institutionalized utilizing state funds at the University of Hawai'i in 2008. Recruitment activities include a summer residential academic and health enrichment program, college campus visits for high school and college students interested in the health professions, and health career exploration presentations and activities. Recently HCOP established a formal partnership with the Philippine Medical Association of Hawaii (PMAH) to expand mentoring efforts for students interested in health professions.

Outcomes 2001-2014:

- A total of 414 high school & college students participated in residential summer programs
- Participant Gender: 84.5% (n=350) females, 15% (n=62) males, 0.5% (n=2) unknown
- Participant Ethnicity: 25.5% Native Hawaiian, 48.3% Filipino, 3.1% Samoan, 2.9% Other Pacific Islander
- Conducted 900 hands-on health career exploration activities
- Completed 3,000 on-campus visits for students interested in attending the University of Hawai'i Manoa and Kapi'olani Community College

JABSOM's Faculty Diversity

JABSOM is committed to diversity of both its students and faculty. Prior to faculty recruitment, every department identifies underrepresented groups and promotes faculty diversity that reflects the diversity of Hawai'i. Each department works with JABSOM's Human Resources Office to implement an EO/AA compliant process during active recruitment. JABSOM's Human Resources Office also assists departments by identifying potential additional venues for reaching underrepresented candidates. Retention of underrepresented faculty is strengthened through active community engagement of the faculty with multiple ethnic and cultural groups in the community. Faculty diversity, including department chairs and other administrative roles, reflect a rich mix of ethnicity, gender, life experiences and seniority. For example, JABSOM faculty is comprised of 10% Native Hawaiian/Pacific Islander, 3% Black/African American, 3% Hispanic, 24% Japanese-American, and 7% South Asian/Asian Indian. A majority (9 of 15) of the clinical and basic science department chairs/directors is of ethnic backgrounds.

Conclusion

JABSOM has been successful in achieving its desired diversity goals. As a result, diversity is one of the institution's major strengths. With an approved institutional diversity policy with clear definitions and methods to track and monitor diversity outcomes, JABSOM has demonstrated commitment to the necessary resources and developed the expertise needed to support and expand recruitment and retention initiatives that ensure student and faculty diversity.

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Community Involvement in Developing a Human Papillomavirus (HPV) Vaccine Brochure Made for Parents in Hawai'i

May Rose I. Dela Cruz DrPH; Jo Ann U. Tsark MPH; Reni Soon MD, MPH; Cheryl L. Albright PhD, MPH; and Kathryn L. Braun DrPH

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 Ranjani R. Starr MPH and Lance K. Ching PhD, MPH from the Hawai'i Department of Health.

Introduction

The human papillomavirus (HPV) vaccine reduces HPV-associated diseases such as cervical cancer, vulvar cancer, anal cancer, and genital warts. Three doses over 6 months are recommended for adolescents at age 11 or 12 before they become sexually active.¹ Since HPV causes 70% of cervical cancers, compliance with HPV vaccination would especially benefit Native Hawaiian and Filipino populations who have low cancer screening prevalence and the highest incidence and mortality rates of cervical cancer.²⁻⁵

Unfortunately, HPV vaccination rates are extremely low. In 2014, completion of all three doses of the HPV vaccine for 13 to 17 year olds was estimated at only 40% for girls and 22% for boys nationally, and at only 38% for girls and 31% for boys in Hawai'i.⁶ HPV vaccine intervention studies have found that parent and physician education are needed to increase uptake.⁷⁻⁹ To be successful, parent education materials need to address known barriers to vaccine uptake, including cultural barriers.¹⁰⁻¹¹

In Hawai'i's 2016 legislative session, Senate Bill 2316 was introduced to require boys and girls to be vaccinated with at least one dose of the HPV vaccine by the time they started 7th grade. There was much support for this bill from members of the medical field, but other individuals gave testimony in opposition to the bill. Many opponents demonstrated in their testimony that they did not understand the vaccine, for example expressing fear of the vaccine as a cause of autism. Nevertheless, this bill, along with its companion bill (HB 1910) and other HPV vaccine related bills (SB 394 and HB 458), did not pass. For legislation to pass, it was clear that the general public needed better access to accurate information on the HPV vaccine.

A locally produced health education brochure could aid in increasing low vaccination rates and in increasing accurate HPV vaccination knowledge. Since there was no current Hawai'i brochure for the HPV vaccine, the overall project goal was to develop a local HPV vaccine brochure and test it locally for attractiveness, readability, and comprehension. The methods

of brochure creation followed the recommendations of Kulu-kulualani, et al (2008), of a four-step protocol to create cancer education brochures.¹² The four steps are: (1) draft brochures using information from literature reviews and interviews, (2) ensure health information specialist and physician review and seek preliminary endorsement, (3) test the brochures with the community, and (4) receive endorsement and final review from physicians and community members.

The brochure was initially developed based on interviews with 20 parents of 11 to 18 year old children who were Native Hawaiian (n=5), Filipino (n=4), Japanese (n=5), and Caucasian (n=6).¹³ In response to knowledge, attitudes, and preferences heard from these parents, the brochure featured bulleted points, pictures of children that reflected local faces, testimonials, vivid colors, and an immunization chart. Health educators and nine physicians also reviewed the brochure. This publication highlights Step 3 of the four-step process of brochure development—testing the brochure with a different Hawai'i sample that was representative of the audience for whom the brochure was developed.

Many of Hawai'i's cancer prevention and education materials have been developed, pretested, and distributed by 'Imi Hale Native Hawaiian Cancer Network ('Imi Hale), a program of Papa Ola Lokahi, which is a community-based, non-governmental entity that oversees the Native Hawaiian Health Care Improvement Act, Hawaiian health policy and health care. 'Imi Hale's work is guided by principles of community-based participatory research (CBPR).¹⁴ Health information, including the HPV vaccine benefits, can be disseminated effectively by including target populations in the development of the educational materials process.⁹ The most effective cancer prevention outreach efforts involve community-based partners who have provided feedback on a material's style, content, and delivery routes.¹⁵⁻¹⁶ 'Imi Hale has developed and tested more than 80 culturally appropriate educational items designed to improve cancer-related knowledge, attitudes, and behaviors in Hawai'i.¹²

Methods

Participants were eligible if they were the parents of an 11 to 18 year old child in Hawai‘i, and usually the person responsible for taking the child to get vaccinated. The parents were recruited through several venues. Some had participated in a random-digit-dial survey on the HPV vaccine conducted by the authors.¹⁷ Others were recruited through local parent groups and by referrals from participating parents. A total of 52 parents provided feedback on the brochure.

Participants were mailed a mock-up of the HPV vaccine brochure and a material feedback survey. The latter included questions on the brochure’s attractiveness, acceptability, messenger effectiveness (testimonies), personal relevancy, readability, suggestions for improvement, parent demographics, and child vaccination status. Data about the brochure’s attractiveness, acceptability, and comprehension were coded by theme and used to iteratively revise the brochure. All 52 parents answered “yes”

or “no” on each measure and were given additional space to comment. Additional questions asked parents to confirm comprehension, new words they have encountered, and suggestions for improvements for the brochure.

A \$20 gift card was provided to participants. This study was approved by the Western Institutional Review Board.

Results

Demographic data are provided in Table 1. Of the 52 parents, 90% were mothers; 31% were Japanese, 31% were Caucasian, 27% were Native Hawaiian, and 12% were Filipino. Most of the parents were married (79%) and were college graduates (70%). The majority of parents had vaccinated their children against HPV (69%).

Material Feedback from All Parents


Table 2 shows the material feedback by parents from the draft brochure. The final brochure is included as Figure 1.

	Parents with HPV vaccinated child(ren) n=36	Parents with HPV unvaccinated child(ren) n=16	Total N=52
Gender			
Female	32 (88.9)	15 (93.8)	47 (90.4)
Male	4 (11.1)	1 (6.3)	5 (9.6)
Ethnicity			
Native Hawaiian	10 (27.8)	3 (19.9)	14 (26.9)
Filipino	3 (8.3)	3 (18.8)	6 (11.5)
Japanese	12 (33.3)	4 (25.0)	16 (30.8)
Caucasian	11 (30.6)	5 (37.5)	16 (30.8)
Relationship Status			
Married	28 (77.8)	13 (81.3)	41 (78.8)
Single	8 (24.2)	3 (18.8)	11 (21.2)
Educational Attainment			
High School Graduate	3 (8.3)	1 (6.3)	4 (7.7)
Some College	8 (22.2)	4 (25.0)	12 (23.1)
College Graduate or More	25 (69.4)	11 (68.8)	36 (69.2)

Measure	Yes (n, %)	No (n,%)
Attractiveness		
If I saw this in a doctor's office, I would pick it up.	44 (84.6)	8 (15.4)
The messages, visuals, colors and voices are appealing to me.	50 (96.2)	2 (3.8)
The people shown look like someone I know.	50 (96.2)	2 (3.8)
Acceptability		
I feel comfortable sharing this brochure with another parent.	52 (100.0)	
I think other parents of adolescents would benefit from this brochure.	52 (100.0)	
Messenger Effectiveness/Testimonies		
I found the quote from the doctor to be helpful.	51 (98.1)	1 (1.9)
I found the quote from the mother something I can relate to.	50 (96.2)	2 (3.8)
Personal Relevancy		
The messages and pictures are meaningful to me as a parent.	50 (96.2)	2 (3.8)
Readability		
I found this brochure easy to read.	52 (100.0)	
Were there words new to you?	4 (7.7)	48 (92.3)

A

The HPV vaccine will protect your daughters and sons from some cancers



B

What is HPV?

Human Papilloma Virus

- HPV is a virus. Some types of this virus cause cancer and infections, like genital warts in males and females.
- A person can have the virus and show no symptoms. If a person has the virus, he/she can pass it on to someone else.
- There is no cure for the virus. But there are two vaccines that can prevent most of the cancers and infections that it causes.

What cancers and infections can this virus cause?


This virus can cause:

- Cervical cancer
- Cancer of the anus and penis
- Cancers of the mouth and throat
- Other genital cancers
- Genital warts

The HPV vaccine can prevent most of the cancers and infections that this virus causes.

“We vaccinated our kids from birth to protect them from polio, measles, whooping cough and other illnesses. Why not also protect them from cancers they might get from this virus in the future? It was an easy decision.”

—May with Kevin and Leiki (Kalen, Ashley, Taylor) Wahiawa, O’ahu



A: front cover

B and C: inside panel

C The vaccine is most effective when given at ages 11 to 12 years.

Common questions parents have about the HPV vaccine

Protect your child by getting them the recommended shots.

Recommended immunizations for your child & when to get them.

CHILD'S AGE	SHOT
11-12 Years	HPV (Human Papillomavirus), Tdap (Tetanus, diphtheria & pertussis), MCV (Meningococcal disease)
4-6 Years (before starting school)	MMR (Measles, Mumps and Rubella), Tdap, IPV (Polio), Varicella (Chicken Pox)
15-18 Months	Tdap
12-23 Months	Hep A (Hepatitis A), with 2 doses needed 6-18 months apart
12-15 Months	Hib (Haemophilus influenzae type b), MMR, PCV (Pneumococcal disease), Varicella
6 Mos. - 18 Yrs (yearly)	Influenza
6-18 Months	Hep B (Hepatitis B), IPV
6 Months	Tdap, Hib (if needed), PCV, RV (if needed)
4 Months	Tdap, IPV, Hib, PCV, RV
2 Months	Tdap, IPV, Hib, PCV, RV
1-2 Months	Hep B
Birth	Hep B

If your child has missed shots or you have questions or concerns, follow up with your child's doctor.

Is the HPV vaccine safe?

Yes. It is monitored by the Centers for Disease and Control (CDC) and the Food and Drug Administration (FDA). More than 57 million doses have been given out, and there have been no serious safety concerns.

Yes. Doctors have given the HPV vaccine safely with other recommended vaccines for Tdap, meningococcal, and influenza.

Are there side effects?

- Side effects are rare and are usually mild. Common side effects include soreness where the shot was given (usually in the arm), fever, dizziness, and nausea.
- Be sure to read the Vaccine Information Statement given by your child's doctor and discuss all risks with the doctor.

What if the doctor did not bring it up?

- If your child's doctor has not mentioned it, you should ask about the HPV vaccine.
- Let your child's doctor know that you heard about the HPV vaccine. Ask if it is something your child should get.

Since HPV can be passed on during sexual activity, why does my child need the vaccine when he/she is not having sex yet?

Getting the vaccine early, at ages 11 or 12, before sexual activity begins, protects your child in the future. The vaccine can prevent 70% of cervical cancers and 90% of genital warts.

Why does my son need the HPV vaccine?


Boys are recommended to receive the Gardasil® vaccine for protection from genital warts and other cancers caused by HPV (anal, penile, and oral cancers).

How much does it cost?

- Most health insurance plans in Hawai'i cover the cost of the vaccine series of 3 shots.
- Programs like Vaccines for Children (VFC) can provide the vaccine free or at low cost.

“Surviving cervical cancer was a tough journey. I would not want another girl to go through that. Parents, be sure to vaccinate your daughters and sons. It could save their lives!”

—Beth
Cervical cancer survivor, Kailua, Hawai'i



Doctors and experts recommend the vaccine for girls and boys, ages 11 & 12 years before sexual activity begins and HPV infection can occur.

If your daughter or son has not yet been vaccinated, it is not too late!

- Also recommended for:
 - Girls ages 13-26
 - Boys ages 13-21
- Some doctors may recommend the vaccine as early as age 9 years old.

Ask your child's doctor about the HPV vaccine.

- There are two HPV vaccines now available, Gardasil® and Cervarix®.
- Both vaccines are given as a series of 3 shots in a 6 month period.
- This vaccine is on the recommended list for Hawai'i schools.

“The HPV vaccine is better than a cure for cancer. It prevents cancer! As an OB-GYN doctor and a parent myself, I strongly recommend the vaccine.”

—Dr. Rani Soori, MD, MPH
Obstetrician-Gynecologist and parent
Honolulu, Hawai'i




Figure 1. HPV vaccine brochure created for parents in Hawai'i

Attractiveness

The majority of parents (85%) answered “yes” when asked if they would pick up the brochure if they saw it at the doctor’s office. The remaining 15% stated that they would not because they already knew about the vaccine or felt that the brochure was not meant for them. A Caucasian mother who did not vaccinate her daughter answered “no,” and commented: “The kids (pictured in the brochure) are younger than my kid and all are non-Caucasians, which makes me think I’m not the audience.” Over 96% of the parents agreed that the messages, visuals, colors, and voices of the brochure were appealing to them. Nine parents commented that the colors were “vibrant,” and the green and blue colors were nice.

Acceptability

All 52 parents were comfortable sharing the brochure with another parent and believed that other parents of adolescents would benefit from this brochure. Six parents noted that the brochure was “easy to read,” and three commented that doctors should give it to parents. A parent of a vaccinated daughter noted that when talking with another parent, “if the subject of vaccinations came up I would not have problem/concerns sharing this brochure.”

Messenger effectiveness/testimonies

The quote from an obstetrician-gynecologist (Ob-Gyn) stated, “The HPV vaccine is better than a cure for cancer. It prevents cancer! As an Ob-Gyn doctor and a parent, myself, I strongly recommend the vaccine.” The majority of parents (98%) found the quote from the doctor to be helpful. A father of an unvaccinated daughter commented that the doctor’s quote “added authority.”

Most parents felt they could relate to the mother in the brochure (96%). Her quote stated, “We vaccinated our kids from birth to protect them from polio, measles, whooping cough and other illnesses. Why not also protect them from cancers they might get from this virus in the future? It was an easy decision.” A mother of vaccinated daughters answered positively to the testimony: “(It) reminds parents of other vaccines our children got, so why not this one?” Another parent with a vaccinated daughter found the testimony impractical: “It ignores the outreach to boys and doesn’t add any more information – it is simply an emotional appeal.” However, six parents commented that they found the mother’s testimony helpful and also “relatable” and “heartfelt.”

Personal relevancy

The messages and pictures were meaningful to 50 parents (96%). When asked if the people shown in the brochure looked like the people they know, 96% of parents agreed and 2 parents disagreed. Five parents specifically commented that the people in the brochure looked “local” (ie, from Hawai‘i).

A mother of a vaccinated son commented, “Kids (pictured in the brochure) are multi-ethnic and look like my kids – messages are very straightforward.” Two mothers with unvaccinated children commented how the brochure affected their intent to

vaccinate their children. One mother of an unvaccinated daughter stated, “It speaks to why I should do this and where I can get more info.” A mother of unvaccinated children commented: “It made me more aware about getting my boys also vaccinated.”

Readability

The Fry Readability Test found the readability of this brochure high at 11th grade level. Readability was checked using the Fry Readability Test that calculated the grade reading level of the brochure.¹⁸ All parents found it easy to read, regardless of many multi-syllable words such as “vaccination,” “papillomavirus,” “immunization,” etc. Four parents identified words that were new to them, which were the names of the vaccine (Gardasil© and Cervarix©) and the word “papilloma.”

Comprehension

In the field test phase, parents were asked: “What is this brochure about?” The most frequent answer to this question was that it was about the HPV vaccine and how it can prevent cancer (44%). Twenty (38%) of the 52 parents also indicated that the vaccine protected “children,” and “boys and girls.” There were a variety of answers that included, “the importance of the HPV vaccine,” “the prevention of disease,” and “information about HPV.”

Other Feedback

Participants offered various comments on additional aspects of the brochure. The immunization chart featured on its own panel was helpful to 11 parents who specifically commented on it. A parent of an unvaccinated daughter mentioned that the chart “was helpful in showing this vaccine as being a ‘normal’ childhood vaccine.” Two mothers of vaccinated daughters commented that the availability of a HPV vaccine brochure would have aided them in deciding to vaccinate their children sooner. One mother stated: “The brochure was a good source of information. I do not recall my doctor telling me about ‘cancer,’ mostly...genital warts. Had I been provided a brochure such as this I would have been quicker to say, ‘Yes,’ and have them vaccinated. The brochure is well done as is (and) should be provided at every doctor’s office and available online.” Another mother explained how a brochure and education of the HPV vaccine is important: “The brochure is brief, easy reading. (It’s) informative without being too overwhelming. (I) wish (the vaccine) was around when my oldest was young. She has genital warts and now has cervical cancer.”

Discussion

Community participation was critical for modifying the HPV brochure for local relevance. This aspect was integral to the study because the final HPV brochure product will be housed and utilized by providers in clinics as a tool for parents. Incorporating messages and the target audience in the brochure’s developmental process is important to increase acceptability and utilization by the target audience.

‘Imi Hale’s protocol has been useful in assessing the HPV vaccine brochure’s attractiveness, acceptability, messenger

effectiveness, personal relevancy, and readability. Nearly all (over 90%) of parents answered “yes” in all the major categories of consumer testing in appearance, comprehension, and utilization. Parents found the brochure easy to read, informative, appropriate and useful. In addition, parents were impacted by the testimonies. Overall, they reported that the brochure increased their knowledge of the vaccine and their intent to vaccinate their child.

A key component of evaluating the utility of a brochure is to assess the target audience’s comprehension of the brochure. Specific information was highlighted, such as the benefits of the vaccine for cancer prevention and the rationale for targeting boys and girls ages 11 to 18 years old. Twenty-three parents (44%) wrote how the HPV vaccine prevented cancer when asked, “What is this brochure about?” and twenty knew that it protected boys and girls, which were both vital take-home messages of the brochure. Previous studies verified that there is a lack of parental knowledge that the HPV vaccine is also for boys 11 to 12 years old.¹⁹⁻²¹

This study was limited by the small sample sizes recruited to evaluate HPV vaccination uptake, self-reported vaccination status, and short material feedback duration and reach. All vaccination uptake results were reported by the parent and not verified with health care providers. This brochure was mainly designed for Native Hawaiian and Filipino parents, yet there were very few (6) Filipino respondents. This posed another limitation to this study. However, respondents of all racial groups found the brochure appealing.

Although the brochure development and vetting process conducted by ‘Imi Hale normally includes a survey of at least 250 people, study constraints limited such an extensive feedback process. However, many parents had overlapping comments and suggestions to the improvement of the brochure, and a saturation of themes was reached.

In conclusion, this study fulfilled a need for a local HPV vaccine brochure for parents in Hawai‘i. Parents reported that it increased their knowledge about the HPV vaccine and that they would share the brochure with their provider and with other parents. All feedback was taken into consideration in the final product of the brochure and used to improve its content. After receiving endorsement from community members, 40,000 brochures were printed for clinics, community health centers, the Native Hawaiian Health Care Systems, and other health offices in the state of Hawai‘i. Two large posters were also created for clinics and health offices to enhance provider and parent discussions about the HPV vaccine.

The creation of this local brochure was timely. Because of the measles outbreak in Hawai‘i and across the nation in 2015, there is a resurgence of attention to educating the public on the importance of vaccines. It is essential to connect the message of prevention with any vaccination information. If health education materials on vaccines are more accessible and promoted in our communities, misinformation could be dispelled. It is our hope that these health materials will help increase HPV vaccination uptake in Hawai‘i.

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THE DANIEL K. INOUYE COLLEGE OF PHARMACY SCRIPTS

The Development of Antimicrobial Stewardship Programs in Hawai'i

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Abstract

In recent years the misuse of antimicrobials has contributed to the growing problem of antimicrobial resistance. Antimicrobial Stewardship Programs (ASP) decrease the misuse of antimicrobials by supporting a rational, systematic approach. ASP strategies vary from broad-ranging policies and other decision support tools to prospective audit review of patients on antimicrobials. Many healthcare facilities, however, have been slow to adopt stewardship attributable to the fact that early ASP models required individuals with specialized training, and a significant amount of time and infrastructural investment from facilities. In response to the increasing need for ASPs in Hawai'i, the Hawai'i Department of Health (HDOH) partnered with the Daniel K. Inouye College of Pharmacy (DKICP) to develop the Hawai'i Antimicrobial Stewardship Collaborative (HASC), a voluntary collaboration whose main objective is to assist hospital institutions in the implementation of a simplified model of the Centers for Disease Control and Prevention's Core Elements of Hospital Antimicrobial Stewardship Programs. The work of HASC places Hawai'i's health care institutions in an advantageous position to be able to comply with impending accreditation standards relating to antibiotics and infections.

Introduction

In recent years the misuse of antimicrobials has contributed to the growing problem of antimicrobial resistance.¹ It is estimated that as much as 50% of all antimicrobial use is inappropriate leading to subsequent antimicrobial resistance.² In particular, pathogens including extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBLs), carbapenem resistant *Enterobacteriaceae* (CRE), *Pseudomonas aeruginosa*, vancomycin-resistant *Enterococci*, and methicillin-resistant *Staphylococcus aureus* have become a challenge to manage with limited therapeutic options available.³ This problem impacts patient morbidity, mortality, and increases complications such as *Clostridium difficile* associated diseases as well as increased health care costs.² Antibiotic resistance is recognized as a top priority for the federal government, prompting President Obama to create Executive Order 13676 in September 2014 that launched federal efforts to combat the rise in antibiotic resistant bacteria.⁴

Inappropriate use of antibiotics often includes:

1. Use of antibiotics for non-infectious conditions
2. Unnecessary initiation or continued use of broad spectrum antibiotics

3. Inappropriate or suboptimal dosing
4. Inappropriate duration of therapy

Antimicrobial Stewardship Programs (ASP) support a rational, systematic approach for the use of antimicrobial agents to achieve optimal patient outcomes. Multiple examples in the literature demonstrate that ASP programs can improve patient outcomes and be financially self-supporting.² Studies show that ASP programs will decrease antimicrobial usage, leading to a decline in associated drug acquisition costs by 22%-36% in both large and small healthcare institutions.⁵ Many healthcare facilities, however, have been slow to adopt stewardship attributable because early ASP models required individuals with specialized training and a significant amount of time and infrastructural investment for facilities. For example, the 2007 Infectious Disease Society of America guidelines² stated that an ASP should include an infectious disease physician and a clinical pharmacist with infectious disease training in order to perform the following activities:

1. Prospective audit of antimicrobial use with intervention and feedback to prescribers
2. Formulary restriction and preauthorization requirements for specific antimicrobial agents
3. Staff education pertaining to antimicrobial use
4. Development of guidelines and clinical pathways
5. Scheduled antimicrobial cycling
6. Automatic stop orders or "time outs"
7. Streamlining or de-escalation of therapy
8. Dose optimization
9. Conversion from parenteral intravenous therapy to oral dosage forms
10. Development of computer surveillance and decision support

Although individually, some, or all of these activities might be achievable by facilities, such requirements in the context of competing priorities and limited resources pose a barrier to incorporating stewardship.

In November of 2013, the Hawai'i State Department of Health (HDOH) conducted a survey regarding the establishment of ASP's in acute care institutions across the state. Of the 21 respondents, 12 (57%) reported that the most commonly reported barriers were staffing constraints or that the development of an ASP had not been identified as a priority.

Shortly thereafter, the CDC published a *Vital Signs* report highlighting the need for improved antibiotic stewardship among hospitalized patients.⁶ Additionally, the President's Council of Advisors of Science and Technology (PCAST) published their report on Combating Antibiotic Resistance that emphasized the need for ASP's in healthcare.⁷

Development of the Hawai'i Antimicrobial Stewardship Collaborative (HASC)

In response to the increasing need for ASPs in Hawai'i, the HDOH partnered with the Daniel K. Inouye College of Pharmacy (DKICP) to develop a voluntary collaboration with multiple Hawai'i healthcare facilities to form the Hawai'i Antimicrobial Stewardship Collaborative (HASC). HASC's main objective was to assist hospital institutions in implementing a simplified model of the CDC Core Elements of Hospital Antimicrobial Stewardship Programs.⁸ The seven core components include:

1. Leadership Commitment
2. Accountability
3. Drug Expertise
4. Action
5. Tracking
6. Reporting
7. Education

HASC's primary end goal was that each individual institution be able to sustain a self-sufficient ASP program utilizing various decision support tool-kits that encourage antimicrobial best practices. Figure 1 depicts the 12 original HASC facilities that began in October 2014. By October 2015, two additional facilities joined HASC. All of the 14 HASC participating facilities have committed to selecting and implementing antimicrobial stewardship strategies that best fit the staffing constraints and practice environments of their individual institutions. Each facility obtained administrative support and identified a program lead, most frequently a pharmacist or physician. HDOH and faculty from DKICP provide webinars, facility specific technical assistance, and collaborative support forums as each ASP program is implemented.

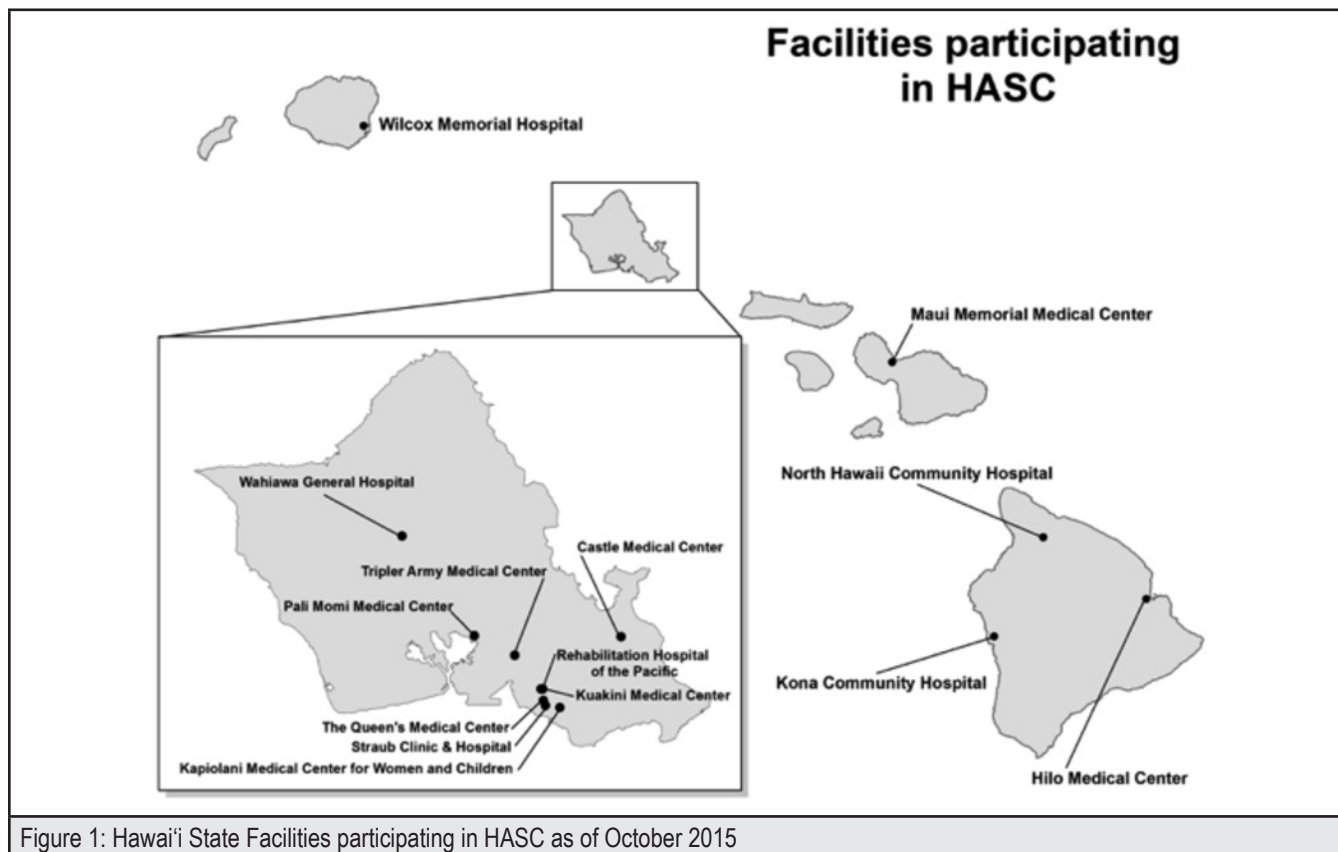


Figure 1: Hawai'i State Facilities participating in HASC as of October 2015

ASP Strategies and Development of Decision Support Tools

ASP strategies vary from broad-ranging policies and other decision support tools to prospective audit review of patients on antimicrobials. The development of decision support tools such as protocols, formulary restrictions or order sets may help to decrease a labor-intensive strategy on a day-to-day basis. These types of strategies have fared well in the smaller sized institutions.

A commonly implemented protocol is the conversion of an intravenous (IV) formulation to the usually lower costing but equally effective oral (PO) dosage form. For instance, IV fluoroquinolones, a class of drugs that have a high oral bioavailability, would be automatically substituted to the PO dosage form based on pre-defined criteria agreed upon by the medical staff and the ASP team. Formulary restriction of selected classes of antibiotics after meeting specific criteria represents another strategy as described in Table 1. Development of order sets supports the appropriate use of empiric antibiotics by offering a finite list of combinations from which providers may choose for treating particular infections.

Some institutions have taken a multi-faceted approach targeting several concurrent initiatives. For example, at Castle Medical Center (Kailua, O'ahu) pharmacists utilize the electronic medical record (EMR) system to print a daily report of all patients on antibiotics and a list of all patients with positive culture results. The pharmacist reviews each patient's chart to ensure the appropriate antibiotic selection and dosing based on the type of infection and patient specific factors. This comprehensive review leads to pharmacist driven changes that may include bug-drug mismatches, IV to PO conversion, renal- and indication-based dosing adjustments, narrowing antibiotic spectrum as well as encouraging an ID consult when broad-spectrum antibiotics are ordered. All pharmacist recommendations are documented in an electronic database that will be used to evaluate the success of each type of ASP activity.

Prospective Review

Although the multi-faceted approach described in the above example is both effective and successful, not all institutions have the ability to perform such a comprehensive review due to limited manpower and workflow challenges. A more streamlined strategy is the prospective review of antibiotic usage in a targeted subset of patients. This strategy utilizes predetermined ASP criteria to identify patients at risk for antibiotic misuse (eg, patients on multiple IV antibiotics, antibiotics with narrow

Antimicrobial Agent	Recommend alternative agent(s) if patient does not meet at least one of the following criteria
Carbapenems	<ul style="list-style-type: none"> • Infectious Disease (ID) Consult • Documented treatment failure with Piperacillin/Tazobactam • Documented suspicion for Extended Spectrum Beta Lactamase (ESBL producing organism)

therapeutic ranges, broad-spectrum antibiotics, antibiotics easily converted from IV to PO, or those on antibiotics for an extended period of time; the pharmacist and ASP team then review the medical record for selected patients to identify opportunities to improve antimicrobial utilization. Facilities that have limited manpower may make use of student pharmacists who are readily available through partnerships with the DKICP. This strategy was implemented at a small rural Hawai'i community hospital. Table 2 lists the criteria that were developed to help identify patients included for prospective review. Student pharmacists were tasked with obtaining data for patients who met the predefined criteria. Issues requiring immediate attention were presented to the overseeing pharmacist and addressed promptly. Less emergent issues and recommendations were presented and discussed during daily patient care rounds and the ASP team as well as the attending physician agreed upon decisions.

Through this type of prospective review, the ASP model can improve antimicrobial prescribing practices, provide opportunities to educate providers, and strengthen the relationships between prescribers and the ASP team. Institutions that opt for this strategy can also collect data regarding the type of recommendations provided and assess trends to identify areas for process improvement or development of new policies and procedures. Recommendations can generally be grouped into 15 categories (Table 3). ASP teams may opt to focus on a select number of recommendation types, depending on resources available and the comfort level of pharmacy staff with making antibiotic-related recommendations.

Challenges and the Future of HASC

Since the inception of HASC, discussions during site-visits or open forums have brought up various site-specific challenges. The biggest challenge has been the ability to maintain ASP initiatives due to rapid staff and leadership turnover at the various facilities. The collaborative HASC team continues

Patients Medical Records are assessed if they meet any of the following criteria:
<ul style="list-style-type: none"> • Two or more intravenous antimicrobials
<ul style="list-style-type: none"> • Broad spectrum/expensive antimicrobials <ul style="list-style-type: none"> o Daptomycin (Cubicin®) o Doripenem (Doribax®) o Ertapenem (Invanz®) o Imipenem/Cilastatin (Primaxin®) o Linezolid (Zyvox®) o Meropenem (Merrem®) o Tigecycline (Tygacil®)
<ul style="list-style-type: none"> • Antimicrobials that require laboratory monitoring or dose adjustments for renal function
<ul style="list-style-type: none"> • Antimicrobials eligible for intravenous to oral conversion <ul style="list-style-type: none"> o Fluconazole (Diflucan®) o Levofloxacin (Levaquin®) o Linezolid (Zyvox®) o Metronidazole (Flagyl®)
<ul style="list-style-type: none"> • Intravenous antimicrobials for 14 days or more

Table 3. General Categories of ASP Recommendations		
	Type of Recommendation	Description
1	Intravenous to Oral Conversion	Recommend converting an IV antimicrobial agent to an equivalent oral agent
2	Narrow Empiric Therapy	Recommend discontinuing antimicrobial coverage of a certain (but not all) pathogen, based on lack of risk BEFORE culture results
3	Broaden Empiric Therapy	Recommend adding additional coverage of antimicrobial for pathogens not being covered by current regimen based on patient specific risk factors BEFORE culture results
4	Streamline Based on Culture Results	Recommend discontinuing coverage of antimicrobial for certain (but not all) pathogens, based on culture results
5	Change Therapy based on culture- treatment mismatch	Recommend changing antimicrobial therapy based on the presence of a pathogen in culture results that was not previously being covered by antimicrobial regimen
6	Change to less expensive agent with similar spectrum	Recommend changing to a cheaper antimicrobial agent
7	Change due to risk of adverse event	Recommend changing antimicrobial agent due to risk of adverse effects
8	Discontinue based on lack of indication	Recommend discontinuing antimicrobials due to lack of infectious condition
9	Discontinue duplicate therapy	Recommend discontinuing an antimicrobial agent due to duplication in spectrum of activity with another agent
10	Clarify Indication	Request documentation of infectious indication
11	Change in duration of therapy	Request change in duration of therapy based on recommendations for specific infection
12	Reorder antibiotics stopped by automatic stop order	Request new order for an antibiotics stopped by an automatic stop order
13	Order laboratory monitoring	Order a laboratory test to better monitor and assess efficacy or safety of antimicrobial agent
14	Recommend infectious disease consult	Recommend further evaluation by infectious disease specialist
15	Dose of frequency change	Recommend change in dose to optimize efficacy and safety

to work with each individual site to overcome these constant personnel changes.

Another challenge has been the ability to collect uniform data metrics from each of the 14 facilities. Due to differences in EMR software and institution specific data-mining techniques, not all institutions were able to provide the original metric of total patient antibiotic days. Subsequently, the uniform metric collected changed to the total daily dose (TDD) with respect to the antibiotic(s) of interest for each institution and this data is submitted to HASC.

Data collection continues from each of the participating institutions in order to determine standards of care with respect to antimicrobial stewardship. Preliminary results collected will be used to seek continued funding to fulfill HASC's primary end goal of sustaining that each individual institution be able to sustain a self-sufficient ASP program utilizing various decision support tool-kits that encourage antimicrobial best practices.

Conclusion

HDOH, DKICP, and the 14 HASC facilities have demonstrated their commitment to combating the development of antibiotic resistant organisms through the creation and implementation of ASPs. The accrediting body for health care institutions, The Joint Commission, recently released their preliminary standards for ASP's.⁹ The work of HASC places Hawai'i's health care institutions in an advantageous position to comply with impending accreditation standards relating to antibiotics and infections.

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General Recommendations on Data Presentation and Statistical Reporting (Biostatistical Guideline for HJM&PH) [Adapted from Annals of Internal Medicine & American Journal of Public Health]

The following guidelines are developed based on many common errors we see in manuscripts submitted to HJM&PH. They are not meant to be all encompassing, or be restrictive to authors who feel that their data must be presented differently for legitimate reasons. We hope they are helpful to you; in turn, following these guidelines will reduce or eliminate the common errors we address with authors later in the publication process.

Percentages: Report percentages to one decimal place (eg, 26.7%) when sample size is ≥ 200 . For smaller samples (< 200), do not use decimal places (eg, 26%, not 26.7%), to avoid the appearance of a level of precision that is not present.

Standard deviations (SD)/standard errors (SE): Please specify the measures used: using “mean (SD)” for data summary and description; to show sampling variability, consider reporting confidence intervals, rather than standard errors, when possible to avoid confusion.

Population parameters versus sample statistics: Using Greek letters to represent population parameters and Roman letters to represent estimates of those parameters in tables and text. For example, when reporting regression analysis results, Greek symbol (β), or Beta (b) should only be used in the text when describing the equations or parameters being estimated, never in reference to the results based on sample data. Instead, one can use “b” or β for unstandardized regression parameter estimates, and “B” or β for standardized regression parameter estimates.

P values: Using *P* values to present statistical significance, the actual observed *P* value should be presented. For *P* values between .001 and .20, please report the value to the nearest thousandth (eg, $P = .123$). For *P* values greater than .20, please report the value to the nearest hundredth (eg, $P = .34$). If the observed *P* value is great than .999, it should be expressed as “ $P > .99$ ”. For a *P* value less than .001, report as “ $P < .001$ ”. Under no circumstance should the symbol “NS” or “ns” (for not significant) be used in place of actual *P* values.

“Trend”: Use the word trend when describing a test for trend or dose-response. Avoid using it to refer to *P* values near but not below .05. In such instances, simply report a difference and the confidence interval of the difference (if appropriate), with or without the *P* value.

One-sided tests: There are very rare circumstances where a “one-sided” significance test is appropriate, eg, non-inferiority trials. Therefore, “two-sided” significance tests are the rule, not the exception. Do not report one-sided significance test unless it can be justified and presented in the experimental design section.

Statistical software: Specify in the statistical analysis section the statistical software used for analysis (version, manufacturer, and manufacturer’s location), eg, SAS software, version 9.2 (SAS Institute Inc., Cary, NC).

Comparisons of interventions: Focus on between-group differences, with 95% confidence intervals of the differences, and not on within-group differences.

Post-hoc pairwise comparisons: It is important to first test the overall hypothesis. One should conduct *post-hoc* analysis if and only if the overall hypothesis is rejected.

Clinically meaningful estimates: Report results using meaningful metrics rather than reporting raw results. For example, instead of the log odds ratio from a logistic regression, authors should transform coefficients into the appropriate measure of effect size, eg, odds ratio. Avoid using an estimate, such as an odds ratio or relative risk, for a one unit change in the factor of interest when a 1-unit change lacks clinical meaning (age, mm Hg of blood pressure, or any other continuous or interval measurement with small units). Instead, reporting effort for a clinically meaningful change (eg, for every 10 years of increase of age, for an increase of one standard deviation (or interquartile range) of blood pressure), along with 95% confidence intervals.

Risk ratios: Describe the risk ratio accurately. For instance, an odds ratio of 3.94 indicates that the outcome is almost 4 times as likely to occur, compared with the reference group, and indicates a nearly 3-fold increase in risk, not a nearly 4-fold increase in risk.

Longitudinal data: Consider appropriate longitudinal data analyses if the outcome variables were measured at multiple time points, such as mixed-effects models or generalized estimating equation approaches, which can address the within-subject variability.

Sample size, response rate, attrition rate: Please clearly indicate in the methods section: the total number of participants, the time period of the study, response rate (if any), and attrition rate (if any).

Tables (general): Avoid the presentation of raw parameter estimates, if such parameters have no clear interpretation. For instance, the results from Cox proportional hazard models should be presented as the exponentiated parameter estimates, (ie, the hazard ratios) and their corresponding 95% confidence intervals, rather than the raw estimates. The inclusion of *P*-values in tables is unnecessary in the presence of 95% confidence intervals.

Descriptive tables: In tables that simply describe characteristics of 2 or more groups (eg, Table 1 of a clinical trial), report averages with standard deviations, not standard errors, when data are normally distributed. Report median (minimum, maximum) or median (25th, 75th percentile [interquartile range, or IQR]) when data are not normally distributed.

Figures (general): Avoid using pie charts; avoid using simple bar plots or histograms without measures of variability; provide raw data (numerators and denominators) in the margins of meta-analysis forest plots; provide numbers of subjects at risk at different times in survival plots.

Missing values: Always report the frequency of missing variables and how missing data was handled in the analysis. Consider adding a column to tables or a footnote that makes clear the amount of missing data.

Removal of data points: Unless fully justifiable, all subjects included in the study should be analyzed. Any exclusion of values or subjects should be reported and justified. When influential observations exist, it is suggested that the data is analyzed both with and without such influential observations, and the difference in results discussed.

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A RIGHT-TO-TRY LAW SHOULD BE A NO-BRAINER

In 2012 when he was 11 years old, Diego Morris was diagnosed with osteosarcoma of his leg. Prompt surgery removed the tumor, but the prognosis was poor because extensive chemotherapy would not reduce the risk of recurrence. Fortunately, a team at MD Anderson Cancer Center found a revolutionary new drug mifamurtide (MTP) that can prevent osteosarcoma from recurring. The drug resulted in a 30% reduction in osteosarcoma mortality rate at 8 years post surgery. MTP was approved in 2009 by the European Medicines Agency and is currently the standard of care in Europe, Israel and many other countries. MTP was exactly what Diego needed, but was not available in the United States because the Food and Drug Administration had rejected it demanding further studies. He had to travel to London to get the lifesaving drug that could be obtained in virtually every industrialized nation in the world. It now takes, on average, 14 years to bring a new drug to market in the U.S., up from 8 years in the 1960s. Americans with terminal illnesses are supposed to have access to investigational drugs through the “compassionate-use” program. Still, it appears to be failing, because the application process is so long and complex, and takes an average of 100 hours to complete that patients give up. That is why the “right-to-try” movement at the state level is so popular with politicians and voters. Patients with terminal illness have access to investigational drugs that show promise in clinical trials. Now 28 states have passed right-to-try laws (Hawai’i pending?) It would be 29 states but California Governor Brown vetoed the bill, stating “The FDA compassionate use program allows this to happen.” Clearly, it is failing. Each year thousands of Americans die without getting access to promising treatment that might save or extend their lives.

A NON-THREATENING CONTROL OF AEDES AEGYPTI – BUT CAN IT BE USED?

Centers for Disease Control and Prevention (CDC), wants action. CDC is pushing state and local agencies to prepare for Zika spreading in the United States as the weather warms and more mosquitoes hatch. Now, Oxitec Ltd., a British maker of genetically modified mosquitos, has offered a plan to control the Aedes aegypti, called the cockroach of mosquitoes, and the primary mosquito vector for Zika, malaria, dengue and other viruses. The target population is Key Haven, Florida, an island community of roughly 1,000 citizens adjacent to Key West. Oxitec’s bugs pass along a gene that kills the offspring of modified insects before they reach maturity, curbing the infectious mosquitos. The company says its mosquitoes have killed more than 90% of Aedes aegypti populations in previous trials, double the effectiveness of insecticides. The US Food and Drug Administration gave the plan a preliminary approval in March and has received about 1,500 comments both pro and con. Oxitec plans to go door to door in Key Haven to persuade residents, “The risk of Zika is very, very real. The risk of this technology is virtually nonexistent.” Oxitec is a 14-year-old company from Oxford University research, owned by Virginia-based biotechnology firm Intrexon Corp. The United States market could reach \$100 million in annual sales. Opponents say the proposal represents government and corporate overreach that ignores residents concerns. Both sides agree much is at stake. Local officials plan to hold a public vote on the plan in August.

AGE RELATED MACULAR DEGENERATION FOLLOWS PALE SKIN

Fisher, et al, at the University of Wisconsin conducted an eight-year study on age-related macular degeneration (AMD) involving multiple racial groups: white, black, Hispanic and Chinese. Researchers examined 3,811 participants from the multi-ethnic cohort, with ages

ranging from 46 to 86 years and recorded the findings with fundus photography. They found substantial variations in AMD incidence with whites having the highest rate and blacks the lowest. Fundus photos 8 years later noted overall incidence of early and late AMD was 4.1% and 2.3%, respectively. Whites were worst with 5.3% and 4.4%; Chinese and Hispanics were intermediate and blacks the lowest at 1.6% and 0.4%. After adjustment for age and gender, black individuals had a 70% lower risk of developing AMD than whites. Variation would appear to be melanin.

A MEDICAL MILESTONE FOR DIAGNOSIS.

A research team at the University of Illinois Urbana, has transmitted high speed digital data through pork loin and beef liver. The signal passed cleanly through gristle and bone so clearly it can permit streaming and be visualized like Netflix, according to the team. This is a crucial diagnostic breakthrough. Patients can swallow the transmitter and physicians can view inner workings of the body in real time with externally controlled implanted devices, such as defibrillators and cranial sensors.

DOC’S AD PHOTO — IS IT THE REAL THING?

There is no quarrel that Doc Pemberton, the 19th century pharmacist, mixed naturally fermented kola nuts with coca leaves (obviously containing cocaine) to yield a drink called Coca Cola. Coke today doesn’t have much to say about whether the original drink contained cocaine, but leans on the legend. Doc was born in 1831 in Georgia, was wounded in 1865 while a lieutenant colonel in the CSA, established the state’s first agricultural chemical testing labs and invented several tonics, including French Wine of Coca, a copy of Vin Mariani, a coca-laced cordial developed in France. However, a debate prevails about Docs looks. Coke’s marketing photos portray a handsome robustly bearded dude, but some claim that picture is actually an unpopular Confederate General. They say an 1888 photo sold at auction in Fairfield, Maine, depicts a man in the doorway next to the sign “Pemberton’s French Wine Coca.” Maine auctioneer Richard Lipack, says the man in the doorway is a dead ringer for Doc, who is portrayed in a painting commissioned by Coke, that hangs on the second floor of its headquarters. Sadly, Doc Pemberton, impoverished and probably addicted to morphine, died in 1888. By then he had sold his stakes in the company. Asa Candler, who gained control of Coke, ordered many of the company’s earliest records burned in 1910.

ADDENDA

- There are five species of Gecko in Hawai’i. Four of them have been here for about 1500 years, possibly stowaways in canoes. The fifth – the “house gecko” – came after WWII and quickly pushed the others to the outdoors. It is more aggressive and will eat other geckos, including their own.
- Eskimo language has 50 words to describe snow, but Hawaiian language has 130 words for “rain,” noting location, intensity, volume, duration.
- If it weren’t for electricity we would all be watching television by candle light.
- The difference between the blues and the blahs is you can’t sing the blahs.
- Without music life would be a mistake.

ALOHA AND KEEP THE FAITH rts

(Editorial comment is strictly that of the writer.)

HAWAI'I JOURNAL OF MEDICINE & PUBLIC HEALTH

The Hawai'i Journal of Medicine & Public Health invites students and professionals at public health, medical, nursing, pharmacy, and dental schools or programs to enter in its **2nd Annual Writing Contest**.

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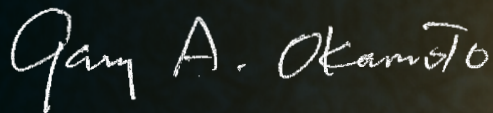


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