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# Factors Affecting the Influenza Vaccination of High Risk Adults in Hawaiʻi

James W. Davis PhD; Ronald Y. Fujimoto DO; Henry Chan BS; and Deborah T. Juarez ScD

# Abstract

Influenza infections cause a substantial toll in respiratory infections. hospitalizations, and death: and immunization has proven effective in reducing these outcomes. This article describes a study to understand variations in influenza vaccination rates for a population ages 50 and older using data from a large insurer in Hawai'i. Vaccination rates were lower in adults without than with a chronic disease, and especially low in those without chronic disease of ages 50-64. People who had been vaccinated in the past year were likely to become vaccinated again, and people with a history of regular physician visits were more likely than others to become vaccinated. Having vaccine available at the worksite led to improved vaccination rates. By ethnicity Japanese, Koreans, and Chinese were most likely to obtain influenza vaccinations; the greatest ethnic differences occurred among adults ages 50 to 64 without a chronic disease. People seeing a physician during the influenza season were especially likely to become vaccinated during the week of the visit. Patients were more likely to become vaccinated by an existing physician than if seeing a new one. The percentage of office visits in weeks in which patients became vaccinated varied four-fold by physician specialty. Internal medicine and family medicine physicians had the highest percentages whereas gynecologists and cardiologists had the lowest. The results suggest multiple reasons that high risk adults may fail to become vaccinated. Better understanding barriers may lead to improved strategies to improve influenza vaccination rates.

# Introduction

In the United States an average of 36,000 deaths annually are attributable to influenza.<sup>1</sup> Ninety percent occur to people aged 65 years and older. One study reported 47% of influenza cases of death occurred in people with heart disease and 23% in people with lung disease.<sup>2</sup> Hospitalizations in the United States with diagnoses of influenza or pneumonia average 133,900 per year.<sup>3</sup> An estimated 294,000 hospitalizations are associated with influenza for all respiratory and circulatory conditions. With the aging of the population, the number of hospitalizations has increased substantially over the recent decades.

A number of studies have documented that influenza vaccination can reduce the risks of deaths and hospitalizations. Investigators analyzing data from a large HMO, including 18 annual cohorts from several geographic regions, reported influenza vaccination was associated with a 27% reduction in the risk of hospitalization for pneumonia or influenza and a 48% reduction in the risk of death.<sup>4</sup> A meta-analysis pooling 15 studies estimated hospitalizations for pneumonia and influenza were reduced by 33%, mortality following hospitalization for pneumonia and influenza were reduced by 47%, and mortality from all causes were reduced by 50%.<sup>5</sup> A study in Hawai'i confirmed that people receiving influenza vaccine had reduced hospitalizations for respiratory conditions.<sup>6</sup> Associations were strongest in those under 80 years old. Studies including a randomized trial suggest that vaccination of persons with cardiovascular disease protects against mortality.<sup>7.8</sup>

In 2000 the Centers for Disease Control extended the definition of high risk populations to include everyone age 50 and older.<sup>9</sup> Given the serious consequences of influenza infection and the effectiveness of vaccination, high risk populations should be heavily targeted for vaccination. A Healthy People 2010 objective is to raise the percent of high risk adults who receive vaccination to 60%; for those over age 65 the goal is 90%.<sup>10</sup> In this article we report analyses of data from a large insurer in Hawai'i examining factors associated with influenza vaccination in adult, high risk members. Factors examined include demographic characteristics, clinical history in the past year, and physician encounters during the flu season.

#### Methods

The study was an analysis of existing administrative data from 2005-2007 provided by a large insurer in Hawai'i. Members were included if age 50 or older on August 1, 2006 and if continuously enrolled for the past year and through January 31, 2007. Nearly all influenza vaccinations occurred during this interval. People living in nursing homes were excluded because influenza immunization status is difficult to determine from nursing homes.<sup>11</sup> People with chronic diseases were identified using an algorithm from the insurer's physician award program, a program giving physicians points toward a financial bonus if their patients had high vaccination rates. Members were considered to have a chronic disease if they had one inpatient claim or three physician outpatient claims with appropriate diagnoses in the past year. Chronic diseases included diabetes, cardiovascular disease, pulmonary disease, kidney disease, liver disease, lymphoma, leukemia, and other malignancies. A few additional diseases affecting small numbers of members were identified in the insurer's algorithm. Because of the small numbers people with these diseases were excluded from the study. The study was granted an exemption from institutional review board (IRB) review by the University of Hawai'i IRB.

The primary outcome was a submitted bill for influenza vaccination. Covariates tested for associations with vaccination included member demographics, past year history of office visits, vaccination in the previous season, vaccine available at work place, and high risk conditions identified in the past year. For some analyses members who had seen one or more physicians in the past year were assigned to the physician they had visited the most often, or to the physician seen most recently before the influenza season in case of ties. Ethnicity was examined in some analyses using self-reported data from member satisfaction surveys. A random sample of members is mailed the surveys each year with typical response rates of 40 to 50 percent. The insurer has not tracked the overall response rate across multiple years.

Vaccination (yes or no) during the 2006-2007 season was analyzed using logistic regression. Additional logistic regression models were fit including all eligible participants who had a known ethnicity. Other analyses using longitudinal data employed the discrete time variation of logistic regression.12 For the discrete time models separate records were created for each week of follow-up. The intent of these analyses was to measure the strength of the association between having a physician visit and influenza vaccination. Visits were characterized by whether they were with a physician seen in the past year and by physician specialty. The physician visits were treated as time-varying covariates classified by the week of the visit. The outcome was influenza vaccination (yes or no) in the same week. Members were followed until they became vaccinated or until the end of follow-up. Results are presented separately by age and chronic disease groups for ease of comparison.

#### Results

Results show substantial variation in vaccination rates by age group and by the presence or absence of chronic disease (Table 1). Of the study population, 12.4% had chronic disease. Vaccination percentages varied two-fold comparing people ages 50 to 64 without chronic disease to people ages 65 and older with chronic disease. At the younger age ranges those with chronic disease had 25% greater vaccination rates than those without.

Women were a majority in all age groups (varying from 1 to 6 percent higher than males [Table 2]). Between one-forth to one-third of the members in the age and gender groups lived on Neighbor Islands. The proportions with known ethnicity varied by age and the presence of chronic disease: 33.2% had known ethnicity for those 50-54 without chronic disease, 54.1% for those 65 and older without chronic disease, and 58.3% for those with chronic disease.

In logistic regression models the strongest predictor of vaccination in the current year was having been vaccinated in the previous season (Table 3). The association was strongest for members ages 50-54 without chronic disease. Members in this group as well as members with chronic disease had 20% to 30% greater odds of vaccination if vaccine was available at their worksite. For the majority of patients who had seen two or fewer physicians in the past year, vaccination percentages increased with the number of office visits. Among patients seeing three or more physicians, the patients with 6 or more office visits had slightly higher vaccination rates than those with three to five. Of patients with chronic disease those with diabetes had the highest odds of influenza vaccination and those with kidney or cardiovascular disease had the lowest.

Japanese, Korean, and Chinese had the highest rates of vaccination compared to Caucasians (20% to 80% higher [Table 4]). The greatest ethnic differences in influenza vaccination occurred among people ages 50-54 who did not have chronic disease. Hawaiians were 20% higher than Caucasians among this population, but 20% lower among the people with chronic disease.

Overall, 23.6% of healthy members ages 50-54, 45.6% of healthy members ages 65 and older, and 55.4% of members with high risk conditions saw a physician during the vaccination season. Seeing a doctor during a week of the flu season increased the odds of vaccination during the same week 17 to 36-fold (Table 5). If the physician also was one seen in the past year the odds increased even more: from 19 to 48 fold. Odds ratios also varied substantially by the physician specialties seen. Visits to internal and family medicine physicians had the highest associations with influenza vaccination, whereas visits to cardiologists and gynecologists had the lowest. Of all three high risk categories, and excluding office visits after vaccination, 40.7% of visits with internal medicine physicians, 38.7% of visits with family practice physicians, 30.7% of visits with general practice physicians, 28.3% of visits with endocrinologists, 17.2% of visits with cardiologists, and 9.6% of visits with gynecologists were in weeks in which patients received influenza vaccination.

Table 1.— Number and percent receiving influenza vaccination by presence or absence of chronic disease and by age categories.					
Chronic Disease	Age Category	Number	Percent		
No	50 to 64	36,630	35.1%		
No	65 and older	45,365	63.3%		
Yes	50 to 64	6,044	59.3%		
Yes	65 and older	10,732	73.4%		

Table 2.— Number and percent of members by gender, island, ethnicity, and presence or absence of chronic disease.

Characteristics	Chronic Disease Absent		Chronic Disease Present
	Ages 50-64	Ages 65+	
Gender			
Women	54,225 (52.0%)	41,707 (58.2%)	12,559 (50.6%)
Men	50,099 (48.0%)	29,935 (41.8%)	12,249 (49.4%)
Island			
Neighbor island	32,533 (31.2%)	18,340 (25.6%)	6,069 (24.5%)
Oʻahu	71,791 (68.8%)	53,302 (74.4%)	18,739 (75.5%)
Ethnicity			
Japanese	12,145 (35.1%)	20,873 (53.9%)	7,227 (46.4%)
Caucasian	8,749 (25.3%)	5,697 (14.7%)	1,756 (13.0%)
Filipino	4,504 (13.0%)	3,617 (9.3%)	1,689 (12.5%)
Hawaiian	4,091 (11.8%)	2,952 (7.6%)	1,653 (12.3%)
Chinese	2,777 (8.9%)	3,353 (8.7%)	1,231 (9.1%)
Korean	610 (1.8%)	636 (1.6%)	206 (1.5%)
Pacific Islander	257 (0.7%)	100 (0.3%)	77 (0.6%)
Other	1,479 (4.3%)	1,502 (3.9%)	615 (4.6%)

Percentages for ethnicity are based on a subset of members with known ethnicity

## Discussion

Both individual characteristics and clinical history were associated with influenza vaccination. At the start of the flu season the strongest indicators of whom might get vaccinated were having been vaccinated in the previous season, and having a history of physician office visits. Regular office visits may identify people likely to visit a physician during the flu season. Having the vaccine available at the work site also boosted the likelihood of vaccination. The association, however, was not seen for members over age 65, many of whom would be retired.

Longitudinal analyses reinforced the importance of physician visits but also illustrated that many people – even of high risk or over age 65 – do not see a physician during the flu season. A physician visit had the strongest effect among people without chronic disease in the 50-54 age range. They may be less inclined to seek out opportunities for vaccination, but agree to vaccination if recommended during a physician visit. Analyses looking at physician visits by weeks into the flu season found that a visit greatly increased the likelihood of vaccination during the same week. Not all physician visits, however, had equal effect. A low percentage of visits in weeks without vaccination suggests missed opportunities. Seeing a physician visited in the past year increased the likelihood of vaccination more than seeing a new physician; and the effect of visits varied by physician specialty. Office visits with internal medicine or family practice physicians were the most effective, whereas visits to cardiologists and gynecologists were the least effective. A low percentage of visits in weeks without vaccination suggests missed opportunities in certain specialties.

A study surveying gynecologists reported that only half worked in practices that offer influenza vaccine.13 A common reason for not offering vaccine was the belief that vaccines should be provided elsewhere. One publication noted that cardiologists do not frequently stock and administer influenza vaccine although the American Heart Association and American College of Cardiology recommends immunization.<sup>7</sup> A study of cardiologists, endocrinologists, and pulmonologists who provided outpatient care to adults aged 18-64 years old reported the majority did stock influenza vaccine in their practices.<sup>14</sup> Cardiologists, however, were the least likely to do so. Among non-stockers the decision was most commonly based on the perception that their patients would receive the vaccine elsewhere.

The greatest differences by ethnicity were for people without chronic disease in the 50-54 age range. Studies in other populations have also reported ethnic differences in influenza vaccination rates. Within the Veteran Affairs Healthcare System, a system where everyone has access to care, non-Hispanic blacks were significantly less likely to be vaccinated than non-Hispanic whites.<sup>15</sup> Differences of 75% versus 81% were estimated in a multiply adjusted regression model. Among those who received vaccination, a reminder from the patients' healthcare team was most often cited as the reason for getting a flu shot. An analysis of the National Health Interview Survey (2000-2001) found influenza coverage levels were 66% for non-Hispanic whites, 48% for non-Hispanic blacks, and 32% for Hispanics.<sup>16</sup> In a multiply-adjusted regression model non-Hispanic blacks remained less likely to obtain flu vaccination than non-Hispanic whites (odds ratio (OR)=0.7,95%CI=0.6-0.8). Hispanics and non-Hispanic whites by contrast were comparable (OR=0.9, 95% CI=0.7-1.1).

Anumber of studies have asked patients about attitudes toward vaccination.<sup>17-19</sup> Patient concerns include costs, side-effects, pain, access, undisclosed shot contents, and concern the vaccine causes influenza. Attitudes regarding barriers to vaccination by nurses and physicians include lack of patient recall systems, practitioner work load, cost of vaccine, and lack of public education campaigns.20

The current study has a number of limitations that should be considered in interpreting the results. The data on influenza vaccinations are limited to vaccinations billed to the insurer. Thus the data may be incomplete to some extent, and less complete for some subgroups than for others. The low apparent vaccination rates of patients with kidney disease may occur for this reason. The study population is privately insured members from a single insurer. Consequently, the results cannot be generalized to the state's population. Results for ethnicity are limited to members who responded to member satisfaction surveys, and may have a response bias.

This study results show that vaccination rates vary by individual characteristics, clinical history, worksite availability of vaccine, age, and risk of adverse events. The results suggest challenges to make vaccine easily available to people who routinely seek vaccination, and to overcome additional barriers for those who do not. Public education regarding the risk of hospitalizations and mortality and the proven effectiveness of influenza vaccines offers one strategy. Educational information might be included in reminder letters to high risk individuals to get their annual flu shot. The Hawai'i Department of Health reported that reminder letters to newly enrolled Medicare beneficiaries led to increased vaccination percentages.<sup>21</sup> Compared to a control group that did not receive reminders, people sent a letter encouraging influenza vaccination had 2.7% increased rates, and people sent a letter encouraging both influenza and pneumococcal vaccinations had 3.8% increased rates. Among even hard-to-reach populations recommendations can increase immunizations.<sup>22</sup> The recent campaign by the Hawai'i Department of Health to vaccinate school children should benefit high risk adults as well by reducing exposure from infected children.<sup>23</sup> The limited months for vaccination means many patients may not see a physician when vaccine supplies are available. Physicians who see high-risk patients should be encouraged to stock and recommend influenza vaccine. Efforts to reduce barriers to physicians such as allowing return of unused vaccine may prove helpful.<sup>24</sup> Renewed efforts are needed to achieve sustainable, high rates of influenza vaccination in Hawai'i.

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Table 3.— Odd ratios with 95% confidence intervals of receiving influenza vaccination by subject and physician characteristics in the past year and by the presence or absence of chronic disease.

Characteristics	Chronic Dis	ease Absent	Chronic Disease	
	Ages 50-64	Ages 65+	Present	
Gender				
Women	1.1 (1.1, 1.1)	1.1 (1.0, 1.1)	1.0 (1.0, 1.1)	
Men	1.0	1.0	1.0	
Neighbor island				
Yes	0.8 (0.7,0.8)	0.7 (0.7, 0.8)	0.9 (0.8, 1.0)	
No	1.0	1.0	1.0	
Vaccine available at wo	rk place			
Yes	1.3 (1.2, 1.4)	0.9 (0.8, 1.0)	1.2 (1.1, 1.4)	
No	1.0	1.0	1.0	
Vaccinated in past seas	on			
Yes	11.3 (11.0, 11.7)	5.9 (5.7, 6.1)	5.3 (5.0, 5.6)	
No	1.0	1.0	1.0	
Primary physician spec	ialty			
Family medicine	0.9 (0.8, 0.9)	0.9 (0.9, 1.0)	1.1 (1.0, 1.2)	
Gynecology	0.8 (0.8, 0.9)	0.8 (0.7, 0.9)	1.0 (0.9, 1.3)	
General practice	0.6 (0.6, 0.7)	0.6 (0.5, 0.7)	0.7 (0.6, 0.8)	
Cardiology	1.1 (1.0, 1.2)	1.0 (0.9, 1.0)	0.9 (0.8, 1.1)	
Endocrinology	1.0 (0.8, 1.2)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	
Internal medicine	1.0	1.0	1.0	
Number of physicians a	nd visits			
≥ 3 physicians, ≥ 6 visits	3.1 (2.8, 3.5)	3.4 (3.1, 3.8)	1.5 (1.3, 1.7)	
≥ 3 physicians, 3-5 visits	2.3 (2.1, 2.6)	2.9 (2.5, 3.3)	1.4 (1.1, 1.7)	
1-2 physicians, ≥ 6 visits	3.1 (2.9, 3.3)	3.6 (3.3, 3.8)	1.7 (1.6, 2.0)	
1-2 physicians, 3-5 visits	2.6 (2.5, 2.8)	3.1 (3.0, 3.3)	1.7 (1.5, 1.9)	
1-2 physicians, 1-2 visits	2.0 (1.9, 2.1)	2.3 (2.1, 2.4)	1.6 (1.4, 1.8)	
No physician visits	1.0	1.0	1.0	
High risk category				
Diabetes			1.2 (1.0, 1.3)	
Other malignancy			1.0 (0.8, 1.0)	
Pulmonary disease			1.1 (1.0, 1.3)	
Cardiovascular disease			0.8 (0.7, 0.9)	
Kidney disease			0.4 (0.4, 0.5)	
Lymphoma			1.2 (0.8, 1.3)	
Liver disease			1.0 (0.7, 1.4)	
Leukemia			0.9 (0.6, 1.3)	

All listed variables were included in the regression models. The analysis of higher risk members was adjusted in addition for age group.

Table 4.— Odds ratios with 95% confidence intervals of receiving influenza vaccine by ethnicity and by the presence or absence of chronic disease.

Ethnicity	Chronic Dis	Chronic Disease	
	Ages 50-64	Ages 65+	Present
Japanese	1.6 (1.5, 1.7)	1.5 (1.4, 1.5)	1.3 (1.2, 1.4)
Korean	1.8 (1.5, 2.2)	1.2 (1.0, 1.5)	1.3 (0.9, 1.9)
Chinese	1.4 (1.3, 1.5)	1.3 (1.2, 1.4)	1.1 (0.9, 1.2)
Hawaiian	1.2 (1.1, 1.3)	1.0 (0.9, 1.0)	0.8 (0.7, 0.9)
Filipino	1.1 (1.0, 1.2)	1.0 (0.9, 1.0)	1.0 (0.9, 1.1)
Pacific Islander	1.1 (0.8, 1.5)	1.5 (1.0, 2.4)	0.7 (0.4, 1.2)
Other	1.1 (1.0, 1.3)	0.9 (0.8, 1.1)	0.9 (0.8, 1.1)
Caucasian	1.0	1.0	1.0

All analyses were adjusted gender, neighbor island, vaccination available at work place, vaccination in past season, number of doctors seen, the number of visits, and specialty of primary physician. Analysis for higher risk members were adjusted in addition for age group and for chronic diseases.

Table 5.— Odds ratios with 95% confidence intervals of receiving influenza vaccine from three regression models examining physician visits during the flu season by age and by the presence or absence of chronic disease.

Model	Variables	Chronic Dis	ease Absent	Chronic Disease		
		Ages 50-64	Ages 65+	Present		
1	Physician visit dur	ing the week				
	Yes	36.3 (35.3, 37.2)	23.4 (22.8, 23.9)	17.5 (16.9, 18.2)		
	No	1.0	1.0	1.0		
2	Physician visit dur	ing the week				
	Physician seen in past year	48.7 (47.4, 50.1)	27.8 (27.1, 28.5)	19.6 (18.9, 20.3)		
	Physician new to patient	28.8 (27.3, 30.4)	12.8 (12.1, 13.6)	5.4 (4.8, 5.9)		
	No physician visit	1.0	1.0	1.0		
3	Specialist visit during the week					
	Internal medicine	41.8 (40.5, 43.1)	27.4 (26.7, 28.1)	21.6 (20.7, 22.5)		
	Family medicine	41.7 (39.2, 44.3)	25.8 (24.4, 27.3)	22.0 (20.1, 24.1)		
	General practice	31.6 (28.5, 35.0)	14.3 (12.7, 16.1)	13.7 (11.7, 16.0)		
	Endocrinology	14.5 (11.6, 18.2)	14.7 (12.2, 17.7)	10.8 (10.0, 12.2)		
	Cardiology	6.8 (6.0, 7.7)	4.9 (4.5, 5.3)	2.4 (2.1, 2.7)		
	Gynecology	3.0 (2.6, 3.5)	1.5 (1.3, 1.8)	2.0 (1.6, 2.6)		

All analyses were adjusted gender, neighbor island, vaccination available at work place, vaccination in past season, number of doctors seen, the number of visits, and specialty of primary physician. Analysis for higher risk members were adjusted in addition for age group and for chronic diseases.

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# Immune Globulin-responsive Thrombocytopenia in Acute Post-Streptococcal Glomerulonephritis: Report of a Case in Hawai'i

Anthony P.S. Guerrero MD; James E. Musgrave MD; and Eric K.W. Lee

## Abstract

A 9-year-old boy in Hawai'i presented with bleeding and thrombocytopenia and was subsequently found to have post-streptococcal glomerulonephritis. He recovered completely with intravenous immune globulin, antibiotics, short-term antihypertensive therapy, and supportive management. This case was similar to the 5 cases previously reported in the literature, with the exception that steroids were not used as the primary immune-modulating therapy.

#### Introduction

Acute immune-mediated thrombocytopenia occurring in the context of post-streptococcal glomerulonephritis (PSGN) has been rarely reported in the literature: in a 4-year-old boy in Macedonia,<sup>1</sup> a 4year-old boy in Japan,<sup>2</sup> a 5½-year-old boy in Saudi Arabia,<sup>3</sup> and a 7-year-old girl and 5½-year-old boy in Canada.<sup>4</sup> In this article, we report on a case of thrombocytopenia associated with PSGN in Honolulu, Hawai'i.

# **Case Report**

The patient was a 9-year-old Samoan-Hawaiian-Filipino boy who initially presented to the primary care physician with the complaint of fever to 103°F and significant bleeding from the gums and lips, which had a scab and swelling. A complete blood count (CBC) obtained showed a platelet count of 4 x  $10^3/\mu$ L. The remainder of the CBC showed a hemoglobin (Hb) of 12.7g/dL, a hematocrit (Hct) of 37.1%, and a white blood cell (WBC) count of 8.1 x  $10^3/\mu$ L, with 77% segmented neutrophils, 18% bands, 3% lymphocytes, and 2% monocytes. There were slight toxic granulations. There was no evidence of hemolysis on peripheral smear. He was referred to the emergency room for further assessment.

By the time of his emergency room visit, he was noted to have petechiae. A repeat CBC confirmed the initial low platelet count. Additional labs showed a lactate dehydrogenase of 280 units/L, an erythrocyte sedimentation rate (ESR) of 59 mm/h, a C-reactive protein of 4.9 mg/L, a prothrombin time of 13.5 seconds, a partial thromboplastin time of 35 seconds, fibrin degradation products of 5 to less than 20 mcg/mL, and fibrinogen of 473 mg/dL. A urinalysis, performed because the review of systems (ROS) was positive for cola-colored urine, showed 100 mg/dL protein, 5-10 WBC's per high power field (hpf), greater than 100 RBC's per hpf, and 3-5 granular casts per hpf. Computerized tomography scan of the head, performed because of headache and dizziness, was normal except for significant sinusitis. Given the significant thrombocytopenia and symptoms of an acute illness, the patient was admitted to the hospital for further evaluation and management.

Additional history revealed that a few weeks prior to the admission, the patient had experienced a fever and upper respiratory infection with sore throat, which appeared to resolve spontaneously, without need for physician contact. However, a few days prior to the admission, he seemed to become ill once again with a fever. Past medical history was significant for allergies to azithromycin and amoxicillin/clavulanic acid. Past medical history was otherwise negative. He had not previously been on any other medications, including herbal medications. Family history was significant only for a maternal grandfather with easy bruisability. There was no family history of any other blood diseases, cancer, or rheumatologic illnesses. Social history was negative for any history of ingestion of uncooked beef or close contacts with similar symptoms. Social history was also negative for any freshwater exposure. He was known to be an active, athletic boy. Review of systems was negative for previous unexplained fevers, night sweats, weight loss, or fatigue; recent gastrointestinal symptoms, including bloody stools; joint pain or swelling; or rashes. Admitting physical examination was significant for dry lips and mucous membranes, slightly enlarged tonsils (2-3+) without exudate, and small palpable nontender rubbery mobile cervical lymph nodes. There was no hepatosplenomegaly.

The patient was started on intravenous (IV) fluids for presumed hypovolemia and IV cefotaxime for sinusitis and possible other bacterial infection. In consultation with the pediatric hematologist, he was also given IV immune globulin (IVIG) at a dosage of 1g/kg, which he tolerated without incident.

Within the next day, the patient developed decreased urine output, weight gain of 2.5 kg, systolic blood pressures in the 120-140 range, and edema. Repeat UA showed 100-300 g/dL protein, too numerous to count RBC's, and granular and RBC casts. Blood tests were as follows: uric acid 10 mg/dL, LDH 292 units/L, blood urea nitrogen (BUN) 51 mg/dL, creatinine 1.67 mg/dL, calcium 8.5 mg/dL, cholesterol 135 mg/dL. Renal ultrasound was normal. In consultation with the pediatric nephrologist, the patient was started on hydralazine and furosemide. Because the clinical and laboratory findings suggested a nephritic syndrome, the differential diagnosis included immune-mediated renal disease, vasculitic syndromes, and sepsis. Of note, the blood culture from the initial presentation was negative. Additional laboratory studies, again obtained per the pediatric nephrologist's recommendation, included a positive streptozyme at 200 units; a positive antistreptolysin-O titer (ASOT) at 449 IU/mL (normal range below 206); a positive anti-DNA-ase at 1:1920 (normal range 1:170 or less); and a low complement-3 (C3) level at 11 mg/dL (normal range 79-179). These findings provided confirmation of a likely post-streptococcal glomerulonephritis. Of note, the urine protein-to-creatinine ratio was 167:85 (approximately 2) and the serum albumin was 3.2 g/dL, which did not support a nephrotic syndrome. Rheumatologic studies showed: positive antinuclear antibody (ANA) at 1:80 (normal range less than 40), with a predominantly nucleolar pattern; negative anti-double-stranded DNA (anti-ds-DNA); negative rheumatoid factor (RF); negative antineutrophil cytoplasmic antibody (ANCA) titer; positive antisingle-stranded DNA titer of 134 units/mL (normal range 0-19); negative anti-extractable nuclear antigen (ENA) titer; and negative Sjögren's antibody. He had a positive Epstein-Barr virus IgG level of 2.81 mg/dL but a negative Epstein-Barr virus IgM level of 0.12 mg/dL (normal range 0 to 0.99).

Over the next few days, there was a steady increase in urine output, reduction in weight, normalization of the blood pressure, normalization of the coagulation parameters, reduction in the creatinine, and improvement in the platelet count. There was no drop in the Hb or Hct. A summary of the platelet counts is shown in Table 1. The patient was discharged 5 days after the initial presentation. The IV cefotaxime was switched to oral cefuroxime.

On outpatient follow-up 2 days following discharge, the patient once again had an elevated blood pressure at 150/110, along with increased weight and edema. He was therefore re-hospitalized and re-started on hydralazine and furosemide. Over the next 6 days, his condition stabilized nicely once again, and he was discharged on oral hydralazine. His weight and blood pressure remained stable on outpatient follow-up. There was further improvement of the renal function parameters, to the point where BUN and creatinine were normal at 15 mg/dL and 0.63 mg/dL, respectively, at 40 days. Urinary casts had disappeared by 29 days.

Approximately 5 weeks after initial presentation, the platelet count had dropped to 15 x  $10^{3}/\mu$ L, as shown in Table 1. At that time, the patient also noted easy bruisability. Of note, the following day, he was coincidentally treated in the emergency room with dexamethasone for croup. The platelet count subsequently increased, without any need for additional IVIG treatments. With normalization of the blood pressure and platelet count, the hydralazine was tapered and fully discontinued approximately 2 months after initial presentation. The platelet count was monitored periodically over the next several months and remained in the normal range. A repeat ANA, obtained approximately 2 months after initial presentation, was negative, and an anti-single-stranded DNA was within normal range. Approximately 1 year later, the urine was completely normal, without protein, RBC's, or casts.

# Discussion

Table 2 summarizes the characteristics of all cases, described in the literature, of thrombocytopenia associated with PSGN. The characteristics of this case that were similar to most of the cases previously reported include: occurrence in middle childhood, which is the age when streptococcal infections are common (although this child was slightly older than the others); presence of a prodromal or recent illness; clinically significant thrombocytopenia that improved with time-limited immune-modulating treatment; abnormal renal function; urinalysis findings that suggested glomerular inflammation or injury; immunologic evidence of recent streptococcal infection; decreased C3, consistent with the known pathophysiology of PSGN<sup>5</sup>; absence, on peripheral smear, of any evidence for hemolytic disease, as would be expected if hemolytic uremic syndrome (HUS) were occurring; negative rheumatologic workup; treatment with an antibiotic likely to eradicate group A beta-hemolytic streptococcus; supportive treatments for other sequelae of PSGN such as hypertension; and overall complete recovery.

Although the etiologic link between PSGN and thrombocytopenia is yet to be definitively proven, Muguruma et al<sup>2</sup> and Tasic and Polenakovic<sup>1</sup> have hypothesized that autoantibodies cross-reactive against group A beta-hemolytic streptococci and platelets may play a role, for which reason, time-limited immune-modulating treatments appear to be beneficial. One aspect of this case that is different from the others is that IVIG, rather than steroids (given for a duration of

Table 1.— Platelet count during the course of this child's illness					
Time from initial presentation	Platelet count (x 103/µL)	Comments			
0	4 (primary care physician's office); 6 (emergency room)				
1 day		IVIG given			
2 days	26				
4 days	96				
7 days	82				
14 days	22				
17 days	37				
29 days	44				
38 days	15				
39 days		Dexamethasone coinciden- tally given for croup			
40 days	57				
59 days	102				
66 days	154				
80 days	205				
4 months	248				
6 months	257				
10 months	251				

4-6 weeks), was used as the primary immune-modulating treatment. In this case, there seemed to be a noticeable improvement platelet count with IVIG treatment (with an expected nadir observed 6-7 weeks following treatment) and resolution of the renal dysfunction even prior to the coincidentally administered single steroid dose. In essence, there seemed to be improvement with the standard treatments for each component (acute immune-mediated thrombocytopenia and PSGN) of the child's illness.

Given that rheumatic fever has continued to be a concern in Hawai'i, even with declines in incidence in the rest of the country;<sup>6,7,8</sup> that the incidence of rheumatic fever in Native Hawaiian and Samoan children has consistently been found to be much higher than in other ethnic groups in Hawai'i;67,8,9 and that (based on the authors' clinical experience) PSGN appears more commonly in Polynesian and Filipino children; it is perhaps of interest that this illness was found in a child living in Hawai'i and of an ethnic background at epidemiological risk of immunological sequelae of streptococcal infections. Although it is yet to be determined if this rare association of immune-mediated thrombocytopenia with PSGN is more prevalent in certain populations or locales, it is probably reasonable to consider streptococcal infections somewhere in the differential diagnosis of immune-mediated thrombocytopenia, particularly in populations where streptococcal infections or their immune sequelae are relatively common.

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Table 2.— Selected characteristics of patients (described in the literature) with acute thrombocytopenia and PSGN									
Study	Demographics	Presenting clinical findings and BP (mm Hg)	Platelet counts (x 103/ μL)	Renal function: BUN (mg/dL)/creati- nine (mg/dL); UA; other nephrologic tests	ASO titer (IU/ mL) and C3 (mg/dL)	Other hematologic tests	Other rheumatologic tests	Medications	Clinical course
Kaplan and Esseltine, 1978	7-year old girl in Canada	Otitis media, then petechiae, bruises, epistaxis, sub-mucosal lip bleeding, gross hematuria; BP normal	2	26/0.9 Many RBC's, occasional RBC casts, 4+ protein	833 52	Hb 10.6 g/dL, anisocytes, atypical lymphocytes, and decreased large platelets Bone marrow normal except for mega- karyocytes not producing platelets	Anti-nuclear factor and ANA negative	Initially, penicillin, then erythromycin Prednisone for 6 weeks	Normal renal function and platelets three months later
	5-year old boy in Canada	Initial upper re- spiratory infec- tion, followed by bruises and epistaxis; BP normal	3	19/0.4 20-40 RBC/ hpf, 2 RBC casts, no proteinuria	833 76	Hb 12.6 g/dL, reticulocyte count 1.6%, no atypical cells Bone marrow with abundant megakaryo- cytes and erythroid hyperplasia but no abnormal cells	ANA negative	Initially penicil- lin, also took aspirin Prednisone for 4 weeks total	Normalization of platelet count after 4 weeks
Rizkallah et al, 1984	5-year old boy in Saudi Arabia	Initial fine papular skin rash, then desquamation, periorbital edema, and gross hematu- ria, then diffuse petechiae and epistaxis; BP 170/100	4	12.5/1 2+ protein, many RBC's, 6-8 granular casts Renal bi- opsy confirmed PSGN Renal scan with adequate excretion	1536 46	Hb 9.5 g/dL, reticulocyte count 4.4%, no fragmented RBC's, normal PT, PTT and FDP Bone marrow normocel- lular with megakaryocytic hyperplasia	Rheumatoid factor negative, ANA 1:120 with anti-DNA of 17%	Prednisone for 4 weeks Hydralazine and reserpine Penicillin	Normalization of blood pres- sure and renal function within 3 weeks
Muguruma et al, 2000	4-year old boy in Japan	Initial need for antibiotic treatment, fol- lowed by gross hematuria; BP normal	16 minimum	16/0.39 2+ protein, >50 RBC's, 10-20 WBC's, occasional RBC and WBC casts	1283 21	Elevated platelet-associ- ated IgG Bone marrow: mildly decreased megakaryo- cytes without abnormal cells	Negative ANA	Cefdinir IV hydrocorti- sone, then oral prednisolone, for a total of 5 weeks of steroids	Improvement in platelet count within a couple months
Tasic and Polenakovic, 2003	4-year old boy in Turkey	Initial fever and exudative pharyngitis, followed by epistaxis and petechiae; BP 135/100 maximum	1 minimum	BUN 44.8 mg/ dL (16 mmol/L)/ creatinine 1.67 mg/dL (148 µmol/L) 2+ proteinuria, 3+ hematuria (dipstick), numerous RBC's with dysmorphology	640 42 mg/ dL (0.42 g/l)	Negative plate- let-associated IgG antibodies Normal RBC morphology	Negative ANA and anti-DNA	Penicillin Prednisone for 4 weeks	Improvement and resolution over 5-year follow-up

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# Late Presentation of Diaphragmatic Hernia in a Pacific Island Pediatric Population

Sherreen Batts DO; Mark W. Thompson MD; and Donald A. Person MD

# Abstract

**Background:** Congenital diaphragmatic hernia (CDH) usually presents at birth with respiratory distress syndrome (RDS) and has a high mortality rate if not promptly recognized and treated. The incidence of CDH is reported to be 0.8 - 1.0/10,000 registered births. Less than 3% present after the neonatal period. In the latter, ie. late-presenting CDH (L-pCDH), the prognosis is improved because pulmonary hypoplasia does not develop. With the creation and application of a store-and-forward telemedicine system to the Pacific Island Health Care Project (PIHCP), we have come to realize that this rare condition ie., (L-pCDH) occurs with unusual frequency in the United States Associated Pacific Islands (USAPIs), especially those of the Federated States of Micronesia (FSM).

**Methods:** Information concerning CDH was identified from the archived data base of the over 3,100 cases of the PIHCP, as well as the composite data base of Tripler Army Medical Center (TAMC). The cases of CDH diagnosed after the neonatal period (>30 days of age) were considered to have L-pCDH. The study period was from 1997 – 2006.

**Results:** During the study period (1997-2006), 12 cases of CDH were referred from the PIHCP. There was 1 case of CDH born at TAMC (beneficiary from Micronesia) during the same period. The number of births over the 10-year period of study was similar for the referral base (PIHCP) and TAMC. Five of the 12 cases in which the age at diagnosis could be established, were L-pCDH from the PIHCP. The one case of CDH born at TAMC, during the 10 year period, was diagnosed in the neonatal period (<30 days of age).

Discussion: These results confirm that CDH occurs with increased frequency in the USAPIs as contrasted to the frequency in the developed world. The incidence of L-p CDH is far in excess in the USAPIs. This review highlights the fact that this group of patients can be easily identified using tele-techology (attached chest X-rays demonstrating stomach and/or bowel gas in the chest) thus allowing remote diagnosis and referral for ultimate surgical correction of this potentially lethal condition. Infants and children with CDH: provided excellent graduate medical education (GME) for residents-in-training; are afforded advanced surgical treatment unavailable in the remote jurisdictions of the Pacific; and, following surgery, are restored to health to return to their homes so as to become contributing members of society.

**Conclusion:** CDH, especially L-pCDH occurs with increased frequency in the USAPIs. The Web-based-store-and-forward telemedicine PIHCP allows for remote diagnosis. Patients so identified are transported to TAMC for definitive treatment. These patients provide excellent GME to our residents-in-training. Following surgical correction these patients are restored to health to return to their homes to mature and become contributing members of society.

## Introduction

The Pacific Island Health Care Project (PIHCP) is a Congressionally funded program allowing patients from underserved areas of the United States Associated Pacific Islands (USAPIs) to be referred to Tripler Army Medical Center (TAMC) for evaluation and treatment. The islands involved are the former Trust Territories of the Pacific. The USAPIs include three Flag territories: American Samoa (AS); Guam; and the Commonwealth of the Northern Mariana Islands

(CNMI) and the three freely associated states: the Federated States of Micronesia (FSM) including; Chuuk, Kosrae, Pohnpei and Yap States; the Republic of the Marshall Islands (RMIs); and the Republic of Palau (ROP). The program has been in place for nearly 20 years and is unique for several reasons. Indigenous patients from the USAPIs comprise a small population (approximately 500,000) in medically underserved and remote areas, but they provide an enormous benefit to graduate medical education (GME) and the training of TAMC residents in surgery, pediatrics, orthopedics, urology, otolaryngology, internal medicine, and obstetrics and gynecology. The program has allowed patients to obtain definitive, advanced medical and surgical treatment for often life-threatening conditions from which, without such treatment, they would not otherwise survive. This care is free of charge to the patient. Within the past decade, a Web-based telemedicine system was created allowing timely consultations from the Pacific Basin.<sup>1-3</sup> The majority of the referrals come from the FSM (Chuuk, Pohnpei, Kosrea, Yap), the Republic of the Marshall Islands, Republic of Palau and America Samoa.

Throughout the history of the referral program, a number of children have been referred for repair of congenital diaphragmatic hernia (CDH). Of note, several of these patients have been referred with what would be described as late-presentation congenital diaphragmatic hernia (L-pCDH). L-pCDH has been defined as diagnosis of the condition after the neonatal period (> 30 days of age). The purpose of this review is to describe patients from the Pacific Island Health Care Project (PIHCP) who presented with CDH and to compare the data with current cases in literature. The incidence of CDH is reported to be 0.8 - 1.0 cases/10,000 registered births.<sup>4</sup> L-pCDH is a rare subset of CDH and a recent study establishes that only 79 (2.6%) of 3,098 cases of CDH from 30 major centers worldwide had L-pCDH.<sup>5</sup>

## Methods

We reviewed all cases of CDH referred through the PIHCP from 1997-2006. A simple Web-based, store-and-forward methodology was developed and has been utilized since December 1997<sup>(1-3)</sup>. Over 3,100 cases have been consulted or referred since the inception of the telemedicine system. All cases are archived for easy retrieval and review. Patients were identified using a key word search of the database using the search strings of "diaphragmatic hernia", "congenital diaphragmatic hernia", and "hernia". Once patients were identified, a chart review was performed from the archived electronic record of the PIHCP as well as TAMC inpatient records. Not all patients identified from the referral database were transported to TAMC so detailed clinical information was not available for them. All patient identifiers were removed from the clinical information. The review of the database and subsequent chart review was approved by the TAMC Institutional Review Board and a HIPPA waiver was obtained. HIPPA waiver was in addition to the fact that all patients/parents provided informed consent (a basic provision of the PIHCP telemedicine system) prior to consultation and/or referral.

# Results

A total of 12 cases of CDH were found within the PIHCP database for the period 1997-2006. Table 1 includes a description of each of the individual cases. The majority of cases presented from Pohnpei State (5), followed by Chuuk State (3), and Majuro (3), the capital of the Republic of the Marshall Islands. One case was referred from AS. The age at presentation ranged from birth to 15 months with a mean age of 4 months. Four of the 12 cases presented at birth. All patients had decreased breath sounds over the affected side, audible bowel sounds on the involved side of the thorax, and a chest radiograph demonstrating abdominal contents in the chest. The most common associated anomalies were malrotation (2/10 cases), and micro-opthalmia (2/10 cases). The most common type of hernia described was left Bochdalek hernia (10/12) cases. Two of the twelve cases died in the early perinatal period prior to transport to TAMC. The most common presenting symptom at birth was respiratory distress, while recurrent cough and shortness of breath were more commonly reported with L-pCDH. Less common presenting symptoms were failure-to-thrive and feeding difficulties. Of the 10 cases referred to TAMC, all were repaired surgically and all had excellent outcomes. All were returned to their homes without residual disease. The majority of cases were male (9/12 cases). By report, all infants were of term gestation. Five of the 12 cases from the PIHCP fulfilled the criteria for a diagnosis of L-pCDH. Search of the database using ICD 9 code 756.6 (anomalies of the diaphragm) resulted in the identification of one case of CDH born at TAMC during the period 1997 – 2006. This case was diagnosed in the early neonatal period (<30 days of age). Table 2 contrasts the 12 cases from the PIHCP with the one case from TAMC. Finally, Table 3 compares the cases of CDH, and L-pCDH, from the PIHCP with those from the international database.<sup>5</sup>

#### Discussion

Two types of CDH have been described: Bochdalek hernia and Morgagni hernia. Bochdalek hernia occurs secondary to failure of the pleuroperitoneal folds to close the foramen at the point where the septum transversum of the diaphragm grows backward and meets the dorsal mesentery. Formation of a hernia sac is dependent on timing of closure of the pleuroperitoneal canal. Most Bochdalek hernias occur on the left side because the left septum transversum closes after the right. Additionally, the liver appears to provide protection from right herniation. The more uncommon Morgagni hernia occurs when there is incomplete extension of the septum transversum to the thoracic wall with defective attachment of anteromedial diaphragmatic bands to the sternum and ribs. The timing of closure of pleuroperitoneal folds usually occurs in the 8-10th week of gestation. A peritoneal sac is present in less than 10 of all hernias which would suggest that herniation occurs during the first trimester.

Most Bochdalek hernias occur on the left side with displacement of stomach, intestine, and spleen usually without hernia sac. The stomach and colon are the most frequent organs to herniate. CDH most commonly presents shortly after birth with evidence of respiratory distress. Presentation in the early newborn period carries a high mortality (50-60%) with death most frequently due to pulmonary hypoplasia. Most cases in the developed world are quickly recognized at birth when the newborn presents with respiratory distress, absent breath sounds on the side of the herniation, shift of heart sounds to the contralateral side, presence of bowel sounds in the chest and the appearance of a scaphoid abdomen.

L-pCDH, as indicated, is defined by diagnosis of CDH outside

the neonatal period (30 days or greater). This entity is rare, and the diagnosis is often delayed because the presentation can be more subtle. It is assumed that the defect in the diaphragm is occluded by the liver or spleen thus preventing more severe symptoms associated with long term displacement of abdominal contents into chest.

In the recent review by the Congenital Diaphragmatic Hernia Study Group of 3,098 cases of CDH from 30 major medical centers around the world for the years 1995-2004 only 79 cases of L-pCDH were ascertained. This is the first time a major study establishes, with certainty the actual incidence of L-pCDH. Although the authors do not report the population from whence these cases were obtained, one might extrapolate, based on the figures from the United Kingdom (0.8-1.0 cases/10,000 births) that 24 to 31 million total births or 2.4 million to 3 million births annually were the origin of the cases. The incidence of L-pCDH in the USAPIs is clearly in excess of that seen in the developed world. It appears that CDH is more common in the USAPIs than that seen at TAMC, but the numbers are too small for a meaningful full comparison. Probably less than 50% of births in the USAPIs occur in hospitals. Infants born at home who develop respiratory distress die. Many Pacific Islands are virtually inaccessible; some are 400-600 nautical miles from the only hospital in the jurisdiction. Even infants born in the hospitals of the USAPIs with severe RDS do not survive as infant ventilators are non-existent. The death of the two infants with CDH in Marjuro and Pohnpei attest to that fact. In contrast to the recent large review<sup>(5)</sup>, none of our patients had cardiac or chromosomal anomalies, reported in 15% of their cases. 2/10 (20%) of our patients have intestinal malrotation and 2/10 (20%) of our patients had micro-opthalmia (both from Chuuk).

The signs, symptoms and clinical course of both CDH and L-pCDH cases reported in the literature and those we report here from the USAPIs are similar. Respiratory distress was seen in the early or neonatal CDH cases. L-pCDH cases tended to have recurrent cough, recurrent respiratory infections, and shortness of breath. In all of our cases, bowel sounds were auscultated over the chest. Right sided heart sounds were detected in several patients. A scaphoid abdomen was reported in most patients both early and L-pCDH. All of our cases from the Pacific were reported to be term births. The male to female ratio for all of the cases from the PIHCP was 3:1. This contrasts with 1.5-2:1 derived from the literature. The most common anomalies reported by the Congenital Diaphragmatic Hernia Study Group were cardiac defects or chromsonal anomalies (primarily trisomy 21). None of our reported cases had cardiac defects or trisomy 21. We have two cases (20%) with malrotation of the bowel. Two additional cases (20%) had associated micro-opthalmia. The latter cases were from Chuuk State where some 35-40 cases of micro or anophthalmia have been indentified in recent years.

We may be missing L-pCDH cases in the Pacific. Asymptomatic or minimally symptomatic patients are unlikely to have a routine chest x-ray. This possibility was recently confirmed when the senior author (DAP) was consulted on a 72-year-old Marshallese man with a respiratory syndrome who was discovered on imaging to have a diaphragmatic hernia consistent with L-pCDH. All of these observations are of interest and are worthy of future study. The incidence of CDH is higher in the Pacific than in the developed world. The incidence of L-pCDH in the Pacific is very much higher. Although there may be a number of possible explanations, the real importance of this review is that infants and children with L-pCDH from the remote Pacific can easily be diagnosed remotely using the simple store-and-forward telemedicine program of the PIHCP. Once

Table 1.— C	Table 1.— Congenital Diagphragmatic Hernia (CDH) cases from the USAPIs									
Pt	Region	Age	Symptoms	Signs	Anomalies	Defect	Outcomes	Sex	Birth Weight	Maternal History
1	Pohnpei	Birth	RDS	Scaphoid Abdomen Chest-BS	Malrotation	Left	Excellent	М	6.5 lbs	Uncomp/term
2	Chuuk	8 days	Tachypnea cyanosis	Scaphoid Abdomen Chest-BS	Malrotation	Left	Excellent	F	7 lbs	Uncomp/term
3	Pohnpei	2.5 mos	Cough Tachypnea	Chest-BS	None	Eventration Left Morgagni	Excellent	М	7lbs 1 oz	Uncomp/term
4	Pohnpei	7 days	RDS	Right heart sounds Chest-BS	None	Left	Excellent	F	Unknown	Term
5	Majuro	4.6 mos	Cough, SOB, fever	Scaphoid abd Chest-BS	None	Left	Excellent	М	Unknown	Term
6	Pohnpei	15 mos	Recurrent uri, SOB, feeding	Chest-BS	None	Eventration	Excellent	М	Not charted	Not charted
7	Am Samoa	15 mos	Fever, SOB, cough		None	Left	Excellent	М	8 lbs	Term
8	Pohnpei	Birth	RDS	Right heart sounds, scaphoid abd	None	Left	Died+	М	8 lbs	Term, PIH
9	Majuro	Birth	RDS	Diminished right breath sounds	None	Right	Died+	М	7 lbs 15 oz	PROM
10	Majuro	Birth	Нурохіа	Diminished right breath sounds	None	Left	Excellent	М	6 lbs	Term
11	Chuuk	3 weeks	Asymptomatic	Prominent right heart sounds	Micro- ophthalmia	Left	Excellent	F	Unknown	Term
12	Chuuk	11 mos	Recurrent cough, SOB, fever		Micro- ophthalmia	Left	Excellent	М	Unknown	Unknown

1. USAPIs, United States Associated Pacific Islands; 2. RDS, respiratory distress syndrome; 3. BS, bowel sounds; 4. SOB, shortness of breath; 5. +, died prior to transport; 6. PROM, premature rupture of membrane

identified, they are transported to TAMC for corrective surgery. They provide invaluable experience to our residents-in-training in pediatrics and general surgery. The humanitarian benefits are incalculable. These patients are expeditiously treated and returned home restored to health.

The opinions or assertions contained herein are those of the authors and are not to be construed as reflecting the views of the Department of the Army, Department of the Air Force, or the Department of Defense.

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Table 2.— Comparison of CDH cases from the FSM and TAMC (1997 – 2006)					
	CDH	L-pCDH	Births	Р	
ТАМС	1	0	22,400	NS	
FSM	8	3	21,720	0.02	

Table 3.— CDH, L-pCDH cases from the PIHCP compared to those reported by the CDHSG

	CDH	L-pCDH	Р			
PIHCP	10	5	<0.0001			
CDHSG*	3,098	79	<0.0001			

\*CDHSG, Congenital Diaphragmatic Hernia Study Group. Late-presenting congenital diaphragmatic hernia. *J.Pediatric Surg*, 2004, 40:1839-1843.

Fisher's Exact Test used to test difference in proportions. P<0.05 considered significant. The incidence of L-pCDH not significantly different due to low sample size at TAMC of CDH. Incidence of CDH at TAMC versus FSM is significantly different. The proportion of L-pCDH iks higher (50%) than national CDHSG (2.6%).

# Assessment of Pain in Older Asian Americans with Cancer

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## Abstract

This cross-sectional study focused on pain assessment in a group of older Asian Americans with cancer. Thirty-six participants and their primary nurses were interviewed, and pain intensity was measured using 3 different scales: the Numeric pain intensity 0-10 scale, the Faces expression scale,<sup>1</sup> and Visual analog scale (VAS).<sup>2</sup> Overall, 56% of participants reported pain. Younger age (65-75 years old) was significantly associated with higher pain intensity (p < 0.05). High correlation was found between the participants' and their nurses' pain intensity ratings (r = 0.69, p < 0.0001). High correlation was also found among different pain intensity scales, with a Spearman correlation coefficient ranging from 0.89 to 0.96 (p<0.0001), suggesting that they are reliable measures in this population.

#### Introduction

Pain and symptom management has been consistently identified by patients as one of the key dimensions in defining quality end-of-life care.3 The 1995 landmark SUPPORT4 study, which showed the common occurrence of uncontrolled pain, has since started a nation-wide effort to improve pain management. While the incidence of cancer rises with age, up to 80% of older patients with cancer continue to experience daily pain.<sup>5</sup> Considering the rapidly growing US senior population (37.3 million people  $\geq 65$  years old in 2006),<sup>6</sup> cancer pain in older adults deserves special attention.

Barriers to effective pain management include time and cost in pain assessment and treatment, fear of addiction, medication side effects, and other patient, clinician, and health system-related factors.<sup>7,8</sup> Studies have also found that older age and minority background are associated with under-treatment of pain.9,10 Presently, there are few studies on ethnic disparities on pain assessment and management in older cancer patients.<sup>11</sup> Data on Asian Americans are even fewer, with most studies being limited by small numbers and subgroup analyses. In fact, the most widely used pain intensity scales have not been directly validated in older Asian American populations. Therefore, the focus of this study is pain assessment in older Asian Americans with cancer.

#### **Objectives**

Elderly Asian Americans with cancer were the target of this study. The objectives of this study were (1) to determine differences in selfreported pain based on age group (65-75 years versus  $\geq$  76 years); (2) to determine the reliability of nurses' assessment of pain, and (3)to measure the reliability of 3 commonly used pain scales.

#### **Methods**

Participants of this study were recruited patients undergoing active cancer treatment at Kuakini Medical Center in Honolulu, Hawai'i. We also included the nurses who had provided care to these patients within the 24 hours preceding our assessment. Potential participants were identified from rosters of the inpatient oncology ward and the outpatient chemotherapy unit. Exclusion criteria were: age < 65 years and non-Asian ethnicity (confirmed by demographic information in the medical chart and by directly questioning the participants or

their families). This project was approved by the Institutional Review Board of Kuakini Medical Center. Patients gave written informed consent while the nurses gave verbal informed consent.

The lead author reviewed all medical charts, performed one-on-one interviews with participants, and collected the nurses' written pain surveys. She also performed Mini Mental Status Exams (MMSE)<sup>12</sup> on the participants. From chart review, information was gathered on demographics, type of health insurance, diagnosis of cancer, past medical history, and analgesic and antidepressant medication usage. During the interviews, participants were asked questions about other aspects of their background, including first language, confirmation of their ethnic origin, and religion. The interviews included a Pain Assessment Survey, consisting of participants' self-report on pain intensity, pain frequency, average duration of pain over the past 24 hours, and other pain characteristics including onset, quality, and location.

Pain intensity was measured using 3 pain scales: (1) Numeric pain intensity scale, with 0 indicating no pain to 10 indicating worst possible pain, (2) faces expression pain scale, with 1 indicating happiest pain-free face to 6 indicating worst pain with crying face,  $^{1}$  and (3)visual analog pain scale (VAS), with 0 mm indicating no pain to 100 mm indicating worst possible pain.<sup>2</sup> Participants were also questioned about the impact of pain on their activities of daily living (ADL) on a 1-5 scale, with 1="no interference" to 5="disabling/excruciating interference." They were questioned on satisfaction with pain treatment also on a 1-5 scale, with 1="very satisfied" to 5="very unsatisfied". In addition, participants were asked about quality of life (QOL) on a 1-4 scale, with 1="excellent" to 4="poor." Finally, mood was assessed by asking "How often do you feel sad?" on a 1-5 scale, 1="never" to 5="all the time."

On the same day, their nurses completed a written pain assessment survey. Nurses were asked to assess their patients' pain intensity averaged over past 24 hours using the numeric pain intensity scale (0-10), pain frequency, impact of pain on ADL (1-5 scale), and their patients' satisfaction with pain treatment (1-5 scale).

To study differences in participants' self reported pain based on age, they were divided into two age groups for analysis: "young" defined as ages 65-75 years (n=20), and "old" defined as  $\geq$ 76 years (n=16). We compared baseline characteristics and reporting of pain by participant age groups using T-tests, Fisher's exact tests and chi-squared tests.

To determine the reliability of nurses' pain assessment, we first compared answers given by participants and nurses on the same pain assessment questions and created 3 groups: 1) nurses overestimated pain, 2) nurses assessed pain the same as the participant, 3) nurses underestimated pain. Inter-rater reliability between participants' and the nurses' pain assessment was then measured using Spearman correlation coefficient (r). Finally, the reliability of the 3 pain intensity scales was also determined using Spearman correlation models. All analyses were performed using SAS versions 6.12 and 8.0.

# Results

A total of 44 participants were identified from the oncology ward rosters. Four declined interview due to fatigue. Four were excluded because they were not of Asian descent. The final study population consisted of 36 Asian Americans (31 Japanese Americans and 5 Chinese Americans) and their nurses (n=36). There were 21 males and 15 females who were between the ages of 66 and 85 years (mean=74). All had Medicare with or without other supplemental or private health insurance. None of the patients had Medicaid. The majority (86.1%) reported English as their first language. The mean MMSE score was  $25.9\pm3.5$ , with the average years of education being  $13.2\pm3.5$ .

When participants were asked about their average pain for the past 24 hours on the 0-10 pain intensity scale: 16 (44%) reported no pain, 10 (28%) had mild pain of 1-3, and 10 (28%) had moderate-to-severe pain of  $\geq 4$  out of 10. Overall, participants reported relatively low pain intensity scores across all 3 pain scales, which are correlated with good self-reported QOL and functional (ADL) status. Of patients who reported pain on any of the 3 different pain scales, 12/23 (52%) had their pain directly caused by cancer (as determined by lead author via chart review and location of pain). The rest had their pain due to surgery, musculoskeletal causes including arthritis and injury, and other causes. When asked about satisfaction with pain treatment, only 1 participant reported dissatisfaction.

Table 1 summarizes participants' characteristics and reporting of pain by age groups. On both the numeric pain intensity scale and the faces expression pain intensity scale, the younger group had significantly higher pain intensity compared to the older group, p < 0.05. The younger group also had non-significant trends of more pain on the visual analog pain scale (p=0.056), increased pain frequency (p=0.09), and greater impact of pain on ADL (p=0.16). Similarly, nurses reported higher pain intensity (p=0.04), greater impact of pain on ADL (p=0.03), and less satisfaction with pain treatment (p=0.03) in younger patients compared to older patients. In addition, there was a non-significant trend of greater use of analgesic medications in the younger age group compared to the older (65% versus 37.5%, p=0.10). None of the patients were on antidepressants or carried a prior diagnosis of depression. However, when asked "how often do you feel sad", 14 (39%) reported "sometimes" while 2 (6%) reported "most of the time."

Figure 1 compares the nurses' and their patients' reporting of pain intensity, frequency, impact on ADL and satisfaction with pain treatment. Spearman correlation models found statistically significant correlations between participants' and their respective nurses' reporting of pain intensity (r=0.69, p<0.0001), pain frequency (r=0.51, p=0.002), impact of pain on ADL (r=0.51, p=0.03), and satisfaction with pain treatment (r=0.64, p=0.02).

To determine the reliability of the 3 most commonly used pain intensity scales in this older Asian American population with cancer, Spearman correlations were done. All 3 scales were found to be highly correlated, with r values ranging from 0.89 to 0.96, and p < 0.0001.

# Discussion

In this study, pain continued to be a common problem for older Asian Americans undergoing active cancer treatment, with 56% of participants reporting pain in the preceding 24 hours. Pain prevalence, however, also appears to decrease with advancing age. We found that participants ages 76 and older reported significantly less pain compared to those between the ages of 65 and 75. Our results are consistent with an earlier multicenter study showing that age >60 years was significantly associated with less pain intensity in both univariate and multivariate analyses.<sup>13</sup> This was theorized to be related to decreased pain perception associated with advancing age.<sup>14</sup> In addition, age related perceptions of health could contribute to older patients reporting less pain.

Similarly, provider attitudes and prescribing patterns appeared to be influenced by the patient's age, with previous research suggesting that less pain experienced by older patients should result in less use of analgesics.<sup>15</sup> In our study, only 37.5% of participants ages  $\geq$  76 years used analgesic medication either on routine or asneeded basis, compared to 65% of those <76 years of age. Because of relatively small numbers (n=36) in this study, this result did not reach statistical significance.

Overall, we found significant correlation between the nurses' and the patients' assessment of pain intensity and frequency, impact of pain on ADL, and pain treatment satisfaction. The Spearman correlation coefficient for pain intensity was 0.69 with a p<0.0001. The nurses had an overall accuracy of 45.7%, but 31.4% still underestimated patients' pain intensity. This finding is consistent with earlier studies.<sup>16,17</sup> In a retrospective study of 41 charts, nurses had a 90% specificity but only 45% sensitivity in assessing moderate to severe pain defined as  $\geq$  4 on the numeric 0-10 scale.<sup>18</sup> Another study found that nurses were more accurate than physicians in assessing pain, but both groups continued to underestimate patients' burden of pain.<sup>19</sup> The discrepancies in pain assessment suggest that further education for health care providers could be beneficial.<sup>20</sup>

Thus far, little research has examined the reliability and validity of commonly used pain intensity scales in older minority patients.<sup>21</sup> Most of the minority research focused on African Americans, of which one study reported correlations ranging from 0.50-0.93 using faces expression pain scale, numeric pain scale, verbal descriptor scale, and visual analog scale.<sup>22</sup> Previous studies on Asian Americans were even fewer, with most being limited by small numbers, limited subgroup analysis, and vague definition of race.<sup>23,24</sup>

We were able to directly assess pain in an older Asian American population, with the racial identity confirmed twice by medical chart demographics and then questioning the participant or their family. We found high correlation among 3 commonly used pain intensity scales (r=0.89 to 0.96, p<0.0001), suggesting that they can be used reliably in the clinical setting. Although participants in this study had an average MMSE score of 25.9 $\pm$ 3.5, other studies have found comparable reliability in similar pain scales for cognitively impaired minorities.<sup>25</sup>

Feelings of sadness were reported by 45% of the patients in the study. There are no validated tools to screen for depression in older Asian American cancer patients. Earlier studies demonstrated correlation between depression and pain,<sup>26</sup> with treatment of depression improving pain and QOL. The assessment of depression is especially important in cancer patients, especially when more than three-fourths were found to have signs of depression in advanced cancer.<sup>27</sup>

There are several limitations to this study. Patients were recruited form a single medical center in Hawai'i which may limit generalizability to Asian-Americans of different ethnicities, immigration

Table 1.— Baseline Characteristics and Reporting of Pain by Age Groups.						
Participant Characteristics and Reporting of Pain	"Young" Group (Age 65-75 yrs) N = 20	"Old" Group (Age ≥ 76 yrs) N = 16	p value			
Male	60%	56.3%	0.82			
English as 1st Language	80%	93.8%	0.35			
Religion:						
Buddhist	25%	50%				
Christian	40%	31.3%	0.28			
Other	35%	18.7%				
Years of Education	13.42 (±3.69)	13 (±3.33)	0.73			
Inpatient (vs Outpatient)	55%	37.5%	0.30			
Any Analgesic medication(s) Use (routine or as needed)	65 %	37.5 %	0.10			
Self-reported Numeric pain intensity scale (0-10)	2.60 (±2.41)	1.13 (± 1.75)	< 0.05			
Nurses' assessment of patients' pain on Numeric pain intensity scale (0-10)	2.26 (±2.21)	0.88 (± 1.41)	0.04			
Self-reported Faces expression pain scale (1-6)	2.55 (±1.32)	1.75 (±0.86)	< 0.05			
Self-reported Visual analog pain scale (0-100 mm)	27.05 (±25.53)	12.13 (± 17.94)	0.056			
Self-reported pain frequency (0 = no pain to 6 = all the time)	3.2 (±2.31)	1.75 (±2.59)	0.09			
Nurses' assessment of patients' pain frequency $(0 = no pain to 6 = all the time)$	2.74 (±2.40)	2.00 (±2.48)	0.38			
Self-reported impact of pain on ADL (1 = no effect of pain on ADL to 5 = worst effect)	2.54 (±1.05)	1.83 (±0.75)	0.16			
Nurses' assessment of pain's effects on patients' ADL (1 = no effect to 5 = worst effect)	2.00 (±0.82)	1.44 (±0.63)	0.03			
Self-reported satisfaction with pain treatment (1 = very satisfied to 5 = very dissatisfied)	2.36 (±1.21)	2.33 (±0.58)	0.97			
Nurses' assessment of patients' satisfaction with pain treatment (1 = very satisfied to 5 = very dissatisfied)	2.11 (±0.76)	1.53 (±0.64)	0.03			
Self-reported quality of life (1 = excellent to 4 = poor)	2.58 (±0.90)	2.00 (±0.82)	0.057			
Self-reported sadness (1= never to 5=all the time)	2.42 (±0.84)	2.19 (±0.91)	0.44			



history, English language comprehension, geographic area, and socioeconomic status. This was a group of Asian Americans with non-Medicaid health insurance. The majority spoke English as a primary language and had at least high school level of education. The sample size was also small, limiting statistical power. Strengths of the study come from directly examining pain in elderly Asian Americans and demonstrating reliability of 3 commonly used pain scales for this unique population. This is the first study on pain that we are aware of focusing primarily on non-Medicaid, older Asian Americans with cancer. Data collection was consistent since it was performed by a single investigator, the lead author.

Until now, Asian Americans have received little attention in studies of assessing and managing cancer pain. Future pain research should include a greater number of Asian Americans and other minority groups. Thus far, all studies on ethnic disparities in pain management have analyzed the data with the presumption that all Asian Americans are homogeneous, when in reality they may belong to different ethnic groups, with varying degrees of acculturation, insurance status, education, and income level among other socioeconomic indicators. This can potentially lead to stereotyping and miscommunication with patients and their families.

While obtaining ethnic statistics to fuel fair policy changes and improve community resource allocation, health care providers need to keep in mind that each patient is unique. Individualizing pain management with particular attention to the patient's functional status, frailty, co-morbid conditions, medication history, and preferences can vastly improve outcomes. Multiple pain guidelines from the American Geriatrics Society<sup>28</sup> and National Comprehensive Cancer Network<sup>29</sup> are available. The healthcare provider's awareness of pain and its implication on the patient's quality of life are the first steps in changing the national trend of pain under-treatment, including high risk groups such as older minority populations with cancer.

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# Selection Criteria for Expander/Implant Breast Reconstruction Following Radiation Therapy

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# Abstract

**Purpose:** Breast reconstruction with expander/implants is generally discouraged in patients who have undergone radiation therapy. However, not every patient treated with radiation develops sequelae severe enough to preclude the use of prostheses. To date, there have been no studies that have established criteria for selecting which patients may still be considered for expander/implant reconstruction. We present a series of 27 patients—the largest of its kind to date—all of whom underwent bilateral mastectomies, radiation therapy to only one chest wall, and delayed reconstruction with submuscular expander/implants. The aesthetic outcomes of the irradiated and the non-irradiated breasts were compared, and a classification of post-radiation skin changes was devised for selecting candidates for expander/implant reconstruction.

**Methods:** Patient records were reviewed to identify those who had undergone bilateral mastectomies, radiation treatment to only one chest wall, and delayed expander/implant reconstructions of both breasts. Twenty-seven patients were identified who met our inclusion criteria. Early post-radiation skin changes were classified as "moderate" or "severe," while aesthetic assessments were classified as "good," "acceptable" or "poor."

**Results:** Irradiated chest walls with moderate skin changes and absent induration have aesthetic outcomes comparable to the nonirradiated chest walls (p > 0.50). In contrast, patients who develop induration or severe post-radiation skin changes have a greater rate of modified Baker class IV capsular contracture and poor results that range from 75% to 100% of reconstructed breasts.

**Conclusions:** A history of chest wall radiation should not itself exclude patients from receiving expander/implant reconstruction. Patients who develop neither severe skin changes nor induration may still be considered for prostheses.

## Introduction

Post-mastectomy breast reconstruction with expander/implants is an ideal procedure for patients who neither desire nor qualify for reconstruction with autogenous flaps. However, the use of prostheses is generally discouraged in patients who have received prior radiation therapy-even in those who would be otherwise prime candidates for an implant. The apprehension with which most plastic surgeons approach expander/implant reconstruction in an irradiated chest wall is based on the deleterious effects of radiation on skin and subcutaneous tissues<sup>1-8</sup> and the concomitant poor aesthetic outcomes resulting from a higher rate of capsular contracture, poor skin expansion, and implant extrusion.<sup>1-7</sup> Yet not every patient who receives radiation therapy develops soft tissue sequelae severe enough to compromise the integrity of a prosthetic reconstruction. Unfortunately, determining which patients would be suitable candidates for post-radiation expander/implant breast reconstruction is ambiguous, as there have been no studies to date that have established reliable selection criteria.

The authors present a series of 27 patients—the largest study of its kind to date—all of whom underwent bilateral mastectomies, subsequent radiation therapy to only one of the mastectomy sites,

and delayed reconstruction with submuscular expander/implants. The final aesthetic outcomes of the reconstructed breasts were compared between the irradiated and the non-irradiated breasts in the same patient. We then established selection criteria based upon the severity of post-radiation skin changes for identifying potential candidates for expander/implant reconstruction.

# **Patients and Methods**

Patient records of the senior authors (FDP and YI) between 1982 and 2008 were reviewed to identify those who had undergone bilateral expander/implant reconstruction following mastectomy with radiation treatment to only one breast. To be included in the study, clear documentation of skin appearance and the presence of any post-radiation changes was necessary. Patients whose records lacked such documentation, who received radiation therapy after implant insertion, or those who received immediate reconstruction—defined as earlier than 6 months after mastectomy or earlier than 6 months after completion of radiation therapy—were excluded.

Twenty-seven patients met the above inclusion criteria. The mean age was 51.3 years. Nineteen patients (70.3%) were of Japanese or of various Asian ancestries. The remaining patients were either Caucasian or belonged to other ethnicities.

Indications for contralateral mastectomy included extensive ductal carcinoma *in situ* of the index breast, BRCA positivity, genetic abnormality, extensive lobular carcinoma of the index breast, history of multiple biopsies with atypia, strong family history of breast cancer, breast asymmetry, and patient's fear of cancer recurrence. Seven patients (26%) smoked tobacco and all had been asked to cease smoking at least two weeks before surgery. Eighteen patients in this series received similar regimens and doses of radiation therapy. In these cases, the chest wall was treated with tangential 6 MeV X-ray beams to a dose of 50 Gy in 25-28 daily fractions. Many patients received additional 10-14 Gy boosts to the lumpectomy or mastectomy site, usually with custom-contoured electron beams. The lymphatic areas—supraclavicular, axillary, internal mammary—were treated with 45 Gy.

Breast reconstruction was performed at a mean of 38.2 months (3.2 years) following radiation therapy (range 6 months to 18.2 years). All expander/implants were placed in the subpectoral space. Capsulotomies or partial capsulectomies were performed in all patients at the time of implant exchange. Prior to 1991, 11 patients received Becker double lumen expander implants (Mentor Medical Systems, Santa Barbara, CA); after 1991, the remaining 16 patients received either McGhan Biospan textured expanders (INAMED Aesthetics, Santa Barbara, CA) or Mentor smooth expander/implants (Mentor Corporation, Santa Barbara, CA). The mean follow-up period after reconstruction was 19.8 months (range 3 months to 26 years). During the follow-up period, the original tissue expanders were replaced with regular implants in 21 patients (78%). The remaining patients

did not exchange expanders, refused exchange, or were lost to follow-up.

The authors have classified early post-radiation skin changes as either moderate or severe. (Table 1) Moderate skin changes include erythema, desquamation, and hyperpigmentation, whereas severe skin changes include edema, ulceration, blistering, and fold formation with or without induration developing at a later date. Late skin changes encompassed skin induration at the time of reconstruction.. Aesthetic assessment was performed by the two senior surgeons, the patient, and two additional case-blinded surgeons using color photographs taken at 6 to 12 months following reconstruction. Appearances were rated as good, acceptable or poor. These subjective ratings corresponded with a numerical score, with "good" being given a score of 3, "acceptable" 2, and "poor" 1. Special attention was paid to radiation induced skin changes, degree of capsular contracture, seroma or hematoma formation, infection, and implant extrusion. Capsular contracture was classified according to the modified Baker classification.9

Data analysis was performed using *Epi Info 3.3.2* (Centers for Disease Control and Prevention, Washington, DC) and *SPSS for Windows* version 11 (SPSS, Chicago, IL).

## Results

Post-radiation skin changes were absent in all of the 27 non-irradiated chest walls. Among the irradiated chest walls, 12 (44.5%) developed moderate skin changes without any induration at the time of breast reconstruction. The remaining 15 chest walls (55.5 %) showed severe skin changes of which 7 (46.7%) developed induration. (Table 2)

The incidence of capsular contracture is reported in Table 3. Of note, there were no breasts in either the non-irradiated or irradiated groups with undetectable prostheses, or modified Baker class IA. Of the non-irradiated chest walls, 14 (51.8%) were class IB, 5 (18.5%) class II, and 8 (29.6%) class III. Of the irradiated chest walls 6 (22.2%) were class IB, 1 (3.7%) class II, 5 (25.9%) class III, and 13 (48.1%) class IV. The rate of class II capsular contracture was not significantly different (p>0.20) when comparing the non-irradiated (29.6%) to the irradiated (22.2%) chest walls. However, there was a significant difference in rate of class III (p<0.05) and IV (p<0.01) contracture.

Aesthetic assessments are reported in Table 3. Of the 27 non-irradiated chest walls, 21 (77.7%) were judged as good and 6 (22.2%) as acceptable. Among the irradiated chest walls, a good appearance was present in 10 (37%), 9 of which showed moderate skin changes and 1 severe changes other than induration. An acceptable rating was given to 4 (14.8%) of the irradiated breasts, 3 of which showed moderate skin changes and 1 severe changes other than induration. A poor rating was given to 13 (48%) breasts, 6 of which showed severe skin changes other than induration. All 7 of the chest walls that developed induration were judged to have a poor outcome. (Tables 1-3)

The rate of good outcomes was significantly different (p < 0.05) when comparing non-irradiated (77.7%) with irradiated chest walls (37%). An even greater significance (p < 0.001) was found in the rate of poor outcomes between these same two groups, 0% and 48.1% respectively.

Complications developed in three patients, all of which occurred on the irradiated side and all associated with both class IV contracture and a poor aesthetic outcome. Two patients developed seromas between days 7 and 14 days following implant insertion, one of whom responded to closed drainage and oral cephalexin, while the Table 1.— Early post-radiation skin changes have been classified as either moderate or severe. In order to ensure accurate documentation of these sequelae, we recommend that patients be given a card resembling this table so as they may check-off which skin changes they experience.

Moderate	Severe
Erythema	Blister formation
Desquamation	Persistent edema
Hyperpigmentation	Skin fold
Temporary edema	Leathery induration

Table 2.— Post-irradiation skin changes as observed in non-irradiated and irradiated chest walls.

	Non-Irradiated Chest Walls	Irradiated Chest Walls		
Induration	Absent	Absent	Absent	Present
Skin changes	Absent	Moderate	Severe	Severe
Number of patients	27 (100%)	12 (44.4%)	8 (29.6%)	7 (25.9%)

Table 3.— Aesthetic outcomes of reconstructed breasts as related to the presence of post-radiation skin changes. Modified Baker classes are provided in italics along with the corresponding number of patients.

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	Good	Acceptable	Poor
Non-irradiated chest walls (n = 27)	<b>21</b> (77.7%) B:14 II:3 III:4	<b>6</b> (22.2%) II:2 III:4	0
Irradiated chest walls with moderate skin changes and absent induration (n = 12)	<b>9</b> (75.0 %) IB:6 II:1 III:3	<b>3</b> (25.0%) III:3	0
Irradiated chest walls with severe skin changes and absent induration $(n=8)$	<b>1</b> (12.5%) III:1	<b>1</b> (12.5%) III:1	<b>6</b> (75.0%) IV:6
Irradiated chest walls with induration. $(n = 7)$	0	0	<b>7</b> (100%) IV:7

other was found to be infected with *S. aureus* and required implant removal with delayed reconstruction 9 months later. The third patient developed an implant infection approximately three weeks after insertion that necessitated explantation and capsulectomy with delayed reconstruction.

# Discussion

The use of expander/implant reconstruction in previously irradiated chest walls is almost universally discouraged due to the potentially deleterious effects of radiation on soft tissue.<sup>1,3,4,5,6,13,15</sup> To avoid these potential sequelae, many plastic surgeons subscribe to the routine use of myocutaneous flaps<sup>1,2,5,14,15</sup> even if an implant would otherwise be the best or safest reconstructive option. One reason for this aversion may be due to the paucity of studies establishing criteria for determining which post-radiation patients may still be considered candidates for an implant. We have found comparable aesthetic outcomes between non-irradiated and irradiated chest walls that developed only moderate skin changes with the incidences of "good" and "acceptable" outcomes in these two groups of 77.8% and 22.2% compared to 75.5% and 25% respectively (p < 0.05). We can therefore confidently recommend that patients who have demonstrated neither severe skin changes nor leathery induration still be considered for expander/implant reconstruction. Among the 13 irradiated chest walls that developed a "poor" outcome 7 (53.8%)

demonstrated inducation at the time of reconstruction while the remaining 6 (46.2%) had supple skin. This finding strongly suggests the importance of documenting post-radiation skin changes. as 75% of patients with "poor" results in the sub-group of 8 patients with "severe" skin changes had no inducation at the time of expander/ implant breast reconstruction. (Table 3) In other words, the absence of inducation at the time of breast

reconstruction is meaningful only if a history of post-radiation skin changes is available.

Although our study group is relatively small (n = 27) it is the largest study of its kind to date. The only comparable studies are those by McCarthy who reports on 12 patients, all of whom had received radiation after, rather than before, expander/implant reconstruction,<sup>15</sup> and Rosato and Dowden, who likewise report on 4 patients receiving post-reconstruction irradiation.<sup>16</sup>

Greater than 90% of patients receiving radiation therapy develop some form of cutaneous sequelae.<sup>17</sup> The severity of these skin changes is dependent upon both treatment and patient related factors, and may range from subtle erythema and hyperpigmentation to severe blistering, edema, fold formation, and necrosis.<sup>18,19</sup> Capsular contracture following radiotherapy is also a common complication, with an incidence reported anywhere from 20 to 100 per cent.<sup>1,8,14,15,20-22</sup> Unfortunately, the literature is sparse with data establishing an optimal timeline for delivering radiation therapy when tissue expander/implants are to be used. Krueger noted a six-fold increase in complications in patients receiving radiation, although the timing of radiation therapy and reconstruction varied.<sup>23</sup> Comparing irradiated with non-irradiated breasts, Cordeiro found the overall contracture rate to be significantly greater in the latter group-68% versus 40%-where immediate reconstruction was performed and radiation begun 4 weeks following mastectomy.<sup>22</sup> Several studies have shown that there is no correlation between the occurrence or severity early skin changes and later fibrosis.<sup>19,24,25</sup> The development of some degree of fibrosis has been found to occur up to 11 years following radiation therapy.<sup>26</sup> Our study has found that the presence of induration or a history of other severe skin changes at a mean time of 3.2 years following irradiation to be significantly related to a poor appearance as well as more severe capsular contracture. Although we have found that aesthetics do not necessarily parallel the degree of capsular contracture-good results were obtained in 77% of non-irradiated patients with classes varying from IB to III-we did find an association between poor aesthetic outcomes and class IV contracture as all 13 breasts rated as poor also had class IV contracture.

#### Conclusion

A history of post-mastectomy radiation therapy should not itself exclude patients from receiving expander/implant breast reconstruction. Patients who meet the following criteria may be confidently selected for post-radiation reconstruction with prostheses: 1. Absence of post-radiation skin induration; 2. Absence of severe post-radiation skin changes. Furthermore, the presence of either of these above sequelae should be considered an absolute contraindication for the use of expander/implants. In patients in whom a history of post-radiation skin changes is not available and induration is absent, expander/implant reconstruction may still be performed with the understanding that there is a 51.8% of obtaining good or acceptable outcome.

This study further demonstrates the importance of documenting of post-radiation skin changes, as reconstructive options may potentially be limited in the absence of this information. Unfortunately, skin changes are not always clearly recorded by physicians, whether they be surgeons or oncologists. In order to ensure adequate documentation, we recommend physicians take time to educate their patients about post-radiation skin changes. Patients should also be provided a card, similar to Table 1, so as they may check-off which changes they experience. Patients should further be asked to photograph any skin changes so as they can provide this information to the plastic surgeon.

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MEDICAL SCHOOL HOTLINE SATORU IZUTSU PHD, CONTRIBUTING EDITOR

# The Use of Nontransplantable Human Tissues

# Scott Lozanoff PhD; Chair, Department of Anatomy, Biochemistry & Physiology, University of Hawai'i School of Medicine, John A. Burns School of Medicine (JABSOM)

Anatomical dissection is indispensible for the proper understanding of the human body for the purpose of medical treatment. The cadaver enables the student to understand spatial relationships in three dimensions that otherwise are impossible to fully understand from two-dimensional depictions in books or computer programs. In many instances, the cadaver is the first experience that a student has with death and it provides a source of humility and compassion. The dissection process also facilitates teamwork among the dissection group and promotes a sense of cooperation and mutual understanding among students. Thus, the availability of cadavers is critical to the medical and allied medical education curriculum at JABSOM advancing the health status of our entire community. The policies of JABSOM's Willed Body Program have been published in the Hawai'i Medical Journal and thus available for public review.1 Numerous altruistic community members and their families have unselfishly donated their bodies to JABSOM's Willed Body Program for the purpose of medical and allied medical education and training.

During the 19th century, an insufficient supply of cadavers existed for medical education and commercial exploitation was rampant resulting in the promulgation of the Uniform Anatomical Gift Act. This law contributed to the demise of grave robbing by unscrupulous individuals who attempted to benefit financially from families of less fortunate individuals who did not have the financial means to insure proper disposition of the remains following death. Under current Hawai'i State Statutes, business people could benefit financially from the procurement, display and sale of human remains, particularly unclaimed bodies in much the same fashion. The indigent population is especially at risk since they have no financial means to insure proper handling of their bodies after death. Commercial exploitation has the potential to impact negatively on the University of Hawai'i School of Medicine since the public associates these exploitative activities with our program, even though absolutely no relationship exists.

Downturn in body donations are seen when activities concerning unethical procurement, display, and body disposition occur in Hawai'i, diminishing the credibility of our program and sustaining a negative impact on educational activities as well as community health in general. Specific examples exist that have impacted negatively or have the potential to do so. Recently, Premier Exhibits debuted "Bodies The Exhibition" at Ala Moana shopping center. This exhibition displayed plastinated human specimens for profit, and was sued in New York by the State Attorney General because "it is not able to confirm that the bodies on display are not Chinese prisoners who may have been tortured and executed" (NY Times, Saturday, May 31, 2008). Another example is a commercial website link ("dot.com") posted for a company in Hawai'i requesting body donations for what is described as medically related activities, but

simultaneously indicates on a downloadable Donation Consent form that the company "may provide my body or tissues derived thereof to other appropriate institutions, domestic and abroad, to maximize the Medical, Scientific, and Educational benefits of my donation." It would appear that this company is prepared to accept body donations from Hawai'i residents and distribute them beyond state and federal borders. This begs the question: Why should human remains leave the state and how does a human body procurement company finance its operation for such extensive distribution?

The problem of commercial display and distribution of human remains is not unique to Hawai'i. Numerous states, including California, Pennsylvania and New York, have enacted laws to prohibit commercial display of human remains, particularly plastinated material. Minnesota, in particular, has enumerated several problems associated with human remains related to a lack of reporting to the Department of Health that also apply to Hawai'i. Serology testing is not required and human remains can leave the state through commercial carriers theoretically packed in the same containers as food packaging. These remains could harbor disease that would be almost impossible to track. Human remains are used in displays or seminars in the same facilities where functions such as banquets are held. Plastinated human remains have been used in commercial displays and can 'leak' liquefied fat if not cured (hardened) properly. The "Bodies Exhibit" recently shown at the Ala Moana Shopping Center is an example a commercial display that poses potential risk in terms of the origin of material, transportation, and handling. Commercial distribution of unclaimed human bodies and parts presents a significantly greater risk if used in commercially related activities involving anatomical dissection, particularly in a public venue lacking verifiable safety regulations related to anatomical dissection.

An argument frequently presented by the operators of commercial displays of human remains is that an educational objective is achieved. This contention is weak. Anatomy education consists of the meticulous and systematic deconstruction of the human body. Careful attention must be paid to anatomical attachments, in situ spatial relationships and morphological variations. Yet, displayed bodies typically are positioned in awkward orientations with anatomical structures lacking spatial relationships, articulations and attachments, or functional relevance. Although these displays profess educational values, they teach us no more about anatomy than television reality shows instruct the viewer about human psychology. Unfortunately, presentations are meant to shock and extract money under the guise of education.

The Chair of the Finance Committee, Hawai'i State Legislature, in response to these issues, has introduced legislation that relates to the prohibition against buying and selling dead human bodies. including plastinated bodies and body parts. The Bill increases the fine for buying or selling a dead human body to up to \$5,000. In addition, a companion Bill prohibits the commercial display of dead human bodies without a permit from the department of health. These proposed legislations address ethical and public health issues related to nontransplantable human tissue use. A human remains tracking system coordinated through the Department of Health seems to be the most logical approach to ensure public safety and ethical treatment of human remains for the purpose of medical education and research. The Willed Body Program at JABSOM represents such a system that has been in place since 1967 demonstrating that human remains can be tracked and administered in a safe and effective fashion promoting ethical procurement and disposition for the purpose of medical education and research.

The use of human remains after death is interpreted differently by individuals based on their own spiritual or cultural perceptions. Some might argue that procuring, selling, and public display of postmortem human remains is an individual's right to pursue commercial business superseding rules introduced by the government. However, commercialization of postmortem remains reduces the human body to a commodity potentially ignoring donor rights, particularly in the case of an unclaimed body, and a procurer's ethical responsibilities to the next-of-kin and society. In the final analysis, a government must ensure, through legislation, proper respect and final disposition of human remains. Otherwise it is a small step to objectifying and commodifying human body parts prior to death.

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# UPCOMING CME EVENTS

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May 2009								
5/16-5/17	OBG	Department of Obstetrics, Gynecology and Women's Health, John A. Burns School of Medicine and Ian Donald Interuniversity School of Medical Ultrasound Hawai'i	Ala Moana Hotel, Honolulu	Contemporary OB/GYN Ultrasound: Recent Advances and Clinical Practice	Tel: (808) 203-6563 Email: treevesman@ucera.org			
July 2009								
7/27-7/30	R	Standford Radiology	Hyatt Regency Maui, Ka'anapali Beach, Maui	3rd Annual LAVA: Latest Advances in interVentionAl Techniques	Tel: (888) 556-2230 Email: radiologycme@med. stanford.edu Web: radiologycme.stanford. edu/dest/			
October 2009		•	•	•	•			
10/20-10/24	Multi	American Society of Human Genetics	ТВА	2009 Annual Meeting	Web: www.faseb.org/genet- ics/ashg			
10/27-11/1	СНР	American Academy of Child and Adolescent Psychiatry	Hilton Hawaiian Village, Honolulu	56th Annual Meeting	Tel: (202) 966-2891			
10/25-10/28	OBG	Central Association of Obstetricians & Gynecologists	Maui, Hawai'i	2009 Annual Meeting	Tel: (701) 838-8323			
January 2010								
1/1-1/7	D	Skin Disease Education Foundation	Maui, Hawai'i	New Era: Psoriasis Therapy	Tel: (312) 988-7700			
February 2010								
2/14-2/19	IM, ID	University of California San Francisco School of Medicine	The Fairmont Orchid, Kohala Coast, Hawaiʻi	Infectious Diseases in Clinical Practice: Update on Inpatient and Outpatient Infectious Diseases	Tel: (415) 476-4251 Web: www.cme.ucsf.edu/cme			



# THE WEATHERVANE russell t. stodd md, contributing editor

#### ♦ WE HAVE SEEN THE PRESENT AND IT DOES NOT WORK.

A New Jersey rheumatologist cared for a deaf female patient with lupus for over a year including more than twenty office visits. According to her testimony at trial she claimed that she repeatedly requested a sign language interpreter, but that he refused. He stated that a sign language interpreter would cost \$150 to \$200 per visit which was more than he was reimbursed for her office visit. He exchanged written notes with the patient and members of her family. The patient was not required to show that anything was wrong with her care nor did she claim any negligence, two facts the doctor was not allowed to present in his defense. Instead she claimed that she "never had a real understanding" of the diagnosis, treatment or prognosis of her disease and that she was deprived of an opportunity to participate in her care. A jury awarded her \$400,000 in granting her claim of disability discrimination.

#### ♦ HERE. TRY MY SWITCHBLADE.

"Wrap rage" is the latest lexicon addition for the puncture or laceration which results from struggling to open the "oyster" or "clamshell" package enclosing an electronic device, toy or other product A report from the Consumer Product Safety Commission states that more than 6,000 people each year seek help in emergency rooms for repair of injuries sustained while opening a package, and who knows how many thousands more such accidents do not get to the ER. Everyone who has tried to open these packages reaches for a knife or pair of scissors, because no amount of tugging, prying or biting will suffice. Moreover, once the package is open the cut edges of the wrapper provide a threat of further injury. In an effort to stem the blood flow, Amazon.com has instituted a program where 19 products are available without the plastic hard shell, and are shipped in an easy-toopen cardboard box. Happy Birthday!

#### ✤ I CAME, I SAW, I ORDERED TAKE OUT.

One more weird disease comes to these lovely islands via our not-so-friendly immigrant, the wharf rat. Limited to warmer climes where snails proliferate, the round worm angiostrongyliasis cantonensis loves the rat brain where it luxuriates in its peculiar and complex life cycle. Larval forms move through the vascular tree into the brain and lungs where adults produce ova that become larva, and migrate up the trachea, down the esophagus, into the gut, and ultimately out with the feces. The intermediate host, snails and slugs, pick up the larva which convert to a different larval form when ingested by the rat and move through the vascular tree to harbor in the rat brain. Human beings come into the cycle when some unlucky person eats a snail or unwashed vegetables with snail or slug slime containing worm larva. Modest fever, neck pain, headache, nausea and vomiting, most of the typical manifestations of meningoencephalitisitis will ensue. The diagnostic sign is a proliferation of eosinophils in the cerebrospinal fluid. The good (?) part is that the worm larva require the rat brain (an uncommon finding in humans) to survive, so they soon expire in humans after a period of inflammation.

#### ✤ I'VE ENJOYED AS MUCH OF AARP AS I CAN STAND.

"They are making money on the backs of old people," according to one member of American Association of Retired Persons (AARP) who found that he paid \$1079 more for his auto insurance than a policy offered by Mutual of Omaha. In fact, AARP is a big-time money-generating organization with a half billion dollars coming in from fees insurers paid for AARP endorsement. Royalties and fees were 43% of its 2007 income (not to mention the float that brought in \$40 million alone). Annual dues of \$5 in the 1980s have expanded five fold. According to a 2007 Harris poll AARP is third behind Consumer Reports and American Red Cross as a trusted advocacy group yet the spendy brass and marble headquarters in Washington, D.C. is closed to visitors. AARP is considered the most powerful interest group in the United States and threatens to defeat politicians who oppose its issues. The political agenda is very liberal, and many conservative members have voiced disapproval.

#### ♦ IT'S A GOOD LAW. RUSSIAN ROULETTE IS SO MESSY.

No sooner was the ink dry on the 'death with dignity' law for the state of Washington than a third state in the US of A joined the limited group. In Montana there was no prolonged legislative wrangling, but instead a ruling by Judge Dorothy McCarter which will take effect immediately. The judge ruled that "The Montana constitutional rights of individual privacy and human dignity, taken together, encompass the right of a competent terminally ill patient to die with dignity." Defending the prevailing law, Montana Attorney General Mike McGrath disagreed and filed a motion to stay the decision, pending an appeal to the Montana Supreme Court.

# ♦ ILLINOIS – THE ONLY STATE WHERE THE GOVERNOR MAKES YOUR LICENSE PLATE.

The Illinois legislature voted \$8 million dollars to fund a medical coalition through Children's Memorial Hospital of Chicago. Because the medicaid funding for child care is so low in Illinois, very few doctors can afford to care for these children. The "We Care for Illinois Kids" coalition included Children's Memorial Hospital, University of Chicago Medical Center, La Rabida Children's Hospital and groups representing Illinois pediatricians. Because Governor Blagojovich would not release the \$8 million the coalition collapsed. According to the FBI allegation, Patrick Magoon, CEO of the Children's Memorial Hospital, refused to contribute \$50,000 (he gave a mere \$1,000) to the Governor's campaign fund, so the funds were never allocated. We all know that a few politicians are slimy, but obstructing children's medical care is below absolute zero.

# ♦ THE REAL PROBLEM WITH HUMPTY DUMPTY WAS THAT HE LET HIS INSURANCE LAPSE.

The latest data released by the Insurance Research Council does not bode well for everybody on the road. Several hundred thousand drivers dropped their auto insurance in the past year as the unemployment numbers have climbed. New Hampshire and Wisconsin do not require drivers to purchase insurance, but the other 48 states do. Many motorists are reducing their coverage to the absolute minimum liability policy required by law. Even with no-fault insurance, a large claim can cause an increase in premium when the other driver is at fault. Moreover, it is sadly true that unlicensed and uninsured drivers are more often involved in fatal accidents. So, drive more defensively than ever, put down your cell phone, do not drink and drive, and stay alert and in control at all times.

# ◆ EVEN ADAM FAILED TO GET A TAX REDUCTION FOR HIS TISSUE DONATION.

In 1984 Congress passed the National Organ Transplant Act, sponsored by Senator Al Gore. The act created a bureaucracy to allocate donated livers, kidneys and other organs. The outrage with a potentially good law is that Congress added a provision making donors and patients subject to criminal prosecution with penalties of up to five years in prison and a \$50,000 fine if it is found that "valuable consideration" was provided to the donor. The law wipes out virtually all incentives to donate organs, including tax deductions. When Pennsylvania offered a pilot program in 1994 to pay only burial expenses for organ donors, state employees refused to act for fear of federal prosecution. Meanwhile, since that date the waiting list for transplant organs has quadrupled. Fewer than 100 Good Samaritans show up at transplant centers each year to provide living donations to strangers.

#### ✤ THE LARGE PRINT GIVETH. THE FINE PRINT TAKETH AWAY.

A West Palm Beach, Florida couple divorced in 2001. The ex-husband agreed to pay \$2,000 alimony each month, but the payments would cease if the woman remarried or "cohabitated" with another person for more than three months. Subsequently, the ex-wife was convicted of felony drunk driving (with serious injury to two women) and sentenced to nine years in prison. Because the woman shares space in prison with another woman the exhusband ceased alimony payments based on the divorce agreement. The 4th District Court of Appeals agreed that living in prison with another woman was "cohabitation" despite being enforced, and canceled the alimony. So, it seems that there is a God!

#### ♦ A START, A FINISH AND A TIME CLOCK. WHAT'S THE PROBLEM?

A runner finished first in the San Francisco women's marathon, but was not declared the winner. Instead another competitor who ran 11 minutes slower "won" and was awarded the medal. Nike had promoted some elite runners to start 20 minutes earlier and apparently expected one of them to finish first, but a "non-elite" competitor from the following pack had a faster time. After a storm of protest the company ultimately declared that both runners "won" the marathon. Nike promised to fix the format in the future.

#### ADDENDA

- Every day people are straying from the church and going back to God.
- I am not a born again Christian. Please forgive me for getting it right the first time.
- ✤ Alpo is now \$3 per can that's \$21 in dog money.
- ♦ If your dog is fat you are not getting enough exercise.

#### ALOHA AND KEEP THE FAITH - rts

Editorial comment is strictly that of the writer.