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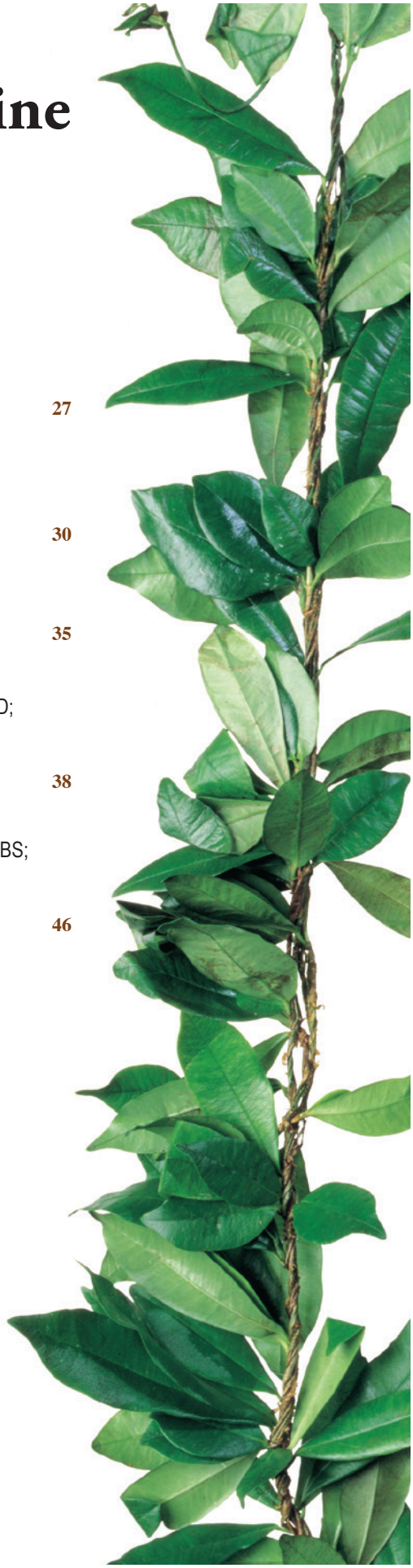

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D. Varez

Systemic Mastocytosis: The Difficult Patient with a Rare Disease. Case Presentation and Brief Review

Daniel H. Desmond MD and Mark G. Carmichael MD

Abstract

Mastocytosis is a rare process involving the activation and accumulation of clonal mast cells categorized by cutaneous or systemic involvement. Although the diagnosis of cutaneous disease can be straightforward and confirmed via skin biopsy, systemic disease mimics more common disease processes making diagnosis a challenge. The widespread physiologic distribution of mast cells causes a variety of symptoms with aberrant expression including fatigue, headache, depression, dyspnea, dyspepsia, nausea, and abdominal pain. We present a patient with a three-year history of multiple, non-specific complaints prompting extensive evaluation at significant financial and emotional cost without therapeutic relief. This case presentation illustrates some of the pitfalls of evaluation and management of mastocytosis when symptoms are treated in isolation. Ultimately, our patient was diagnosed with indolent systemic mastocytosis (ISM), which has a good overall prognosis but no curative treatment. Providers must maintain a high index of suspicion for mastocytosis in order to make the diagnosis and facilitate appropriate treatment and screening.

Keywords

Mastocytosis, urticaria, c-KIT

Introduction

Mast cells are tissue-fixed cells of inflammatory and allergic reactions derived from hematopoietic progenitors that have variability in function depending on their terminally differentiated location.[1,2] This partly explains the nonspecific symptoms described among patients with abnormal mast cell expression. Associated symptoms are classically characterized by allergic-type reactions ranging from localized urticaria to angioedema. In addition, gastrointestinal symptoms, headache, depression and bone pain are all associated findings.[3-5] Secretory granules located within the mast cells release histamine, serotonin, tumor necrosis factor (TNF), and proteases such as tryptase causing both local and systemic symptoms. Activation of these immune cells is usually the result of mast cell surface receptor (FcεRI) responding to stimulation by IgE. Multiple other stimuli can also lead to degranulation including: anaphylatoxins, complement, aggregated IgG, drugs, venoms, physical stimuli, emotional stress, cytokines and neuropeptides.[2] Mastocytosis comprises a heterogenous group of conditions associated with aberrant proliferation and expression of clonal mast cells.[1] It is a rare disease with a prevalence of approximately 13 in 100,000 cases.[3] The pathogenesis of this aberrant phenotype is unknown although there are characteristic genetic and phenotypic markers that make up the diagnostic criteria (Table 1). Specifically, mastocytosis is associated with the presence of a gain-of-function mutation in the associated oncogene, c-KIT in 80% of cases.[2] This oncogene encodes a transmembrane tyrosine kinase receptor, KIT (CD117), found in early hematopoietic progenitor cells and in terminally differentiated cells located in tissues exposed to the environment (gut, respiratory epithelium, skin, etc).[6]

Table 1. Major and minor criteria for the diagnosis of systemic mastocytosis (SM).[7]

Major Criteria	Minor Criteria
• Multifocal, dense aggregates of mast cells (15 or more) detected in sections of extracutaneous tissues (commonly bone marrow) confirmed by tryptase immunohistochemistry and/or KIT immunohistochemistry	• In biopsy section, more than 25% of the mast cells in the infiltrate have atypical morphology, or, of all the mast cells in the aspirate smear, more than 25% are immature or atypical • Mast cells coexpress CD117 with CD2 and/or CD25 • Detection of KIT point mutation at codon 816 in bone marrow, blood, or other extracutaneous organs • Serum total tryptase persistently >20 ng/ml
Diagnosis requires either 1 major and 1 minor criterion or 3 minor criteria.	

*Adapted with permission from World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC, Lyon, 2008.

Presentation

A 29-year-old Caucasian woman presented to clinic with a brownish macular rash that had intermittently been present for 2-3 years but, recently developed over her arms and progressed to her torso and abdomen over a period of weeks (Figure 1). The rash involved mostly the patient's torso and extremities although, her hands, feet, head, and neck were spared. She described her rash as erythematous and pruritic when scratched (Darier's Sign) and reported that it became irritated and erythematous during exercise and with exposure to heat and humidity. These symptoms became worse with a move from the northeastern United States to the South Pacific. Review of systems revealed intermittent dyspnea on exertion associated with a previous diagnosis of allergic-type asthma and a 3-year history of abdominal complaints including pain, constipation and bloating. Her abdominal discomfort prompted the patient to present to multiple providers during this time period and resulted in considerable diagnostic evaluation. In late 2013 she was diagnosed with cholecystitis and received a cholecystectomy, however, she continued to experience bouts of severe abdominal pain prompting multiple visits to the emergency department where serial computed tomography(CT) scans were negative. Ultimately she was offered an esophagoduodenoscopy (EGD) by her surgeon which showed mild esophagitis and gastritis and she was treated a trial of proton-pump inhibitor therapy. The patient was referred to gynecology due to concomitant menorrhagia and irregular bleeding and was diagnosed with endometriosis. Confirmatory biopsy was not obtained, due to pregnancy and reluctance to perform an invasive procedure. In one of the patient's abdominal CT scans in late 2015 a small

nodule was noted in the left lung, and a dedicated chest CT revealed mild hilar lymphadenopathy and a 5mm nodule in the left hilum. Biopsy of the hilar nodule via endobronchial ultrasound-guided fine-needle aspiration (EBUS-FNA) showed a granulomatous process with CD4/CD8 ratio of 3.76 consistent with the diagnosis of sarcoidosis.

The patient was eventually referred to dermatology for her macular rash. Skin biopsy showed increased perivascular and interstitial mast cell proliferation and serum tryptase of 36.5 ng/mL. Bone marrow biopsy was pursued to obtain extracutaneous tissue to confirm the suspected diagnosis of systemic mastocytosis. Her bone marrow was normocellular with < 10% mast cells but, flow cytometry was positive for CD117 and CD25 (negative for CD3, CD20, and CD34) and molecular studies showed the KIT D817V mutation. Given the patient's symptoms, persistently elevated tryptase, mast cell proliferation on skin and bone marrow biopsy, flow cytometry, and the presence of KIT D817V mutation, she met the criteria for the diagnosis of systemic mastocytosis (SM). (Table 1) The patient did not have any evidence of end-organ infiltration by malignant cells such as cytopenias, hepatosplenomegaly, lymphadenopathy, malabsorption, or osteopenia. These findings are referred to as B (indicating high burden of mast cell expansion) or C (infiltration associated with organ damage) and can indicate aggressive disease.[1] As the patient did not have B or C findings she was diagnosed with indolent systemic mastocytosis (ISM).

Discussion

Mastocytosis is broadly subcategorized into cutaneous and systemic disease. Cutaneous mastocytosis (CM) is associated with gain-of-function KIT mutations in approximately 60 to 80% of cases and is defined by lack of infiltration into non-cutaneous organs.[2] In comparison to systemic disease, CM is more common in the pediatric population, is less severe, and often resolves with time. There are three described subtypes of cutaneous disease: urticaria pigmentosa, diffuse mastocytosis, and mastocytoma. Urticaria pigmentosa, the most common subtype, is generally diagnosed on physical exam by eliciting Darier's sign, an immediate urticarial response to physical manipulation of an affected area.[4] Interestingly patients with only cutaneous disease can present with non-cutaneous manifestations including gastrointestinal upset and anaphylaxis.[3]

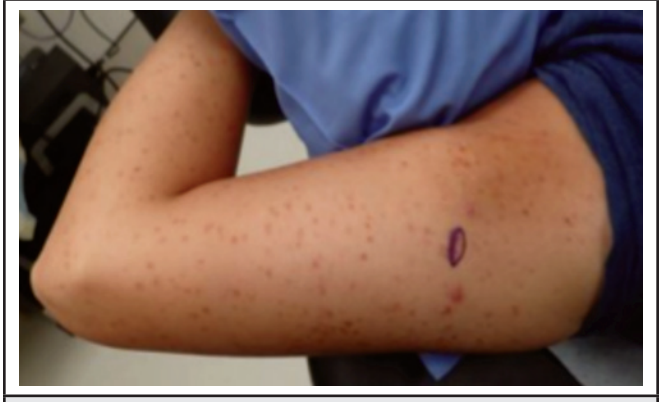

Figure 1. Patient's arm after skin biopsy

Among adults, 95% of mastocytosis manifests as systemic mastocytosis (SM).[6] The World Health Organization published updated classification criteria in 2016 and removed mastocytosis from the category of myeloproliferative neoplasms creating a new category for mastocytosis due to disease heterogeneity. Systemic disease is categorized into the following types (listed in order of worsening prognosis): ISM, smoldering SM, SM with an associated hematological neoplasm (SM-AHN), aggressive SM, and mast cell leukemia.[8] Mast cell sarcoma continues to exist as its own category. ISM is by far the most common subtype with a prevalence of 90-95% among patients with systemic disease.[3] Mast cell degranulation causes the symptoms that are associated with ISM including the most common, maculopapular rash and gastrointestinal symptoms which have a reported prevalence of 70-80%.[4] The evolution of ISM into a more aggressive subtype is a rare occurrence and therefore patients with ISM have a favorable prognosis. Advanced mastocytosis is differentiated by increased mast cell tissue invasion and expansion resulting in B and/or C-symptoms. Notably, osteoporosis and vertebral fractures are frequent in all types of SM.[3,4] Aggressive SM describes an infiltrative process leading to organ failure.[3] Finally, mast-cell leukemia is diagnosed when greater than 20% mast cells are present in marrow or more than 10% immature mast cells are present in peripheral blood. Mast cell sarcoma is a locally aggressive tumor that doesn't meet any of the criteria for SM.

Identification of SM requires a high degree of suspicion given the nonspecific findings. Past reviews and case reports alike discuss a wide variety of presentations consistent with the ubiquitous nature of mast cell distribution in the body (Table 2). Prior to her final unifying diagnosis, our patient was seen by the emergency department, primary care, gastroenterology, pulmonary, gynecology, and surgery. She received multiple diagnoses to include seasonal allergies, asthma, GERD, irritable bowel syndrome, chronic constipation, depression and sarcoidosis. It wasn't until she was referred to dermatology and her cutaneous symptoms were managed primarily that a biopsy was performed and a unifying diagnosis was made. The rarity of mastocytosis and its nonspecific symptoms result in a previously reported phenomenon of patients receiving diagnoses contained within the purview of the sub-specialist treating the patient.[2] Often these patients do not receive adequate diagnostic or therapeutic satisfaction despite seeking treatment from multiple institutions and specialties, as in the case of our patient. Additionally, mast cell pathology in the brain has been implicated in the development of depression and mild cognitive impairment.[5] The marriage of predisposing physiology, rarity of disease presentation and the tendency for these patient's to be high-utilizing patients can result in frustration and grief for both the provider and patient.

Table 2. Symptoms by systems affected by aberrant expression/proliferation of mast cells			
Cardiovascular Hypotension Syncope Pre-syncope Lightheadedness Tachycardia	**Cutaneous** Flushing Pruritus Urticaria Angioedema	**Gastrointestinal** Abdominal cramps Diarrhea Esophageal reflux Nausea and vomiting	**Musculoskeletal** Aches Bone Pain Osteopenia Osteoporosis
Neurologic Anxiety Depression Mild Cognitive Impairment Insomnia Migraines	**Respiratory** Nasal Congestion Nasal Pruritus Dyspnea Throat swelling Wheezing	**Systemic** Fatigue Generalized malaise Weight loss	

Knowing when to consult a hematologist for assistance with making the diagnosis is complicated by the nonspecific features of mastocytosis. If the patient is presenting with C-symptoms, a consult is warranted. Given the prevalence of systemic involvement in adults with mastocytosis (90%-95%), it is reasonable to refer if this diagnosis is being entertained. The most common presenting symptoms include a maculopapular rash that demonstrates a typical urticarial response when scratched (Darier's sign), gastrointestinal upset and headache.

Treatment for systemic mastocytosis remains limited although there are new developments. ISM is treated with supportive care, trigger avoidance, antihistamines, and oral cromolyn (GI symptoms). Leukotriene antagonists, H2 antagonists, or proton pump inhibitors are used adjunctively, if needed. Other options include omalizumab (IgE humanized monoclonal antibody), steroids, cytoreductive agents, and tyrosine kinase inhibitors in specific cases.[9] Advanced mastocytosis subtypes have previously been devoid of curative options outside of bone marrow transplantation which is associated with high morbidity and mortality. Median overall survival in patients with advanced systemic mastocytosis is 3.5 years.[9] Previously tested treatments include cytoreductive therapy (cladribine, steroids, IFN-α) and the tyrosine kinase inhibitor, imatinib, in limited cases with varied success.[6] Recent phase II clinical trial data was released regarding the treatment of aggressive mastocytosis with a multi-kinase inhibitor with activity against KIT, midostaurin.[10] In this study, 45% of patients had a major response which was defined as complete resolution of at least one type of mastocytosis-related organ damage. In April 2017, midostaurin was approved by the FDA for use in patients with aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm or mast cell leukemia. Further study remains to determine if this treatment may be used in patients with ISM and recalcitrant symptoms.

Conclusion

Systemic mastocytosis is a rare disease process driven by aberrant activation and infiltration of mast cells that presents in adults with nonspecific symptoms and can follow an indolent or aggressive course. In adults, the most common form is ISM, as seen in the patient presented above. Clinicians need to keep a high index of suspicion in order to identify patients with ISM due to the low prevalence of disease and nonspecific symptoms. Referral to hematology should be made in severely symptomatic patients and those with high pretest probability for systemic disease. Treatment for systemic mastocytosis is difficult and largely focused on symptom amelioration; however, there is an emerging role for the multi-tyrosine kinase inhibitor, midostaurin, for advanced subtypes of disease.

The views expressed in this manuscript are those of the author(s) and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the US Government.

Conflict of Interest

None of the authors identify any conflicts of interest.

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Impact of Laboratory Practice Changes on the Diagnosis of Tuberculosis with the Introduction of Xpert MTB/RIF in Kiribati

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Abstract

The Republic of Kiribati, Central Pacific, has the largest tuberculosis epidemic in the region. There is a national tuberculosis control program, which has used smear microscopy for acid-fast bacilli as the main diagnostic tool for many years. In 2015, an Xpert MTB/RIF machine was procured and became functional within the tuberculosis hospital. The aim of this cross-sectional study, using routinely collected data, was to determine the effects of introducing Xpert MTB/RIF on laboratory smear microscopy practices and the pattern of registered tuberculosis cases. Between February 2015 and January 2016, there were 220 Xpert MTB/RIF assays performed with 6.4% errors and 15% detection of Mycobacterium tuberculosis*: one patient showed rifampicin-resistance. One year before and after introducing Xpert MTB/RIF, the number of presumptive tuberculosis patients increased by 9% from 2,138 to 2,322. There were no changes in demographic characteristics, smear-positive results, or acid-fast bacilli grade between the two periods. The number of specimens cultured for* Mycobacterium tuberculosis *significantly declined from 638 to zero, with 76 positive MTB cultures before and none after introducing Xpert MTB/RIF. There was a significant change in the profile of registered tuberculosis cases with more children (34% versus 21%) and fewer bacteriologically-confirmed cases (29% versus 43%) – P < .001. Since the deployment of Xpert MTB/RIF in Kiribati, there have been a small number of assays performed and this has been associated with no adverse effects on smear microscopy, a stoppage in mycobacterial cultures, and a change in the types and categories of diagnosed tuberculosis.*

Keywords

Xpert MTB/RIF; tuberculosis; Kiribati; smear microscopy services; culture for Mycobacterium tuberculosis*; types of tuberculosis*

Introduction

Sputum smear microscopy for acid-fast bacilli is still the most widely used method for the diagnosis of pulmonary tuberculosis (TB) in low- and middle-income countries.[1] Although inexpensive to perform and despite attempts made to improve its sensitivity and specificity, smear microscopy is cumbersome, costly for patients (although the test is free, patients have to pay for several trips to the hospital and they also incur lost wages from time off work), and does not detect drug-resistant disease.[1,2] With over 10 million people estimated to have developed new TB globally in 2015, and 580,000 having multidrug-resistant or rifampicin-resistant (MDR or RR) TB (ie, resistant to rifampicin or both rifampicin and isoniazid), new diagnostic tools to replace or complement smear microscopy are urgently needed.[3,4]

The most important recent diagnostic development to the Xpert MTB/RIF machine and assay (Cepheid Inc, Sunnyvale, CA, USA) for use with sputum and other body specimens.[5] The cartridge-based system means there is no need for prior sputum processing, minimal laboratory expertise is needed to perform the assay, the results are provided in less than two hours, sensitivity and specificity for the diagnosis of TB is high, and the investigator is provided with information about susceptibility or resistance to rifampicin.[5-7]

In 2011, the World Health Organization (WHO) strongly recommended the widespread use of Xpert MTB/RIF, especially for individuals suspected of having MDR-TB and Human Immunodeficiency Virus (HIV)-associated TB.[8,9] In 2013, the WHO updated this guidance, recommending that Xpert MTB/RIF be used as the initial diagnostic test for all patients with presumptive TB.[10]

Kiribati is an island republic in the Central Pacific, comprising 32 coral atolls, reef islands, and one raised coral atoll stretching along the equator.[11] The population is 103,058, with South Tarawa being the Capital.[12] In 2014, the country had a GDP per capita of USD$1,605 and is recognised as one of the poorest and least developed countries in the Pacific.[13] Kiribati has the largest per capita TB rate in the region with 420 cases in 2013.[14] Estimated MDR-TB cases for that year were 4.5 and 24 per 100,000 for new and previously treated TB respectively, although there were no actual diagnosed MDR-TB cases in 2013.[14] There is a national TB control program (NTP) that has followed the WHO Directly Observed Treatment, Short-course (DOTS)strategy and has used smear microscopy as the main diagnostic tool for many years. Current TB control efforts include 6-months of directly observed chemotherapy for diagnosed TB cases using the standardized regimens recommended by WHO,[15] contact tracing, isoniazid prophylaxis for contacts under five years of age and those diagnosed with diabetes, and screening of community members for TB in identified TB hotspots. All TB control efforts take place within the NTP and no TB cases are managed in the private sector.

With funding and technical support from the Australian AID Program and the Pacific Community (SPC), the Kiribati NTP procured an Xpert MTB/RIF machine in early 2015, which became functional within the NTP hospital February 5, 2015. After one year of use, there has been no published information about the number of Xpert tests performed or the results. Additionally, there are a number of other issues of interest. First, we wanted to assess the community response to the introduction of this new assay—the arrival and capability of the Xpert MTB/RIF assay was published in the newspaper and aired in the news over the radio, and we wanted to know whether this may have prompted more patients with presumptive TB to come forward and submit sputum specimens. Second, we wanted to assess the impact of this new technology on the proficiency of

laboratory technicians performing smear microscopy as we were concerned that smear microscopy would be underused resulting in a decline in the quality of acid-fast bacilli detection. Third, with the introduction of Xpert MTB/RIF, a decision was made to stop sending specimens for *Mycobacterium tuberculosis* (*MTB*) culture and drug-susceptibility, and we needed to know whether this had actually happened. Finally, we were interested in assessing whether there was any association between the introduction of Xpert MTB/RIF and the diagnosed and registered types and categories of TB.

We therefore carried out a retrospective study using secondary data to assess whether the introduction of Xpert MTB/RIF was associated with a change in diagnostic practices and the profile of TB in Kiribati. Specific objectives were to determine: 1) use of Xpert MTB/RIF over one year between February 2015 and January 2016 in terms of number of tests performed along with errors and results and 2) for one year before (February 2014 to January 2015) and one year after (February 2015 to January 2016) the introduction of Xpert MTB/RIF, the numbers and characteristics of patients submitting sputum specimens along with the results, the number having *MTB* cultures performed along with positive cultures, and the types and categories of diagnosed TB.

Methods

Patient Population

All patients with presumptive and diagnosed TB registered at Kiribati NTP between February 2014 and January 2016 were included in the study and divided into the pre-Xpert period (February 2014 to January 2015) and the post-Xpert period (February 2015 to January 2016).

Study Design

This was a cross-sectional retrospective study using routinely collected data from laboratory and patient TB registers.

Setting

Tuberculosis and TB control in Tungaru Central Hospital, South Tarawa:

The study was carried out at the NTP unit, Tungaru Central Hospital, South Tarawa. Presumptive cases of TB are referred from peripheral health clinics, outpatient clinics, inpatient services and emergency units on the main and outlying islands to the NTP unit.

Diagnostic Criteria and Treatment

TB diagnosis before introduction of Xpert MTB/RIF:

All presumptive TB patients submitted two sputum specimens for smear microscopy. Those with positive smears - scanty, 1+, 2+ and 3+ acid-fast bacilli (AFB)—were diagnosed as smear-positive pulmonary TB while those with negative smears followed a clinical and radiographic algorithm for the diagnosis of smear-negative pulmonary TB. Extra-pulmonary TB was diagnosed based on clinical, microbiological and radiographic characteristics. *MTB* cultures were done on patients highly suspected to have smear-negative pulmonary TB while culture and drug-susceptibility testing was done on patients with previously treated TB, with HIV, or with persistently smear-positive sputum specimens during treatment. Drug-susceptibility testing was performed outside the island in the SA Pathology Laboratory, Adelaide, Australia.

TB diagnosis after introduction of Xpert MTB/RIF:

All presumptive TB patients still submitted two sputum specimens to the laboratory for smear microscopy. Those with positive smears were diagnosed as smear-positive pulmonary TB. Those with negative sputum smears who were highly suspected to have TB on chest radiography had one of the two sputum specimens examined by Xpert MTB/RIF. All presumptive TB patients with HIV-infection, at high risk of MDR-TB (previously treated cases, contacts of MDR-TB cases, and cases still smear-positive after three months of treatment), who were aged less than 15 years or had suspected extra-pulmonary TB had their sputum or other specimens examined by Xpert MTB/RIF, regardless of smear microscopy. No specimens were sent for culture and drug-susceptibility testing, unless the Xpert MTB/RIF showed resistance to rifampicin when culture and drug-susceptibility testing were used to confirm the result.

Registration and Treatment:

Diagnosed patients were registered as new or previously treated and as bacteriologically confirmed pulmonary TB (smear-positive, culture-positive or Xpert-positive), not-bacteriologically confirmed pulmonary TB and extra-pulmonary TB. Anti-tuberculosis treatment followed standard WHO TB treatment guidelines.[15,16]

Data Variables, Sources of Data and Data Collection

Data variables included: 1) for the use of Xpert MTB/RIF - laboratory register number, year, month, age, sex, Xpert test number, an error (unsuccessful result caused for example by the reaction tube being filled improperly, a reagent probe integrity problem, maximum pressure limits exceeded, or module failure), a positive TB diagnosis, and a positive rifampicin resistance result. The data source was the NTP laboratory register for the Xpert MTB/RIF assay; 2) for laboratory sputum smear and culture examination—laboratory registration number, year, month, age, sex, sputum result, highest positive sputum grade (3+, 2+, 1+ or scanty), culture done, and culture positive for *MTB*. Drug-susceptibility results were not collected as these were done overseas in Australia and the results were inconsistently documented in Kiribati. The data source was the NTP laboratory register for sputum smear microscopy; 3) for registered TB patients –TB registration number, year, month, age, sex, type of TB (bacteriologically confirmed, not bacteriologically confirmed, extra-pulmonary), and category of TB (new, relapse, failed previous treatment, returned after default, other recurrent TB, transfer-in). The data source was the TB patient register. Data collection was carried out between February and June 2016 using paper-based questionnaire form.

Analysis and Statistics

Data were single-entered into Epinfo Version 7.0 (Centers for Disease Control and Prevention, Atlanta, USA). A descriptive analysis of the use of Xpert MTB/RIF was performed using absolute numbers, frequencies and proportions. Comparisons were made before and after the introduction of Xpert MTB/RIF using the chi-square test or chi-square test for trend with respect to numbers and characteristics of presumptive TB patients and their laboratory parameters and numbers, types and categories of TB, with differences at or below the 5% level being regarded as significant.

Ethics Approval

Permission for the study was obtained from the Kiribati National Tuberculosis Program through the director of public health and ethics approval was obtained in writing from the Ethics Advisory Group, International Union Against Tuberculosis and Lung Disease, Paris, France. Patient consent was not required as secondary data were used throughout.

Results

The results of Xpert MTB/RIF assays are shown in Table 1. Of the 220 assays performed, 185 were in persons aged ≥ 15 years while 35 were in children < 15 years. Just over 6% of assays had errors. From the remainder of the successful assays, there were 31 (15%) showing MTB: 2 were in children (6% positive detection) and 29 (16% positive detection) were in persons aged ≥ 15 years. All but one sample showed sensitivity to rifampicin (that one sample had rifampicin mono-resistance diagnosed by culture and drug-susceptibility testing).

Characteristics of patients with presumptive TB and their laboratory results before and after the introduction of Xpert MTB/RIF are shown in Table 2. There was a 9% increase in the number of patients identified with presumptive TB after Xpert MTB/RIF was introduced, although no differences were noted in gender or age group distributions between the two groups. Although there was a slight decrease in smear-positive detection in the post Xpert period, this was not statistically significant and AFB grading distribution in those with positive sputum smears was also not significant. The number of MTB cultures performed in the post Xpert period dropped to zero.

Characteristics of patients registered with TB for one year before and after the introduction of Xpert MTB/RIF are shown in Table 3. The main differences in the post Xpert MTB/RIF period compared with the previous period were in age group distributions where significantly more children were registered with TB and in types of TB where significantly fewer patients were registered with bacteriologically confirmed TB.

Table 1. Number of Xpert MTB/RIF tests done between February 2015 and January 2016 in Kiribati along with errors and results

Characteristics	N	(%)
Xpert tests done	220	
Xpert tests with errors	14	(6.4)
Xpert tests completed with no errors	206	(93.6)
Xpert results showing Mycobacterium tuberculosis (MTB)	31	(15.0%)[a]
MTB showing rifampicin resistance	1	(3.2%)[b]
MTB showing no rifampicin resistance	30	(96.8%)[b]

[a]denominator = Xpert tests completed with no errors (n=206)
[b]denominator = Xpert results showing Mycobacterium tuberculosis (MTB) (n=31)

Table 2. Demographic and laboratory characteristics of patients presenting for the investigation of tuberculosis before and after the introduction of Xpert MTB/RIF on Kiribati

Characteristics	Before Xpert n (%)	After Xpert n (%)	*P*-Value*
All Patients	2138 (100)	2322 (100)	
Gender			
Male	1167 (55)	1225 (53)	.20
Female	969 (45)	1094 (47)	
Not Known	2 (<1)	3 (<1)	
Age Group in Years			
1-14	261 (12)	312 (13)	.07
15-49	1027 (48)	1142 (49)	
50-69	519 (24)	551 (24)	
70+	114 (7)	122 (5)	
Not Known	187 (9)	195 (9)	
Sputum Smear Examination			
Positive AFB	157 (7)	137 (6)	.80
Negative AFB	1981 (93)	2171 (93)	
No Result Documented	0	14 (1)	
Grade of AFB			
3+	38 (24)	34 (25)	.47
2+	32 (21)	27 (20)	
1+	46 (29)	53 (38)	
Scanty	41 (26)	23 (17)	
Culture Done for MTB			
Culture Performed	638 (30)	0 (0)	<.001
Culture Not Performed	1498 (70)	2315 (99)	
No Result Documented	2 (<1)	7 (7)	
Culture positive for MTB	76 (12)	0	

*using chi-square test or chi-square test for trend
AFB = acid-fast bacilli; *MTB* = *Mycobacterium tuberculosis*

Table 3. Demographic and clinical characteristics of patients diagnosed with tuberculosis before and after the introduction of Xpert MTB/RIF on Kiribati

Characteristics	Before Xpert n (%)	After Xpert n (%)	*P*-Value
All Patients	472 (100)	550	
Gender			
Male	248 (53)	295 (54)	.70
Female	224 (47)	255 (46)	
Age Group in Years			
1-14	99 (21)	186 (34)	<.001
15-49	252 (53)	267 (49)	
50-69	108 (23)	87 (16)	
70+	13 (3)	10 (1)	
Category of TB			
New	446 (94)	524 (95)	.85
Relapse	12 (3)	7 (1)	
Failed Previous Treatment	2 (<1)	3 (<1)	
Returned After Default	0	0	
Other Recurrent TB	12 (3)	15 (3)	
Transfer In	0	1 (<1)	
Type of TB			
Bacteriologically Confirmed	201 (43)	161 (29)	.47
Not bacteriologically confirmed	221 (45)	304 (55)	
Scanty	60 (12)	85 (167)	

*using chi-square test or chi-square test for trend
TB = tuberculosis

Discussion

This is the first study from Kiribati reporting on 12-months usage of the newly introduced Xpert MTB/RIF assay and assessing whether this had any effect on numbers of patients with presumptive TB, laboratory practices and the types and categories of diagnosed TB.

Given the size of the TB epidemic in Kiribati, the number of Xpert MTB/RIF assays performed per 100,000 people was relatively small compared with what has been observed in several African countries.[17,18] In terms of Xpert MTB/RIF results, error rates were similar and MTB detection rates slightly higher than those found in sub-Saharan Africa. One published study from Fiji on the use of Xpert MTB/RIF in the Pacific region showed similar findings to those of our study.[19] It was reassuring that only one case of rifampicin mono-resistance was found in Kiribati and this is in line with findings from Fiji where there were no detected cases of MDR-TB.

There was a small increase in the number of patients presenting with presumptive TB after the introduction of Xpert MTB/RIF. This period coincided with active TB case finding in the community and this may have been the main reason for the increase in presumptive TB cases rather than the introduction of new technology. Although general concerns were raised several years ago that the introduction of Xpert MTB/RIF might adversely affect sputum smear microscopy services,[20] we found no significant effect in Kiribati. It was also reassuring to see that no sputum specimens were submitted for MTB culture after Xpert MTB/RIF was introduced in accordance with national recommendations.

The main differences in the types and categories of TB before and after Xpert MTB/RIF were a higher proportion of children diagnosed with TB and a lower proportion diagnosed with bacteriologically confirmed TB. We do not know why there was an increase in children diagnosed with TB in the post Xpert MTB/RIF period, but it was not due to the new technology which only resulted in two pediatric confirmed cases in the year. The lower proportion diagnosed with bacteriologically confirmed TB may have been due to more children diagnosed who tend to be smear-negative,[21-23] and no MTB cultures performed which were not compensated for by Xpert MTB/RIF positive cases. The small discrepancies between the numbers with bacteriologically-confirmed TB in the TB registers and numbers with smear-positive AFB in the laboratory registers are not surprising as it takes time for patients diagnosed in the laboratory to be registered and started on anti-TB treatment, so the time periods for patients in each register do not exactly match.

An important strength of this study was that the NTP Unit in Tungaru Central Hospital, South Tarawa, provided services for presumptive TB patients coming from over 90% of Kiribati, and the study was therefore nationally representative. The conduct and reporting of the study also adhered to STROBE and RECORD guidelines.[24,25] Limitations related to the operational and retrospective nature of the study with missing data for some of the variables in the laboratory register. We also did not collect data on why patients with presumptive TB were referred for Xpert MTB/RIF (because this was not recorded consistently in the forms or registers) as this would have been important and helpful to understand why few tests were done in the first 12 months.

There are a number of programmatic implications from this study. First, there should be a scaling up of the Xpert MTB/RIF technology as the number of tests performed in the first 12 months was small. Kiribati has now procured a second instrument in 2016 and this has become functional since the conclusion of the current study. Current WHO recommendations are that Xpert MTB/RIF is used for all patients with presumptive TB,[10] and Kiribati needs to decide whether to widen its use to all patients. Second, there needs to be an improvement in the Xpert MTB/RIF register so that reasons for being tested are being recorded. Third, if the country decides to scale up Xpert MTB/RIF to all presumptive TB patients in the country, a decision would have to be made about smear microscopy services. This study suggests that the quantity and quality of these services has not been adversely affected and it would seem prudent to continue in the first few years with these services in case there are technical or other issues with the Xpert instruments. The skill base for performing smear microscopy would thus be

retained. Finally, a decision will also need to be made about whether to re-establish the use of *Mycobacterium tuberculosis* culture and drug-susceptibility testing. Before the introduction of Xpert MTB/RIF, culture and drug-susceptibility testing were performed in patients with previously treated TB, with HIV, or with persistently smear-positive sputum specimens during treatment. The main purpose of this was to identify and diagnose MDR-TB, including rifampicin-resistant TB, both of which are treated with MDR-TB treatment regimens.[4] Since the introduction of Xpert MTB/RIF, no cultures or drug-susceptibility testing were carried out with the molecular assay replacing this function, thus saving money and removing the logistic challenges of transporting the specimens to the SA Pathology Laboratory, Adelaide, Australia. However, the downside is that there is no information about isoniazid or other primary drug resistance, excluding rifampicin. In the 2010 WHO Tuberculosis Guidelines,[15] and further endorsed in the most recent 2017 WHO Tuberculosis Guidelines,[26] the recommendation is that ethambutol can be added to the continuation phase of isoniazid and rifampicin if there are high levels of isoniazid resistance. This is something that the Kiribati NTP may wish to consider including the re-establishment of culture and DST.

In conclusion, despite the introduction of Xpert MTB/RIF in Kiribati, only a small number of Xpert tests were performed with an MTB case detection rate of 15%. Sputum smear microscopy services were unaffected while the numbers of specimens being sent for MTB culture dropped to zero. The pattern of registered TB changed with fewer numbers of bacteriologically confirmed TB. Reasons for these changes and programmatic implications are discussed.

Conflict of Interest

None of the authors identify any conflict of interest.

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MEDICAL SCHOOL HOTLINE

School of Medicine Departments — Year in Review 2017, Part 2

Sandra P. Chang PhD; Maria Chun PhD; Anthony Guerrero MD; Chessa Harris MBA; Joseph Keawe'aimoku Kaholokula PhD; Marjorie L.M. Mau MD; Kenneth Nakamura MD; Karen Thompson, MD; Ivica Zalud MD

In 1993, the Medical School Hotline was founded by Satoru Izutsu PhD (former vice-dean UH JABSOM), it is a monthly column from the University of Hawai'i John A. Burns School of Medicine and is edited by Kathleen Kihmm Connolly PhD; HJMPH Contributing Editor.

This article is a continuation of highlights from each department in areas of scholarly, research, and service activities for calendar year 2017. This issue includes the following departments: Native Hawaiian health; obstetrics, gynecology, and women's health; pathology; pediatrics; psychiatry; surgery; and tropical medicine, medical microbiology, and pharmacology.

Native Hawaiian Health

The Department of Native Hawaiian Health continues to be a center of excellence in medical education, health disparities research, clinical services, and community engagement aimed at improving the health of Native Hawaiians and other Pacific Peoples. The 2017 year was exciting and productive for the department as it worked toward enhancing its mission and outreach.

In the medical education division, the department received an additional five years of funding from the Health Resources and Services Administration (HRSA) of the US Department of Health and Human Services to support the Native Hawaiian Center for Excellence (NHCOE). The NHCOE has been in existence for 26 years. Its mission is to recruit students into health professions, promote faculty and student development, implement cultural competence development training, and disseminate information resources relevant to the health of Native Hawaiians.

In the research division, the department expanded its NIH-funded basic biomedical science research. In partnership with the John A. Burn's School of Medicine's (JABSOM) new Diabetes Center of Biomedical Research Excellence, new clinical and community-based research programs were developed. The internal medicine practice, Lau Ola Clinic, transitioned to the Department of Medicine's primary care clinic on Queen's Medical Center's Punchbowl campus. The clinic is expanding its behavioral health services.

The community engagement division has grown the Ulu Network of community-based organizations across Hawai'i and Southern California to include 38 organizations with over 80 sites. A number of these organizations were supported with funds for dissemination of research innovations and programs. In addition, the department was also involved with the Native Hawaiian Health Task Force, that authorized a Hawai'i State Senate resolution to advance policy and program recommendations to improve the health of Native Hawaiians.

The clinical division provided medical support for the Polynesian Voyaging Society's World Wide Voyage (2014-2017). Drs. Marjorie Mau, Dee-Ann Carpenter and Martina Kamaka served on board as Medical Officers.

Please visit the department's new website for more information at http://dnhh.hawaii.edu/.

Obstetrics, Gynecology, and Women's Health

The core values of the Department of Obstetrics, Gynecology, and Women's Health (OB/GYN), integrity and excellence, inspire the department to achieve its mission of advancing women's health in Hawai'i through excellence in education, research, clinical care, and community service in perpetuity.

The department maintains a large, diverse faculty team who serve in numerous leadership capacities in our medical school and national and international clinical societies. Within this year, seven new faculty members have joined the department. This includes Dr. Kareem Khozaim, who fulfills the department's initiative to improve access to health care on the neighbor islands by expanding care to Hawai'i Island (Hilo). Four faculty members were promoted. Twelve faculty members are listed among Hawaii's "Best Doctors." Last academic year faculty, fellows, residents and students published 33 peer reviewed publications and presented original research with 26 peer-reviewed abstracts. Maternal Fetal Medicine faculty Dr. Stacy Tsai was awarded the prestigious NIH funded Reproductive Scientist Award. Drs. Tod Aeby, Mark Hiraoka, and Holly Olson are examiners with the American Board of OB/GYN, a national honor for educators in this field. Additionally, Dr. Ivica Zalud, Professor and Department Chair, was recognized as the 2017 Physician of the Year by the Hawai'i Medical Association (HMA) and elected as the only fellow from Hawai'i to the American Gynecological and Obstetrical Society.

The department provides a wide range of highly specialized women's health care in areas such as general obstetrics and gynecology, maternal fetal medicine, obstetric and gynecologic ultrasound, gynecologic oncology, urogynecology and pelvic reconstructive surgery, menopause, family planning, reproductive endocrinology and infertility, addiction medicine, and critical care. The clinical practice is a part of the University Health Partners of Hawai'i, JABSOM's faculty practice plan. The nationally recognized OB/GYN residency program, since 1948, is among the top 5% programs in the country. The department hosts two nationally recognized post residency fellowships in family planning and maternal-fetal medicine. The third year medical student clerkship and fourth year electives are consistently some of the highest rated rotations by students from JABSOM and those visiting from other medical schools. The department continues to serve communities in Wai'anae, Kalihi-Palama, Waimanalo, Lana'i and now in Hilo. In addition, our subspecialists serve Kaua'i, Maui, Lana'i and Hawai'i.

The department experienced major philanthropic investments; more than $8 million dollars were donated by its community and department members. Currently, the Ob/Gyn Department has two endowed chairs, five endowed professorships, and two endowed programs. Each philanthropic contribution plays a vital part in advancing medical education and research, community outreach, and professional development, in addition to supporting women's health care and the people of Hawai'i.

Pathology

The Department of Pathology faculty members continue to provide high quality anatomic and clinical pathology services to the state of Hawai'i at various practice sites. The department continues to play a role in JABSOM's teaching where faculty members serve as course directors, tutors, and pathology laboratory instructors in problem-based learning units. The department also facilitates medical student autopsy rotations, and third and fourth year laboratory elective rotations. Three residents graduated from the pathology residency program in June; all obtained competitive fellowship positions at University of California – Davis, University of California – Los Angeles, MD Anderson Cancer Center, and Vanderbilt University. The department welcomed three first year pathology residents for the 2017-2018 year. Residents have opportunities to work with faculty in research projects. Faculty members published 15 journal articles over the last year. Faculty members at the Blood Bank of Hawai'i presented at the Transfusion Medicine Symposium in May, which was highly valued by blood bank personnel, clinicians, and the community. Dr. Jane Uyehara-Lock is congratulated for completing the Professional Mentoring Skills Enhancing Diversity (PROMISED) Program at the University of Pittsburgh over the summer, earning a certificate in Research Leadership aimed at developing skills for mentoring diverse trainees pursuing biomedical research careers.

Pediatrics

The Department of Pediatrics continues to grow to meet the clinical service expectations of the community for specialty care with a safety net for all children throughout the state. Growth has included increasing partnerships within the community, including Queen's Health Care Centers, Kaiser Permanente, Tripler Amy Medical Center, and Shriners Hospitals for Children. Due to the organized system for pediatric care, the clinical learning environment for medical students, residents, and neonatology fellows remains strong. Ten JABSOM students chose a career in pediatrics in 2017.

In research, the Department of Pediatrics was awarded a National Institutes of Health grant: Hawai'i IDeA Center for Pediatric and Adolescent Clinical Trials (HIPACT). This opportunity supports an infrastructure in partnership with Kapi'olani Medical Center for Women & Children and Wai'anae Coast Comprehensive Health Center to make available clinical studies to improve the health of children in Hawai'i. As part of the program, faculty members will have opportunities to participate in professional development activities.

Psychiatry

The year 2017 was a positive year for the Department of Psychiatry. Among the faculty, two were promoted: Dr. Asad Ghiasuddin to Clinical Associate Professor and Dr. Susana Helm to Professor. Several faculty won important awards: Dr. Gretchen Gavero received the University of Hawai'i at Mānoa's (UHM) Chancellor's Citation for Meritorious Teaching; Dr. Jeanelle Sugimoto-Matsuda received the Outstanding Community Mental Health Leader award from Mental Health America of Hawai'i; and Dr. William Haning and Dr. Satoru Izutsu received the inaugural Judge James S. Burns Award for Community Service.

The department continued to cover high-volume, high-value clinical services in support of the clinical learning environment at the partner healthcare systems, including Queen's Health Systems/Queen's Medical Center, Department of Health Child and Adolescent Mental Health Division, Kapi'olani Medical Center for Women & Children/Kapi'olani Behavioral Health Services. The department expanded involvement with community sites and initiated new school-based contracts at Kamehameha Schools and the University of Hawai'i (UH) School of Nursing/Department of Education.

In medical student recruitment, approximately 14.3% of UH-JABSOM's graduating seniors chose psychiatry. This represents more than double the national average. This year, the department matched medical students into seven positions in general psychiatry and three in child and adolescent psychiatry.

In research, the department was productive with numerous peer-reviewed publications, national and international presentations, and extramural grants and contracts. See website for the department's list of publications and abstracts (http://blog.hawaii.edu/dop/research/publications-abstracts/).

Finally, through the generosity and diligent efforts of the people in the department and colleagues in the community, the *Walter F. Char, MD, John F. McDermott, MD, and Naleen N. Andrade, MD, Endowed Professorship in Psychiatry*, through UH Foundation, achieved the endowment level of endowed professorship.

Surgery

2017 was a year of continued growth and expansion for the UHM Department of Surgery. The department opened the University Health Partners of Hawai'i (UHP) outpatient clinic at Queen's Medical Center (POB 2, 207) in January, where Drs. Kenric Murayama, Dean Mikami, and Stacey Woodruff now see patients. The department's UHP outpatient clinic at Kuakini Medical Center experienced increased business with the addition of two new surgeons: Dr. Carl "Joey" Tadaki in late 2016; and Dr. Chad Cryer in September 2017. At Queen's Medical Center – West O'ahu, the department hired Dr. Irminne Van Dyken in July 2017 to serve as Director of Surgical Education. The department's over 40 compensated and over 300 noncompensated faculty members continue to support the academic mission of JABSOM by teaching medical students and residents.

The department's philanthropic efforts also continued to thrive in February 2017. With generous funding from an anonymous donor, the department is on its way to funding an endowed chair position named after past Department Chair Thomas Whelan. A Whelan Society was created and annually a prominent surgeon is invited to speak on a cutting edge topic. In November 2017, the first Whelan Visiting Professor was Dr. John Hunter, Chair of Surgery at Oregon Health & Science University, his topic was "Surgical Residency Redesign: Is It Time?"

In addition, the department hosted its very first Surgical Innovation, Technology, and Education (SITE) conference in February 2017, overseen by Dr. Mikami. Covering the latest in complex general surgery techniques, the conference is now an annual event. In February 2017, the department hosted its 5th biennial Cross-Cultural Health Care Conference, which included local (UH and JABSOM), national, and international experts in cross-cultural health care.

Tropical Medicine, Medical Microbiology, and Pharmacology

The Department of Tropical Medicine, Medical Microbiology, and Pharmacology has had a productive year for faculty and students in 2017. Tropical medicine PhD graduate, Glen Chew, received the 2017 UH Manoa Student Excellence in Research Award (Doctoral Level). Tropical medicine graduate faculty Dr. Richard Yanagihara was recognized as the Advancing Science in America Foundation Honolulu Scientist of the Year. Six faculty members received new or renewal NIH grants in 2017: Dr. Saguna Verma - R21 Zika Response grant; Dr. Lishomwa Ndhlovu -R21 on HIV glycomic interactions; Dr. Axel Lehrer - R01 grant on a thermostable trivalent filovirus vaccine; Dr. Mukesh Kumar - R21 grant for a guinea pig model of Zika virus disease; Dr. Bruce Shiramizu - R21 grant on anal neoplasia in HIV and HPV co-infected individuals; and Dr. Vivek Nerurkar - D43 grant to support the Northern Pacific Global Health Research Fellows Training Consortium. PhD student Liana Medina was awarded an NIH Minority Supplement Award to support her dissertation research on filovirus vaccines under the mentorship of Dr. Lehrer. Two undergraduate students participating in the Minority Health International Research Training Program; Michael Fernandez and Jovikka Antallan, received travel awards to attend a national conference in Arizona during which they both received outstanding research presentation awards. Postdoctoral fellow Dr. Wen-Yang Tsai received a travel award to present his Zika virus and dengue virus research at the annual American Society for Tropical Medicine and Hygiene meeting in November.

Tropical Medicine faculty and students have been active in community outreach. Drs. Kenton Kramer, William Gosnell, and De Wolfe Miller were appointed by Governor David Ige to the Rat Lungworm Joint Task Force, chaired by Dr. Kramer. Tropical medicine graduate students organized the Student Immunization Initiative (SII), which has spearheaded several projects to promote vaccination education and disease prevention in the community as well as health career recruitment events for middle school, high school, and undergraduate students and teachers. SII received a Student Equity, Equality and Diversity (SEED) Award and supplemental funding from the Pacific Center for Emerging Infectious Diseases Research which enabled 10 Tropical Medicine graduate students to visit Kalaupapa to experience and share the history of Hansen's disease in Hawai'i.

The Tropical Medicine Graduate Program graduated in the 2016-17 academic year six MS and seven PhD students. In the same year, the new, one-year Tropical Medicine Graduate Certificate program was awarded to three students.

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In What Ways are Hawaii's HIV Prevention Services Engaging Gay Male Couples and Using Technology?

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

Abstract

Partner-oriented services and Health Information and Communication technology (HICT) in the forms of mHealth (eg, smartphone applications), eHealth (eg, interactive websites), telemedicine, and social media play an important and growing role in HIV prevention. Accordingly, the present study sought to describe: (1) the primary and secondary HIV prevention services available in Hawai'i, (2) the prevention services that are available for gay male couples and partners, and (3) the prevention services that use HICT. Information about prevention services and use of HICT were obtained from websites and phone calls made to 19 organizations in the state, including the Hawai'i Department of Health. Overall, partner-oriented services were limited and only 1 couples-based service was currently being offered. Technology, namely social media, was used by 14 organizations, primarily to increase HIV awareness and advertise events. These findings may inform how best to adapt and better leverage the use of innovative technological tools to help expand access to HIV testing and counseling, sexual health education, and case management services for gay male couples and other MSM populations in the state.

Keywords

HIV prevention; men who have sex with men; gay male couples; technology; eHealth; mHealth; telehealth

Introduction

Epidemiology of HIV in Hawai'i

Since mandatory reporting of HIV and AIDS cases began in 1983 in Hawai'i, there have been a cumulative total of 4,779 HIV/AIDS cases.[1] Among the four counties in the state, Honolulu county — due to being the most densely populated – has the highest proportion of HIV/AIDS (73%).[1] Similar to the continental United States (U.S.), the majority of people living with HIV in Hawai'i are males (89%), between the ages of 25-44 years old (65%), and/or have been exposed through male-to-male sexual contact (71%) (ie, men who have sex with men [MSM]).[1]

The HIV epidemic in Hawai'i does differ from the continental U.S. with respect to race and ethnicity: a higher proportion of individuals who self-identify as Asian, Hawaiian or Pacific Islander, American Indian or Alaskan Indian, multiple races, or other races are affected by HIV in Hawai'i versus the U.S. generally.

Behavioral and Biomedical Approaches of HIV Prevention

Since the HIV epidemic began over three decades ago, a number of approaches have been developed to help prevent the acquisition and transmission of HIV across a wide variety of at-risk groups, including MSM. These prevention services can broadly be categorized as either primary or secondary prevention.

Primary prevention services are primarily for individuals who are HIV-negative and/or are unaware of their serostatus. These services consist of HIV education, condom distribution, syringe exchange, HIV testing and counseling, and referral and uptake of non-occupational post-exposure prophylaxis (nPEP) and/or pre-exposure prophylaxis (PrEP). Non-occupational PEP is a 28-day course of 3 antiretroviral medications that should be taken within 72 hours after a potential exposure to HIV.[2-4] In contrast, pre-exposure prophylaxis (PrEP) is a regimen of antiretroviral therapy (ART) (ie, Truvada) that is taken daily by those who are HIV-negative to prevent the acquisition of HIV. Efficacy trials have demonstrated that use of PrEP can greatly reduce the risk of sexual acquisition of HIV infection.[5-9] Since findings from these trials, the U.S. Food and Drug Administration approved Truvada for PrEP in 2012.[10]

Secondary prevention services are primarily for persons living with HIV/AIDS (PLWHA) and those newly diagnosed. These services include partner notification services, management of ART, case management, HIV counseling, and support groups. Partner notification is a free, confidential, and voluntary prevention resource to assist PLWHA with notifying their sex and/or injection drug use partners about a potential HIV exposure.[11] Once notified, partners are offered a variety of prevention services, which vary depending on their individual needs. HIV counseling for PLWHA can include discussion of sensitive issues, such as lack of social support, isolation, low self-esteem, and trauma associated with diagnosis. In case management, a case manager connects PLWHA with community resources for medical and dental care, health insurance programs, financial resources, food stamps, housing, and other support services.[12,

[13] Most importantly, case management is responsible for making sure individuals have access to an HIV doctor and ART.[12, 13] Support groups provide safe and confidential settings for PLWHA to connect with one another to obtain support about living with HIV, ranging from the changes associated with being diagnosed, their experiences with health and health care, to HIV-related stigma.[14]

How are Couple-focused Strategies Currently Used in HIV Prevention?

A burgeoning body of evidence has identified relationship partners as important influencers in promoting positive health behaviors and influencing health behavior change, including reducing HIV risk and onward transmission among MSM.[15] There is growing interest in providing HIV prevention services for gay male couples.[16] Couples' HIV testing and counseling (CHTC) is a testing method where gay male couples are counseled and receive their HIV test results together.[17] After a couple receives their results, counseling is provided based on partner serostatus and relationship characteristics.[17] CHTC is currently a CDC sponsored strategy for increasing HIV testing and linkage to care for gay male couples, and is currently offered throughout the U.S.[18] Previous research reported high willingness among MSM in same-sex relationships to use CHTC, if it were available to them.[19-21] In addition, the influence that relationship partners have with respect to the attitudes and uptake of a variety of available HIV prevention services is important to consider given the high proportion of MSM who acquire HIV within the context of a same-sex relationship. Although evidence is limited in Hawai'i, recent epidemiological estimates suggest between one- and two-thirds of MSM in the U.S. acquire HIV from their sex and romantic partners.[22, 23]

How is Technology Currently Used in HIV Prevention?

Health Information and Communication technology (HICT) is any form of technology associated with the internet, smartphone applications, computer applications, and social media that can be used for receiving and/or providing health care information.[24] eHealth, mHealth, and telehealth are specific forms of HICT that can be used to connect current and future patients with health care providers all over the world.[25]

A term, eHealth, coined to bridge the gap between technology and health care, provides health care that is accessible, entertaining, and made available in a variety of different environments, from homes to clinics.[26] Examples of eHealth services include, but are not limited to online consultations with a health care provider (eg, video-based portals), online health education programs, and programs which include a web-chat portal to allow patients to have a quick conversation with a nurse or physician without needing to make an in-person appointment. Within the context of HIV prevention, eHealth has been used to deliver web-based sexual health interventions to help reduce HIV risk among MSM.[27-31]

While eHealth focuses on larger intersections of technology and health, mHealth is the use of mobile communication, such as smartphone applications (apps) and SMS (short message service / text), to gain information or to access various health services.[25] For example, iPhone's Apple HealthKit app provides users with the ability to track their heart rate and eating habits with the option of enabling them to share this information with their health care provider.[32] In addition, apps for Facebook and Twitter often have advertisements regarding new health products as they come on the market. Also, mHealth can also be used in a variety of ways for HIV prevention. For example, mHealth has been used to link and engage newly diagnosed MSM into HIV care post diagnosis through the receipt of SMS and other confidential messages on social media.[33] Also, mHealth has been used to help bolster other aspects of HIV prevention, ranging from promotion of routine HIV testing[34, 35] to supporting ART adherence for viral suppression.[36]

Telemedicine is becoming widely used in a variety of places around the world, and is often referred to as "healing at a distance."[37] Telemedicine is often used to provide access to care and medical information when distance is a critical factor.[37] Examples of telemedicine may include a patient using email to describe symptoms to a medical provider, the use of videoconferencing to help providers located elsewhere to meet and discuss a case, or to provide counseling over the phone. With respect to HIV prevention, telemedicine has been used to provide therapy for aging MSM living with HIV,[38] and for HIV testing and counseling to gay male couples from the comfort of their homes.[39]

Specific Aims

In summary, there are a number of ways in which partner-focused interventions and technological tools, such as those of eHealth, mHealth, and telemedicine, could benefit the residents of Hawai'i in HIV prevention. However, it remains unknown which HIV prevention services in Hawai'i are available for gay male couples, as well as which ones leverage the use of HICT. In this descriptive, cross-sectional study, we sought to briefly describe the primary and secondary HIV prevention services currently available in Hawai'i and for which target populations, including MSM. We then assessed which of the prevention services are currently available for gay male couples, including whether services account for the influence that sex and romantic partners may have on an individual's prevention behaviors. Next, we assessed which of the prevention services use HICT, and in what specific ways. Lastly, recommendations are provided for how some of the current prevention services could be adapted for gay male couples and/or be provided through the use of technology in Hawai'i.

Methods

Five of the seven research team members collected data online from websites maintained by local community-based organizations (CBOs) and AIDS service organizations (ASOs), as well

as from the Hawai'i Department of Health (HDOH); phone calls were also made to the organizations if some data were not readily available on their website. Four of the five team members collected data for one specific county; the fifth member collected data about the HDOH. The data collection phase for this study occurred between September and November 2017. For each organization within a specific county, data collected were categorized by type of prevention service(s) (primary, secondary) provided, population(s) targeted (eg, MSM, gay male couples), and what types of technology and social media were used. Technology was defined as any use of social media, SMS/text message, mHealth, eHealth, and telemedicine. Once data were collected and organized into a table format, the lead and senior authors fact checked the data collected by visiting each organization's website and calling the organization.

Findings

Which Primary and Secondary HIV Prevention Services are Available in Hawai'i and for Whom?

Overall, nineteen organizations in the state provide primary prevention services (Table 1). The majority are available to the general population. However, some services appear to be targeted for at-risk MSM, PWID (persons who inject drugs), heterosexual women, and transgender individuals based on either the type of services provided (eg, syringe exchange program) or the content provided on the organization's website. All 19 organizations offer HIV testing and/or counseling. These organizations also offer additional services including HIV education, safe sex education, condom distribution, and STI testing. In regards to PrEP services, eight organizations provide PrEP services in Hawai'i; one in each county except for Honolulu County, which had five organizations. In addition, the HDOH Harm Reduction Services Branch provides a directory of PrEP providers across the state. Less commonly offered primary prevention services include safer sex kits (1 organization in Honolulu County and 1 organization in Maui County), and syringe exchange programs (1 organization in Hawai'i County, 2 in Honolulu County).

Among the secondary prevention services provided in the state (Table 1), HIV counseling was the most commonly offered service among organizations (n=9), with two offering it in Hawai'i County, six in Honolulu County, and 1 in Kaua'i County. Case management was the second most commonly offered service among organizations (n=5), with one organization offering it in Hawai'i County, two in Honolulu County, one in Kaua'i County, and one in Maui County. Partner notification services were limited across the state (n=4), with two organizations offering it in Honolulu, and one in Hawai'i and Maui Counties, respectively. Other secondary prevention services include ART/ HIV treatment service (n=5), housing assistance (n=4), support groups (n=3), and referral services (n=2).

Which Primary and Secondary HIV Prevention Services in Hawai'i are Available for Couples and/or Address the Influence of Partners?

Overall, no ASOs or CBOs in Hawai'i explicitly state that the HIV prevention services they provide are for couples. However, one organization offers a relationship empowerment program for heterosexual, lesbian, gay, bisexual, and/or transgender couples to increase partner communication and education about HIV prevention, including safer sex practices. Additionally, partner notification services are offered as part of secondary HIV prevention in four organizations across the state, with coverage in all counties except Kaua'i County. According to one organization, these services are offered to help prevent onward transmission of HIV and to help partners get earlier access to individualized counseling, HIV testing, medical treatment, and other prevention activities.[40]

Which Prevention Services Use Technology, and in What Ways?

Many organizations use social media to increase awareness of services they offer and to promote events in their communities. Specifically, 15 organizations in the state use social media, with Facebook being the most popular platform used, followed by Twitter, Instagram, and mobile dating apps. For example, one organization uses Facebook and Twitter to raise awareness about HIV related topics and inform the community about events whereas another organization uses a variety of social media platforms, such as Instagram, YouTube, and dating/sex apps, to provide information about their free testing services, PrEP, and case management. Lastly, one organization uses public service announcements on the radio to raise awareness about HIV prevention and their community events.

With respect to mHealth, two organizations use an SMS/text system. One organization uses a text system to provide clients with appointment reminders, while the other organization uses a text system for test result notifications. Based on the information provided by the organizations' websites, no services were being offered via eHealth or telemedicine.

Recommendations for How Current Prevention Services Could be Adapted for Gay Male Couples

Organizations that offer couple-focused methods of prevention may better meet the HIV prevention needs of gay male couples in Hawai'i. There are several examples in which prevention services could be adapted to better serve this particular population in the state. For example, ASOs and CBOs could consider offering CHTC in addition to individual HIV testing and counseling. With respect to HIV counseling and case management services, ASOs and CBOs should consider involving and including sex and romantic partners of PLWHA. Previous research has found that social support received from sex and romantic partners helps

with secondary HIV prevention efforts, namely ART initiation and adherence,[41,42] and thus helps to reduce transmission within the relationship.[43,44] As such, organizations may want to consider how best to involve sex and romantic partners in these services to help their clients achieve better HIV care-related outcomes.

To begin to consider offering these services for gay male couples, organizations must first identify what training, personnel, and other resources they would need to offer CHTC[45] and/or involve sex and romantic partners in HIV counseling and case management services.

Recommendations on How Current Prevention Services Could be Adapted to Use Other Forms of Technology

The potential use for technology in HIV prevention is growing because it can help provide: (1) services beyond clinical settings; and (2) help alleviate potential logistical barriers to primary and secondary services for those living in Hawai'i. For instance, individuals living in rural areas of the state who have access to the Internet and/or a smartphone could benefit by having HIV prevention services available to them through a variety of technological tools. Moreover, some individuals may feel uncomfortable accessing services in-person or close to their residence due to stigma pertaining to their sexuality and/or HIV serostatus. Thus, these individuals could also benefit from accessing prevention services via mHealth, eHealth, or telemedicine. Although several examples of HIV prevention and sexual health programs that use eHealth are currently in development in the U.S. (according to NIH RePORTER: https://projectreporter.nih.gov/reporter.cfm), we describe two examples of nation-wide, online pilot programs that have reported promising preliminary results. These programs may soon become available to a variety of MSM populations throughout the U.S. once they are found to be efficacious. These examples also illustrate novel ways to enhance HIV prevention and sexual health education online for two different populations of MSM, which may appeal to those living in Hawai'i.

The Male Couples Agreement Project (MCAP) is an eHealth toolkit intervention for gay male couples with a foundation in relationship science including sexual agreements, sexual health education and HIV prevention. The premise of the toolkit is to provide gay male couples with informational modules about sexual health and HIV prevention strategies (eg, testing, PrEP), and help them form and adhere to a sexual agreement that meets the needs of both men of the couple. Sexual agreements are the explicit conversations that couples have that lead them to creating a mutual decision about which sexual and other relational behaviors are allowed to occur within their relationship and if applicable, with outside sex partners.[46,47] A pilot randomized controlled trial was conducted to assess the feasibility that couples who received the toolkit would be more likely to reduce their HIV risk compared to couples who did not receive the toolkit (control arm). Findings from this study indicate that gay male couples who received the toolkit were more likely to form and adhere to their sexual agreement and were also more likely to not engage in condomless anal sex with casual sex partners, thereby reducing their risk for HIV compared to couples in the control arm.[48]

Another on-going eHealth project is called the myDex Project: A six session (10 minute per session) sexual health education program that provides interactive storytelling, case scenarios, information about HIV risk reduction strategies, graphics and videos for young MSM (YMSM).[49] The overarching goals of myDex are to increase HIV testing, and decrease sexual risk behaviors (eg, condomless sex) and the number of sexual partners among YMSM.[49] Enrollment for this project is ongoing.

These two examples provide ideas of how eHealth could help expand current primary prevention services in the areas of sexual health and HIV education with current in-person HIV prevention efforts. However, acceptability of these two programs among MSM and male couples in Hawai'i should be explored given the racial and ethnic differences of the HIV epidemic between the state and the rest of the continental U.S.

Conclusion

A variety of primary and secondary HIV prevention services are offered throughout Hawai'i. Some prevention services are limited, such as partner-notification, and may benefit from expansion. In addition, other services could be offered to gay male couples and/or through the use of technology. These changes could help expand prevention services to reach additional at-risk individuals throughout the state, especially to those who are located in more rural areas. However, ASOs and CBOs must first consider their ability and capacity to make such changes in the services they provide. Further, data are needed to assess whether MSM in Hawai'i are interested in services that are relationship-oriented and/or are offered through a technologically-based platform. While the use of technology for HIV prevention may help reduce geographical or logistical barriers to healthcare[50] and alleviate privacy concerns for Hawai'i residents, barriers to using these technologies (eg, language, familiarity, and access to technologies) must first be considered and addressed before implementation.

Table 1. HIV Prevention Services in Hawai'i

	Primary HIV Prevention services[a]	Secondary HIV Prevention services[b]	Target Population(s)[c]	Technology/social media use for services
Hawai'i County - Big Island (Hawai'i Island)				
1) Hamakua-Kohala Health Center (http://www.hamakua-health.org/; data extracted on 11/3/17)	• HIV testing and counseling • STI testing and counseling	• HIV counseling • STI treatment		• Facebook used to provide organizational information (not specific to HIV services) • Text reminder system used for appointment reminders
2) Hawai'i Island HIV/AIDS Foundation (HIHAF) (http://hihaf.org/; data extracted on 11/3/17)	• HIV testing • PrEP referral • STI testing • Syringe exchange program	• Case management • Counseling and referral • Housing assistance • Job placement assistance	• PWID	• Facebook used to increase awareness of HIV and community events
3) Waiakea Health Center (Hawai'i District Health Office) (http://health.hawaii.gov/harmreduction/where-to-get-tested/hawaii-island-testing-resources/; data extracted on 11/3/17)	• Condom distribution • Free anonymous HIV testing in correctional facilities • HIV testing • STI testing	• Partner notification services • STI treatment		
Honolulu County				
4) Hawai'i State Department of Health (HDOH) - Harm Reduction Services Branch (http://health.hawaii.gov/harmreduction/hiv-aids/; data extracted on 11/3/17)	• PrEP referral	• Partner notification services		• Contract with ASOs for out reach through social media • Use social media in partner services under DOH policies
a)HIV Case Management and Support Services (http://health.hawaii.gov/harmreduction/hiv-aids/hiv-programs/hiv-case-management-support-services/; data extracted on 11/3/17)		• a) Access to medical care • a) Medical case management • a) Specialized case management • a) Social services case management • a) Client support services	• a) PLWHA	
b) HIV Medical Management Services including Hawai'i Insurance Continuation Program (H-COBRA); Hawai'i Seropositivity and Medical Management Program (HSPAMM); HIV Drug Assistance Program (HDAP) (http://health.hawaii.gov/harmreduction/hiv-aids/hiv-programs/hiv-medical-management-services/; data extracted on 11/3/17)		• b) H-COBRA: Assistance with health insurance premiums for HIV+ • b) HSPAMM: Link-to-care services (provides HIV+ individuals with access to routine lab tests and medical care) • b) HDAP: Treat HIV infection, opportunistic infections, HIV-associated anemia and wasting, co-occurring conditions, and treat or improve HIV side effects, Prevention for HIV positive individuals (P4P) • b) Referrals	• b) PLWHA	
c) STD/AIDS Education and Risk Reduction Services (http://health.hawaii.gov/harmreduction/hiv-aids/hiv-programs/stdhiv-education-and-risk-reduction-services/	• c) HIV testing, education, counseling, and referrals • c) Syringe exchange • c) STI referrals for screening and treatment • c) Prevention case management	• c) PLWHA • c) MSM • c) MSM who inject drugs • c) PWID • c) At-risk women • c) Transgender men and women at risk		
d) PrEP Provider Directory (https://health.hawaii.gov/harmreduction/files/2015/01/HIV-PrEP-Provider-List-March-2017-Final.pdf; data extracted on 11/3/17)	• d) PrEP Provider Directory across the state	• d) MSM • d) MSM who inject drugs • d) PWID • d) At-risk women • d) Transgender men and women at risk		

Table 1. HIV Prevention Services in Hawai'i (continued)				
5) The Community Health Outreach Work to Prevent AIDS Project (The CHOW Project, locations on Maui, Kaua'i, Hawai'i Island) (http://www.chowproject.org/about-us.html -- will merge with the Life Foundation; data extracted on 11/3/17)	• Condom distribution • HIV testing, education, and referrals • Syringe exchange program	• HIV counseling • Drug assistance services	• PWID	• Facebook used for outreach and to increase awareness of HIV and community events
6) Diamond Head Health Center (Part of HDOH) (http://health.hawaii.gov/harmreduction/where-to-get-tested/oahu-testing-resources/; data extracted on 11/3/17)	• HIV testing and education • STI testing and education	• HIV counseling • Partner notification services • STI treatment services • STI counseling	• PLWHA and their partners	• Text or email notification to receive test results
7) Kaiser Permanente Moanalua Medical Center (https://healthy.kaiserpermanente.org/health/care/!ut/p/a0/FchBCoMwEAXQs3iA8KGISHbSdcVN0WQ3ZIIONBMxQa9fXb4HjwVe6ZSVqmSl320XotZ42FK5GFI2m5yGhAtmePj9oDURnGYTKGzxOc0cheHmabL2M7av_t11X-wp9dfQNH_KzV0i/; data extracted on 11/3/17)	• HIV testing • Health and wellness information online • PrEP – on site • Safer sex practices	• HIV counseling • Medication (ART)	• Kaiser members	• Facebook used to provide organizational information (not specific to HIV services)
8) Kalihi-Palama Health Center (http://www.kphc.org/patient/medical/ and http://www.kphc.org/patient/health-education/family-planning/; data extracted on 11/3/17)	• HIV testing • STI prevention presentations • STI testing	• HIV treatment • STI treatment		• Facebook used to provide organizational information (not specific to HIV services)
9) Kokua Kalihi Valley Comprehensive Family Services (http://www.kkv.net/index.php/services-and-activities; data extracted on 11/3/17)	• Condom distribution • HIV testing and counseling • HIV/AIDS prevention and education • STI prevention and education • STI testing • Safer sex education	• HIV counseling • Safer sex education		• Facebook used to provide organizational information (not specific to HIV services)
10) Life Foundation: HIV Prevention Department (https://www.lifefoundationhawaii.org/gettestedsub; data extracted on 11/3/17)	• Condom distribution • HIV testing and counseling • HIV prevention and education • PrEP services • Safer sex kits	• Case management • Client support: support groups, emergency food pantry, hygiene items • HIV counseling • Housing assistance	• Individuals at-risk for acquiring HIV • PLWHA • Transgender men and women	• Facebook, Instagram, Twitter, and YouTube used to increase awareness of HIV and community events
11) Planned Parenthood - Honolulu Health Center (Another location on Maui) (https://www.plannedparenthood.org/get-care/our-services/hiv-services; data extracted on 11/3/17)	• Condom distribution • HIV test education • HIV testing and counseling • PrEP – on site	• HIV counseling • HIV treatment referrals • STI Treatment services	• HIV-positive individuals and their partners	• Facebook, Instagram, Twitter, YouTube, and Tumblr used to provide organizational information (not specific to HIV services in Hawai'i)
12) Waianae Coast Comprehensive Health Center (http://www.wcchc.com/Contact/Waipahu-Family-Health-Center-Primary-Care; data extracted on 11/3/17)	• HIV testing and counseling • HIV/AIDS prevention and education • PrEP – on site • STI testing and counseling • Safer sex education	• HIV treatment and counseling • STI treatment • Safer sex education		• Facebook and Instagram used to provide organizational information (not specific to HIV services)
13) Waikiki Health (http://waikikihc.org/patients/services/hiv-services/; data extracted on 11/3/17)	• Health education for HIV/AIDS risk factors • HIV/AIDS testing • HIV/AIDS prevention • HIV/AIDS Early Intervention Services (HEIS) Outreach Program	• Treatment • Medication counseling • Nutrition counseling • HIV/AIDS Early Intervention • Services (HEIS) Outreach Program		• Facebook and Twitter used to increase awareness of HIV and community events
14) Waimanalo Health Center (http://waimanalohealth.org/becoming-a-patient; data extracted on 11/3/17)*	• Family planning to discuss STI prevention • HIV testing (refer to DOH) • STI testing	• Follow up with providers (referrals for HIV-positive patients to Infectious Disease Specialist for follow-up and treatment)		• Facebook and Instagram used to provide organizational information (not specific to HIV services)

Table 1. HIV Prevention Services in Hawai'i				
Kaua'i County				
15) Kaua'i Community College - Wellness Center (Family Planning Health Clinic) (https://kauaiccwc.weebly.com/; data extracted on 11/3/17)	• HIV testing and counseling • STI testing	• Referral to Mala Pono Health Services if test is positive	• College students • Faculty • Staff • Special populations (family planning for teens, uninsured, and sexual assault victims)	• Facebook used to provide organizational information (not specific to HIV services)
16) Kaua'i District Health Office (Part of HDOH - includes 5 testing centers) (http://health.hawaii.gov/harmreduction/where-to-get-tested/kauai-testing-resources; data extracted on 11/3/17)	• HIV testing • STI testing			
17) Malama Pono Health Services (http://mphskauai.org; data extracted on 11/3/17)	• Community HIV/AIDS education program • Community STI education program • Condom distribution • HIV testing • PrEP – on site • Relationship skills – Love notes • STI testing	• Case management treatment referrals • Drug assistance program • Food pantry • HIV counseling • Housing assistance • STI treatment	• MSM • Partners/couples	• Facebook, dating apps (Grindr, Scruff), and Craigslist used to increase awareness of HIV and community events • Public service announcements via live radio announcements
Maui County				
18) Maui AIDS Foundation (http://www.mauiaids.org/; data extracted on 11/3/17)	• Condom distribution • HIV 101 education • HIV testing and counseling • STI testing • PrEP Clinic – on site • Safer sex kits	• Case management • HIV treatment • HIV-positive social support group • Medical assistance • Partner notification services are referred to Maui DOH • Prevention for HIV positive individuals (P4P) • Food pantry • Housing assistance • Safer sex kits		• Facebook, Twitter, Instagram, YouTube, Tumblr, and Snapchat used for STI and HIV testing information, awareness, and events • MSM dating apps used for HIV testing services, test scheduling, and information on PrEP and case management • Craigslist used for free testing
19) Maui District Health Office (Part of HDOH - includes 2 locations) (http://health.hawaii.gov/maui/hiv-testing/; data extracted on 11/3/17)	• Condom distribution • HIV testing and counseling • STI testing and counseling	• HIV treatment referral • Partner notification services		

Data represented in this table characterizes HIV prevention services in four counties of Hawai'i and were collected from organizational websites; and via phone call for some of the organizations.

HEIS services include education, risk factors, and prevention of HIV/AIDS, including case management.

[a]Services target individuals of HIV-negative or unknown serostatus, as well as at risk groups, such as MSM, PWID, transgender men and women, and heterosexual women.

[b]Services target individuals living with HIV and recently diagnosed

[c]Specific target populations other than PLWHA and individuals of HIV-negative or unknown serostatus

ART represents antiretroviral therapy
ASO represents AIDS Service Organization
MSM represents men who have sex with men
P4P represents prevention for positives
PLWHA represents persons living with HIV/AIDS
PrEP represents pre-exposure prophylaxis
PWID represents persons who inject drugs
STI represents sexually transmitted infection

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THE WEATHERVANE

RUSSELL T. STODD MD; CONTRIBUTING EDITOR

PLEASE MR. TRUMP FORGET THE TWITTER.

Our President who frequently has his foot in his mouth, made the statement that women who undergo abortion should "face some sort of punishment." He was greeted with widespread condemnation. He backed off and then released a statement that the doctors who perform these services are the ones who should be punished. Subsequently, he revised his remarks to state that if Congress were to pass legislation making abortion illegal, and the federal courts upheld the bill, the doctor or the one performing the services should be punished. Our leader failed to note the issue was decided by the Supreme Court three and one-half decades past with the landmark decision Roe v Wade. The court recognized that a human being has a right to one's own body.

THE VACCINATION NEEDLE IS HEADED OUT.

DIY (Do it yourself) patch vaccinations are likely on the way. The patch eliminates the need for sterile needle disposal, does not require refrigeration, and flu vaccine is stable at room temperature for at least a year. A study published in Lancet on flu vaccines nearly all users described the experience as painless. One side of the patch looks like a regular bandage. The other side holds a small array of 100 hard cone-shaped micro-needles, each about a half millimeter tall, made of polyvinyl alcohol, sugar and vaccine. When the bandage is pushed into the back of the wrist, the micro needles penetrate the outer layer of skin and dissolve. Regardless of how the vaccine is given the mild side effects remain the same, fatigue or headache and occasional nausea. The patch could help with mass vaccination campaigns in countries with limited resources and minimally trained personnel. A similar program for polio eradication efforts using a patch with polio vaccine in planned.

FIRST I TELLS THEM. THEN I TELLS THEM WHAT I TOLD THEM. THEN I TELLS THEM AGAIN.

No matter how often the warning message comes through the media, or directly from the eye surgeon, too many people still stare at an eclipse. In New York, about 22 people came into the Eye and Ear Infirmary after the event worried that they had stared at the sun without proper protection. Among them was a young woman who had a "hole in my vision." She told the doctors she had viewed the eclipse for six seconds or so without any protection and then, using borrowed glasses watched it for 15 or 20 seconds. To define the damage, Dr. Deobhakta and his colleagues used a new technique called adaptive optics scanning which gives unusually clear and previse view of retinal cells. They could see the lesion resembled the solar rim during the partial eclipse. It's an amazing leap forward in imaging where one can see individual photo receptors that were damaged in that pattern.

TOO MUCH FACEBOOK? WHAT IS NEEDED IS MORE FACEBOOK!

A downside admission on Facebook, Inc. acknowledged that social media can be harmful to mental health. Several former executives raised questions about the platform's imprint on the world. Originally Facebook was offered as a way for families and friends to maintain contact with pictures of newborns, and small children and share material of mutual interest. Now their own top researcher pointed to external studies showing the negative effects of passive use of social media sites to read news but not interact with anyone. Facebook said the solution to mental malaise was more Facebook. The claim is that more active use could improve a person's mood and well-being. Their research and other academic studies suggest it's about how you use social media that matters. This downside admission by Facebook is a turnaround from previous criticism that was ignored until research revealed that Facebook was connected to negative feelings.

THESE CARS ARE ABOUT TO HIT THE ROAD WITHOUT ANY RULES.

Federal auto safety regulators are struggling with approval of automated-driving technology before the vehicles are on the street. Existing motor vehicle safety rules don't address autonomous cars, so regulators have no authority to obstruct them. That absence allowed Tesla Motors Inc. to roll out its so-called Autopilot automated driving system via a software update to many of its electric vehicles. A fatal crash in May involving the system gave regulators an opportunity to scrutinize the technology. There is no express prohibition of autonomous vehicles in federal safety standards according to Anthony Foxx, Secretary Department of Transportation. He offered that US regulators may soon demand a voice in the issue. A pre-market approval process could slow the adoption of driver-less technology.

HOW BRAIN-EATING AMOEBAS REALLY KILL.

On July 9, just a few days after swimming in Minnesota's Lake Minnewaska, a fourteen year-old girl was dead. Doctors believe the culprit was the water-dwelling Amoeba *Naegleria fowleri*. Most people know it by its other name, the brain eating amoeba. Right out of horror films, the amoeba crawls up the nose to the brain where it wreaks havoc, ultimately killing 97% of its victims. The amoeba thrives in freshwater and causes numerous deaths in Pakistan. Only 133 cases were reported in the United States from 1962 to 2014 according to the Centers for Disease Control and Prevention. Dr. Abdul Mannan Baig of Aga Khan University in Karachi, Pakistan, where numerous infections have been reported thinks that the death is actually an "inside job" caused by the immune system's attempt to fight the invader. When *N. fowleri* attacks the brain, it sets off a cascade of inflammatory responses that lead to dangerous cerebral edema and death.

ADDENDA

- Accident report – 75% of industrial accidents happen to people who skipped breakfast that day.
- Of all the lakes in the world, over half are in Canada.
- Classical music is music written by famous dead foreigners.
- I had a nest egg, but I lost it gambling. I was betting I'd be dead by now.
- My wife doesn't understand pornography. She's always fast-forwarding to get the story.
- The hands on my biological clock are giving me the finger.
- Pregnancy is amazing. To think you can create a human being with just the things you have around the house.

ALOHA AND KEEP THE FAITH rts

(Editorial comment is strictly that of the writer.)

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