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Contents

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"Nene"

Depicting the official Hawai'i state bird which is making a come-back from near extinction.

HE MANA'O: THOUGHTS FROM THE EDITOR

HAWAI'I MEDICAL JOURNAL

October 2006

S. Kalani Brady MD, MPH, FACP
Editor, Hawai'i Medical Journal

The Hawai'i Medical Journal is the peer-reviewed publication of the Hawai'i Medical Association. Our Association has 1300 members. One of the most important events for the HMA is the Annual Meeting, occurring this year on October 20-22 at the Hawai'i Convention Center. This meeting celebrates the 150th anniversary of the Association. It provides the opportunity to network with our peers; continue our education in medicine and health care issues with the Scientific Sessions; deliberate on the state of our organization, both present and future; direct the leadership as to how to represent us as physicians with the Legislature and the larger community; attend the Exhibit Fair with your office staff and family for quick learning points and useful material; and have a great time at the Ola Pono Ike Medical Ball & Silent Auction.

Based on the needs surveys you completed, the Scientific Session planning committee developed presentations on legal issues which affect medical practice, minimizing the risk of being sued, building a new system of health care financing, care for the uninsured and underinsured, a debate on pay for performance, a panel on electronic medical records, integrative and complementary medicine, pearls in the management of chronic kidney disease, and an update by executives of Hawai'i's major medical centers. The faculty is dynamic and informative. The learning opportunity is great.

With shrinking reimbursement for patient encounters and increasingly complex diagnostic modalities and management plans, we physicians are at risk of becoming solely absorbed with the daily intensity of our practices. The Annual Meeting provides the opportunity to step back and regain perspective on the larger issues confronting our profession. It is through meetings like this that we can be most effective in guiding the future of medicine. Take the opportunity! Call today and register for this important meeting.

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Overweight and At-Risk for Overweight Among Hawai'i Public School Students Entering Kindergarten, 2002-2003

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Abstract

Recent studies have pointed to an increasing problem of overweight and obesity in children in Hawai'i, but all of these studies have been conducted in specific communities or special population groups. No broad population-based studies have been conducted to document the extent of overweight in the general population of children in Hawai'i. To provide a population based estimate of overweight in Hawai'i's children, this study examined Student Health Records for 10,199 children entering kindergarten in public schools during 2002-2003. Data on age, gender, height, and weight were used to calculate BMI (body mass index) scores. Because records for all students entering public school kindergarten were available for analysis, the data presented here represents the broadest estimates of overweight and at risk for overweight in Hawai'i's children published to date. The results illustrate that almost one-third of the children aged 4-6 years old entering Hawai'i public schools are either overweight or at risk for overweight. Rates are higher in rural school complexes than urban ones. Compared to a 1984 study that found 'no significant under or over nutrition' in Hawai'i's school children, our results suggest that almost one-third of children aged 4-6 entering Hawai'i public schools are either overweight or at risk for overweight. Physicians should be aware of this growing problem, and seek to implement practices to combat overweight among their pediatric patients and families.

Introduction

The number of overweight children in the United States has doubled in the past 20-30 years, with similar patterns occurring throughout the world.[1] Data from the 1999-2002 National Health and Nutrition Examination Survey (NHANES),[2] which uses actual height and weight measurements, indicated that an estimated 16% of children and adolescents ages 6-19 years were overweight. Studies have also shown that children in certain minority ethnic groups (American Indians, Hispanics, African-Americans) in the United States are particularly at risk for overweight and obesity.[3] The Centers for Disease Control and Prevention (CDC) 1999 Youth Risk Behavior Survey (YRBS)[4] found no difference between adolescents in Hawai'i and nationally in terms of the proportions at risk for overweight (14.3%) or overweight (10%), illustrating that Hawai'i is clearly following nationwide patterns for overweight and obesity.

The health problems that overweight or obese children and youth develop are similar to problems of overweight or obese adults. They are at increased risk for numerous health conditions, including type 2 diabetes,[5,6] hypertension, cardiovascular disease,[7] dyslipidemia (high triglyceride levels), some specific cancers, gallstones, osteoarthritis, rheumatoid arthritis, premature death, sleep apnea and respiratory problems, as well as poorer physical functioning status,[8] and lower life expectancy.[9]

Background

More than 20 years ago, researchers at the University of Hawai'i conducted a study on the anthropometry of Hawai'i school children, which provides an important background to current studies.[10] Lichton and his colleagues were able to measure the height, weight and measurements of the non-dominant arm (both upper arm circumference and triceps skin-fold thickness) of more than 14,000 children ages 5 to 15 years, attending both public and private schools in Hawai'i. Their purpose was to establish growth standards for specific race and ethnic groups in Hawai'i and to examine whether or not there was evidence of what they termed "significant under or over nutrition" within any groups of children. They compared their measurements with mainland children sampled for the National Center for Health Statistics (NCHS) growth curves in 1977, and found Hawai'i children had heights and weights similar or greater, except for Samoan children who were consistently taller and heavier than the other school children. Comparisons of children of Asian ancestry were done based on studies conducted in several Asian countries (Philippines, Taiwan and South Korea), mainly because of the high rates of immigration from Asian countries to Hawai'i. Comparing Asian ethnic school children with their counterparts in Asia found that Hawai'i's Filipino, Chinese and Korean schoolchildren were taller and heavier than their counterparts in Asia. The

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authors suggested however, that Filipino children in Hawai'i stored less fat than other children. They did not find any evidence of over or under-nutrition among Hawai'i's school children. They further suggested that Samoan children may, for genetic reasons, be taller and heavier than other groups and their greater weight and storage of fat was not considered over-nutrition because this fit with their greater height. Numerous studies of Pacific populations have illustrated that the problems of dietary related chronic diseases, especially diabetes and obesity, are pervasive for Pacific Islanders (e.g. Native Hawaiians, Samoans and Micronesians).[11-13]

Recent research studies suggest that Hawai'i has a significant problem with childhood overweight. Most estimates are for infants and very young children and youths or adolescents; only a few studies include elementary school students. These studies have also found ethnic differences in the proportions of overweight or at risk.

A 1997-1998 cross-sectional study of more than 20,000 children aged 1-4 years participating in the United States Department of Agriculture (USDA) Women, Infants and Children (WIC) food program in Hawai'i found that the prevalence of overweight in all ethnic groups was above the expected 15%.[14] The data also demonstrated significant differences across ethnic groups. Among 2-4 year olds, Samoan children were the tallest (16.9%) and the heaviest (27% were overweight), while Filipino children were the shortest (19.0% were short) and the lightest (11.8% were underweight) (based upon the CDC percentile cut-off points). Hawaiians (13.6%), Asians (12.2%), and Others (10.1%) also had high percentages of short children. The prevalence of overweight was lowest among 1-year-olds, but it increased at age 2 and remained high until age 4.

A longitudinal study examining body size and overweight, which took anthropometric measurements of more than 1,400 public school students ages 6-17 years on Moloka'i, suggested a childhood obesity problem in Hawai'i, disproportionately affecting those of Hawaiian ancestry.[15] Obesity rates in that study were twice as high as national rates.

Data from the 2003 Hawai'i Youth Risk Behavior Survey (YRBS) show that 27.1% of the middle school students surveyed considered themselves to be slightly or very overweight. Other survey data collected between 2000-2004 from the Nutrition Education Needs Assessment Survey (NENAS) conducted in the Hawai'i public schools every 10 years, also showed an overweight problem among youth and teenagers. More than one-third of the 4th graders and high school students surveyed for the NENAS were either overweight or at risk for overweight.

While the studies mentioned above support a significant problem of overweight among young children and youths and adolescents in Hawai'i, the lack of sufficient and current data on elementary school age children was one driving force behind this study. Another reason for this study was to assess the utility of the Student Health Records as a source of surveillance data for childhood weight measurement.

Methods

Student Health Records are required for students entering public schools by Hawai'i Administrative Rules.[16] Under an agreement with the Superintendent's Office of the Department of Education and the Department of Health, this study was conducted to examine childhood overweight among public school students, and to assess the feasibility of using the Student Health Records as a means of surveillance of childhood overweight. The study protocol was reviewed and approved by the Department of Health's Institutional Review Board and the Superintendent's Office of the Department of Education.

The Student Health Record document contains the student's required immunizations history and must be stamped or signed by a medical practitioner, medical personnel, or a clinic. It also contains the student's information on the forms, including the age and gender of the child along with information regarding existing chronic conditions, such as asthma. Height and weight are measured and recorded by the medical personnel completing the form.

Of the 12,682 children who entered the Hawai'i public school system in 2002-2003, there were 12,452 Student Health Records available from the DOH Immunization Branch. 2,253 records were excluded from the study: records which were not complete for age, sex, weight ,and height or had implausible anthropometric values, and children who did not meet the age criteria of the study (e.g. older students transferring into a school). The study population was limited to those students from ages 4 to 6 years (48 to 71 months), resulting in a total of 10,199 students; the mean age was 57 months old. EpiInfo 2000 NutStat was used to calculate percentiles for BMI (body mass index), height for age and weight for height based on the 2000 CDC reference population.

The CDC reference population is based on national health surveys from 1963 to 1994 along with supplemental sources, including NHES II &II, NHANES I, II & III and others.[17] It is important to note that the CDC reference population is actually an "idealized population". The CDC reference population can be described as a normal distribution with cut off points using z-scores (standard deviation units) or percentiles. In this study we are using the percentile cut-off points. The CDC uses the following definitions as cut-off points for percentiles: overweight is defined as BMI $\geq$ 95th percentile and at-risk for overweight was defined as being between $\geq$ 85th and < 95th percentiles. In an idealized population, 10% of children would be

at-risk for overweight and 5% would be overweight, with a total of 15% combined at-risk for overweight and overweight.

One limitation of this study is that kindergarten is not required in Hawai'i; therefore, this study population is not representative of children aged 4-6 throughout the state of Hawai'i in 2002-2003, so we do not know the total number of children who could have entered kindergarten during 2002-2003. We estimate therefore, that this group of kindergartners (n=10,199) accounts for at least one-third of the population of children aged 4 to 6 in the state of Hawai'i in 2002-2003 (e.g. there were more than 30,000 children aged 4 to 6 in the state of Hawai'i in 2002-2003). Furthermore, this group of children is only comprised of public schools students and does not provide any estimates of the proportions of children entering kindergarten who are overweight or at-risk for overweight children in private schools.

Results

Table 1 lists the percentages of children overweight and at risk for overweight for each of the school complexes in Hawai'i. The maps show these percentages for each island. School complexes in Hawai'i are grouped geographically and comprise those elementary and middle schools that feed into a particular high school, similar to a school district. Although information on individual schools was available for the study, and was provided to the Department of Education, to ensure privacy, results of individual schools were suppressed under an agreement between the Department of Health and the Department of Education.

Overall, the state totals (Table 1) reveal high proportions of 4 & 5-year-olds entering Hawai'i public schools overweight and at-risk for overweight (28.5%). Variation between complexes range from a low of 17.6% at the Kaiser complex on O'ahu, to a high of 47.1% at the Hana complex on Maui. In general, this study suggests that rural communities on O'ahu and O'ahu's Neighbor island communities are more likely to have kindergarteners entering schools overweight or at risk for overweight.

Discussion

Since these data represent the status of children entering kindergarten, overweight and obesity is clearly a problem which exists before children begin school in many communities throughout Hawai'i. There are some notable differences between school complexes, as different school complexes reflect the ethnic and other social characteristics of the communities of which they are a part. For examples of the diverse ethnic, social, economic, and other characteristics of Hawai'i's school complexes, refer to the University of Hawai'i's Center on the Family Data Center interactive website.[18] Further research is currently being conducted to determine some of the school and community factors that may be associ-

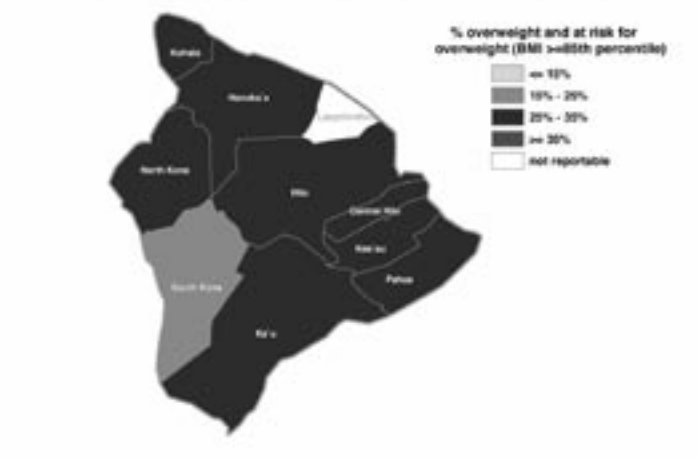
Table 1: Hawaii 4 & 5 year olds entering public schools in 2002-2003 by complex area and percentage overweight or obese.

	Complex Area	% overweight (BMI >=95)	% at risk for overweight (BMI >= 85 and < 95)	Total
State total (N=10,199)		14.4	14.1	28.5
(Oahu N=7,234)		13.9	13.8	27.7
	Aiea (N=247)	8.1	17.8	25.9
	Campbell (N=440)	16.4	13.0	29.4
	Castle (N=370)	15.4	13.5	28.9
	Farrington(N=483)	15.5	17.2	32.7
	Kahuku (N=188)	19.7	16.0	35.7
	Kailua (N=204)	15.2	13.7	28.9
	Kaimuki (N=343)	15.5	13.7	29.2
	Kaiser (N=119)	7.6	10.1	17.6
	Kalaheo (N=305)	9.5	12.8	22.3
	Kalani (N=249)	7.6	12.9	20.5
	Kapolei (N=334)	13.2	10.5	23.7
	Leilehua (N=553)	13.4	15.9	29.3
	McKinley (N=373)	14.5	13.4	27.9
	Mililani (N=315)	10.8	13.7	24.5
	Moanalua (N=241)	12.5	12.0	24.5
	Nanakuli (N=148)	17.6	10.8	28.4
	Pearl City (N=446)	13.2	12.8	26.0
	Radford (N=588)	12.2	15.1	27.3
	Roosevelt (N=407)	11.1	11.8	22.9
	Waialua (N=59)	22.0	17.0	39.0
	Waianae (N=302)	15.9	14.2	30.1
	Waipahu (N=483)	19.9	12.6	32.5
Hawaii (N=1,310)		15.1	15.2	30.3
	Central Hilo (N=215)	16.3	14.0	30.3
	Hilo (N=241)	17.0	14.5	31.5
	Honokaa (N=200)	16.5	18.0	34.5
	Kau (N=41)	14.6	17.1	31.7
	Keeau (N=152)	15.1	17.1	32.2
	Kohala (N=34)	11.8	20.6	32.4
	North Kona (N=221)	15.4	13.1	28.5
	Pahoa (N=86)	14.0	14.0	28.0
	South Kona (N=120)	8.3	14.2	22.5
Kauai (N=488)		12.5	16.4	28.9
	Central Kauai(N=233)	9.0	14.2	23.2
	East Kauai (N=150)	16.0	14.7	30.7
	West Kauai (N=141)	14.9	22.0	36.9
Maui (N=1,167)		17.9	13.8	31.7
	Baldwin (N=203)	17.2	17.7	34.9
	Hana (N=17)	35.3	11.8	47.1
	Kekaulike (N=275)	15.6	12.7	28.3
	Lahainaluna (N=124)	27.4	17.7	45.1
	Lanai (N=30)	20.0	26.7	46.7
	Maui (N=452)	15.9	11.1	27.0
	Molokai (N=67)	17.9	13.4	31.3

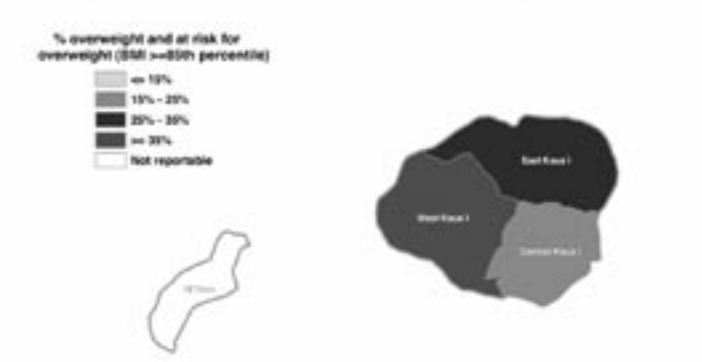
Source: Department of Health, Community Health Division.

Note: Laupahoehoe and Niihau are not reportable due to small numbers.

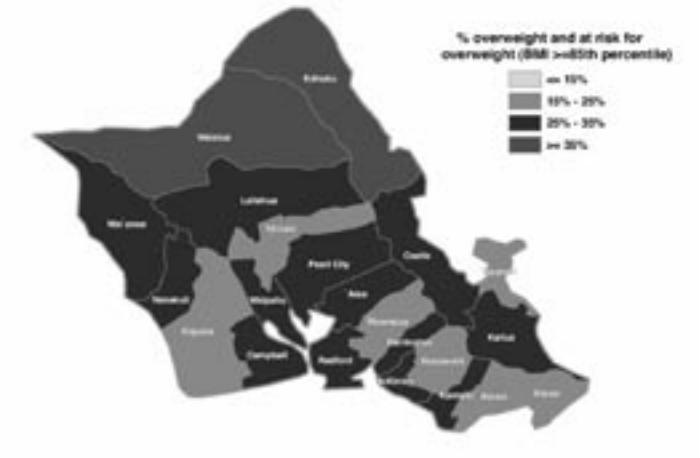
Percent Overweight And At Risk for Overweight, Public School Students Entering Kindergarten By School Complex, Hawai`i County, 2002 - 2003



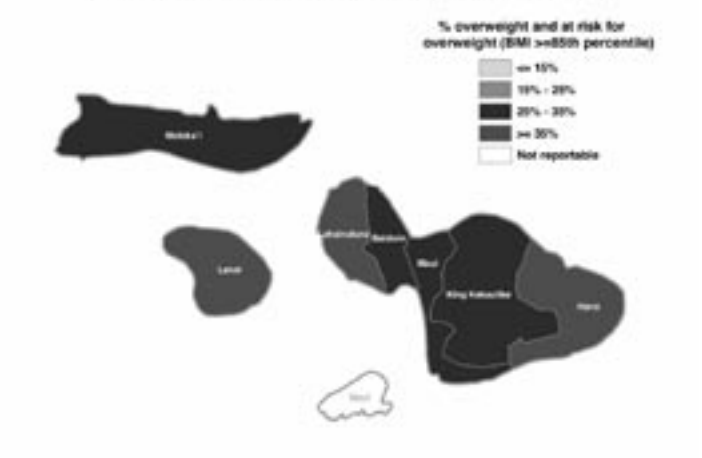
Percent Overweight And At Risk for Overweight, Public School Students Entering Kindergarten By School Complex, Kaua`i County, 2002 - 2003



Percent Overweight And At Risk for Overweight, Public School Students Entering Kindergarten By School Complex, Honolulu County, 2002 - 2003



Percent Overweight And At Risk for Overweight, Public School Students Entering Kindergarten By School Complex, County of Maui, 2002 - 2003



ated with the observed differences between the school complexes. School level indicators for which data are available include ethnicity, the proportions of children receiving subsidized school lunches, the proportion of families receiving TANF (Temporary Assistance for Needy Families) and proportions of children for whom English is a Second Language (ESL). Community level indicators for which data are available include ethnicity, income, and occupation.

This study supports the findings of other recent studies, illustrating that childhood obesity is a serious problem in Hawai'i, for both the individuals involved and communities that will experience an increased burden of providing care for individuals with chronic diseases. It is important that a comprehensive system of prevention, early detection and treatment be developed. Trends in reported physical activity levels on the YRBS also indicate that the percentage of Hawai'i middle school students who attended physical education classes daily has decreased by 50% from 1993 to 1999. The overall proportion of these students participating in daily physical activity was much lower compared to the United States.[19]

Surveillance is an essential element of a coordinated public health response, developing and implementing a system for monitoring childhood obesity is an essential foundation of obesity prevention. It is evident from this study that it is feasible to use Student Health Records (Form 14) data as a basis for developing a system of on-going childhood obesity surveillance. Such a surveillance system needs to include Student Health Records from private schools as well in order to be state-based. Private schools also require students to have completed Student Health records for immunizations, therefore the potential for a state-wide surveillance system for children entering schools is feasible.

The findings from this study suggest that there is a significant and growing problem of overweight among Hawai'i's children. Physicians need to be aware of this growing problem, and should seek to implement strategies within their practices to combat overweight among their pediatric patients and families. Guidance on the role of physicians in the prevention of pediatric overweight obesity is available through the American Academy of Pediatrics.[20]

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Conjugate Heptavalent Pneumococcal Vaccine Outcome Improvements

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Abstract

Heptavalent conjugate pneumococcal vaccine (PCV7) is now routinely administered to infants. Medical records from a pediatric outpatient clinic were used to identify two study groups: 1) those born between January 1995 – May 1997 (controls), 2) those born between April 2000 – May 2001 (PCV7 group). The PCV7 group showed a lower incidence of otitis media episodes, clinic visits for fever and respiratory symptoms, antibiotic prescriptions, ceftriaxone use, and hospitalizations (singled sided probabilities).

Introduction

The heptavalaent conjugate pneumococcal vaccine (PCV7) (trade name Prevnar©) has been shown to induce an effective T-cell-dependant response against the seven most-common serotypes of *Streptococcus pneumoniae*. While initially licensed to prevent invasive pneumococcal disease, several studies over the past two years have documented modest efficacy against other, more common childhood pneumococcus-related illnesses such as otitis media[1-3] and community-acquired pneumonia.[4,5]

Numerous serological surveys have shown wide geographical variations in *S. pneumoniae* serotypes,[6-9] with theoretical protection via the 7-valent conjugate vaccine ranging from nearly complete to well below 50%. Populations thus far studied have been primarily Caucasian, African-American, and Native American.[10,11] Hawai'i, with its larger proportion of Asian and Pacific Islanders, may show differing patterns of conferred immunity with PCV7. Some of these studies have shown equivocal results in the prevention of otitis media in their study populations,[2,3,12] raising the question of vaccine efficacy against otitis media.

The purpose of this study is to add further data to assess PCV7 efficacy against familiar pneumococcal-related illnesses in Hawai'i.

Methods

All medical records from a pediatric outpatient clinic were screened for patients falling into one of two groups. Those born between January 1995 – May 1997 were placed in the "control group," and those born between April 2000 – May 2001 were placed in the "PCV7 group." Records for each group were examined, and patients were removed from the study if they met any of the following exclusion criteria, which place the patient at a higher risk of pneumococcal related infections, pneumonia in general, or lack of sufficient follow-up:

- history of meconium aspiration requiring mechanical ventilation
- congenital heart disease or pulmonary abnormality
- immunocompromising condition
- chronic renal disease
- neurologic conditions other than febrile seizures and meningitis
- language or developmental delay
- changed doctors or died prior to 36 months of age

Additionally, patients in the control group were excluded if they received any doses of the PCV7 vaccine prior to 36 months of age; patients in the PCV7 group were excluded if they did not receive three doses of the PCV7 vaccine prior to 12 months of age. Following these exclusions, 72 patients remained in the sample group and 83 patients remained in the control group.

All outpatient, inpatient, and emergency department records were reviewed for these patients, and basic demographic data, disease incidences, and visits to providers were recorded. Patients receiving care at this outpatient clinic are registered primary care patients, nearly all of which have medical insurance plans that require primary care and non-emergent care to be obtained exclusively at this clinic. Because of this, inpatient care and emergency department care are almost exclusively provided at the same medical center. This set of circumstances makes it extremely likely that all outpatient clinic, emergency department, and inpatient encounters will be captured by reviewing the patient's medical record.

Differences between groups were analyzed using univariate analysis. The null hypothesis is phrased such that single sided (one tailed) probabilities apply. In other words, we are only interested in the whether PCV7 group has improved outcomes (lower disease

incidence). P values listed in the results are single sided probability values.

Results

72 children born between 2000–2001, who received three doses of PCV7 prior to 12 months of age, were compared to 83 controls who did not receive PCV7. The groups were similar in birth weight, gestational age, and asthma prevalence. The results are tabulated in Table 1. The PCV7 group showed a significantly lower incidence of otitis media episodes, clinic visits for fever, clinic visits for respiratory symptoms, antibiotic prescriptions, ceftriaxone use, and hospitalizations. No significant differences were observed in the mean episodes of urinary tract infections, CBC, urinalyses ordered, or emergency department visits for chief complaints of fever or respiratory symptoms.

Table 1.— Outcome incidence means (+SD) in control versus PCV7 groups. Significant p values are single sided probabilities.

	PCV7	Controls	p value
Gender	45M/27F	41M/42F	NS
Gestational age	39.2 ± 1.4	39.3 ± 1.4	NS
Well child check visits	8.2 ± 1.4	8.7 ± 1.3	NS
Asthmatics	31 (43%)	38 (46%)	NS
Clinic visits for fever	3.4 ± 3.0	5.0 ± 4.0	0.003
Clinic visits for respiratory symptoms	3.9 ± 3.4	6.1 ± 5.2	0.0014
ED visits for fever	1.8 ± 2.2	1.8 ± 2.2	NS
Other ED visits	1.0 ± 1.1	0.9 ± 1.1	NS
Pneumonia episodes	0.39 ± 0.72	0.60 ± 0.95	0.06
Otitis media episodes	2.5 ± 3.4	4.2 ± 4.0	0.003
Urinary tract infections	0.07 ± 0.26	0.05 ± 0.22	NS
Bacteremia episodes	0.014 ± 0.12	0.048 ± 0.22	NS
CBC	1.3 ± 1.8	1.5 ± 1.6	NS
Urinalysis	0.76 ± 0.97	0.80 ± 1.0	NS
Blood culture	0.9 ± 1.1	1.3 ± 1.6	0.045
Antibiotic prescriptions	4.5 ± 4.3	7.2 ± 5.8	0.0009
Ceftriaxone doses	3.9 ± 3.4	6.1 ± 5.2	0.0014
Hospitalizations	0.26 ± 0.56	0.47 ± 0.86	0.042

Discussion

Comparison of demographic data showed that the two groups were statistically similar in terms of gender, birth weight, gestational age, and prevalence rates for asthma.

Analysis of disease incidence showed a statistically-significant decrease in the rate of otitis media following pneumococcal-conjugate vaccination, as were total antibiotic prescriptions written, hospitalizations, ceftriaxone use, and blood cultures. For the latter three findings, the double sided probability is greater than 0.05. However, using a single sided probability is valid in this analysis. The single sided p value of 0.06 for the incidence of community-acquired pneumonia, almost achieved statistical significance as well. This was most likely due to the small size of the study population and the likelihood that most pneumonias in this age group are of viral etiology which is not likely to be affected by PCV7. It would be particularly difficult (a larger sample size would be needed) to demonstrate PCV7 efficacy in reducing the overall incidence of pneumonia of which only some cases are caused by pneumococcus.

Several indicators of health-resource utilization were also decreased in the vaccinated group, specifically clinic visits for fever and respiratory complaints. However, emergency department visits for the same complaints were not decreased, though this may be ascribable to a documented increase in ED utilization between the time-periods examined. In the same vein, CBC and urinalysis testing did not decrease between groups (though there were fewer blood cultures obtained in the PCV7 group), reflecting the fact that the vast majority of these tests are ordered out of the emergency department, rather than outpatient clinics. Further study will be necessary to determine whether the decrease in clinic utilization, admissions, and antibiotic-usage translate into cost-effectiveness of the vaccine in this state. Since the two study groups sustained their illnesses and events during different periods of time, the possibility that changes in test ordering and antibiotic use behavior during these periods is partially or entirely responsible for these results. However, it is likely that ceftriaxone use has overall increased or stayed the same over the years rather than decreased. Thus, a decline in ceftriaxone use for PCV7 group is particularly remarkable. This effect on test ordering behavior is less clear.

In conclusion, the results of this study confirm many of the findings of other studies. In this small study conducted in Honolulu, the pneumococcal-conjugate vaccine has resulted in significant declines in otitis media, antibiotic usage, and hospitalization in children under the age of 3.

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Oral Antibiotic Treatment for Methicillin-Resistant Staphylococcus aureus Skin and Soft Tissue Infections: Review of the literature

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Abstract

*Background: The emergence of methicillin-resistant **Staphylococcus aureus** (MRSA) as a cause of hospital- and community-associated infection has been reported worldwide and has become an increasing health care problem. Treatment options for MRSA infection are limited, complicated and expensive. Oral antibiotics have been used in the outpatient setting for less severe MRSA infections such as skin and soft tissue infections (SSTIs), but their efficacy has not been well studied.*

Methods: We reviewed the literature and Internet information sources as well as recent abstracts for factors relevant to the in-vitro and in-vivo activity and adverse effects of oral antibiotics of possible value in treating MRSA SSTI.

Results: Most of MRSA isolates are still susceptible to linezolid, TMP-SMX, and the tetracyclines but less susceptible to the quinolones, clindamycin, and erythromycin. Only the quinolones have bactericidal activity, which may be a relevant factor if there is bacteremia. In-vivo studies indicate a high clinical cure rate with linezolid, TMP-SMX, doxycycline and minocycline. Adverse effects are different among the drugs and are a significant factor. Antibiotics with once-daily dosing such as the quinolones have advantage in regard to compliance. Linezolid has the highest daily cost of treatment whereas the cost of the tetracyclines, erythromycin, and TMP-SMX is much lower.

Conclusion: The antibiotics available for MRSA SSTI vary widely in chances of resistance, activity, adverse effects, and cost. More clinical studies of clinical efficacy are needed, especially with comparative trials. Selection of the most appropriate antibiotic will depend upon local antibiotic resistance, type of infection, potential adverse effects, and cost for the individual.

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) has gradually evolved over the past 40 years in hospitals and more recently with new strains in the community.[1] This formidable pathogen has become an increasing problem with a spectrum of infection that often threatens human lives as well as the resources of the health care system.[2] Skin and soft tissues are common sites for MRSA infection in both hospital and community settings.[2-5] The options for treatment of MRSA are limited, especially with oral antimicrobials. Hospitalization and parenteral therapies are expensive and complex. Intravenous vancomycin continues to be the mainstay of therapy for hospitalized patients with severe MRSA infections. However, oral anti-MRSA medications are often used in patients with less severe infection, such as skin and soft tissue infection (SSTI), or in those who can be switched from intravenous therapy.[6] The benefits of oral antibiotics for MRSA infection, in terms of lower cost, convenience, and length of hospital stay reduction, have been shown in previous studies.[5,7,8] Oral antibiotics of potential value in treating MRSA include linezolid, trimethoprim-sulfamethoxazole (TMP-SMX), clindamycin, tetracyclines, macrolides and fluoroquinolones. Their relative risks and benefits have not been well studied and their comparative efficacy is uncertain. We reviewed the literature on in-vitro and in-vivo studies, clinical trials, adverse effects, cost, and the use of these oral antibiotics for MRSA SSTI.

Methods

Information about the likelihood of antimicrobial resistance in Hawai'i was derived through reports available from Diagnostic Laboratory Services (DLS) on the Internet.[9] In-vitro studies of these antibiotics on *Staphylococcus aureus* were researched using the MEDLINE database (which includes citations from 1966 to the present). The terms used were "*Staphylococcus aureus*", "MRSA", "skin and soft tissue infection", "linezolid", "trimethoprim-sulfamethoxazole (TMP-SMX)", "clindamycin", "erythromycin", "tetracycline", "doxycycline", "minocycline", "ciprofloxacin", "levofloxacin", "gatifloxacin" and "moxifloxacin". The English-language literature was searched for clinical trials on MRSA skin and soft tissue infection treated with linezolid, trimethoprim-sulfamethoxazole (TMP-SMX), clindamycin, erythromycin, tetracyclines, and fluoroquinolones. Abstracts from the 43rd Annual Meeting of Infectious Diseases Society of America (IDSA) (2005) and drug information on these antibiotics from

the Food and Drug Administration (FDA) Website were reviewed.[10]

The activity of the different antibiotics was reviewed based on that reported in the literature in regard to their in-vitro activity as judged by their minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC), and concentration of the antibiotics compared with their MIC. The calculated ratio of the area under the curve to the minimal inhibitory concentration (AUC/MIC) was selected as the best parameter of in-vitro activity.[11]

In-vivo activity was estimated through the clinical studies that have been done for *Staphylococcus aureus*. In addition, a separate analysis was done for MRSA.

Dosing and adverse effect information was gathered from the Physician Desk Reference compendium of package inserts authorized by the Food and Drug Administration.[12] Cost figures were derived from the price of the Long's pharmacy as of February 1, 2006.

Results

The in-vitro considerations in regard to the antibiotic choice are listed in table 1. Susceptibility data is taken from the DLS Website as available in December, 2005. Linezolid is reported only on request in most labs but all strains in Hawai'i have been reported susceptible so far. Minocycline and doxycycline are not usually tested but the bacteria may be assumed susceptible if the strains are susceptible to tetracycline. Ciprofloxacin, moxifloxacin, and gatifloxacin can be assumed to be active if the strains are against levofloxacin. Outpatient results are distinguished by site of origin, which may consist of doctor offices or clinics. Inpatient results were derived from hospitals.

Only the quinolone antibiotics are considered bactericidal as defined by the MBC being at least two tube dilutions (4-fold) higher than the MIC.[13] The AUC/MIC ratio was derived from the expected serum concentrations over time divided by the MIC as shown in the column 6. The AUC/MIC ratio is generally considered the best pharmacokinetic-pharmacodynamic parameter for determination of drug efficacy.[13] However, many of the older antibiotics have not been modeled for the AUC/MIC activity.

Table 2 displays the information published from clinical studies which evaluated any strain of *Staphylococcus aureus* susceptible to methicillin. It is difficult to compare results of clinical trials because of the variation in study methodology, patient inclusion criteria, treatment variation, and measures of success. The best data exists for linezolid and the quinolones, which are the only oral anti-staphylococcal antibiotics granted Food and Drug Administration (FDA) approval for this organism within the last three decades.[10] The clinical response rates were 89% or greater for linezolid and the quinolones, with hundreds of patients analyzed for the recent trials required for FDA approval. We could find only 54 cases reported for doxycycline or minocycline and only one randomized controlled trial for minocycline. Results were not as good with minocycline for the simple randomized trial reported against penicillin or for two recent chart reviews of 10 cases. For macrolides, most of the studies were done with azithromycin although some were done with erythromycin. The rate of eradication of *Staphylococci* was reported only for azithromycin, gatifloxacin, levofloxacin, linezolid and moxifloxacin with all showing greater than 88% elimination.

Table 1.— In-vitro activity against methicillin-resistant *Staphylococcus aureus* of the oral antibiotics

Antibiotics	Susceptibility (%)			Antibacterial activity (MBC/MIC)	AUC/MIC ratio (hours)
	DLS[9]	Outpatient[15]	Inpatient[15]		
Ciprofloxacin	NA	64	15	Bactericidal	125[16]
Clindamycin	65	63	25	Bacteriostatic	NA
Doxycycline	NA	NA	84[6]	Bacteriostatic	NA
Erythromycin	41	46	16	Bacteriostatic	NA
Gatifloxacin	NA	NA	NA	Bactericidal	35[17]
Levofloxacin	66	61	21	Bactericidal	130[16]
Linezolid	100	NA	100	Bacteriostatic	50-80
Minocycline	NA	NA	84[9]	Bacteriostatic	NA
Moxifloxacin	73	NA	NA	Bactericidal	80[18]
Tetracycline	90	80	63	Bacteriostatic	NA
Trimethoprim-sulfamethoxazole	97	95	90	Bacteriostatic	NA

AUC/MIC = area under the curve/minimal inhibitory concentration; NA = not available.

Table 3 shows the studies that have been performed for MRSA. Four of the seven studies included a comparison with vancomycin and three of those were with linezolid. The linezolid studies all used initial intravenous therapy with a switch to oral when possible. The variations in clinical response to both linezolid and vancomycin were great and likely related to the severity of infection. In all three studies, however, linezolid appeared better in clinical results and in two of three, it appeared better in microbiological outcomes. The TMP-SMX compared against vancomycin study conducted by Markowitz et al was a randomized and controlled one with disappointing and statistically significant results.[14] We could find no studies comparing one oral drug with another.

Table 4 displays the pharmacological characteristics of the antibiotics and their costs. Only the quinolones can be given once a day in an otherwise normal person. Erythromycin, clindamycin and tetracycline have frequencies of administration, which may be a problem with compliance.

Discussion

The oral antibiotics available for therapy of MRSA differ considerably in the features we are able to analyze from prior studies. Local susceptibility testing is a critical part of decision making, especially as antibiotics are usually prescribed before resistance is known. Linezolid, the tetracyclines and TMP-SMX all have 90% or greater likelihood of in-vitro activity. Erythromycin and clindamycin have approximately a 50% likelihood of susceptibility. Susceptibility to the quinolones ranges up to 73% for moxifloxacin but is lower for the others.

From an in-vitro perspective, only the quinolones are bactericidal, a factor which may be relevant with possible bacteremia. The activity of an antibiotic calculated from the AUC/MIC ratio suggests the quinolones are very active but the results of the other antibiotics have not been reported.

Table 2.— Summary of clinical trials reporting treatment of methicillin-susceptible *Staphylococcus aureus* skin and soft tissue infections

Antibiotics vs. comparator	Study design	Number of cases vs. comparator	Clinical cure rate vs. comparator (%)[a]	Microbiological success rate vs. comparator (%)[b]	References (Year)
Azithromycin vs. cefadroxil	MC, RCT	152 vs. 139	97.0 vs. 96.0	94.0 vs. 86.0	Jennings et al.[19] (2003)
Azithromycin vs. dicloxacillin	DB, RCT	62 vs. 60	83.3 vs. 83.9	90.0 vs. 87.1	Amaya-Tapia et al.[20] (1993)
Azithromycin vs. dicloxacillin	MC, RCT	60 vs. 58	97.0 vs. 98.0	91.0 vs. 97.0	Rodriguez-Solares et al.[21] (1993)
Azithromycin vs. cephalexin	RCT	74 vs. 74	99.0 vs. 96.0	98.0 vs. 98.0	Mallory[22] (1991)
Clindamycin vs. cloxacillin	RCT	31 vs. 30	87.1 vs. 60.0	NA	Pusponegoro et al.[23] (1990)
Doxycycline vs. none	CR	13 vs. 0	100.0	NA	Ruhe et al.[6] (2005)
Erythromycin vs. mupirocin	RCT	51 vs. 51	73.0 vs. 95.0	NA	Dagan et al.[24] (1992)
Erythromycin vs. dicloxacillin	RCT	20 vs. 30	96.6 vs. 96.7	NA	Barton et al.[25] (1988)
Gatifloxacin vs. levofloxacin	DB, RCT	202 vs. 205	90.3 vs. 85.0	92.2 vs. 91.9	Fung et al.[26] (2003)
Levofloxacin vs. ciprofloxacin	RCT	231 vs. 238	97.8 vs. 94.3	97.5 vs. 93.5	Nichols et al.[27] (2003)
Linezolid vs. dicloxacillin	MC, DB, RCT	400 vs. 419	88.6 vs. 85.8	88.1 vs. 86.1	Fung et al.[26] (2003)
Minocycline vs. none	CR	10 vs. 0	80.0	NA	Ruhe et al.[6] (2005)
Minocycline vs. none	CR	15 vs. 0	100.0	NA	Ruhe et al.[6] (2005)
Minocycline vs. penicillin-V	RCT	115 vs. 128	74.0 vs. 54.0*	NA	Keeney et al.[28] (1979)
Moxifloxacin vs. none	DB, RCT	171 vs. 170	90.0 vs. 91.0	92.0 vs. 93.0	Parish et al.[29] (2003)

a: Rate of resolution of clinical signs and symptoms of infection, b: Rate of documented eradication of all pathogens presented at baseline, * = Statistically significant ($p < 0.05$)
CR = chart review; DB = double-blinded; MC = multicenter; NA = not available; RCT = randomized controlled trial.

Table 3.— Summary of clinical trials reporting treatment of methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections

Antibiotics vs. comparator	Study design	Number of cases vs. comparator	Clinical cure rate vs. comparator (%)[a]	Microbiological success rate vs. comparator (%)[b]	References (Year)
Doxycycline vs. none	CR	11 vs. 0	91.0	NA	Ruhe et al.[6] (2005)
Linezolid vs. vancomycin	RCT	30 vs. 30	50.0 vs. 20.0*	97.0 vs. 77.0	Sharpe et al.[5] (2005)
Linezolid vs. vancomycin	MC, OL, C	600 vs. 600	94.4 vs. 90.4	94.5 vs. 89.7	Weigelt et al.[8] (2005)
Linezolid vs. vancomycin	RCT	240 vs. 220	73.2 vs.7 3.1	58.9 vs. 63.2	Stevens, et al.[7] (2002)
Minocycline vs. none	CR	5 vs. 0	100.0	NA	Ruhe et al.[6] (2005)
Trimethoprim-sulfamethoxazole vs. none	CR	284 vs. 0	75.0	NA	Billeter et al.[30] (2005)
Trimethoprim-sulfamethoxazole vs. vancomycin	DB,RCT	43 vs. 58	86.0 vs. 98.3*	NA	Markowitz et al.[14] (2005)

a: Rate of resolution of clinical signs and symptoms of infection; b: Rate of documented eradication of all pathogens presented at baseline, * = Statistically significant ($p < 0.05$)
C = controlled; CR = chart review; DB = double-blinded; MC = multicenter; NA = not available; OL = open-label; RCT = randomized controlled trial

Table 4.— Administrative doses, cost and common adverse reactions of the oral anti-staphylococcal antibiotics

Antibiotics	Dosing and frequency for normal host[a]	Daily cost L*	Adverse reactions[a]	
			High likelihood	Low likelihood
Ciprofloxacin	500 mg Q 12 hrs	$2.49	Nausea, vomiting, diarrhea, headache	QTc prolongation, hyperglycemia, hepatitis
Clindamycin	300-450 mg Q 8 hrs	$8.98	Diarrhea, antibiotic-associated colitis, rash	Neutropenia, polyarthritis
Doxycycline	100 mg Q 12 hrs	$0.88	Photosensitivity, rash, diarrhea, joint pain	Neutropenia, increased intracranial pressure
Erythromycin	500 mg Q 6 hrs	$1.55	Headache, abdominal cramp, rash, diarrhea	QTc prolongation, seizure
Gatifloxacin	400 mg Q 24 hrs	$11.48	Nausea, vomiting, diarrhea, headache	QTc prolongation, hyperglycemia, hepatitis
Levofloxacin	500 mg Q 24 hrs	$12.89	Nausea, vomiting, diarrhea, headache	QTc prolongation, hyperglycemia, hepatitis
Linezolid	600 mg Q 12 hrs	$129.68	Rash, headache, nausea, vomiting	Thrombocytopenia, pancytopenia
Minocycline	100 mg Q 12 hrs	$2.98	Photosensitivity, rash, diarrhea, joint pain	Neutropenia, increased intracranial pressure
Moxifloxacin	400 mg Q 24 hrs	$13.53	Nausea, vomiting, diarrhea, headache	QTc prolongation, hyperglycemia, hepatitis
Tetracycline	500 mg Q 6hrs	$0.80	Photosensitivity, rash, diarrhea, joint pain	Neutropenia, increased intracranial pressure
Trimethoprim(TMP)-sulfamethoxazole(SMX)	TMP 160 mg-SMX 800mg Q 12 hrs	$1.23	Rash, nausea, vomiting	Megaloblastic anemia, hepatitis, arthralgia

a: Physician Desk Reference (PDR) 2005; L: Long's Pharmacy; * = Minimal daily cost for 14-day course

Reports of in-vivo studies are few with even fewer of them comparative. Some of the reported efficacy is from the research performed decades ago with older methodology and likely different organisms than present today. Vancomycin has been used as a comparator for linezolid and TMP-SMX activity for MRSA but provides little insight as the studies are few and the outcomes varied considerably.

Other considerations in antibiotic selection include dosing, especially in regard to compliance, which is generally less with more frequent administration such as with erythromycin and tetracycline. Tolerance and frequency of adverse effects must also be considered, especially if there is a history of allergies to any of the antibiotics being considered. The cost of antibiotics has become a concern as well, especially with linezolid, which may cost more than $120 per day. This is certainly an important factor in decision making as many patients can not pay the price and insurance companies may refuse to cover the charges or create such administrative and prior authorization barriers that the work of prescribing becomes prohibitive.

Linezolid - a good oral-bioavailable, oxazolidone antibiotic, has broad in-vitro activity against most gram positive bacteria and virtually all *Staphylococci*[7] although it is bacteristatic. It was approved by the FDA for use in complicated skin infections due to MRSA. Recent studies have demonstrated the excellent in-vivo efficacy of linezolid in MRSA SSTI comparable or superior to vancomycin.[5,7,8] However, its high cost and limited formulary access have been limiting factors in its use.

Erythromycin and clindamycin have been considered valuable antibiotics for community-associated MRSA (CA-MRSA) in adults but only half of the strains in Hawai'i appear susceptible.[31,32] Clindamycin has been used successfully in the treatment of systemic MRSA infection in children[1,33] but similar data are not available in adults. Clindamycin also has the advantage of inhibiting toxin production and relatively low cost.[13] The disadvantage is in its side effect of antibiotic associated colitis and multiple dosing. Clindamycin should not be used when the isolates are D-zone positive in double-disk diffusion test indicating the inducible macrolide-lincosamide-streptogarmin B (iMLS) form of resistance. This test can be performed by placing clindamycin and erythromycin disks 15-20 mm apart on Mueller-Hinton agar. The presence of iMLS results in a D-shaped blunting of the circular zone of inhibition around the clindamycin disk on the side facing the erythromycin disk. Clinical laboratories should test all *Staphylococcus aureus* isolates for this form of resistance before reporting clindamycin susceptibility.[34,35]

Trimethoprim-sulfamethoxazole (TMP-SMX) is an inexpensive oral antibiotic for MRSA SSTI with convenient twice-daily dosing. Most MRSA strains, especially CA-MRSA, are susceptible to TMP-SMX.[4,30,31,36] However, one study has demonstrated that TMP-SMX was not as effective as vancomycin in treating intravenous drug abusers with MRSA infection.[30] The disadvantage of TMP-SMX includes side effects such as drug rash and megaloblastic anemia.

Fluoroquinolones (ciprofloxacin, levofloxacin, gatifloxacin and moxifloxacin) have the advantage of good in-vitro antistaphylococcal activity and once daily dosing (levofloxacin, gatifloxacin and moxifloxacin). However, resistance is rising with time and can develop during therapy.[1,35] The new generation fluoroquinolones such as moxifloxacin and gatifloxacin have greater in-vitro activity and may be different. They are reported to be able to maintain serum concentration well enough to block the growth of the least susceptible mutant.[37]

Tetracyclines (tetracycline, doxycycline and minocycline) have the advantage of good in-vitro anti-MRSA activity, low cost and convenient dosing. However, they are bacteriostatic and comparative studies with other antibiotics are lacking. Doxycycline and minocycline can be used successfully in the treatment of MRSA SSTI[6] and may be better tolerated than tetracycline. The disadvantage is in their side effects such as gastrointestinal intolerance, vestibular toxicity and photosensitivity.

It is clear that more research is necessary to understand the clinical efficacy of the antibiotics available for MRSA. Clinical trials with randomized direct comparisons would be extremely valuable. However, more research funding is limited as most of these drugs are off-patent. Real cost factors, such as those for failures and adverse effects also need to be assessed. The ability to avoid hospitalization for intravenous antibiotic therapy should also be considered, especially at a cost of more than $1,000 per day. The fact that some patients with simple MRSA SSTIs such as abscess, folliculitis or carbuncle get better with surgical intervention alone or in combination with ineffective antibiotic treatment, indicates that antibiotic treatment is not always necessary in every infections. Even with better clinical information, however, decision making will remain a challenge to the clinicians. The evolving epidemic of MRSA is one that requires a good history and physical examination as well as more cultures for identification and resistance testing of the pathogen. Selection of the best antibiotic for the individual is often a complex and difficult process and may result in a recommendation different for each patient.

Conclusion

Oral antibiotic therapy should be considered for uncomplicated MRSA SSTI. Clinical studies suggest that linezolid, the quinolones, the tetracyclines, and TMP-SMX are useful against MRSA if the organism is susceptible, but their relative effectiveness is not clear. Only linezolid and some of the quinolones appear comparable to vancomycin but MRSA is developing resistance to the quinolones. Treatment consideration should be made based on local susceptibility data, individual patient evaluation, and economic factors. Practitioners should also be aware of increasing antimicrobial resistance problem in the clinical practice. More clinical trials which compare these antibiotics are urgently needed.

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*See **"References"** p. 299*

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White Coat Ceremony Keynote Address

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White Coat Ceremony* Key Note Address
August 4, 2006
Hawaii Prince Hotel

**Conceived by the Arnold P. Gold Foundation, a public foundation dedicated to fostering humanism in medicine, the White Coat Ceremony impresses upon students the importance of professionalism, excellence in science, compassion, and honor. At each ceremony, white coats, "cloaks of compassion" are placed on the shoulders of each student and they recite the Hippocratic Oath for the first time.*

Dean Shomaker, honored guests, faculty and staff, family and friends, students of the Class of 2010, I feel very fortunate to be with you this evening; on such a proud occasion, for these talented future physicians and colleagues. This is the night we don our first white coat, the cloak of compassion, and reflect on its importance to our personal and professional lives.

As medical students, there are three groups with whom you must share your compassion. You must have compassion for yourself, your family, and finally, and most importantly, your patients. Tonight I hope to make you smile then touch your heart by highlighting these three areas with personal reflections that illustrate the importance of sharing your kindness with these three groups.

Let's begin with the compassion you must have for yourself.

I recall in my first year of medical school preparing with my classmates for our first exam on microscopic anatomy. We studied all night long, until dawn. Since the test was in the afternoon, I decided to leave campus and drive to my grandmother's house, to take a short nap before the test.

I woke up in time, in fact with plenty of time to review my notes before the exam. Aah, I remember my precious notes…the key to my success, all the little cells and structures were drawn with colored pencils. Each structure was labeled. I knew I had all the answers.

I started flipping through my notes as I walked to my car. I put my notes on the top of my car as I opened the door, I threw my backpack in the front seat, and started driving to campus…

Well, it was a minute or so before I began to notice all these papers flying around behind me, as I looked in my rearview mirror. I remembered thinking to myself, "Hawai'i is such a beautiful place - why do so many people litter?"

And then I realized what was happening. Oh my God! Those are my notes! I panicked. I slammed on the brakes, hopped out of the car and began trying to pick up the papers. People on the sidewalk saw me and started to help. I was so freaked out when I discovered my notes flying away that when I stopped the car, I forgot to put it in park. And as I turned to look behind me, there was my car rolling up King Street with no driver inside!

I had now reached a seminal point in my medical school life. Should I get my notes, or get my car?

Well, I decided to run after my car. And when I finally caught up with it, my papers were so dispersed that I just took the ones I recovered and drove to school. I took the exam; did just fine, and often reflect on this story today.

My point is that when it comes to tests and other academic challenges in medical school, you must keep the proper perspective. Tests are very important. And while I'll be the first to tell you to study hard, remember that your performances on medical school exams do not define your worth as a person. So give yourself permission to approach each school day with a smile on your face. And when you get home in the evening, give yourself permission to sleep well. Permit yourself to grow into a seasoned clinician and avoid demanding of yourself that you achieve it immediately. Pay attention to your health and happiness, and have compassion for yourself.

And now, let me talk about the compassion you must have for your family and loved ones who must tolerate you as a medical student for the next four years. Permit me to share a little about an important person in my life, my grandmother.

In my first memory of my grandmother she is cooking pancakes for breakfast. I had spent the morning catching small fish with a bamboo pole on a reef in Makaha and I was very hungry. The pancakes smelled so good.

Each day after school I would go to her house and she'd cook me dinner. She always cooked something incredible, but my favorite was her roast chicken. When it came out of the oven you could hear the skin crackling and I used to smother it with her gravy. She always had corn on the cob and cornbread. And during dinner she'd tell me stories about her life and what it was like when she was a child. Our conversations ended her by saying, "Damon, I just want to live to see you graduate from high school." Well, she did.

Saying goodbye to her before getting on the plane for college was difficult. Every month for my entire four years at college I would receive a letter from her that also included a crisp twenty dollar bill. It was unbelievable, how many times I had forgotten to get some money from the bank for the weekend and would find grandma's letter in my mailbox. She saved the day! I would visit her during each Christmas vacation. Whenever I visited, there was always roast chicken, gravy, corn on the cob, and cornbread waiting. She told me the same thing on each visit. "I just want to live to see you graduate from college." And she did.

Grandma was happy when I came back home to Hawai'i for medical school. I made it a point to have dinner with her every Monday night, without fail. And yes, we often had roast chicken and gravy. And in between our conversations she would often say, "I just want to live to see you graduate from medical school." Grandma was at my medical school graduation at the Kennedy Theatre in 1991.

Throughout my internal medicine residency training I still managed to have dinner with grandma once a week where we often talked for a long time.

One evening, she said, "Your grandfather wanted to be a doctor. He had a plan with his older brother. His older brother would graduate from high school and immediately go to work to support your grandfather through medical school. And when he became a doctor, he would work to support his brother through medical school. That was their dream. But one summer while in high school, grandpa's brother died, and their dream of being doctors together died with him. Grandpa often talked about how bright his brother was… That's why I'm glad you became a doctor."

"Sometimes becoming a doctor is a family's dream, not that of just an individual."

I often think to myself, where would we be without those who cheer for us our entire lives, whose spirits rise with ours? Many of your supporters are in the audience. What does it mean to them that you are here on this stage? Everything. What will it mean to them to see you graduate in four years? Everything. What could it mean to the people of Hawai'i? Everything. You just need to make it so.

Remember to cherish those that you love. Visit whenever you can, have some roast chicken. And when mom or dad asks you to take the garbage out after dinner, don't think, "Don't you know how much homework I have tonight?" Just say "Sure mom," and carry it out the door.

While compassion for ourselves and those we love enrich our lives, first and foremost, as physicians, we must nurture and protect the compassion we have for our patients. For when all is said and done, what they'll remember about us is our compassion.

A number of years ago I cared for an elderly homeless man who was dying from a cancer in his mouth. He would come to our clinic every two weeks to collect his prescription for pain medication. We eventually learned that the clinic staff and I were his only friends. During our visits, we talked about his adventures and the different people that had come in and out of his life. Soon, his cancer made it impossible for him to speak, and so we communicated with each other by writing on napkins and paper towels. I learned about his personality and that he had a life like many others, filled with ups, downs, and dreams some realized, some left unfulfilled. As his condition worsened, he refused additional treatments choosing to fight on in his own way. But soon he reached a point where admission to a hospice became necessary. I sat by his bedside and he communicated with me in his usual way, by writing on a paper towel. I could see how frail he looked. Always a fighter, he wrote something to me that evening that I'll always remember.

He said, "I've been fighting this cancer for so long now. Is it OK tonight to just rest?"

And I knew what he was trying to tell me. And I said, "Yes John, you've been fighting so hard. Tonight, let's just rest."

And I put my hand on his forehead. He closed his eyes. And he died that evening.

The Tinman they say, is the most compassionate character in the Land of Oz, yet ironically he searches for a heart. Because you've entered medical school already blessed with humanism, your task is not to find your heart, but to hold on to it, despite the adventures that lay ahead of you.

So imagine your compassion is a treasure for which you are the sole guardian. Instead of losing your caring, let your future training experiences lead you to care more.

Emily Dickinson said:

If I can stop one heart from breaking,
I shall not live in vain;
If I can ease one life the aching,
Or cool one pain

Compassion is such a powerful treatment yet it doesn't cost much at all. There are few adverse effects and rarely is there an overdose. It can be given to people of any age, race, or gender. It defines us as physicians. It is a virtue William Shakespeare might call "twice blest."

It blesses him that gives, and him that takes.
It becomes the throned monarch better than his crown.

As it does the physician better than his diplomas.

Tonight you'll receive your first white coat. It will be the first of many. Before it's retired, it will be stained with coffee, stained with blood. Still, I encourage you to keep this first coat, your cloak of compassion, always.

Let it be a reminder of this evening, when you gathered with your colleagues, recited the Hippocratic Oath, and began to believe that the hero in these stories of compassion will be you.

Do Japanese Have an Increased Susceptibility to Colorectal Cancer?

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It is estimated that approximately 10% of colorectal cancers (CRCs) are due to highly penetrant inherited mutations. Genetic factors are expected to also play an important role in the more numerous non-familial CRCs. Indeed, it is generally accepted that most CRCs result from the combined effects of environmental exposures (such as smoking, diet, alcohol, obesity, and physical inactivity) and common genetic susceptibility factors (i.e., common inherited DNA variants). We now know a great deal about environmental risk factors for CRC. However, we know very little about the genetic susceptibility factors involved in sporadic CRC. Our research group has been interested in taking advantage of the differences in cancer risk that exist in the multiethnic population of Hawai'i to identify such genetic susceptibility variants.

Epidemiology of CRC in Hawai'i Japanese

The epidemiology of CRC in Hawai'i is remarkable because of an unexpectedly high risk in Japanese Americans. The almost totality of the 215,000 Japanese who migrated to Hawai'i between 1885 and 1924 came from rural areas in Southern Japan and their descendants have married Japanese originating from the same prefecture.[1] No sizeable migration from Japan to the United States has taken place since the 1920s and, until recently, there has been very little intermarriage with other ethnic groups. CRC rates for Japanese migrants to Hawai'i and California markedly increased upon migration, presumably as a result of dietary change.[2] However, whereas rates for other cancers, such as breast and stomach cancers, took two generations or more to approach those of the Caucasians, Japanese CRC rates matched the Caucasian rates within the first generation.[2] In 1983-1987, Japanese American men in Hawai'i and Los Angeles had the highest incidence rates for CRC among the more than 175 populations followed for cancer incidence worldwide.[3] The Hawai'i Japanese CRC rates remained the highest in 1988-1992[4] and appear to have peaked in 1993-1997[5] (Figure 1). Studies of other migrant groups to Hawai'i (e.g., Filipinos), the United States, or Australia also showed that rates for immigrants and their descendants rapidly reach those of the host country, but usually not in the first generation.

These observations suggest that Hawai'i Japanese may have a particular susceptibility to CRC due to an especially pronounced exposure to lifestyle risk factors in the United States, and/or the modifying influence of genetic susceptibility factors.[6]

Epidemiology of CRC in Japan Japanese

A comparable "epidemic" of CRC is now taking place in Japan. In the mid-20th century, CRC incidence was very low in Japan. However, rates for both colon and rectal cancers have increased there since the 1970's and particularly rapidly, since the 1980's (Figure 1)[7] The highest CRC incidence rates in the world are now reported from

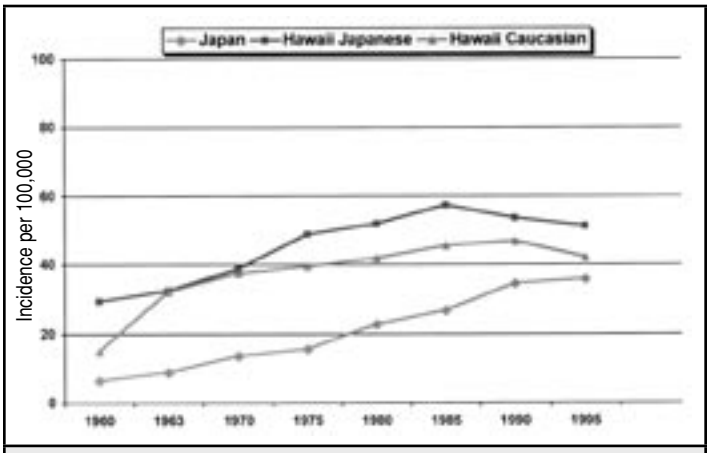

Figure 1— Male Colorectal Cancer Incidence in Hawaii and Japan

Japan.[5] This increase probably reflects lifestyle changes that have been taking place there beginning in the 1950s, such as increased consumption of animal fat and meat, decreased intake of grains (particularly, rice), and decreased energy expenditure. A number of epidemiologic studies of CRC and adenoma have been conducted in Japan and have implicated the very same risk factors as in the West, in particular, a western diet.[8]

Gene-Diet Interactions in Colorectal Cancer

As we explored reasons for the high CRC rates of Hawai'i Japanese, we showed that they consume less energy and fat but more beef and processed meats than Hawai'i Caucasians.[6] Also, their intake of fiber, calcium, and vegetables is lower.[6] We found that all of these variables, as well as smoking and physical activity, are risk factors for CRC in this population.[9] We also showed that family history tended to confer a greater CRC risk in Hawai'i Japanese [OR=3.0 (2.1-4.6)] than in Caucasians [OR=1.8 (1.2-2.9)] (p=0.07).[10] We also observed an interaction between family history and beef intake.[9] The association with beef intake was markedly stronger among individuals with a CRC family history. This led us to study genetic susceptibility and, specifically, common polymorphisms in genes involved in the metabolic activation of meat carcinogens. Most chemical carcinogens, included those formed when meat is cooked by high temperature methods (i.e, grilling/barbecuing, pan-frying and broiling), need to be activated by metabolic enzymes before they can bind to DNA and cause mutations.

Our most recent study showed that Hawai'i Japanese tend to prefer their red meat well-done (27% vs.17% in Caucasians) and that such a preference is associated with a 8.8-fold increased CRC risk (95%CI: 1.7-44.9) among smokers with both the rapid CYP1A2

and rapid NAT2 phenotypes.[11] These two enzymes play a critical role in the bioactivation of heterocyclic amines, a class of putative carcinogens that are formed when meat is cooked well-done. The rapid NAT2 phenotype is more than 10 times as common in Japanese (48%) as in Caucasians (4%), suggesting that this GxE interaction may be particularly important in the Japanese.[6,11]

Similarly, an insert polymorphism in the regulatory region of the *CYP2E1* gene that results in an increased enzyme activity and is frequent in Japanese (23% vs. 2% in Caucasians) was found to increase rectal cancer risk, especially in consumers of high levels of processed or red meats which have been shown to lead to endogenous nitrosamine formation in the large bowel.[12] CYP2E1 is known to play a key role in the metabolic activation of low molecular weight nitrosamines.

Moreover, a common C677T substitution in the gene coding for 5,10-methylenetetrahydrofolate reductase (MTHFR), an enzyme involved in folate metabolism, has been associated with a lower risk of CRC, with a low folate intake and/or high alcohol consumption negating or reversing this effect.[13] We have shown that the protective T allele is somewhat more common in Japanese (0.42) than Caucasians (0.36) and that the TT genotype appeared to consistently decrease CRC risk in this group as well.[13]

Giovannucci et al.[14] have reported an increased risk of colorectal adenoma among individuals with the *ADH3*(2-2) genotype and high alcohol-low folate intake compared with those with low alcohol-high folate intake and the *ADH3*(1-1) genotype (p for interaction = 0.006). Functional variants in the alcohol metabolizing genes (e.g., alcohol dehydrogenases and aldehyde dehydrogenease) are common in Japanese compared to other ethnic groups.

Similarly, we found that the association between pack-years of smoking and CRC was stronger among carriers of the *CYP1A1 Msp*I variant, which is more common in Japanese (37% vs. 9% in Caucasians).[15] CYP1A1 is a key enzyme in the bioactivation of polycyclic aromatic hydrocarbons, one of the main classes of carcinogens in tobacco smoke.

Although Hawai'i Japanese are less obese than their Caucasian counterparts, Asians have been shown to accumulate more intra-abdominal fat at a lower BMI, which is a contributor to insulin resistance and hyperinsulinemia. Indeed, Japanese are more susceptible to diabetes and guidelines in Japan have defined obesity as a BMI≥25, instead of ≥30 as in the US. Hyperinsulinemia is a suspected causal factor for CRC.

Conclusion

In conclusion, Japanese may possess a certain genetic susceptibility, based on multiple gene-environment interactions, that manifested itself when they migrated to the United States (and in more recent years in Japan) due to an increased exposure to meat carcinogens, low vegetable, calcium, and fiber intakes, as well as smoking and, possibly, overnutrition. Thus, the descriptive and analytical epidemiology of CRC in Japanese clearly point to the critical importance of common gene modifiers, acting in various pathways, in CRC etiology.

For more information on the Cancer Research Center of Hawai'i, please visit our web site at www.crch.org.

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Issues in Medical Malpractice IV

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QUESTION: A patient developed severe headache and neck stiffness, which the clinic doctor incorrectly diagnosed as a viral infection. Her condition did not improve, so her husband called the doctor who did not return the page. The call was transferred to the emergency department (ED) doctor who asked some questions but did not encourage re-evaluation, as the ED was extremely busy at the time. The patient's condition deteriorated, and she expired. At autopsy, a subarachnoid bleed was found. Her husband sued the clinic doctor, ED doctor, and hospital for malpractice. The clinic doctor, a hospital employee, is a medical resident just out of medical school. The ED doctor works as an independent contractor and derives no direct salary or fringe benefits from the hospital. A prominent sign at the entrance features these words: "Hospital Emergency Services: Physician on duty 24 hours."

A. The clinic doctor is not liable because he met the standard of care expected of a physician at his stage of training.

B. The ED doctor is not liable because there was no doctor-patient relationship.

C. The hospital is vicariously liable for clinic doctor's conduct but not ED doctor's conduct.

D. The hospital cannot be liable because it is not a person.

E. No liability attaches to any of the three parties because their negligence, if any, did not cause the death of the patient.

ANSWER: ***All Incorrect.*** Whether the clinic doctor is liable will depend on whether the original medical history and physical findings were sufficient to raise the diagnosis of a subarachnoid bleed. That he/she is a medical resident will not in and of itself absolve him/her of liability. Inexperience is not usually regarded as an adequate defense and most jurisdictions will judge the resident by the standard expected of a fully qualified doctor.

By talking to the husband and asking questions about the patient, the ED doctor is probably deemed to have established a doctor-patient relationship. Whether he/she breached the standard of care by failing to ask the patient to immediately come to the hospital will depend on the questions asked and the answers received. Certainly a busy ED is not a good enough reason to keep a patient with a life-threatening condition away.

Any entity, not only a person, can be held liable for civil damages. Hospitals can therefore be asked to pay damages for any number of reasons, e.g., direct negligence, vicarious liability, premise liability, and so on. Although there is still controversy over whether residents are hospital employees, the facts here stipulate an employer-employee relationship, which makes the hospital liable on the basis of *respondeat superior*. That is, the negligence of the servant (employee) is imputed to the master (employer). This is a classic example of what is termed vicarious liability. Since the ED doctor is not an employee but an independent contractor, *respondeat superior* does not apply to his/her case. However, the plaintiff would attempt to cast the ED physician as an ostensible agent of the hospital, and so hold the hospital vicariously liable. As evidence, the plaintiff would point to the hospital sign that ED doctors are working for the hospital 24 hours a day.

Finally, for the defense to be successful, it must counter with expert testimony that the subarachnoid bleed was too far advanced for effective medical intervention, i.e., the disease caused the death, not any delay in diagnosis and treatment. Prompt surgical intervention may be life-saving in a subarachnoid bleed, so the defense faces an uphill fight on the causation issue.

Hospital Liability

Hospitals, like the doctors and nurses who work there, can be sued for wrongful conduct that leads to patient injury. The liabilities can be direct or indirect.

Direct Liability: The hospital can be directly liable for its own negligent acts. Examples are: short-staffing, negligent nurse-hiring practices, or negligent credentialing of doctors. A hospital can also be sued for injuries that occur on its premises (called premise liability) such as a patient or visitor slipping on a wet slippery floor.

There are numerous legal theories to hold hospitals directly liable, e.g., corporate liability, non-delegable duty, EMTALA (Emergency Medical Treatment and Active Labor Act) violations, and strict liability.

Vicarious Liability: In addition to direct liability, how else can hospitals be held liable for the negligent acts of its doctors and staff? Court decisions have generally used the employer-employee or the agency principle to hold hospitals vicariously liable. Where there is an employer-employee relationship, e.g., nurses and some doctors hired by the hospital, *respondeat superior* is the basis for liability. *Respondeat superior* means: 'let the master answer.' So long as an employee (or the old term 'servant') carries out the negligent act during and within the scope of employment, the employer will be

held vicariously, i.e., indirectly, liable. The idea behind this rule is to ensure that the master or employer, as supervisor, will enforce the proper work standards so as to avoid risk of harm. Thus, liability flows back to the master for the negligence of the servant. In the hospital setting, nurses and other employed hospital workers are covered by the *respondeat superior* doctrine. The test is whether the act occurred during and within the scope of employment, and whether the risk of harm was foreseeable.

However, where the negligent actor is an independent contractor rather than an employee, *respondeat* will not apply. An institution usually does not exercise substantial control over the actions of independent contractors, whereas the opposite is true for its employees. Most doctors who work in private hospitals are independent contractors, as they do not draw a hospital salary, nor are their work hours and work duties controlled or defined by the hospital.

However, depending on the facts, some courts have concluded that there may be an agency relationship between the doctor and the hospital. Agency may be established if there is some degree of control, even if minimal, that is exerted on the doctor by the hospital. The relationship may be construed as an ostensible agency, where there is some representation that the doctor works for the hospital. When the patient relies on this relationship in seeking his or her treatment, it is called agency by estoppel. Under any of these formulations, the plaintiff may include the hospital as a co-defendant in a malpractice suit.

Thus, invoking vicarious liability begins with a determination as to whether the tortfeasor is an employee. Then the court will look at whether there is an agency relationship. If both are absent, there will be no vicarious liability. The issue may not always be straight forward, as a recent Florida case illustrates: The ship's doctor aboard a Carnival cruise ship failed to diagnose acute appendicitis in a 14-year-old girl despite several days of abdominal symptoms. The patient ruptured her appendix, and this resulted in sterility. The parents sued the cruise line as a codefendant, which denied liability because the doctor was not an employee and this was specifically spelled out in the cruise ticket. Although the doctor's contract stated that he was an independent contractor, the court reasoned that in a claim based on agency, it is the right of control rather than actual control itself that matters. It therefore held that: *"(1) for purposes of fulfilling cruise line's duty to exercise reasonable care, ship's doctor is an agent of cruise line whose negligence should be imputed to cruise line, regardless of contractual status ascribed to doctor; and (2) to the extent cruise ticket sought to limit cruise line's liability for negligence of doctor, it was invalid."*[1]

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. You may contact the author, S.Y. Tan MD, JD, at email: siang@hawaii.edu or call (808) 526-9784 for more information.

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UPCOMING CME EVENTS

Date	Specialty	Sponsor	Location	Meeting Topic	Contact
October 2006					
10/12-10/16	R, N	Western Neuroradiological Society	Fairmont Orchid, Kohala Coast	38th Annual Meeting	Tel: (630)574-0220 x226 Web: www.wnrs.org
10/20-10-22	Multi	Hawai'i Medical Association	Hawai'i Convention Center, Honolulu	2006 Annual Meeting: Leading the Way… Building on 150 Years of Service	Tel: (808) 536-7702 Web: www.hmaonline.net
10/22-10/27	U	Western Section of the American Association of Urology	Hyatt Regency Resort, Maui	82nd Annual Meeting	Tel: (714) 550-9155 Web: www.wsau.org
10/22 - 10/27	AN	International Trauma Anesthesia & Critical Care Society	Wailea Marriott Resort & Spa	Trauma: The Team Approach to the Clinical Challenge	Tel: (800) 222-6927
10/29-11/2	PMD	University of California, Davis	Grand Wailea, Maui	UCD Review and Update of Pain & Palliative Care Medicine	Tel: (916) 734-5390 Web: www.ucdmc.ucdavis.edu/cme
November 2006					
11/6-11/9	Multi	Kaiser Permanente	Wailea Marriott Resort	Evidence-Based Medicine Conference: The Essentials	Tel: (808) 432-7932
11/8-11/11	OBG	American College of Obstetricians and Gynecologists	Hapuna Beach Prince Hotel, Kohala Coast	Obstetrical and Gynecological Pearls	Tel: (800) 638-8444 x2540 Web: www.acog.org
11/9-11/12	PMR, PMM	American Academy of Physical Medicine and Rehabilitation	Hawai'i Convention Center	67th Annual Assembly	Web: www.aapmr.org
11/13-11/15	PD	Lucile Packard Children's Hospital at Stanford	Mauna Lani Bay Resort, Kohala Coast	Popular Pediatric Clinical Topics	Web: www.cme.lpch.org
January 2007					
1/17-1/22	D	American Academy of Dermatoloty	Wailea Beach Marriot Resort & Spa, Wailea, Maui	3rd Annual Advances in Cosmetic & Medical Dermatology	Tel: (312) 321-0150 Web: www.acmd-derm-hawaii.com
1/21-1/25	ON, FM	American Association for Cancer Research	Hilton Waikoloa Village, Waikoloa	In the Forefront of Basic and Translational Cancer Research AACR/JCA 7th Joint Conference	Tel: (215) 440-9300 Web: www.aacr.org
1/21-1/25	GS, SPI	Mayo Clinic College of Continuing Medical Education	Hapuna Beach Prince Hotel, Kohala Coast	International Spine Surgery Symposium 2007	Tel: (480) 301-4580 Web: www.mayo.edu/cme
1/22-1/25	CD	Mayo Clinic College of Continuing Medical Education	Hapuna Beach Prince Hotel, Kohala Coast	Arrhythmias & the Heart in Hawaii	Tel: (480) 301-4580 Web: www.mayo.edu/cme
1/29-2/3	R, N	NYU School of Medicine	Four Seasons Resort, Hualalai	Neuroradiology (and Head & Neck) on the Big Island	Tel: (212) 263-5295 Web: www.radcme.med.nyu.edu
February 2007					
2/14-2/18	OBG	Ian MacDonald Inter-University of Medical Unltrasound Hawai'i & Department of OB/GYN and Women's Health, JABSOM	Hyatt Regency Waikiki Resort & Spa, Honolulu	Evidence-based OB/GYN: Practical Application of New Advances & Contemporary Ob/Gyn Ultrasound: Recent Advances and Clinical Practice	Tel: (808) 203-6528 Email: ckawahar@hawaii.edu

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❖ **TWO WRONGS DON'T MAKE A WRITER.**
How often do eye surgeons see patients complaining of sudden onset of spots and floating strands in the field of vision? Every day? Twice a week? In the following case, a 54-year-old man consulted with his eye surgeon. The doctor dilated the eyes, saw "4+ cells" in the vitreous, diagnosed pars planitis and prescribed oral steroids. A week later the patient returned, and his symptoms had not improved. Two weeks later he returned with a retinal detachment. A retinal surgeon operated promptly but the retina failed to reattach, and a second attempt failed also. The patient developed headache, double vision, cataracts, and eye strain with reading and writing. The patient sued the initial ophthalmologist stating that he should have seen and treated retinal tears which could have prevented the detachment. He won a $7.5 million award, primarily due to a lack of documentation. The surgeon described the second office visit as "no change to retina." Jurors told the defendant's attorney that his chart failed to state "complete retinal exam performed." The trial attorney's mantra, if you didn't write it down, it didn't happen, and one could add, "You lose!"

❖ **WHEN SOMEONE SAYS HE IS COMING TO DO GOOD, RUN FOR YOUR LIFE!**
In Virginia a 16-year-old boy is suffering with Hodgkin's Disease. He went through three months of chemotherapy, that left him weak and nauseous. When his doctors recommended further chemotherapy he refused, and stated that he did not want any more of that kind of treatment. Responding to an interview, the lad sounds intelligent and quite capable of making such a decision. His parents support him, and say they want to pursue alternate forms of therapy. Subsequently, the matter came to Judge Jesse Demps, who ordered that the parents must share the decisions for his medical treatment with the Accomack County Department of Social Services, and the lad must report to the hospital and accept treatment recommended by his doctors. Wow! Compare that kind of reasoning with the 1914 ruling of Judge Nathan Cardozo, Justice, New York Supreme Court, "Every human being of adult years and sound mind has a right to determine what shall be done to his own body." What kind of big brother social agency and judge feel empowered to override the rights of an intelligent 16-year-old supported by his parents?

❖ **WE'RE NUMBER ONE! WE'RE NUMBER ONE! OH WAIT, WE'RE NUMBER 37!**
The World Health Organization (WHO) ranks the United States number one of 191 countries surveyed in responsiveness to patient's needs, choice of physician, autonomy, dignity, timely care, and confidentiality. Alas however, the United States is ranked 37th among developed nations in failing to require mandatory health insurance thereby failing to meet WHO's fairness and distribution goals. Additionally, 56% of US health care dollars are privately managed while most countries rely on federal financing. Another problem (?) is medical savings accounts (MSAs) which encourage fee-for-service payments, making it difficult to regulate and control treatment practices and prevent central pooling of dollars. Yes, how crazy these Americans who want to control their own pocketbooks, select their own physicians, and decide what medical care they want, if any!

❖ **EVERY DECENT MAN IS ASHAMED OF HIS GOVERNMENT.**
In an effort to scrap the senseless and unfair Medicare reimbursement formula (sustainable growth rate) promulgated during the Clinton years, Representative Michael Burgess MD of Texas has introduced a bill tied to the Medicare Economic Index (MEI). The present mechanism is a built-in negative feedback loop that constantly creates a deficit in health care funding. By using his formula, physicians would receive annual updates equal to the MEI percentage minus 1%. The current plan would be changed from a projected cut of 4.7% in January 2007 to an estimated 1.5% increase. That's a swing of 6.2% for the coming year, and reimbursement would continue to be directly related to medical expenditures. Access to care is already threatened, and without a new formula more doctors will refuse to provide care to the elderly.

❖ **A HANGOVER IS THE WRATH OF GRAPES.**
Using a Center for Communicable Disease and Prevention (CDC) "Behavioral Risk Factor Survey of 2004" as a database, Forbes magazine rated America's drunkest cities. The five parameters were state laws, numbers of drinkers, heavy drinkers, binge drinkers, and alcoholics. Milwaukee, Wisc., was the dubious winner, followed in order by Minnesota's Twin Cities, Columbus, Ohio, Boston, Mass., and Austin, Texas. Milwaukee citizens were upset claiming that it was just an unfair stereotype because of beer production there, and Chicago barkeeps were upset, because the Windy City rated too low at number six. Surprisingly, party cities like New York, Las Vegas and New Orleans were on down the list. San Francisco-Oakland was way down at number 20, party-town Miami was 33rd, and Honolulu didn't even make it into the top 35.

❖ **INSTANT HUMAN. JUST ADD COFFEE.**
In Scotland a seven-year study of 11,000 men and women ages 40 to 59, revealed that heavy coffee drinkers were less likely to have heart disease than tea drinkers. Labeled the Scottish Heart Health Study, the data showed that the heavy coffee drinkers were less likely to die of other conditions as well while the opposite was true for tea lovers. Meanwhile, a study of 125,000 people done by Kaiser Permanente Division of Research in Oakland, Calif., turned up a protective effect of coffee in cutting the risk of liver cirrhosis. Their numbers indicated that one cup of coffee a day reduced the threat of cirrhosis by 20%, and four cups a day cut cirrhosis frequency by an astounding 80%. The figures held true for various ethnic and racial groups. Added to this plus for coffee, is the American Medical Association study demonstrating that coffee drinkers are 30% less likely to develop Parkinson's Disease, and Italian research found an even steeper drop to 80% for Parkinson's.

❖ **IF YOU CAN'T LAUGH OFF AN INSULT, YOU PROBABLY EARNED IT.**
Officials at Waterfront Development Park in Louisville, Ky., found that their public fountains had dangerously high bacteria counts, presumably due to homeless people using them for bathing, as well as diapered toddlers wading in the pools. Signs warning of dangerous contamination had little or no effect. Park Director David Karem decided to post new signs, "DANGER! Water contains high levels of hydrogen KEEP OUT!" The bacteria count plummeted, and the local newspaper (Louisville Courier-Journal) complained that Karem was treating Louisville citizens like fools. If the shoe fits…

❖ **SOME PUSH THE ENVELOPE. OTHERS JUST LICK IT. SOME CAN'T EVEN FIND THE FLAP.**
In Chicago, Ill., a 29-year-old man had a strange looking object in his carry-on bag while going through airport security. When asked by the officer what it was (actually part of a penis pump) he said it was "a bomb." After his arrest he stated that he said that because his mother was nearby, and he did not want her to know about the device. He is charged with felony disorderly conduct and could face up to three years in prison.

ADDENDA
❖Flu was first described by Hippocrates in 412 B.C.
❖Jesus saves sinners – and redeems them for cash and valuable prizes.
❖A smoking section in a restaurant is like a peeing section in a swimming pool.
❖All true wisdom is found on bumper stickers and T-shirts.

ALOHA AND KEEP THE FAITH — rts■

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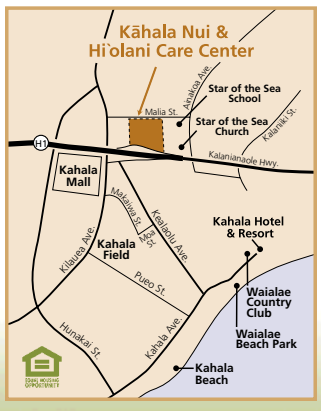

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