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# Neuropsychological test performance of Hawai'i high school athletes: Hawai'i ImPACT normative data

William T. Tsushima PhD; Ross Oshiro MS; and Daniel Zimbra BA



William T. Tsushima PhD



Ross Oshiro MS

#### **Abstract**

**Objective:** Establishing normative data of the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) performance of high school athletes in Hawai'i.

**Study Design:** Pre-season ImPACT testing was performed on 751 participants in football, baseball, basketball, soccer, volleyball, softball, and track from 4 Oahu public high schools. The ImPACT composite scores included measures of Verbal Memory, Visual Memory, Processing Speed, and Reaction Time. The descriptive statistical data collected were the group means, standard deviations, standard errors of measurement, distribution of scores and percentile ranks of (1) 262 boys ages 13 to 15; (2) 297 boys ages 16 to 18; and (3) 192 girls ages 13 to 18.

Results: The means and standard deviations of the 4 ImPACT composite scores for the 751 student-athletes in Hawai'i were similar to the ImPACT scores obtained from a master database of ImPACT test results. Although differences between the Hawai'i and mainland data were nonsignificant, there appeared to be a trend revealing somewhat lower scores in the Hawai'i sample of athletes.

**Discussion:** The similarity in ImPACT test performance of Hawai'i high school athletes as compared to the mainland normative data provides support for the applicability of this computerized neuropsychological battery in Hawai'i. However, in view of a trend reflecting slightly lower ImPACT scores among Hawai'i participants, the use of the normative data produced by this study may be desirable in assessing Hawai'i high school athletes.

#### Introduction

The diagnosis and treatment of head injuries sustained in athletic activities have drawn increasing attention in recent years. Annually an estimated 300,000 mild traumatic brain injuries (MTBI) occur in sports events. At the high school level alone, an estimated 62,000 varsity athletes sustain an MTBI each year, of which about 63% are football players. The obvious seriousness of the impact of closed head injuries, such as impaired cognitive and emotional functioning, calls for improved methods of assessing the neuropsychological sequelae of sports-related concussions.

In the late 1990s, researchers at the University of Pittsburgh Medical Center, as part of their work with the Pittsburgh Steelers football team concussion program, developed a reliable, sensitive and practical approach to the neuropsychological assessment of MTBI. Instead of the labor intensive conventional paper-and-pencil neuropsychological test instruments, the research team constructed a computerized neurocognitive assessment method, referred to as ImPACT (Immediate Post-Concussion Assessment and Cognitive Testing), that evaluates verbal and visual memory, processing speed, and reaction time.<sup>3</sup> Computerized neuropsychological testing provides a relatively brief (20 to 30 minutes), cost-efficient evaluation with clinically useful information for the management of head injured athletes.

A growing body of research attests to the reliability and validity of ImPACT in the neuropsychological evaluation of sports-related concussion.<sup>4-6</sup> Currently, ImPACT is utilized by over 125 Division I-A and I-AA colleges, over 300 high schools across the country, as well as the majority of National Football League teams, and professional motor sports participants.<sup>7</sup>

Several high schools in Hawai'i have begun to utilize the ImPACT neuropsychological test battery, employing the descriptive statistics recommended by the authors. 8,9 The present use of the ImPACT presumes that the statistical data and norms obtained by the test developers are applicable to all high school athletes in the United States, as research to challenge this presumption is non-existent. Indeed, despite the growing number of research reports on the ImPACT, the influence of factors such as geographic region or ethnic minority membership on ImPACT test performance has not, to date, been examined.

A number of studies have demonstrated that ethnic minority individuals score more poorly on cognitive tests, <sup>10,11</sup> although the specific effects of culture and bilingualism on standardized tests scores are not clearly understood. <sup>12</sup> Thus, when such scores are relied upon to infer neuropsychological impairment in a minority person based on inappropriate norms, the consequence could be an overestimate of cognitive deficits. <sup>13,14</sup> In sports, false positive errors may result in loss of valuable game time, possible harm to college scholarship opportunities, and emotional losses for the student-athlete.

The athletes in Hawai'i high schools represent a racially diverse Pacific Islander population, including

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Correspondence to: William T. Tsushima PhD Straub Clinic & Hospital 888 South King Street Honolulu, HI 96813 Ph: (808) 522-4521 Fax: (808) 522-3526 Email: wtsushima@straub.net Caucasians, Polynesians, and Asians, as well as Hispanics and African Americans. Normative data that reflect the unique racial, ethnic and cultural backgrounds of the Hawai'i population would appear to be a more relevant reference source than statistical data obtained on the mainland United States.

In 1997 a panel of neurologists and neuropsychologists convened to address issues in sports-related concussion. The panel specifically promoted the establishment of databases for neuropsychological assessments instruments, like ImPACT, and further recommended the investigation of the effect of cultural factors on the neuropsychological test performances of school athletes. The purpose of this research is to establish Hawai'i-based norms by analyzing the ImPACT scores of student-athletes from 4 O'ahu public high schools. Present interpretation of ImPACT test results in Hawai'i assumes that scores obtained with a Pacific Islander population are comparable to data from the present national normative sample. If the Hawai'i ImPACT data deviate from the national norms, then the use of normative standards developed by this research should be considered when interpreting the ImPACT scores of Hawai'i high school athletes.

#### **Methods**

#### **Participants**

The study, in a retrospective archival search, obtained the ImPACT test results of 751 consecutive student-athletes (559 boys, 192 girls), who were healthy at the time of their testing. The athletes were from 4 public high schools on Oʻahu.

The average age of the total sample was 15.91 years (SD=2.04), and 207 (27.6%) of the subjects reported at least one previous concussion. The largest portion of the athletes was football players (47.9%). Other represented sports included basketball (8.4%), baseball (4.1%), soccer (0.8%), softball (0.3%), track (0.8%), volleyball (0.7%), wrestling (9.7%), and "others" (3.6%).

The student-athletes completed an average of 9.40 years (SD=1.96) of education.

For this study, the participants were placed in the following groups: Boys ages 13 to 15, boys ages 16 to 18, and girls ages 13 to 18. The mean age of each group was boys 13-15 (M=14.73, SD=1.78), boys ages 16-18 (M=16.87, SD=1.39, and girls 13-18 (M=15.99, SD=2.6). The mean years of education of each group were 8.42 (SD=1.59), 10.32 (SD=1.82), and 9.47 (SD=2.02), respectively.

#### Materials and Procedure

The participants were administered the ImPACT neuropsychological test battery<sup>3</sup> as part of an ongoing program establishing baseline or pre-injury neuropsychological test data to assist the athletic department staff in making return-to-play decisions after the occurrence of a sports-related concussion. Data were also collected regarding the athlete's concussion history.

The computerized neuropsychological test was administered to each athlete by an athlete trainer trained in the administration of ImPACT. Version 2.0 of ImPACT consists of 6 individual test modules that measure different cognitive abilities. The 4 standard ImPACT composite scores were used for this study, including Verbal Memory, Visual Memory, Processing Speed, and Reaction Time.

#### **Statistics**

Descriptive statistics including means, standard deviations, and standard error of measurement were obtained for each of the four ImPACT composite scores (Verbal Memory, Visual Memory, Processing Speed, and Reaction Time) for the 3 groups of athletes. In addition, the distribution and percentile ranks of the composite scores for each group were calculated.

#### Results

The means (and standard deviations) for each of the 4 ImPACT composite scores of the entire group of 728 athletes were as follows: Verbal Memory 82.49 (9.83), Visual Memory 70.49 (13.36), Processing Speed 34.94 (8.29), and Reaction Time 0.60 (0.10). These scores are very similar to those in the study by McClincy, Lovell, Pardini, Collins, and Spore, 5 who reported the following means (and standard deviations) of 104 athletes: Verbal Memory 85.75 (8.59), Visual Memory 74.04 (13.82), Processing Speed 35.05 (6.90), and Reaction Time 0.57 (0.08).

The means, standard deviations, and standard errors of measurement for the 4 ImPACT composite scores of each of the 3 subgroups of athletes are presented in Table 1.

The Impaired classification, defined as scores < 1.9 percentile rank, are presented in Table 2 for the present sample and the ImPACT normative sample. Almost without exception the Hawai'i cutoff scores identifying "impaired" performances were lower than the cutoffs in the national normative sample. Thus, the classifying of "impaired" scores would vary, depending on the use of local norms versus norms obtained on the Mainland.

Because of space considerations, the distribution and percentile ranks of the composite scores for the 3 groups of participants are not presented in this report, but can be made available by contacting the first author.

#### **Discussion**

The purpose of this research was to examine the test scores of ImPACT, a computerized neuropsychological test battery, when administered to high school athletes in Hawai'i. The results revealed that the ImPACT composite scores of a large sample (n = 751) of Hawai'i high school athletes were similar to those of mainland high school athletes (n = 424), and tentatively support the use of ImPACT in Hawai'i high schools. The present findings were consistent with previous investigations in Hawai'i assessing the applicability of widely used neuropsychological test batteries, the Halstead-Reitan Neuropsychological Battery and the Luria-Nebraska Neuropsychological Battery. <sup>16,17</sup>

A trend revealing slightly lower ImPACT scores among Hawai'i participants was not unexpected. Past research suggests that on many cognitive measures, ethnic minority individuals perform relatively poorly, and are much more likely to be misclassified as impaired than are Caucasians. Using the lower cutoff scores from this study to identify an impaired (< 1.9 percentile rank) performance, there would be fewer athletes identified as impaired than if national cutoff scores were used. However, at this nascent stage of employing the ImPACT, it is probably prudent to consider both the national normative data along with the norms obtained in this research when evaluating a head-injured Hawai'i student-athlete.

Discussion of the implications of these results must consider the limitations in the data collected. The raw data from the mainland norms were not available, thus, a direct statistical comparison between ImPACT scores of the Hawai'i participants and the mainland normative sample was not possible. At best, we were only able to make visual comparisons between these sets of data, in which considerable similarity in ImPACT means and standard deviations was noted.

In this study, the Hawai'i participants were grouped as a single sociocultural entity. A more informative investigation of the effects of ethnicity would identify subgroups of Pacific Islanders, such as those of Polynesian, Caucasian, Asian, African, and Hispanic backgrounds, which was beyond the scope of the present research. The present study raises awareness that diversity is a significant factor in our country that needs to be considered when employing psychometric tests.

Computerized testing, like ImPACT, is useful as a quick, easy to administer neuropsychological measure of head trauma effects, but it is not a substitute for comprehensive neuropsychological testing that consists of a broad battery of test instruments and takes several hours of one-to-one examination. The proper use of ImPACT requires specialized training and experience in clinical neuropsychology, as well as familiarity with the various ImPACT neuropsychological scores. Finally, it should be stressed that the proper evaluation of a head injured high school athlete involves an effective neuropsychological assessment within the context of a multidisciplinary effort headed by the team physician and including the athletic trainer, a neurological consultant, and other sources of clinical data, e.g., neurodiagnostic tests.

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Table 1.— Means, standard deviations, and standard errors of measurement of the three groups of athletes.

	Boys 13-15		Boys 16-18			Girls 13-18			
	М	SD	SEM	М	SD	SEM	М	SD	SEM
Verbal Memory	80.66	10.29	0.64	81.93	11.71	0.68	84.98	8.59	0.62
Visual Memory	70.12	13.54	0.84	72.02	14.95	0.87	70.99	13.14	0.95
Processing Speed	31.18	8.39	0.52	34.83	9.21	0.54	35.35	7.52	0.54
Reaction Time	0.61	0.12	0.01	0.58	0.12	0.01	0.59	0.08	0.01

Table 2.— Impaired\* classification cutoff scores for composite scores of the three groups of athlete.

Age Groups	Verbal I	Memory	Visual Memory		Processing Speed		Reaction Time	
	Hawaiʻi	Norms	Hawaiʻi	Norms	Hawaiʻi	Norms	Hawaiʻi	Norms
Boys 13-15	≤57	≤63	≤45	≤49	≤ 13.6	≤16.2	≤.86	≤.76
Boys 16-18	≤55	≤68	≤37	≤51	≤10.2	≤26.4	≤.81	≤.74
Girls 13-18	≤68	≤68	≤43	≤49	≤19	≤18.9	≤.79	≤.75

\*Impaired = < .19 percentile rank

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## Initial Antihypertensive Prescriptions, Switching Patterns and Adherence Among Insured Patients in Hawai'i

Kikikipa Kretzer PhD; Deborah Taira Juarez ScD; and James Davis PhD

#### **Abstract**

**Purpose:** Practice patterns were investigated for an insured population to determine if prescribing patterns, switching, and relative adherence by drug class for first-line antihypertensive medications adhered to national guidelines.

**Procedures:** Drug use was obtained from pharmaceutical claims. Prescriptions were categorized into 6 drug classes for analyses. Adherence with antihypertensive medications was based on a medication possession ratio or 0.8 or greater. For the analyses, 28,073 patients were categorized into groups: hypertension alone, hypertension plus diabetes, and hypertension plus congestive heart failure. Patient and physician characteristics affecting prescribing, switching, and adherence were analyzed using multivariable logistic regression analysis.

**Findings:** Thiazide diuretics were used and adhered to less often, despite national guideline recommendations. New drug classes were used more highly.

**Conclusions:** Inconsistency exists between guidelines and practice as older, cheaper drugs were used less and more expensive drugs were used more often with better adherence.

#### Introduction

Hypertension as a leading medical risk factor for heart disease and stroke<sup>1</sup> affects approximately 65 million Americans.<sup>2-4</sup>Appropriate treatment and medication use might substantially reduce medical risks of hypertension. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) recommends for most persons with uncomplicated hypertension an initial use of a thiazide-type diuretic alone or in combination with another agent such as an ACE Inhibitor, a beta blocker, an angiotensin receptor blocker (ARB), or calcium channel blocker. <sup>1</sup>

Patients with some disease states and certain ethnicities may have compelling indications requiring additional antihypertensive agents. For instance, the JNC 7 guidelines recommend persons with heart failure use a thiazide-like diuretic, a beta blocker, an ACE Inhibitor, an angiotensin receptor blocker (ARB), or an aldosterone antagonist; but that these persons not use a calcium channel blocker. For persons with diabetes, the guidelines recommend a thiazide-type diuretic, a

beta blocker, an ACE Inhibitor, an ARB, or a calcium channel blocker, but not an aldosterone antagonist.<sup>1</sup>

In the Holmes et al<sup>4</sup> study, the authors reported that prescribing practices of health providers did not match guideline recommendations. Nearly half of the individuals with hypertension and various co-morbidities did not receive first-line treatments. The authors further described substantial social and financial costs of prescribing trends using newer drugs rather than less expensive traditional drugs, like diuretics and beta blockers, and without evidence that the newer drugs offered superior benefits. Holmes et al noted a lack of comparison studies with detailed, individual level prescription information on antihypertensive agents. Recent evidence suggest, on the other hand, that adherence with some newer agents may be better, suggesting a preventive advantage. <sup>5</sup>

In Hawai'i 1 out of 3 deaths is a result of hypertensionrelated problems. <sup>6</sup> Native Hawaiians have exceptionally high risks. This study examines antihypertensive prescribing patterns for the initial drug prescribed and adherence among an ethnically diverse group of patients enrolled in a large health plan in Hawai'i.

#### **Methods**

The design of this study was a non-concurrent longitudinal study analyzing administrative data provided by a large insurer in the state of Hawai'i. A limited data set, included dates of the first prescription, was created for the study. Individual participants could not be identified from this data. An exemption from IRB review was granted prior to initiating the study by the University of Hawai'i Institutional Review Board.

This study population consisted of members with a diagnosis of hypertension based on ICD-9 codes and who were prescribed their first prescription for an antihypertensive medication between the years 2002 and 2004. A minimum of 1 year of continuous enrollment before the first prescription was required to participate. Ninety-two percent of the participants had been continuously enrolled for 2 years or more. All insured members 18 years and older were eligible if they met the diagnosis and enrollment criteria.

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Antihypertensive medications were identified by specific therapeutic class codes. Adherence to a prescribed medication was based on a "medication possession ratio" (the percentage of days with a prescribed medication). 7 A ratio of 0.8 or greater was considered adherent for this study. The maximum allowable gaps between prescription fills were based upon possession ratios, calculated as follows: Possession ratio = days supplied for first prescription (Rx) (fill date of second Rx - fill date of first Rx). A claim separated from a previous claim with a possession ratio of 0.8 or greater was considered adherent. Adherence was examined for 6 drug classes among members who were classified into 3 disease categories: hypertension alone, hypertension with diabetes mellitus, and hypertension with congestive heart failure. Diabetes and congestive heart failure were defined by the insurer's criteria for its disease management program.

Explanatory variables for the study population included: demographic characteristics, island of residence, morbidity, insurance type, and the specialty of prescribing physician. The morbidity index used comes from the Johns' Hopkins' Adjusted Clinical Group case-mix adjustment system, which categorizes patients' clinical conditions from ICD-9 diagnoses into 1 of 6 integer categories ranging between 0 and 5. Higher numbers indicate worse morbidity. This measure of morbidity is a risk adjustment tool that measures the illness burden of patients and their expected consumption of health services.<sup>8</sup>

In descriptive analysis, frequencies were calculated for demographic variables, drug classes used, and physician specialties. Drug adherence during the first year of use was analyzed using multivariable logistic regression analysis. In analyses modeling physician specialties, members were identified as clustered within the practice of their initial prescribing physicians. These analyses were performed using generalized linear mixed effects models<sup>9</sup> and were adjusted for patient characteristics (age, gender, isle of residence, insurance type, morbidity, and if the patient had a diagnosis of diabetes or congestive heart failure). Odds ratios compare specialists to primary care physicians on the likelihood of prescribing the listed drug class relative to thiazide diuretics.

#### Results

Calculations from 2002 to 2004 showing that of 28,073 patients receiving first prescriptions for an antihypertensive medication, 63% were over 50 years of age while 23% were 65 years of age or older (Table 1). The proportion of women to men was about even. Seventy percent of the participants lived on the island of O'ahu in Hawai'i; the remainder lived on rural, outer Hawaiian Islands. A substantial majority (84%) were enrolled in fee for service plans as opposed to health maintenance organizations. About 30% had a high morbidity based upon an assessment of their insurance claims in the past

Table 1.— Demographic characteristics of study population. Total: 28,073						
CHARACTERISTIC	DESCRIPTION	FREQUENCY (PERCENT)				
	20-34	1,701 (6.1%)				
	35-49	8,801 (31.3%)				
Age	50-64	11,023 (39.3%)				
	65-79	5,099 (18.2%)				
	80+	1,449 (5.2%)				
Gender	Female	13,652 (48.6%)				
Gender	Male	14,421 (51.4%)				
	Oʻahu	19,555 (69.7%)				
Island of Residence	Hawaiʻi	3,803 (13.5%)				
Island of Residence	Maui	2,062 (7.3%)				
	Other	2,653 (9.4%)				
Insurance Type	Health Maintenance Organization	4,492 (16.0%)				
,,	Fee-for-service	23,581 (84.0%)				
Morbidity	Low	19,691 (70.1%)				
iviorbialty	High	8,382 (29.9%)				
	Hypertension	23,488 (83.7%)				
Disease Category	Diabetes	3,972 (14.1%)				
	Congestive heart failure	613 (2.2%)				

class and disease category.						
DRUG CLASS Hypertension Diabetes Mellitus Congestive Heal Failure						
Angiotensin receptor blockers (ARB)	29.3%	30.8%	17.5%			
ACE Inhibitors (ACE I)	25.6%	50.5%	49.9%			
Beta blockers (BB)	19.8%	7.4%	17.8%			
Calcium channel blockers (CCB)	11.8%	5.2%	9.0%			
Thiazide diuretics (THZ)	10.9%	4.0%	5.1%			
ACE Inhibitors and CCBs	2.6%	2.1%	0.8%			

year. Fourteen percent of the patients with an initial prescription for an antihypertensive medication were diagnosed with diabetes and about 2% were diagnosed with congestive heart failure.

Of the participants with hypertension alone, 65% were prescribed ARBs or ACE Inhibitors as their initial antihypertensive medication (Table 2). Twenty percent were prescribed beta blockers. Half of the patients with diabetes or congestive heart failure received ACE Inhibitors. An additional 31% of those with diabetes received ARBs. Of the patients with congestive heart failure, about 18% were prescribed ARBs; a similar percentage was prescribed beta blockers. Calcium channel blockers were prescribed almost twice as often as thiazides to patients with congestive heart failure.

About 60% of the prescriptions from primary care physicians were for ARBs or ACE Inhibitors. Beta blockers were prescribed half as often. Cardiologists

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Table 3.— Odds ratios for prescribing listed drug classes relative to thiazide diuretics by the number of patients to which the physician had prescribed antihypertensive medications.<sup>a</sup>

DRUG CLASS	ODDS RATIO PER 20 PATIENTS PRESCRIBED
Angiotensin receptor blockers	1.2 (1.2, 1.3)
Ace Inhibitors	1.0 (1.0, 1.1)
Beta blockers	1.1 (1.0, 1.1)
Calcium channel blockers (CCBs)	1.0 (1.0, 1.1)
Ace Inhibitors and CCBs	1.1 (1.1, 1.2)

<sup>&</sup>lt;sup>a</sup>Regression models treated patients as grouped within the physicians who prescribed their initial antihypertensive medication. Analyses were adjusted for patient age, gender, isle of residence, insurance type, morbidity, and if the patient was diagnosed with diabetes or congestive heart failure.

Table 4.— Drug classes or combinations of class prescribed during first year of antihypertensive medication use by disease category.<sup>a</sup>

hypertensive medicati	on use by disease category."	
DISEASE CATEGORY	DRUG CLASSES	PERCENT
	Angiotensin receptor blocker	25.9%
	Beta blocker	18.5%
	ACE I inhibitor	18.2%
Hypertension alone	Calcium channel blocker	10.4%
	Thiazide diuretics	10.4%
	ACE I inhibitor & calcium channel blocker combination	2.6%
	Ace I inhibitor & beta blocker	2.3%
	ACE I inhibitor	31.9%
	Beta blocker	16.2%
	Angiotensin receptor blocker	12.9%
Diabetes	Ace I inhibitor & beta blocker	8.5%
	Calcium channel blocker	7.8%
	Thiazide diuretics	4.1%
	ACE I inhibitor & Angiotensin receptor blocker	3.9%
	ACE I inhibitor	39.9%
	Angiotensin receptor blocker	27.3%
Congestive heart failure	Beta blocker	6.8%
Congestive near railure	ACE I inhibitor & Angiotensin receptor blocker	5.5%
	Calcium channel blocker	4.4%
	Thiazide diuretics	3.8%

<sup>&</sup>lt;sup>a</sup>Table lists all drug classes or combinations used by 2% or more of patients in a disease category. Ampersand separates different drug classes used by patients during year, and not necessarily at the same time.

and endocrinologists exhibited somewhat contrasting prescription practices. Cardiologists most frequently prescribed beta blockers followed by ACE Inhibitors and then ARBs. Endocrinologists were the reverse: they most frequently prescribed ARBs followed by ACE Inhibitors and then beta blockers. Physician prescribing patterns were further compared in regression models adjusting for patient characteristics. After adjustment, cardiologists and endocrinologists were 3 times as likely as primary care physicians to prescribe ARBs than as to prescribe thiazides. Cardiologists were also significantly more likely to prescribe ACE I inhibitors, beta blockers, and calcium channel blockers. Of all physician specialties, those who prescribed antihypertensive medications to the most patients were the least likely to prescribe thiazide diuretics (Table 3). All comparisons were statistically significant (p<0.05), although the relative odds of prescribing were moderate in magnitude. The median number of patients prescribed was 7,

but a third of the physicians prescribed to 20 or more patients, and 20% prescribed to 40 or more patients. The strongest association with the number of patients treated was for ARBs: for every additional 20 patients treated, the odds of prescribing ARBs relative to thiazide diuretics increased 20%.

When looking at all of the drug classes members used in their first year of treatment, most patients reported using a single drug class (Table 4). ARBs were the most common drug class for patients with hypertension alone, whereas ACE inhibitors were most frequently used by patients with hypertension complicated by diabetes or congestive heart failure.

During their first year of use and depending upon the initial drug used, 3-9% of patients switched drug classes. ARBs and beta blockers were switched least often, whereas the combination of ACE Inhibitors and calcium channel blockers were most commonly switched. Comparing the 2 most established drug classes, beta blockers were switched half as often as thiazides.

Drug adherence relative to thiazide diuretics during the first year of antihypertensive medication use was highest for ARBs, ACE Inhibitors, and beta blockers (Table 5). Among patients with diabetes, adherence was greatest with ARBs; adherence was greatest with ARBs among patients with hypertension alone or hypertension and congestive heart failure. Thiazide diuretics invariably exhibited the worst adherence.

#### **Discussion**

In this Hawai'i study, the newer ARBS and ACE Inhibitors were the most common antihypertensive medications prescribed to patients not known to have been previously treated. This finding was consistent for members with hypertension alone or hypertension in combination with diabetes or congestive heart failure. In apparent contradiction to hypertension guidelines, the older beta-blockers and diuretics were prescribed less frequently than the newer drug classes. These results confirm what other investigators such as Holmes et al<sup>4</sup> have observed: that recommended, first-line antihypertensive agents are not being consistently prescribed to patients with hypertension.

In the current study primary care physicians and endocrinologists wrote prescriptions most often for ARBs and ACE Inhibitors. Cardiologists most often prescribed beta blockers and ACE Inhibitors. Patients adhered best with ARBs followed by beta blockers or ACE Inhibitors, depending upon the patient's co-morbid conditions. The choice of ARBS as a first-line therapy is likened to the results of Greving, Denig, van der Veen, et al<sup>10</sup> in The Netherlands, where angiotensin II receptor blockers were found to be first-line rather than second-line therapy for hypertension.

Reports on best practices vary and results from randomized trials differ in conclusions regarding the

Table 5.— Percent adherence with antihypertensive medications and odds ratios comparing adherence of other drug classes to thiazide diuretics by disease category<sup>a</sup>

DRUG CLASS	HYPERTENSION ALONE		HYPERTEN	SION & DIABETES	HYPTERTENSION & CONGESTIVE HEART FAILURE	
	% adhered	ODDS RATIO (95% CI)	% adhered	ODDS RATIO (95% CI)	% adhered	ODDS RATIO (95% CI)
Angiotensin receptor blockers	55.0%	2.4 (2.2, 2.6)	41.2%	3.1 (2.1, 4.4)	52.3%	3.8 (1.5, 9.8)
Beta blockers	46.2%	1.7 (1.5, 1.9)	44.9%	1.6 (1.1, 2.4)	39.4%	2.3 (0.9, 5.8)
Ace I inhibitors and CCBs	43.3%	1.5 (1.3, 1.8)	41.2%	1.4 (0.8, 2.5)	20.0%	1.0 (0.1, 0.8)
Ace I inhibitors	42.0%	1.4 (1.3, 1.6)	43.4%	1.6 (1.1, 2.2)	45.1%	3.0 (1.2, 7.2)
Calcium channel blockers (CCBs)	41.3%	1.4 (1.2, 1.5)	37.2%	1.2 (0.8, 1.8)	36.4%	2.0 (0.7, 5.6)
Thiazide diuretics	33.4%	1.0	33.1%	1.0	22.6%	1.0

aOdds ratios were adjusted for age, gender, isle of residence, insurance type, morbidity, and whether the patient had coronary artery disease.

most effective antihypertensive medications. For instance, Psaty, Smith, Siscovick, et al<sup>11</sup> concluded that beta-blockers and diuretics were superior as first-line antihypertensive agents to ACE Inhibitors and calcium channel blockers. In a later analysis, Psaty, Lumley, Furberg, et al<sup>12</sup> concluded that low-dose diuretics were the most effective first-line therapy in preventing cardiovascular disease and suggested clinical practice should follow suit. In 2002, the ALLHAT Collaborative Research Group found that low dose thiazide diuretics were superior as first-line therapy and were unsurpassed in lowering blood pressure and with regard to consideration of clinical events, cost and tolerability.<sup>13</sup> In 2007, Einhorn, et al<sup>14</sup> concluded that for prevention of heart failure in high-risk hypertensive patients, thiazide diuretics should be the preferred first-step therapy.

Following national guidelines may yield substantial cost savings. According to a simulation by Fischer & Avorn<sup>15</sup> the cost difference between antihypertensive agents actually prescribed and those suggested by evidence-based guidelines could have saved an estimated \$11.6 million. That study concluded that a vast consideration of resources are being expended on the newer and more expensive drug classes; and without clear evidence from randomized trials that patients benefit from these classes over and above older, less expensive alternatives. Free pharmaceutical samples and type of insurance may influence selection of non-first line prescriptions<sup>16</sup> as might education, costs of treatment, and updates on clinical trials.<sup>17-18</sup>

The results of this study suggest that current practice in Hawai'i does not follow the recommended guidelines since thiazide diuretics were one of the least used drug classes. Most often clinicians started patients diagnosed with hypertension on ARBs, which over the first year of use had better drug adherence. It is possible factors such as undesirable side effects from diuretics may have influenced provider selection of drugs and patient adherence; however, that cannot be confirmed by this study. Some believe that for about two-thirds of people with hypertension and especially those with co-morbidities such as diabetes mellitus, 2 drug classes may be required to provide blood pressure control. In this study of initial drug use for hypertension, the use of multiple drug classes was much less frequent.

The results reported in this article should be interpreted with a number of limitations in mind. First, prescriptions were from billing data and represent filled prescriptions and not actual medications taken. As a consequence, adherence represents refilling of prescriptions, not necessarily the continued taking of antihypertensive

medications. Second, data on free samples are unavailable. As a consequence, the medication identified as the first prescription may not necessarily be the first medication taken. Also, since our data do not report blood pressure measurements or levels, we cannot examine the effectiveness of the various medications. This could be evaluated in future studies along with numbers of patients being prescribed 2 or more antihypertensive drugs since drug combinations were excluded from the data.

Although JNC 7 guidelines and pharmacological treatment options are reasonably broad and open to interpretation the observed prescribing patterns in this study appear inconsistent with the intent of the guidelines. ARBs and ACE Inhibitors were used most often for all disease categories and thiazides were used least often. In a 2005 report, the American Journal of Managed Care<sup>5</sup> notes results similar to these: evidence of increased prescriptions of the newer classes of antihypertensive agents due to better adherence. The report attributes adherence issues with tolerability for patients coupled with reduced side effects. Sustained therapy may afford the greatest protective cardiovascular benefits.

Other factors such as patient lifestyle modifications and preferences, efficacy of individual patient plans, costs, use/abuse of resources, side effects, safety/comfort, risks/benefits, co-morbidities, gender, and drug adherence must also be factored into the equation to help patients achieve optimal outcomes. Investigating the relative risks and benefits of available antihypertensive medications and whether optimum blood pressure control is being achieved using the various drug classes is essential. Together with these factors, approaching an understanding of why providers choose various treatments for hypertension is of utmost importance if we are to reduce the risks of heart disease and stroke related to hypertension while conserving valuable resources.

See REFERENCES p. 111

# Diffuse Pachymeningitis due to Mycobacterium tuberculosis: A Case Report and Review of the Literature

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#### **Abstract**

Diffuse pachymeningitis is an uncommon presentation of tuberculous meningitis (TBM). We present a 78-year-old woman patient with a 1-year history of progressive headache and MRI of the brain compatible with diffuse pachymeningitis. Without strong evidence to support a diagnosis, she subsequently underwent dural biopsy which revealed caseous granulomatous inflammation and was positive for Mycobacterium tuberculosis complex by PCR. The dura tissue culture subsequently confirmed the diagnosis of TBM. Successful treatment with antituberculous drugs and corticosteroid was observed without complications. Literature review on characteristics, diagnoses and treatment of central nervous system tuberculosis was also performed.

#### Introduction

Tuberculous meningitis (TBM) is a serious and lifethreatening presentation of extra-pulmonary tuberculosis. Delay in diagnosis and treatment results in significant morbidity and mortality. Because of the low prevalence of the disease in developed countries, TBM is easily overlooked, especially in immunocompetent hosts. Even in the high prevalent regions, the diagnosis of TBM is difficult and requires a high degree of clinical suspicion. Direct examination of centrifuged cerebrospinal fluid (CSF) pellets and polymerase chain reaction of CSF for Mycobacterium tuberculosis complex (PCR-TB) are specific but have varied sensitivities.1 Culture of M. tuberculosis is time-consuming and not useful for making early diagnosis. While thickening of the basilar leptomeninges suggests TBM, the differential diagnosis for this radiographic finding is broad.<sup>2,3</sup> The authors report a confirmed case of diffuse pachymeningitis due to M. tuberculosis in a woman with a 1-year history of progressive headache who successfully completed dual antituberculous and corticosteroid therapy.

#### **Case Report**

A 78-year-old Thai woman with history of hypertension and osteoarthritis of the knees was admitted with a 1-year history of progressive headaches. The headaches were generalized, nearly continuous, throbbing and with intermittent radiation to the orbits and the back

of the neck. She experienced progressive worsening of the headaches which were not relieved by rest or analgesics. Additionally, the patient had malaise, night sweats and a 5 kg unintentional weight loss over 1 year. She reported no fever, anorexia, visual changes, nausea, or vomiting. She reported history of tuberculosis contact from her father 2 years ago but denied recent travel beyond Thailand or animal exposures. The physical examination, with vital signs, was within normal limits and without evidence of neurological deficits. Laboratory data revealed white blood cell count of 8,200 cell/µl (66% neutrophils, 18% lymphocytes, 12% monocytes, 3% eosinophils and 1% basophils), hemoglobin of 10.4 g/dl, normal transaminases, total protein of 6.0 g/dl and albumin of 2.6 g/dl. Magnetic resonance imaging (MRI) of the brain showed diffusely prominent dural enhancement at both convexities and along the tentorial cerebelli, compatible with diffuse pachymeningitis (Figure 1). Lumbar puncture revealed an opening pressure of 24 cmH<sub>2</sub>O. CSF studies showed no cells, protein of 86 mg/dl and glucose of 94 mg/dl (serum glucose of 100 mg/dl). The centrifuged deposit of 15 ml of CSF was carefully examined and revealed no organisms on Gram stain and acid fast stain. CSF tests for cryptococcal antigen and cytology were negative. The result of the CSF PCR-TB was negative. The CSF PCR-TB was processed based on the amplification of the repeated insertion sequence IS6110 according to the published method.<sup>4</sup> Briefly, the outer primers (primer J; 5'-CGGGACCACCCGCGCAAAGCCCGCAG-GAC-3' and primer K;5'-CATCGTGGAAGCGACCC-GCCAGCCCAGGAT-3') of the IS6110 sequence were used to amplify a 220-bp fragment. The inner primers (primer IS1; 5'-CCTGCGAGCGTAGGCGTCGG-3' and primer IS2; 5'-CTCGTCCAGCGCCGCTTCGG-3') were used to amplify a unique 123-bp fragment of M. tuberculosis complex. PCR were conducted with an initial 4-min denaturation step at 94°C coupled to a repeating cycle of 1.5 min at 94°C, 1.5 min at 63°C, and 1.5 min at 72°C for 20 (first round) and 40 (second round) cycles, followed by 7 min of final extension at 72°C. The two-step PPD skin test was positive but her

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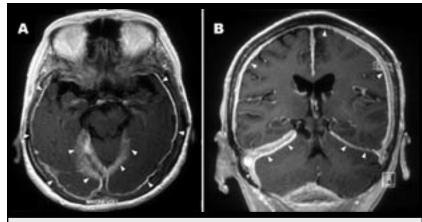


Figure 1.— Post-gadolinium enhanced axial (A) and coronal (B) MR images showed diffusely prominent dural enhancement at both convexities and along the tentorial cerebelli (arrowheads), compatible with pachymeningitis.

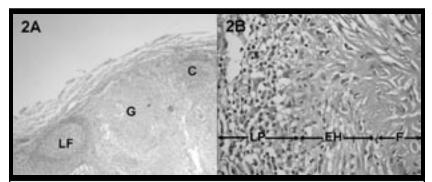


Figure 2.— A: Diffusely fibrotic dural tissue with reactive lymphoid follicle (LF), granulomatous inflammation (G) and chronic inflammatory cell infiltrate (C). (X40) B: Wall of granuloma consisting of outer layer of lymphoplasmacytic infiltrate (LP) and middle layer of epitheloid histiocytes (EH) surrounding central fibrosis (F). (X400)

chest radiograph was unremarkable. Serum antinuclear antibody, HIV antibody, and rapid plasma reagin were all negative. Without strong evidence supporting a specific diagnosis, she subsequently underwent a dural biopsy, which revealed caseating granulomatous inflammation (Figure 2) but was negative for acid-fast bacilli (AFB). The dura tissue was ground in a sterile tissue grinder and a small amount of BHI broth was added to the tissue. A few drops of the tissue/broth mixture were placed onto Löwenstein-Jensen medium, Middle Brook agar and BACTEC Mycobacteria Growth Indicator Tube (MGIT) 960 system (Becton Dickinson, Sparks, MD) which were incubated for 12 weeks. The presumptive diagnosis of tuberculous pachymeningitis was made by the positive PCR of the duratissue for *M. tuberculosis* complex. She completed 2 months of intensive therapy with isoniazid (300 mg/day), rifampicin (600 mg/day), pyrazinamide (2,500 mg/day) and ethambutol (1,500 mg/day) (2IRZE), followed by 7 months of isoniazid (300 mg/day) and rifampicin (600 mg/day) therapy (7IR). In addition, she received adjunctive prednisone 60 mg/day with tapered dosing over 8 weeks. The initial and subsequent CSF cultures for bacteria, fungi, and mycobacteria were all negative but the dura tissue culture grew *M. tuberculosis*. The organism was susceptible to all antituberculous drugs she was on. She responded well to 9 months of treatment with resolution of anemia and no report of adverse events or residual neurological symptoms.

#### **Discussion**

The state of Hawai'i has consistently reported one of the highest annual tuberculosis case rates in the country. The rate was 9.3 cases per 100,000 populations compared with the US nationwide rate of 5.1 cases per 100,000 populations in 2003.5 Extrapulmonary tuberculosis inclusive of central nervous system (CNS) tuberculosis accounted for less than 10% of all cases in Hawai'i.5 TBM is a form of CNS tuberculosis that remains a diagnostic dilemma given the difficulty of confirmatory testing, the severe sequelae of delayed treatment, and the anticipated toxicities of empiric therapy. In countries with a high prevalence of tuberculosis,

TBM most commonly occurs in children, whereas, in countries with low prevalence, it usually affects adults, especially immigrants from high-prevalence areas, immunocompromised hosts, and those with either a history of travel to endemic areas or a tuberculosis exposure. 6 Notably, the common presentations of TBM, including altered mental status, focal neurological deficit, headaches, intracranial hypertension signs, and seizures, are non-specific. Hence, the initial differential diagnoses are broad and include other CNS infections, non-infectious inflammatory diseases of the meninges, intracranial malignancies and idiopathic hypertrophic meningitis. 7,8 Localized basilar meningeal enhancement, with or without hydrocephalus, on both head computed tomography and brain MRI has been reported in patients with TBM.<sup>6</sup> However, pachymeningitis, described as diffuse or localized thickening of the cranial dura mater with or without associated inflammation, is a rare finding.<sup>2,3</sup> Per our review, this is the first reported case of diffuse, whole brain tuberculous pachymeningitis. Characteristics, diagnosis and treatment of tuberculous Authors' Affiliations:

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Table 1.— Comparison of ch	naracteristics of 4 different type	es of central nervous system tu	uberculosis from literature rev	iew <sup>3,6-8,11,12,21-25</sup>
Characteristics	Meningitis	Pachymeningitis	Intracranial tuberculoma	Spinal tuberculous arachnoiditis
	,			1
Onset	Subacute (2-3 weeks)	Insidious (weeks-months)	Insidious (weeks-months)	Insidious (weeks-months)
Common presenting symptoms	Low grade fever, headache, confusion, personality change	Chronic headache, seizure, cranial neuropathies	Focal neurological deficits de- pending on the affected sites <sup>a</sup>	Nerve root and spinal cord com- pression symptoms <sup>b</sup>
Concurrent systemic institutional symptoms°	Common	Uncommon	Uncommon	Uncommon but may present at late stage
Meningeal signs <sup>d</sup>	Common	Uncommon	Uncommon	Uncommon but may present at late stage
Common imaging (MRI) findings	Basilar meningeal enhancement combined with any degree of hydrocephalus	Localized or diffuse thickening of the cranial dura mater	Intracranial ring or nodular contrast-enhancing lesions	Nodular, meningeal or nerve root surface enhancement of the spinal cord
CSF findings	1			
Opening pressure <sup>e</sup>	Elevated	Normal or elevated	Normal or elevated	Elevated
WBC count (cells/µl)	5-1,000	0-1,000	0-1,000	5-1,000
Neutrophil	10-70%	0-70%	0-70%	10-70%
Lymphocyte	30-90%	30-100%	30-100%	30-90%
Protein <sup>f</sup>	Elevated	Normal or elevated	Normal or elevated	Elevated
CSF glucose to blood glucose ratio	Less than 0.5	Normal or less than 0.5	Normal or less than 0.5	Less than 0.5
Positive acid-fast staining	Sensitivity 20-90% Specificity 100%	NA	NA	NA
Positive PCR-TB	Sensitivity 32-100% Specificity 82-100%	NA	NA	NA
Abnormal chest radiograph	Sensitivity 40-50%, lack of specificity in high-prevalent area of pulmonary tuberculosis	NA	NA	NA
Positive PPD skin test	Sensitivity 40-50%, lack of specificity in high-prevalent area of pulmonary tuberculosis	NA	NA	NA
Biopsy for diagnosis	Not required	May be required	May be required	May be required
Treatment	,			,
Antituberculous drugs	IRZE for 2 months followed by IR for 7-10 months	Same as meningitis	Same as meningitis	Same as meningitis
Steroid	Dexamethasone or prednisone with tapering doses over 4-8 weeks	Same as meningitis	Same as meningitis	Same as meningitis

a = Localized weakness, blurry vision, impaired sensation, propioception, and loss of balance

Abbreviations: CSF = cerebrospinal fluid; IR = isoniazid-rifampicin; IRZE = isoniazid-rifampicin-pyrazinamide-ethambutol; MRI = magnetic resonance imaging; NA = not available; PCR-TB = polymerase chain reaction for tuberculosis; PPD = purified protein derivative; WBC = white blood cell

pachymeningitis in comparison with other types of CNS tuberculosis are shown in Table 1.

Previous investigators have suggested that TBM is a result of the bacteremia that follows primary infection or late reactivation of tuberculosis elsewhere in the body. 9,10 However, concomitant non-CNS tuberculosis was found in only 65-75% of the cases. 7.8 Active or previous tuberculosis findings on chest radiographs and

positive PPD skin tests were each present in 40-50% of patients with TBM. 11,12 Consistently, chest radiographs and PPD skin tests have lacked specificity in high-prevalence populations of pulmonary tuberculosis. In contrast, CSF examination is crucial for the diagnosis of TBM. Common CSF profiles for TBM usually include elevated opening pressure, pleocytosis with lymphocyte predominance, high protein, and low CSF to blood glucose ratio.

b = Radicular pain, hypereathesia, paresthesia, paraplegia, and incontinence

c = Fever, night sweats, myalgia, and anorexia

d = Stiff neck, Kernig's sign, and Brudzinski's sign

e = Normal range: 8-20 cmH<sub>2</sub>O

f = Normal range: 15-45 g/dl

However, in tuberculous pachymeningitis cases like ours, these profiles can be normal (Table). The detection of AFB in the CSF is the most rapid, effective, and widely available method for an early diagnosis of TBM yet reported sensitivity is inconsistent (20-90%). 7-9,12 The diagnostic yield significantly improves when at least 4 serial samples of at least 6 ml of CSF specimens are obtained from which 0.02 ml centrifuged deposits are viewed in an area not exceeding 1 cm diameter and examined as 200-500 high-powered fields for at least 30 minutes. 9,10 Another rapid method for detection of M. tuberculosis is the nucleic acid-based amplification test that relies upon the PCR. The CSF PCR-TB test is rapid, specific (82-100%) and of varied sensitivity (32-100%). Hence, a negative CSF PCR-TB test neither excludes the diagnosis nor obviates the need for treatment in a highly-suspected case. Quantiferon assay is a new immunological method for diagnosis of latent tuberculosis with a sensitivity of 80%. 13,14 This method measures the level of interferon-gamma released from T-cell lymphocytes during the M. tuberculosis specific antigen encounter. The benefits of the assay in comparison with the PPD skin test are less subject-to-reader bias and error, ability to complete the test after a single visit and a negative result following the BCG vaccination.<sup>13,14</sup> However, the sensitivity for detection of active tuberculosis was only 64% and its utility for diagnosis of CNS tuberculosis has not been established. 15 Urine anti-M. tuberculosis antibody assay and detection of urine mycobacterium lipoarabinomannan have sensitivity of 53-64% and 50-80% in diagnosis of tuberculosis respectively. 16-18 However, these results are mostly for diagnosis of pulmonary tuberculosis, not for CNS tuberculosis.

The indication of dural biopsy is generally to rule out or confirm diagnosis of serious conditions such as malignancy or infectious diseases in patients with broad differential diagnoses.<sup>19</sup> The procedure's risks or complications include bleeding, hematoma, and infection.<sup>19</sup> However, the post-procedure infection rate is minimal and does not appear to be more than other clean-wound surgical procedures.<sup>20</sup> In this patient, due to lack of strong evidence to support the diagnosis of tuberculous pachymeningitis, a dural biopsy was obtained. The sensitivity and specificity of the PCR-TB method used for formalin-fixed, paraffin-embedded dura tissue were 87% and 100% respectively. Because of the positive PCR-TB and histopathological findings of the dura, the patient was presumptively diagnosed with tuberculous pachymeningitis. The antituberculous 2IRZE + 7IR regimen was selected, based on recommendations from the American Thoracic Society, Centers of Diseases Control and Prevention, and Infectious Diseases Society of America.<sup>21</sup> Notably, the first 2-months treatment regimen should contain 4 drugs for intensive eradication of M. tuberculosis and drug resistance prevention. Isoniazid and pyrazinamide generally pass freely into the CSF and their use may be crucial to a successful outcome. In contrary, the roles of rifampicin and ethambutol are still uncertain given their low concentration in the CSF, especially in the absence of inflammation.<sup>6</sup> Thus, longer duration of maintenance therapy with 2 drugs (7-10 months) compared with the duration of the therapy for pulmonary tuberculosis (4 months) is necessary due to the lower level of rifampicin concentration in CSF. Corticosteroid therapy was added to the regimen for potential survival benefit and minimization of risk for disease and treatment sequelae.<sup>22</sup>

In summary, TBM should be included in the differential diagnosis in patients with diffuse pachymeningitis. Given the diagnostic limitations of CSF PCR-TB for confirming TBM, negative results should not exclude the diagnosis or delay treatment in highly-suspected cases. A high index of clinical suspicion, tissue procurement and PCR method are essential to facilitate early diagnosis and proper management of TBM.

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#### Problem-based Learning: Emergence of Vertically Stable Study Groups Among First and Second-Year JABSOM Students

Joshua Jacobs MD; Jill Omori MD; Yasutomo Oda MD; Richard Kasuya MD; and Leslie Tam PhD

In 1989, the John A. Burns School of Medicine, University of Hawai'i (JABSOM) introduced the problem-based learning (PBL) curriculum of the McMaster University (Ontario, Canada) (Neville and Norman, 2007). A notable feature of the curriculum was the removal of 75% of faculty lectures and the introduction of small group tutorials. Groups of five to six students studied clinical cases, guided by a faculty tutor. Tutorial-based learning was accompanied by large blocks of "unscheduled or protected time" for self-directed learning and discovery by students (Fig. 1). The McMaster rationale for tutorial-based learning was based on the belief that the active exchange of ideas within small groups not only increases interest among the participants, but also and promotes critical thinking.<sup>2</sup> Studies since have shown that cooperative teams achieve at higher levels of thought and retain information longer than students who work individually.<sup>3</sup> In addition, students working in small groups tend to learn more and are more satisfied with their classes.<sup>4</sup>

Problem-based learning has three steps. On Monday, students in tutorials open a case, usually six to seven pages, beginning with the chief complaint, followed by history, physical exam, laboratory tests, and finally treatment and course of illness. Students are encouraged by the tutor to think critically. If a group learns that chest pain in a patient, hypothesized to have pericarditis, is relieved by sitting up and leaning forward, the tutor may ask - "why do you think this happens?" If the case reveals that the patient's EKG demonstrates concave up "saddle" ST segment elevation and PR segment depression, the tutor may ask why. Throughout the session, the tutor will encourage students to think critically. If students cannot offer a satisfactory answer, the question becomes a learning issue. At the end of the session, students will have distilled a list of learning issues, which they feel will help them understand the case and cases like the one being studied. Overall, a PBL session might produce six to twelve learning issues, which are divided among students. Students spend the next two-and-a-half days independently researching and writing their learning issues. The product is a well-digested and formatted two- to three-page study guide, which is duplicated for each tutorial member as well as the tutor. In the next tutorial, students meet for "peer-teaching" and discussion of the learning issues within the context of the case being studied. Thus, the tutorial has been the centerpiece of collaborative learning in PBL.

Recently, JABSOM faculty members have become aware of a new phenomenon. In addition to tutorials, students were meeting in small groups during the week and weekends during time allotted for self-directed learning to work collectively in study groups "outside" of tutorials. Since the Office of Medical Education reforms tutorial groups for each unit (approximately every two months), tutorial memberships change constantly. However, the composition of study groups tends to remain intact vertically as students progress through the eight curricular units that comprise the first two

years of the curriculum. For a quick glimpse at how study groups are formed and what they do, a questionnaire was sent to first and second-year JABSOM students. Eighteen students responded. In addition, two first and two second year students were interviewed. What follows are selected questions asked in the questionnaire, along with representative answers given by the student panel. Additionally, answers from students who responded to the email survey are identified in italics.

Question: About how many hours per week do you spend with your study group?

The average was about four hours, usually on weekends. However, one student had two study groups, spending ten hours with group A and three to four hours with group B. Another student had three study groups and spent a total of about 35 hours.

Questions: What do you cover in your study groups? Is there a schedule? Who decides? Do you case map?

Answer from panel: Most groups reviewed learning issues and also case-mapped.

We decide as a group what material is most important and then we cover that... usually we're in agreement when we set a schedule for next meeting and we take a vote if there is disagreement. We used to case map, but recently we just verbally reviewed the case.

Go over cases. We may read through the case together and try to explain every line. We decide together what cases to go over and what topics we want to cover a few days before we meet. We used to map out the entire case, but now we just map out the important concepts. I try to do a brief map for each case before I meet with the group.

(This student has two study groups.) *Group A: We cover PBL* (issues not clarified in tutorials) *on Sundays and lecture material on Mondays. One student created a schedule at the beginning. Another has compiled a list of learning issues' to study that week. Each student is assigned a lecture that they will outline and summarize then teach to the group. Group B: Mostly PBL.* 

We case map and go over the cases on Wednesdays. On Fridays we review the Basic Science Lecture Series topics (mainly anatomy) each for about 1-2 hrs.

Question: How effective is your study group compared with your PBL tutorial group?

Most students felt that the study groups were more effective than tutorial groups.

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Study group has a higher efficacy because everyone has done independent reading on the specific topic at hand (which is inherently difficult in PBL unless you guessed correctly what the case would be based on the lecture schedule/patient name).

Study group is a great time to consolidate your knowledge. I get to hear what other groups have said in their tutorials and share what was discussed in my group. It is a time to reinforce what you learned in tutorial and through your own reading.

Very effective. Group A: We evaluate as we go to make sure everyone is achieving their learning goals. Group B: Very effective. Everyone is competitive and likes to ask thought provoking questions of the group. Often this is a good test of your knowledge.

In the beginning, the study group was more effective (than tutorial group), because I was afraid to ask the "dumb questions" in my tutorial. Now, if I don't understand, I feel confident to ask my study group or my tutorial group. The study group often brings perspectives from a variety of study groups, which is nice.

Question: How effective is your study group compared to independent study?

Most students responded that both were effective and necessary.

Very effective as long as I spend time preparing for my study group.

Group is always more effective if all the members have done their own research first.

Varies. Usually helpful to explain concepts that I am confused about during independent study.

I need both for my studying. The study group is only effective once I have done my own background reading and have prepared so that I am a valuable group member.

Open-ended: Please ask a question about group study and provide your answer.

What is the ideal size for a good study group? My study groups are all 3-4 people. This is a great size because it gives you the chance to interact more, coordinate schedules better, and I feel that it minimizes conflicts.

What is the maximum number you would allow in your group? Answer: We currently have four. I would not want any more. I have heard of groups with ten.

Would it be useful for the Office of Medical Education to help form study groups at the beginning for individuals? No. I think the benefit comes from discovering who likes to learn in the same way, and building off of that.

How does your study group deal with a problem? My study group evaluates periodically and will discuss how the process is for everyone. We are all very comfortable with each other so we feel safe to share our thoughts and feelings. The study group is an opportunity for learning and if you don't get the most out of it that you want then you need to change something or leave.

	Mon	Tues	Wed	Thur	Fri	Sat	Sun
a.m.	Tutorial (3 hrs)	open	Basic Science Lectures (3 hrs)	Tutorial (3 hrs)	Case Related Lectures (4 hrs)	open	open
p.m.	open	Comm. Health (3 hrs)	Clinical Skills (3 hrs)	open	Gross Anatomy (3 hrs)	open	open

Typical Week of a Student in the Problem-Based Learning Curriculum University of Hawaii John A. Burns School of Medicine (Years 1 and 2) (2008).

Various names have been given to collaborative learning (cooperative learning, collective learning, learning communities, peer-teaching, peer-learning, reciprocal-learning, team-learning, study circles, study groups, and work groups). Three types of collaborative groups exist: informal learning groups, formal learning groups, and study groups. Informal learning groups are temporary clusters of students within a single class session. A teacher may form an informal learning group quickly, for example, by asking students to turn to a neighbor and to spend two minutes discussing a question he as posed. Formal learning groups are formed to complete a specific task, such as write a report or prepare a position paper. Students work together until the task is finished, and their project may be graded. Study groups are long-term teams with stable membership. Study groups provide members with support, motivation, and assistance in completing course requirements and assignments. The more complex the subject matter, the more valuable are study groups.

The PBL tutorial group might be considered a formal learning group. The tutorial exists to examine and understand collectively the ten to twelve clinical cases over the course of a curricular unit. The recent phenomenon of the JABSOM study group fits the description of a long-term study group. The JABSOM study group remains together for over two years of the curriculum. The members within a study group work well together, set goals, and have similar learning philosophies. Some groups even evaluate regularly to assure that both individual and group goals are met. What is prominent in this pilot survey is the characteristic of collaborative, discussion-based learning in the JABSOM PBL curriculum. In addition to tutorials, students have coalesced into stable study groups, which may be more effective than tutorials for collaborative group learning.

This initial analysis into characterizing study groups revealed the JABSOM study group as an important and meaningful phenomenon at JABSOM. Future research in this area should include verifying the existence of vertically stable study groups in other medical schools with predominantly PBL curricula. Additionally, further research characterizing and comparing the study habits of students in different pedagogies, including students in foreign countries, are warranted. Finally, determining the relative contributions to the learning effort of independent study, group study, and the specific type of group study, in what may well be called PBL Step 4, will enhance the understanding of how PBL students learn.

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#### Ethnic Differences in Smoking and Lung Cancer Risk in Hawai'i

Loïc Le Marchand, MD, PhD, Cancer Research Center of Hawai'i

#### **Smoking and Lung Cancer Occurrence**

Lung cancer is the most common malignancy in the world and rates have been increasing rapidly in less-developed countries, especially in Asia and South America.1 Although the incidence for this malignancy has decreased in recent years in the United States, including Hawai'i, and most of Europe, it is still the leading cause of cancer mortality in these regions. Tobacco smoking is universally recognized as the predominant cause of lung cancer. Indeed, in the United States, it is estimated that 90% of deaths from this disease are caused by smoking.1 Risk is known to increase in relation to both intensity and duration of smoking, and a person who smoked a pack a day for 30 years is estimated to carry a lung cancer risk 10- to 20-fold greater than a lifelong nonsmoker. Smoking cessation leads to a reduction in the risk of lung cancer, but not significantly before the 5th year and risk, probably, never returns to the background rate of a lifelong nonsmoker. Among the thousands of compounds in cigarette smoke, at least 55 are considered as being lung carcinogens by the International Agency for Research on Cancer.1

Temporal trends and geographical differences in lung cancer incidence track cigarette consumption patterns with a 20- to 30-year lag, as shown by the sharp rise in lung cancer mortality that occurred in the United States between the 1930s and 1980s as the result of a major increase in cigarette manufacturing that started in the 1910s. Although avoidance of tobacco products is an established way to prevent lung cancer, there will continue to be hundreds of millions of smokers worldwide in the foreseeable future. Thus, it is important to understand the biological mechanisms underlying the strong effect of smoking on the risk of cancers of the lung and other organs (oropharyngeal, larynx, bladder, pancreas, cervix, etc.). The unexplained differences in lung cancer risk that exist among the ethnic/racial populations living in Hawai'i offer opportunities for etiologic research.

#### Incidence of Lung Cancer in Hawai'i

The main source of cancer statistics in Hawai'i is the Hawai'i Tumor Registry (HTR), a program of the Cancer Research Center of Hawai'i (CRCH). The HTR is a statewide registry that has been a member of the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute since 1973. Biostatisticians at CRCH recently updated the cancer incidence rates available for the main ethnic groups in the state using demographic projections from the 2000 US Census. Figures 1A and 1B show the temporal trends in lung cancer incidence for the 5 main ethnic groups in Hawai'i, by sex, for the period 1975-2004. In men, incidence rates have peaked and are now decreasing for all ethnic groups; however, this decrease started in different time periods for these groups. Men's rates peaked first among the Japanese in the early 1980s, then in Caucasians in the early 1990s, in Native Hawaiians in the late 1990s, and most recently among the Chinese and Filipinos. Of importance is that the marked increase in lung cancer incidence

that took place between 1985 and 1999 for Filipino men appears to have peaked. Rates have also started to decrease in women for the 2 high risk groups, Caucasians and Native Hawaiians, in the late 1990s and early 2000s, respectively.

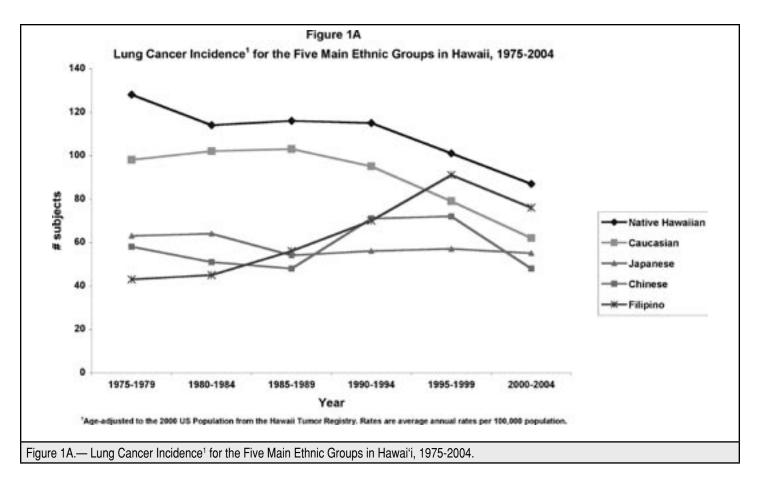
#### **Smoking Rates in Hawai'i**

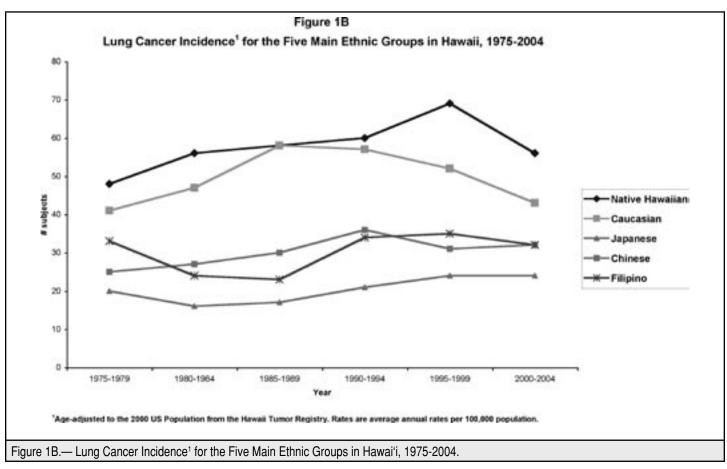
Temporal trends in rates of cigarette smoking in Hawai'i were reported by Maskarinec et al<sup>2</sup> after compiling 19 studies conducted by CRCH epidemiologists between 1975 and 2001. This database includes almost 159,000 research participants. The results showed that smoking rates decreased until 1990-1994 for the main ethnic groups in Hawai'i. Consistent with the lung cancer incidence rates discussed above, Japanese participants had the lowest prevalence of smoking at all times during the study period, while Native Hawaiians had the highest. Caucasians experienced the greatest decline in smoking rates between 1975 and 1994 (55%), compared to Japanese (36%) and Native Hawaiians (31%). No further decrease in smoking prevalence was observed between 1995 and 2001.<sup>2</sup>

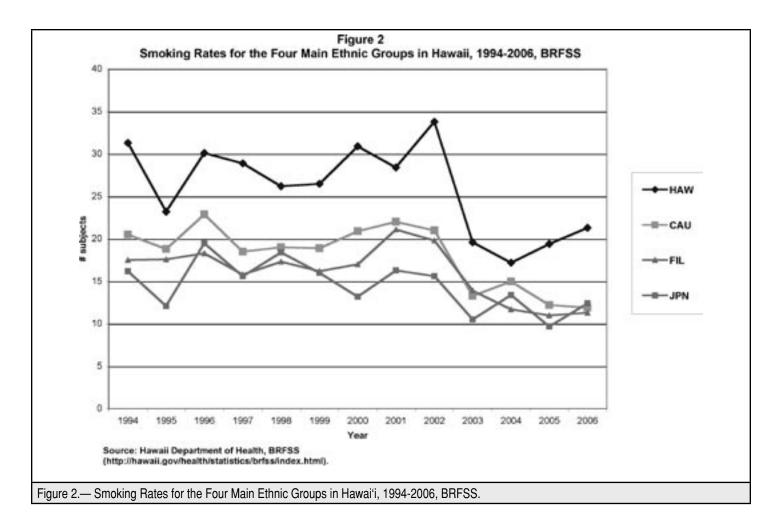
A second source of data on smoking rates is the Behavioral Risk Factor Surveillance Survey (BRFSS) which is an annual random telephone survey conducted since 1994 by the Hawai'i Department of Health in collaboration with the Centers for Disease Control and Prevention (CDC).<sup>2</sup> These rates, presented in Figure 2, show some year to year variability due to sampling variation and, in agreement with the data discussed above, seem to have remained stable between 1994 and 2002. However, a decrease in smoking rates seems to have taken place for the 4 main ethnic groups after 2002, corresponding to the adoption of strict smoking bans in restaurants and public places. This decline in smoking rates should translate into a further reduction in lung cancer rates in the coming years.

### Research on Ethnic Differences in Lung Cancer Risk

CRCH epidemiologists have clearly demonstrated using cross-sectional, 4 retrospective, 5 and prospective 6 data that there exist major (2- to 5-fold) differences among Hawai'i's main ethnic groups in the risk of lung cancer associated with cigarette smoking, even after taking into account dose and duration. These differences are more pronounced at lower smoking doses. 6 Native Hawaiians have a higher risk for lung cancer than Caucasians, who in turn have a higher risk than the Japanese. The CRCH has hypothesized that these differences are related to common genetic variants that vary in frequency across ethnic/racial populations. Indeed, associations were observed between several genetic polymorphisms in a number of metabolic and DNA repair pathways and lung cancer risk. Also, the CRCH has confirmed that these variants vary in frequency across the ethnic groups living in Hawai'i.7 However, it has become apparent that a large number of variants would have to be taken into account in order to explain the ethnic differences in risk observed in Hawai'i's population. In the past several years, the CRCH has







studied phenotypic biomarkers that integrate both individual differences in exposure and genetic susceptibility. For example, it has been hypothesized that the rate of nicotine metabolism may be an important determinant of how much a person smokes. That is, rapid metabolizers would be expected to need more nicotine to obtain the desired pharmacological effects and, therefore, smoke more (or more intensely) than slow metabolizers. Such a smoking pattern could result in an increased uptake of tobacco smoke carcinogens through the lung. The P-450 enzyme CYP2A6 is primarily responsible for the metabolism of nicotine to cotinine and of cotinine to 3-hydroxycotinine. The ratio of urinary 3-hydroxycotinine-to-cotinine can be used as a marker of CYP2A6 activity. This ratio has been shown to be lower in Asians<sup>8</sup> and, therefore, may explain their lower risk. The CRCH has confirmed that Hawai'i Japanese have a lower CYP2A6 activity than Caucasians; however, Native Hawaiians had an activity that was intermediate. Thus, CYP2A6 cannot explain all the observed differences in lung cancer risk observed in Hawai'i. The results to date suggest that a comprehensive study is warranted. This study, which is being planned, will look at a combination of genetic and environmental factors acting on several metabolic pathways (nicotine metabolism, carcinogen bioactivation and detoxification, and DNA repair) in the main ethnic groups.

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#### **Issues in Medical Malpractice XXII**

#### S.Y. Tan MD, JD, Professor of Medicine, John A. Burns School of Medicine, University of Hawai'i

#### **Question:**

Emily developed diabetes and was started on insulin. Two weeks later, she lost her coordination while driving and struck the car in front of her, seriously injuring its driver. In the emergency room, her blood glucose was low at 30 mg/dl. Her doctor had not warned her of this risk of insulin use. Which of the following is (are) correct?

- A. Emily can sue the doctor for negligence because she was not warned of the risk of hypoglycemia.
- B. Her lawsuit will fail because informed consent is about surgical or other invasive procedures, not about medications.
- C. She was herself not hurt, and without physical injuries, there can be no malpractice claim.
- The driver in the other car can sue her for negligent driving.
- E. A lawsuit against the doctor by the injured driver in the other car will probably fail because there is no doctor-patient relationship.

#### Answer to Question: A, D

The doctrine of informed consent requires the healthcare provider to inform patients about procedures, alternatives, and material risks. In order for patient consent to be meaningful, it has to be an informed one. Disclosure of material risks is an especially important part of informed consent, and this applies equally to surgical procedures as well as prescription medications and medical devices. Invasive procedures or hazardous drugs naturally warrant a more detailed explanation of the risks of harm. If it is shown that a reasonably prudent person would want to know about the risk of hypoglycemia and its effect on driving, and if the plaintiff can show that had she been warned, she would not have used insulin, then she will likely prevail in a lawsuit against the doctor.

Malpractice damages can be compensatory or punitive, and they can be based on physical injuries as well as emotional ones. Although the plaintiff in this case suffered no apparent physical injury, she can still claim damages for emotional distress, pain and suffering, etc.

The injured driver can of course sue her for negligent operation of a motor vehicle, but he may not prevail if the accident occurred through no fault of hers. This is why it is likely he will sue the doctor instead, the legal theory being that had the doctor warned her about hypoglycemia (and the precautions to take once symptoms begin to develop), she would not have struck his car. Such a claim is based on whether the doctor owed a duty to him, a third party, independent of any doctor-patient relationship (see below).

#### **Third Party Liability**

Sometimes, a doctor is liable for someone other than his/her immediate patient. In such a circumstance, another person, often referred

to as a 'third party', may sue the doctor absent a doctor-patient relationship. An example is where an obstetrician fails to treat a pregnant woman known to have been exposed to German measles, who then delivers a child with birth defects. A Rhode Island court has ruled that a cause of action could be instituted by the child, called a 'third party.' In another case, a missed diagnosis of meningitis in a mother led to the son contracting and dying from the disease. The lower court found no physician-patient relationship between the doctor and the son, but the appellate court reversed, holding that the physician-mother relationship resulted in a special situation for imposing a duty of care for her son.<sup>2</sup> Similarly, the Supreme Court of Tennessee held that a physician has a duty to warn persons in the patient's immediate family of the risk of a disease such as Rocky Mountain Spotted Fever although it itself was not contagious.<sup>3</sup>

A doctor may even be found to have a duty to a total stranger. The best known case is <u>Tarasoff.</u> where a California court imposed a duty on a psychologist to warn an intended named victim even though that meant breaching confidentiality of a professional relationship.

An emerging area of malpractice litigation affects patients who drive. Consider the following example: Suppose a patient loses control of his car and hits a pedestrian because of a medical condition or drug reaction. The doctor may face a liability claim by the injured pedestrian, a total stranger. Such an issue was recently decided by the Hawai'i Supreme Court which held:

"A physician owes a duty to non-patient third parties injured in an automobile accident caused by an adverse reaction to the medication... where the physician has negligently failed to warn the patient that the medication may impair driving ability and where the circumstances are such that the reasonable patient could not have been expected to be aware of the risk without the physician's warning." 5

The medication in this case was the anti-hypertensive drug Prazosin, which caused the driver to develop hypotension and lose control of his vehicle.

This article is meant to be educational and does not constitute medical, ethical, or legal advice. It is excerpted from the author's book, "Medical Malpractice: Understanding the Law, Managing the Risk" published in 2006 by World Scientific Publishing Co., and available at Amazon.com. You may contact the author, S.Y. Tan MD, JD, at email: <a href="mailto:siang@hawaii.edu">siang@hawaii.edu</a> or call (808) 728-9784 for more information.

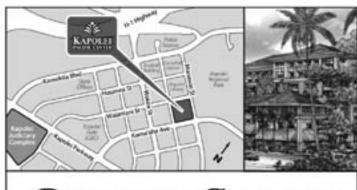
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## **UPCOMING CME EVENTS**

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Date	Specialty	Sponsor	Location	Meeting Topic	Contact
May 2008					
5/2-5/6	PD	Pediatric Academic Societies	ТВА	Annual Meeting 2008	Tel: (281) 419-0052
					Web: www.pas-meeting.org
5/22	IMG	Queen's Medical Center	Koolau Golf Club	The Queen's Medical Center	Tel: (808) 547-4406
				Conference on Geriatric Medicine, "United We Stand, Divided They Fall"	Web: www.queens.org/cme.html
5/23	ADM, ADP, P	Department of Psychiatry, John A. Burns School of Medicine, University of Hawai'i	Queen's Conference Center	Medical Comorbidities of Addiction	Tel: (808) 586-2900
June 2008		1			
6/3-6/4	OSS	American College of Physicians & Surgeons	John A. Burns School of Medicine, University of Hawai'i	Pre-Congress Fresh Cadaver Workshops	Web: www.msmisst.org
6/3-6/7	OSS	American College of Physicians	Hilton Hawaiian Village,	1st World Congress of Minimally	web. www.mamast.org
		& Surgeons	Honolulu	Inasive Spine Surgery & Techniques	Web: www.msmisst.org
6/10-6/15	Multi	Department of Native Hawaiian	Waimea, Kauaʻi	Pacific Region Indigenous	Tel: (808) 587-8570
		Health, John A. Burns School of Medicine, University of Hawai'i		Doctors Congress 2008	
6/15-6/18	PP	Department of Pathology, John A. Burns School of Medicine, University of Hawai'i	Sheraton Maui Resort	Current Concepts in Pediatric Pathology	Tel: (808) 692-1130
6/19-6/20	PD	Kaiser Permanente	Hapuna Beach Prince Hotel,	26th Annual Kaiser Permanente National Pediatric Conference	Tel: (510) 527-9500
			Kohala Coast	National Fediatife Conference	Web: www.meetingsbydesign.
6/21-6/27	PD	American Academy of Pediatrics, California Chapter	Hyatt Regency Maui Resort & Spa, Kaʻanapali Beach, Maui	Pediatrics in the Islands Clinical Pearls 2008	Tel: (808) 354-3263
		& University Children's Medical Group			Web: www.ucmg.org
6/22-6/26	Multi	University of California - Davis	Hapuna Beach Prince Hotel, Kohala Coast	Update on the Management of Thromboembolic Disorders	Tel: (916) 734-5390
			Kondia Coast	Thromboembolic disorders	Web: cme.ucdavis.edu
6/25-6/28	TS	Society for Clinical Vascular	Sheraton Keauhou Bay, Kona, Hawai'i	Western Thoracic Surgical Association 34th Annual Meeting	Tel: (978) 927-8330
		Surgery	nawaii	ASSOCIATION 34th Annual Meeting	Web: www.scvs.org
6/28-7/5	Multi	University of California San	Hapuna Beach Prince Hotel,	Essentials of Women's Health:	Tel: (415) 476-4251
		Francisco School of Medicine	Kohala Coast	An Integrated Approach to Primary Care and Office Gynecology	Web: www.cme.ucsf.edu/cme
July 2008					
7/13-7/18	IM, FM	Kaiser Permanente	Hapuna Beach Prince Hotel	17th Kaiser Permanente	Tel: (510) 527-9500
				National Internal & Family Medicine Symposium	Web: www.meetingsbydesign.
7/18-7/19	Multi	Queen's Medical Center	Hilton Hawaiian Village, Honolulu	Hawaiian Islands Trauma Symposium	Tel: (808) 537-7009
			Tionolulu	Symposium	Web: www.queens.org/cme.html
7/23-7/26	Multi	University of California - Davis	Waikoloa Beach Marriott	UC Davis Update on Emerging Infectious Diseases	Tel: (916) 734-5390
7/00 6/2	1		T.1910.0.1111.1.11	T. 0	Web: cme.ucdavis.edu
7/26-8/2	Multi	Queen's Medical Center	Tahiti & Society Islands Cruise	The Queen's Medical Center Summer Medical Practice	Tel: 808-537-4406
				Seminar - "Carpe Diem - 'Seas' the Day! II"	Web: www.queens.org/cme.html
7/28/-8/01	ORS	Kaiser Permanente	Hyatt Regency Kauaʻi	Kaiser Permanente Orthopaedic Surgery Conference 2008	
					Web: www.cmxtravel.com

August 2008					
8/3-8/4	GS	Hawai'i Chapter, American College of Surgeons	JW Marriott Ihilani Resort & Spa, Honolulu	Oncology: State of the Art, 2007 and Beyond	Tel: (800) 328-2308
0/4 0/7		Object and I had a smaller Oak and at	Our and I have March Co	LAVA Latari Adama da la	Web: www.hawaiifacs.org
8/4-8/7	R	Stanford University School of Medicine	Grand Hyatt, Kaua'i	LAVA: Latest Advances in Interventional Techniques	Tel: (888) 556-2230
				·	Web: med.stanford.edu
8/6-8/9	EM	University of California - Davis	Mauna Lani Resort and Spa	UC Davis Emergency Medicine 2008: Hot Topics	Tel: (916) 734-5390
	5 514 114 614				Web: cme.ucdavis.edu
8/14-8/17	D, FM, IM, ON	Kaua'i Foundation; Hawai'i Dermatology Association	Hyatt Regency Resort & Spa, Koloa, Kaua'i	22nd Annual Hot Spots in Dermatology	Tel: (413) 458-2800
				,	Web: www.hotspotshawaii. blogspot.com
8/19-8/21	Multi	Stanford University School of	Oʻahu	3rd Annual Complex	Tel: (650) 724-9549
		Medicine		Cardiovascular Patient Management	Web: www.cme.stanfordhospital.
October 2008		,			
10/5-10/9	PMM	Kaiser Permanente	Royal Kona Resort, Kailua-Kona	Ironman Sports Medicine Conference	Web: www.cmxtravel.com
10/11-10/15	ОРН	American Society of Retina Specialists	Grand Wailea Resort, Wailea, Maui	26th Annual Meeting	Web: www.asrs.org
10/12-10/17	Multi	Scripps Conference Services	Kaua'i Marriott Resort	Destination Health: Renewing Mind, Body & Soul	Tel: (858) 587-4404
					Web: www.scripps.org/conferenceservices
10/14-10/17	ON	American Association for Cancer	JW Marriott Ihilani Resort & Spa	Chemical and Biological Aspects	Tel: (215) 440-9300
		Research	at KoʻOlina	of Inflammation and Cancer	Web: www.aacr.org
10/20-10/22	PD	Stanford University School of	Mauna Lani Resort and Spa	Popular Pediatric Clinical Topics	l
		Medicine		2008	Web www ome lack are
10/25-10/29	PS	American Conjety of Plactic	Hawai'i Convention Center,	Plactic Curacry 2009	Web: www.cme.lpch.org Tel: (847) 228-9900
10/23-10/29	173	American Society of Plastic Surgeons	Honolulu	Plastic Surgery 2008	
					Web: www.plasticsurgery.org
10/25-10/31	PD	American Academy of Pediatrics, California Chapter	Grand Hyatt Kaua'i	Aloha Update: Pediatrics 2008	Tel: (808) 354-3263
		& University Children's Medical Group			Web: www.ucmg.org
10/26-10/30	CD	University of California - Davis	Hyatt Regency, Maui	UC Davis 28th Annual Current	Tel: (916) 734-5390
				Concepts in Primary Care Cardiology	Web:cme.ucdavis.edu
10/27-10/31	AN	California Society of	The Mauna Lani Bay Hotel,	CSA Hawaiian Seminar	
		Anesthesiologists	Kohala Coast, Hawai'i		Web: www.csahq.org
November 200	)8				1
11/3-11/6	Multi	Methodist Healthcare	Fairmont Orchid, Kona	Advances in Medicine	Tel: (901) 516-8933
			,		' '
		L	J	J	Web: www.methodistmd.org

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Russell T. Stodd MD

#### **❖ CANNABIS JOINS THE FAMILY** OF "WONDER DRUGS."

Whoa! A giant step was taken by the governing body of the American College of Physicians (ACP). The ACP is the second largest medical organization in the country with 124,000 members, and now has endorsed the medical use of marijuana.. The ACP wants the Feds to roll back the prohibition and the report cites studies that show the drug is useful in treating severe weight loss associated with AIDS as well as the nausea and vomiting frequently seen with cancer therapy. Their declaration stated that additional studies are needed to define therapeutic properties of marijuana, standard and optimal doses,

and routes of delivery. The report states that research has been hindered by debate over legalization, the complicated federal approval process, and limited availability of research-grade cannabis. No doubt the issue will be presented at the June meeting of the American Medical Association, and pressure will be on the delegates to follow suit with the ACP. If the AMA House of Delegates joins the ACP on this issue, the door will be open. Perhaps also the American Academy Ophthalmology (AAO) will follow suit and change policy regarding marijuana and glaucoma.

#### ❖ THERE IS NO GREED LIKE THE PHARMACEUTICAL INDUSTRY, NOT EVEN TOBACCO PEOPLE OR THE OIL

Not satisfied that cholesterol-lowering drugs are already prescribed in excess, now Merck wants to dispense 20 mg. doses of Mevacor over the counter without a prescription. Fortunately, the Food and Drug Administration (FDA) said no with a "not approvable" letter. Merck is not to be dissuaded. Edwin Hemwall, Merck's vice president, said Merck would evaluate the conditions outlined in the agency's response to determine the path forward for Mevacor OTC.

#### ❖ THE DIFFERENCE BETWEEN TRUE LOVE AND HERPES HERPES IS FOREVER.

In the not too distant past before specific anti-viral therapy, penetrating keratoplasty (PKP) for corneas scarred by herpes was considered nearly always a loser. Now a study in the American Journal of Ophthalmology has documented the use of acyclovir comparing oral versus topical therapy. Topical use resulted in a rejection rate of more than 50% but oral acyclovir reduced the rejection figure to 20%. Clearly, oral acyclovir should be the prophylactic drug of choice in PKP for eyes scarred with herpes simplex.

#### ❖ HAS ANYBODY SEEN ELVIS LATELY?

The death of big-time movie star Heath Ledger due to a combination of sedatives and prescription pain-killers has served to accentuate the potential dangers of mixing prescription medications. The great majority of patients don't have a clue about the cumulative effects of drugs, especially those designed for sleep or pain or anxiety, and the addition of alcohol further heightens the potential for death. When the medical examiner's report shows death due to drug overdose, the toxicology report often reveals that multiple drugs were ingested. In Ledger's case the report listed hydrocodone, diazepam, oxycodone, temazepam, alprazolam and doxylamine as being found his system. The City of New York Chief Medical Examiner concluded that "the manner of death is accident, resulting from the abuse of prescription medications." Lethal combo - narcotics, sedatives, tranquilizers, and alcohol.

#### ❖ WHAT A CUTE GECKO! THAT'S NO GECKO. IT'S A PANTHER.

According to Pew Research Center data released in 2007, 36% of 18 to 25year-olds have tattoos while 40% of 26 to 40-year-olds have at least one. Beyond age 41 the number drops to 10%. Naturally, some of these people aren't happy with the result and 17% regret their tattoo decision, sometimes because a name inscribed is no longer in favor (Mother?), or the image faded or sagged, or "it was stupid." Technology to the rescue! A company called Freedom-2 in Camden, New Jersey, has developed an ink that can be removed with just one laser treatment and it leaves no scar. So far, old time tattoo artists aren't interested in changing ink says Sailor Bill Johnson, vice president of the National Tattoo Association. "We've had success and we know what is good." The FDA needs to approve tattoo inks before they

can be marketed, but in fact, they seldom bother since there haven't been any widespread concerns about tattoo safety. The actual practice falls under state and local regulations. The threat of disease is real since improperly sterilized tools can transmit HIV, hepatitis, or staph aureus, or all three. One-time US Marine George Schultz, holder of three cabinet posts under two presidents has a tiger tattooed on his behind. We don't know what it looks like today, and let's hope we never will.

#### ❖ I DO NOT FEAR THOSE PALE GREEN PANTS WITH NOBODY INSIDE THEM. I SAID AND SAID AND SAID THOSE WORDS. I SAID THEM, BUT I LIED THEM. (Dr. SEUSS)

Roger Clemens, possibly the best baseball pitcher in modern times, went before the House of Representatives committee investigating baseball, and swore that he did not and has not ever taken or been injected with human growth hormone or anabolic steroids. It is a tough call for Roger because his old teammate Andy Pettite stated under oath that Clemens had told him that he had taken the drug. Moreover, the trainer at the time has testified that he administered the drugs to Clemens during the 1999 and 2000 baseball seasons. Supposedly, he retained needles and syringes to establish his DNA evidence, if it should ever become important to do so. Oh yeah, right!! Like the famous blue dress of President Clinton fame, why would a person keep syringes and needles nearly ten years? It might appear that the trainer had other things on his agenda besides keeping his team's athletes in competitive shape. Do you think? Whatever the Clemens outcome this wonderful game invented in the USA has been dishonored by a few rotten apples.

#### ❖ A NEW SURVEY REVEALS THAT MOST AMERICANS WOULD RATHER GIVE UP SEX THAN THE TELEVISION REMOTE.

No one could claim that the 2008 Super Bowl (XLII) was dull. Often the Super Bowl party is much more interesting than the game, but this time it was white knuckles to the very end as the New York Giants upset the already canonized (by all the sport talking heads), "best of all time" New England Patriots. The Fox network was delighted because the game was the second-most watched television spectacle of all time with 97 million, topped only by the final MASH episode in 1983 (100 million) according to Nielsen Media Research. The audience increased over the course of the game reaching 130 million at the end. The advertisers got their money's worth as they paid out \$2.7 million for a 30-second spot. The fighting balloon floats were judged the best advertisement with the Charlie Brown balloon winning the bottle of Coca-Cola.

#### ❖ ALWAYS YIELD TO A BLIND PEDESTRIAN EVEN THOUGH HE CAN'T READ YOUR LICENSE PLATE.

A study published in the journal Ophthalmology used a managed care data base to evaluate the cost of being blind compared with a similar population of patients with eyesight. Researchers identified 10,796 blind patients and a similar cohort of seeing patients, using total and pharmacy-related direct medical charges for a full year. For the blind population the median charges in the first year were \$6,854 per person, while the non-blind patients' median charges were \$3,778. The analysis by age group revealed significantly higher overall charges in the older age group.

#### GARBAGE IN, GARBAGE OUT!

Not unlike Hawai'i, certain places in Lake County, Calif., attract illegal dumping. A Lucerne man loaded his pick-up with garbage, drove out Robinson Road, stopped and dropped the tailgate, and began to empty his garbage. He fell dead, apparently with shovel in hand, cause of death undetermined. Fate? Karma? Bachi? Be careful where you dump!

#### ❖ JAWS SPRING KID JUST AHEAD OF SPIN CYCLE.

A 4-year-old wanted to investigate the top-loading washing machine (it was not running). He managed to get stuck against the agitator with his knee folded across his chest. Firefighters and the "jaws of life" were required to extricate him without injury, but the washer was never the same.

#### ADDENDA

- ❖ In the Netherlands a man was arrested for licking women's toes while they were sunbathing. Prosecution had to negate the arrest because toe-licking is not defined as a crime since there is no objective sex act.
- ❖ In Melbourne, Australia, a 38-year-old man and his 36-year-old girlfriend planned to rob a restaurant. He grabbed what he thought was a bag of money, but was a bag of rolls. Then he accidentally fired his gun striking his partner in the buttocks. They were arrested.
- ❖ A sex shop in Brasov, Transylvania, was ordered to pay \$1,179 to a man who claimed his inflatable doll had "lost her moan."

#### ALOHA AND KEEP THE FAITH — rts

Contents of this column do not necessarily reflect the opinion or position of the Hawai'i Ophthalmological Society and the Hawai'i Medical Association. Editorial comment is strictly that of the writer.





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—Mitchell B. Miller, MD, physician member of the AMA and his local and state societies

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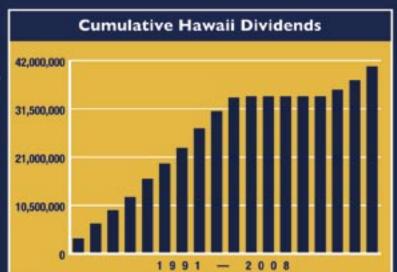


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