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Environmental Factors of Obesity in Communities with Native Hawaiians

Marjorie K. Mau MD; Kara N. Wong BS; Jimmy Efird PhD; Margaret West MPA; Erin P. Saito MSc; and Jay Maddock PhD

Abstract

Objective: To compare the fast food outlets and exercise resources across 3 communities with varying percentages of Native Hawaiians (NH) and to correlate these findings with obesity prevalence.

Methods: Data on all food and exercise resources were collected from January through July 2006 within a 1-mile radius in 3 distinct communities (site A = higher % NH to site C = lower % NH). Comparisons between communities were analyzed in 2007 using Fisher's Exact and ANOVA.

Results: Trends in obesity prevalence paralleled the percentage of NHs. After adjusting for population size, site B had a greater number of fast food outlets (p < 0.001) than site A or C, and more exercise facilities compared to site A (p = 0.05). Availability of fast food outlets was significantly greater at site A compared to site C (p = 0.03). Usage of exercise facilities was not significantly different between sites although exercise resources were in 'poorer' condition at site A compared to site B or C (p < 0.05).

Discussion: Results confirm the increased frequency of obesogenic environmental factors and their correlation with obesity trends across 3 distinct NH communities. These results suggest that environmental factors may offer another means for reducing obesity disparities in minority communities.

Introduction

In the United States, recent studies have highlighted the disproportionate rates of obesity in ethnic/racial minority populations including Native Hawaiians (NHs) with a prevalence of up to 70-80%.1-5 Although the multiple causes for obesity disparities among NHs and other racial minorities are not clearly understood, several studies have found that environmental factors, including the availability of healthy food options or exercise facilities, affect the development of excess weight.⁶⁻⁸ In addition, despite some mixed results, 9-11 the majority of studies suggest a higher prevalence of fast food outlets and lower prevalence of recreational facilities in minority communities compared to non-minority communities. 12-15 To date little is known about access to food outlets or exercise resources in communities that are predominantly Native Hawaiian and/or other Pacific Islander even though they are known to have increased obesity disparities.

The purpose of this study was to examine the quantity, usage, and quality of fast food outlets and exercise

resources in 3 distinct communities distinguished by the proportion of NHs living in each community.

Methods

Assessments of food and exercise resources were collected using the study protocol of the PILI 'Ohana Program – Community Assessment Study from January – July 2006. Three non-contiguous geographical areas on the island of O'ahu were selected for assessment. Each site had varying percentage of NHs with Site A having the highest and Site C with the lowest (See Table 1). Within each geographical area, a 1-mile radius was constructed around a centrally located public facility (i.e., community health center, elementary school, etc.). Due to the coastal geography of Site A, 2 semi-circles were constructed around 2 focal points to approximate a complete 1-mile radius.

Assessments were conducted on both weekdays and weekends at various time points by trained researchers using standardized forms. Food resources were categorized as follows: 1) supermarket (at least 5 aisles of household staple foods), 2) fast food (no wait staff, meal obtained in 10 minutes or less), 3) restaurant (patrons seated at tables and served by wait staff), or 4) specialty food (narrow range of non-meal food, e.g. smoothies, desserts). Exercise resources (excluding those located on private property) were divided into: 1) beaches, 2) swimming pools, 3) gym/exercise facilities, 4) walking/running trails, or 5) playgrounds/fields/courts. Each resource was evaluated visually for physical condition and utilization and assigned a score from 1 (poor condition or low utilization) to 3 (good condition or high utilization).

The distribution of resources was compared using Fisher's Exact test (categorical data) and analysis of variance (ANOVA, continuous data). All data analyses were carried out in 2007 using SAS 9.1 and $p \le 0.05$ was considered statistically significant. This study was approved by the University of Hawai'i, Committee on Human Studies.

Results

The prevalence of obesity paralleled the trend in percentage of Native Hawaiians in each of the 3 sites (Table 1); however, the trend in percent below poverty level did not. Sites A and B had a similar number of

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| Table 1.— Description of Communities by Sites; O'ahu, Hawai'i (2005-2006) | | | | | |
|---|--------|-------|--------|--|--|
| Community Sites | Α | В | С | | |
| | | | | | |
| Community Characteristics | | | | | |
| Native Hawaiian Population (%) ^a | 55.7 | 21.0 | 13.2 | | |
| Estimates of Total Population per Site ^a | 23,824 | 5,845 | 11,576 | | |
| Obesity Prevalence (%)b | 39.4 | 21.8 | 9.2 | | |
| Below Poverty Level (%) ^a | 21.7 | 5.0 | 8.7 | | |
| Environmental resources ^c | | | | | |
| Number of Fast Food Outlets | 29 | 31 | 19 | | |
| Number of Supermarkets | 4 | 3 | 4 | | |
| Number of Other Food Resources ^d | 18 | 22 | 23 | | |
| Number of Exercise Resources | 20 | 14 | 32 | | |

^aEstimate based on Census 2000 adjusted to 1-mile radius using census tracts and/or GIS software.

Other Food Resources defined as all non-Fast Food Resources (including supermarkets).

| Table 2.— Comparison of Fast Food and Exercise Resources Between Communities | | | | | | |
|--|-----|-----|-----|----------------|----------------|----------------|
| Community Sites | Α | В | С | C vs. A | C vs. B | B vs. A |
| Fast Food Resources | | | | | | |
| Relative frequency ^a | | | | 1.3, p=0.59 | 0.3, p=0.00 | 4.4, p=0.00 |
| Mean usage ^b | 2.8 | 1.9 | 2.4 | p≤0.05 | p≤0.05 | p≤0.05 |
| Availabilityc | 57% | 55% | 41% | p=0.03 | p=0.07 | p=0.89 |
| Exercise Resources | | | | | | |
| Relative frequency ^a | | | | 3.5, p=0.02 | 1.2, p=0.69 | 3.0, p=0.05 |
| Mean usage ^b | 2.3 | 2.0 | 2.2 | p>0.05 | p>0.05 | p>0.05 |
| Mean conditiond | 1.8 | 3.0 | 2.6 | p≤0.05 | p>0.05 | p≤0.05 |

^aPer 10,000 population, based on the US Census 2000.

fast food eateries (Site A = 29; Site B = 31) although Site A had a slightly larger proportion of fast food establishments compared to other food resources (n=29 fast food resources; 22 other food resources). Assessment of exercise facilities at each site showed that Site B had the lowest number of exercise resources (n=14) compared to Site A (n=20) or C (n=32).

After adjusting for population density, Site C was found to have a significantly lower frequency of fast food resources or outlets than Site B (p<0.001) and Site B had a significantly higher frequency of fast food outlets compared to site A (p<0.001) (Table 2). Both Site B (p=0.05) and Site C (p=0.02) had significantly more exercise resources compared to Site A even after adjustment for population density.

Site A had the highest usage of fast food outlets (usage score 2.8 of 3.0) compared to all other community sites (all p<0.05) (Table 2). Site B had the lowest usage (usage score 1.9 of 3.0) of fast food outlets despite the higher

absolute number of fast food establishments in Site B. The relative proportion of fast food resources per total food resources in a community site, an estimate of the availability of fast food in a community, was only significant for Site A, which had a significantly higher proportion of fast food outlets per total food resources compared to Site C (p=0.03). By contrast, mean usage of exercise resources was similar in all 3 community sites (all p>0.05). However, the exercise resources at Site A were found to be in 'poorer' condition when compared to either Site B or Site C. (both $p \le 0.05$).

Discussion

Communities with a higher proportion of NHs had a greater proportion of fast food outlets and the least number of exercise facilities per 10,000 population. These results are consistent with previous literature, which suggests that minority communities have a higher availability of fast foods and a lower number and quality of exercise resources.^{8, 15-21} Similarly, the study found that the proportion of NHs in a community is directly correlated to the estimated obesity in the community. The study also found that all 3 sites utilized existing exercise resources in their communities at near maximum. This suggests that even communities with a high proportion of NHs (Site A) are frequent users of exercise resources despite increased obesity prevalence and could probably benefit from increased access to exercise resources of sufficient quality. These results are consistent with prior studies that have shown that public access to exercise resources, i.e. parks, sidewalks, etc., are associated with a greater likelihood of being more physically active.8, 22, 23

One unexpected finding was the high number of fast food eateries with a low number of exercise resources in Site B. This increased availability of fast food eateries may increase the risk for the future development of obesity in Site B. As Site B is an emerging community that is likely to attract younger families, creating more exercise resources may be one means for reducing the risk for obesity in this community as few exercise resources were initially identified in this study.

Limitations of this study include restricting assessments to a 1-mile radius, using obesity estimates derived from self-reported data, and not examining socioeconomic status (SES) and its relationship with environmental factors of obesity. The cross-sectional nature of the study also does not allow for causal inferences. In future studies, multiple assessments should be made of the communities at different time points to gain a better representation of the resources and their utilization.

Despite these limitations, this study is the first to provide confirmatory evidence that increased obesogenic environmental factors are more frequent in communities with a higher proportion of Native Hawaiians and that there is a trend of increasing environmental factors

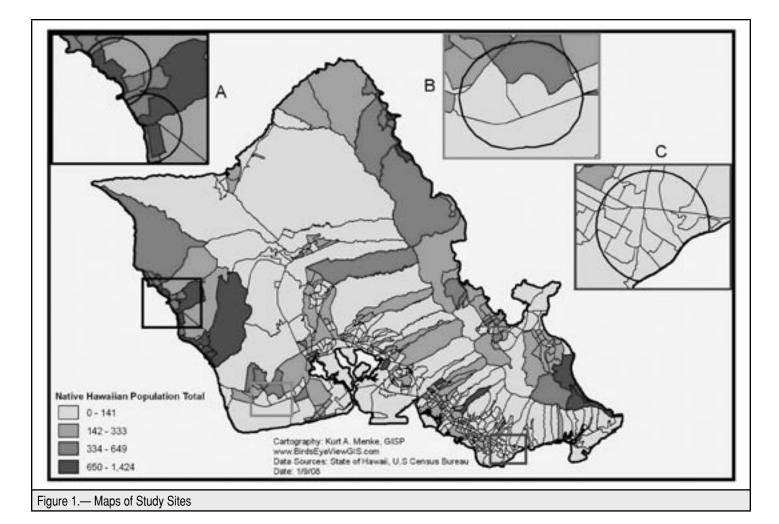
^bEstimate of obesity was based on Behavioral Risk Factor Surveillance System data for 2006 and was defined as body mass index > 30 kg/m2.

^cAscertained within defined 1-mile radius.

^bDefined as the mean ability of the resource to accommodate additional users on a scale of 1-3 where 1 represents minimal utilization and 3 represents utilization that is approaching full capacity.

^{&#}x27;Availability defined as the number of fast food resources divided by the total food resources ascertained in a given community.

[&]quot;Defined as the mean overall condition of the resource on a scale of 1-3 where 1 represents a resource that is not safe or aesthetically welcoming (i.e. "poor physical condition") and 3 represents a resource that is above average in safety and aesthetically appealing (i.e. "good physical condition").



associated with increasing obesity prevalence. In emerging communities, the increased number of fast food outlets and few exercise resources, such as in Site B, poses a potential risk for future obesity trends, especially among young families. The results of this study may help to identify communities at high risk for obesity, and also to inform the development of health policies to encourage built environments that promote and support healthier lifestyle practices.

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Partnerships to Address Obesity Disparities in Hawai'i: The PILI 'Ohana **Project**

Andrea H. Nacapoy MA; Joseph Keawe'aimoku Kaholokula PhD; Margaret R. West MPA; Adrienne Y. Dillard; Anne Leake PhD, APRN-Rx; B. Puni Kekauoha; Donna-Marie Palakiko RN, MS; Andrea Siu BA; Sean W. Mosier BA; and Marjorie K. Mau MD on behalf of the PILI 'Ohana Project

Abstract

Community-based participatory research (CBPR) is an approach to scientific research that is gaining broader application to address persistent problems in health care disparities and other hypothesis-driven research. However, information on how to form CBPR community-academic partnerships and how to best involve community partners in scientific research is not well-defined. The purpose of this paper is to share the experience of the Partnership for Improving Lifestyle Interventions (PILI) 'Ohana Project in forming a co-equal CBPR community-academic partnership that involved 5 different community partners in a scientific research study to address obesity disparities in Native Hawaiians and other Pacific Peoples (i.e., Samoans, Chuukese, and Filipinos). Specifically, the paper discusses 1) the formation of our community-academic partnership including identification of the research topic: 2) the development of the CBPR infrastructure to foster a sustainable co-equal research environment; and 3) the collaboration in designing a community-based and community-led intervention. The paper concludes with a brief summary of the authors' thoughts about CBPR partnerships from both the academic and community perspectives.

Introduction

Community-based participatory research (CBPR) is an approach to scientific inquiry that "equitably involves all partners [community and academic] in the research process and recognizes the unique strengths that each brings." Despite variations in practice, CBPR is becoming more widely accepted in a wide range of contexts and among ethnically diverse communities as an approach for addressing persistent problems in health care disparities and other types of health research.³ As community-based organizations serving Native Hawaiians (NHs) and other Pacific Island Peoples (PIPs) delve deeper into translational research (e.g., effectiveness and dissemination studies), the need for academic-community partnerships that aim to achieve balance between scientific rigor and community wisdom emerges. Although there are many publications on the

principles, approaches, and benefits of CBPR, 2,4,5 little

is known about how to form sustainable CBPR community-academic partnerships as a means to address health disparities particularly in NH and PIP communities. The purpose of this paper is to share the process undertaken and the insights learned by the Partnership for Improving Lifestyle Interventions (PILI) 'Ohana Project (Pili is relationship and 'Ohana is family in the Hawaiian language) in forming a co-equal CBPR community-academic partnership that involved 5 community partners in a scientific research study to address obesity disparities in NH and other PIP (i.e., Samoans, Chuukese, and Filipinos).

Forming a Community-Academic **Partnership**

Researchers from the Department of Native Hawaiian Health (DNHH) began the forging of a CBPR partnership by inviting 10 community-based organizations serving NH and other PIP to discuss the top health concerns of their respective communities. These 10 community-based organizations ranged from community health centers to long-standing civic clubs to grassroots community organizations, but all had a prior relationship with the DNHH through the Ulu Community Network of the Hawai'i EXPORT Center (HEC) and had expressed an interest in participating in research. The *Ulu* Network is a community network of 21 organizations and agencies who serve NH and other PIP throughout the state of Hawai'i and was formed in 2000 as part of the Community Engagement Core of the HEC, whose mission is to reduce and eliminate health disparities via research, training and community engagement.

The initial discussions between DNHH researchers and the 10 community-based organizations were facilitated by a number of experienced CBPR academic leaders including the Director of the Ulu Network and the Director of the HEC who laid the foundation for power sharing and fostering a respectful, collaborative relationship in keeping with the spirit of CBPR.¹⁻² At the first meeting, the top 3 health concerns of the 10

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- Department of Psychology, University of Hawai'i at Manoa, Honolulu, HI (A.H.N.)
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- Kōkua Kalihi Valley Comprehensive Family Services, Honolulu, HI (A.L.)
- School of Nursing and Dental Hygiene, University of Hawai'i at Mānoa (A.L.)
- Ke Ola Mamo, Honolulu, HI (D.M.P., A.S.)

Correspondence to Andrea H. Nacapoy BA Department of Native Hawaiian Health 651 Ilalo Street, MEB 307 Honolulu, HI 96813 Ph: (808) 692-1044 Fax: (808) 692-1255 E-mail: nacapoy@hawaii.edu community organizations were discussed to determine possible interventions, the formation of a formal CBPR partnership, and the potential roles of the partners (communities and academic). Obesity was collaboratively identified as a major concern and high priority health issue by all 10 community organizations. Due to other priorities and commitments, 5 of the 10 original community organizations chose to serve in an active role in a CBPR partnership at the time, while the other 5 agreed to serve in an advisory role. The 5 self-selected community organizations and the academic partner (the DNHH) discussed further who should serve as the lead organization to coordinate and submit the grant proposal on behalf of the newly formed CBPR partnership to the National Center on Minority Health and Health Disparities. The DNHH was nominated to carry out this responsibility.

The name *PILI 'Ohana* Project was discussed and unanimously approved by the CBPR partnership and exemplifies the mission of the partnership – to bring the communities together to eliminate obesity disparities in Hawai'i. The 5 community partners of the *PILI 'Ohana* Project represent 3 different types of community organizations: 1) Grassroots organizations, 2) Native Hawaiian Health Care System, and 3) Community Health Centers. The strengths of each partner are briefly described here:

Grassroots organizations (GRO)

Hawai'i Maoli - The Association of Hawaiian Civic Clubs (HM-AHCC) and Kula No NāPo'e Hawai'i (KNNPH) represent 2 GROs. HM-AHCC is the oldest private, non-profit, community-based Native Hawaiian organization comprised of a confederation of 54 clubs with a collective membership of over 2,800 individuals located throughout the states of Hawai'i, Alaska, California, Colorado, and Nevada. Recently the Association has turned its attention to issues of health and wellness with the recognition that its members are disproportionately affected by chronic illnesses.

KNNPH is also a non-profit organization, formed in 1992 by a group of concerned community women to help improve the educational skills of children from the NH Homestead communities of Papakālea, Kewalo, and Kalawahine located in urban Honolulu. The educational vision of KNNPH has broadened to include activities that raise the awareness of good health, nutrition, and exercise. In 2003, they implemented health screening for diabetes mellitus and cardiovascular risk factors and health education counseling.

Community Health Centers (CHC)

Kalihi-Pālama Health Center (KPHC) and Kākua Kalihi Valley Comprehensive Family Services (KKV) represent the two CHCs. KPHC is a private non-profit CHC that provides primary care services to many PIPs (i.e. Micronesians and Filpinos). KPHC is committed to addressing obesity-related disparities such as diabetes and has implemented a diabetes management program, weekly diabetes clinics, and a diabetes support group tailored to their multi-ethnic population.

KKV is a community-owned and operated non-profit corporation formed in 1972 by community and church leaders to address the lack of adequate and accessible health services in their community. Health services are provided to a primarily low-income PIP population (i.e. Micronesian, Samoan, and other immigrant groups) and include a wide range of services such as dental, medical, and mental

health. KKV has implemented community gardening and diabetes education programs at their CHC and employs an ethnically diverse staff that is fluent in 17 Asian and Pacific Island languages.

Native Hawaiian Health Care System (NHHCS)

Ke Ola Mamo (KOM) is a private, non-profit NHHCS for the island of O'ahu. KOM has 4 locations and provides services to primarily low income NHs and their families that include community outreach, transportation assistance, health education and prevention/wellness programs. KOM has more than 10 years of experience conducting health screenings and implementing health education programs such as the nationally recognized Diabetes Mellitus Awareness Program.

Academic Partner

The **DNHH** is a University of Hawai'i, Board of Regents approved clinical department of the John A. Burns School of Medicine that was formed in 1999 and consists of 4 cores: 1) Administrative, 2) Clinical Teaching and Health Care Services, 3) Medical Education, and 4) Research and Evaluation. Collectively, the DNHH research leadership has 10+ years of NIH-funded research experience in epidemiological, observational, intervention development, program evaluation, and clinical trials research addressing multiple health disparity topics such as diabetes,⁶ cardiovascular disease,⁷ chronic kidney disease, and health behaviors.⁸

Thus, each of the academic and community organizations brought into the CBPR partnership a wealth of experience and community wisdom in serving and working with NH and PIP in Hawai'i via various capacities – from clinical services to social advocacy.

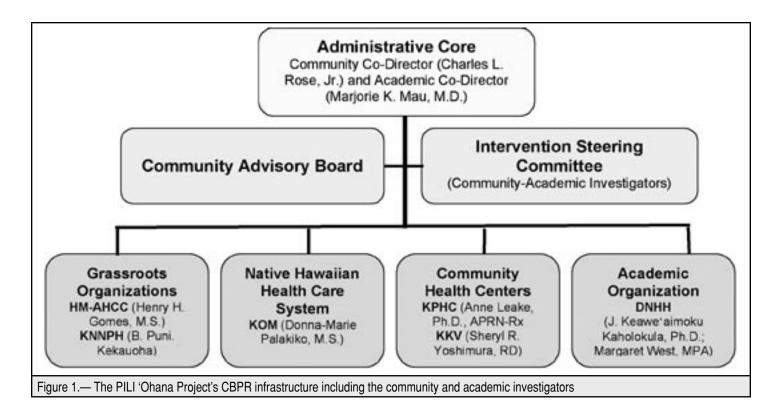
In particular, 2 key elements about the formation of the CBPR partnership were important in developing trust. First, the partnership began with community organizations and academic researchers who collaborated previously and already demonstrated an interest in research. Prior relationships with the members of a CBPR community-academic partnership are helpful as academic researchers must consider the communities' attitudes towards scientific research, particularly the tendency towards mistrust of the academic researchers and their intentions. Similarly, community organizations need to weigh the benefits (e.g., having an effective community-based intervention) and risks (e.g., expenditure of the community resources) of participating in scientific research to their respective communities.

Second, as mentioned previously, communities can be defined in a number of different ways. In the formation of this CBPR partnership, the primary interest was organizations with a significant burden of obesity health disparities in the communities they served (i.e. NH and other PIP), and all of the community organizations involved provided services primarily to these populations.

Establishing a CBPR Infrastructure

The CBPR administrative infrastructure established by the *PILI* 'Ohana Project is depicted in Figure 1.

To ensure a balance of power among all partners (community and academic), an Administrative Core consisting of 2 co-equal leadership positions entitled the Community Director and the Academic Director were created. A Community Advisory Board (CAB) was formed to provide guidance on maintaining the partnership and establishing

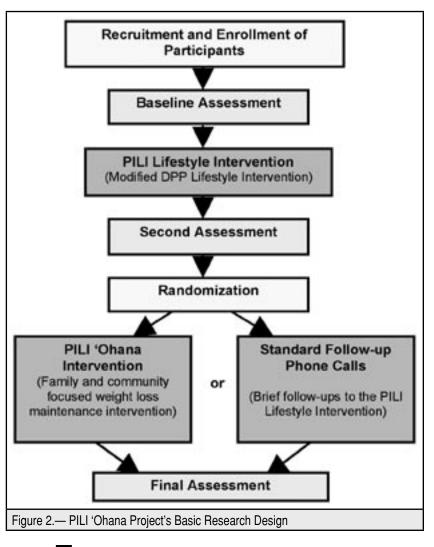


CBPR policies, and consisted of members from the 5 partnering communities as well as the 5 community organizations initially involved in the planning process. An Intervention Steering Committee (ISC) was also formed, which consisted of all partners (5 communities and 1 academic) who would meet monthly to discuss the development, implementation, and evaluation of all research activities and continuous assessment of the CBPR partnership.

The first undertaking of the ISC was the creation of a document that informs and guides the partnership in maintaining a co-equal and mutually respectful research environment. This document entitled the "PILI 'Ohana Project Principle and Guidelines for Overall Governance" documents: (1) purpose, (2) CBPR principles and values, (3) roles and responsibilities of each partner, (4) decision making process, (5) handling and sharing of data, (6) evaluation process of the CBPR partnership, and (7) procedures to amend the document. The establishment of the infrastructure and guiding principles and guidelines was invaluable in providing a framework for day-to-day operations, providing a mechanism to address a myriad of concerns or disputes, and demonstrating the commitment of each partnering organization to the CBPR process, especially the commitment of the academic partner to include the community organizations as co-equal CBPR partners.

Design of a Research Study

Through a series of meetings facilitated by the Community and Academic Co-Directors, the community-academic partnership negotiated a mutually acceptable



research design and protocol that engaged the community partners as well as maintained scientific rigor. The PILI 'Ohana Project partners struggled with the scientific perspective and experimental design issues, such as using a randomized controlled trial (RCT) protocol, in which participants are randomly assigned to either the intervention being evaluated or to a control group. From the community perspective, intervention needed to ensure that no participant was denied or delayed in receiving a possibly effective intervention. In balancing these 2 perspectives, the partners agreed upon a RCT design that ensured all participants would receive an active intervention while still being able to scientifically test the efficacy of the weight loss maintenance intervention. The basic research design is depicted in Figure 2.

It was agreed by all CBPR partners that all study participants would receive a culturally adapted version of the Diabetes Prevention Program's (DPP) Lifestyle Intervention. After completing the intervention, participants would be randomized to either a family-and community-focused intervention (a new intervention designed by the PILI partnership) for weight loss maintenance or to a control group (standard phone-call follow-ups only). In this way, all study participants would be able to receive an intervention which was modified to be used in these populations and found to be efficacious as well as participate in the hypothesis-testing portion of the study to evaluate a weight loss maintenance intervention via an RCT.

The final step was negotiating the roles and responsibilities of each partner in conducting the planned research activities. To build the communities' capacity to engage in research and deliver community-based interventions, it was collectively decided that all the interventions would be delivered, and all data maintained, by community-peer educators and staff from each of the 5 community sites. The DNHH would provide and standardize research training, technical assistance, and collate the de-identified data from each community organization for overall study analyses.

Reflections on the CBPR Partnership

Although the CBPR approach experiences of the *PILI 'Ohana* Project may not be generalizable to all CBPR projects, the collective experience of this project demonstrates that CBPR approaches can provide a framework for engaging the community while maintaining scientific merit and offer hope for ensuring that populations with a disproportionate burden of health disparities become active partners in reversing these health disparities and improving the health of their communities and the larger public.

Academic Partners' Experience and Perspective

Most academic investigators engage in a CBPR partnership with community organizations that are similar in function (e.g., direct services) or type (e.g., civic clubs). The diversity in this CBPR partnership added a layer of complexity because 5 different community perspectives with varying skill sets and priorities needed to be considered and balanced throughout the project. Thus, the choice to engage in CBPR significantly added to the time commitment needed and complexity involved in carrying out the research. For example, more meetings are needed to negotiate research ideas and address the diversity in perspectives and values, which can pose challenges to meeting deadlines. However, the richness of ideas

and perspectives shared by and long-term relationship fostered with community people through CBPR adds enduring value and meaning to a scientific research project.

In this CBPR partnership, the community partners were completely and equally (e.g., individual budget management) involved in all aspects of the research project, which a paucity of projects is able to do in practice. As shared earlier, the community partners identified the research topic and provided input into how the CBPR partnership would be structured and how the study would be designed and implemented. They also own their own data and determine how the information is disseminated in their respective communities. The active involvement of communities for which the research findings are to benefit is vital to developing effective and sustainable community engaged interventions to eliminate health disparities.

Notwithstanding the many benefits of CBPR, there were challenges in implementing the intervention and assessment protocols. One challenge involved the standardization of research protocols and the adherence to these protocols across the 5 different community partners. Scientific investigations, like RCTs, seek to reduce or eliminate biases most often through strict adherence to standardized research and intervention protocols. Despite having standardized protocols in the RCT, it was challenging to maintain consistency and adherence to the protocols across 5 community settings with very different organizational structures. For example, due to the community partners' multiple responsibilities and competing demands, certain parts of the intervention and assessment protocols were difficult to adhere to, such as having the same community-peer educator delivering the intervention or having the required number of assessors available at all times. Another example is variations in the delivery of intervention materials because of differences among community-peer educators in expertise and familiarity with facilitating groups, as well as dissimilarities across bilingual translators in the translation of materials into different Pacific Islander languages. However, the challenges faced by the community partners reminded the group that these are real-world issues, and if interventions are to be effective (vs. efficacious) and transportable across settings, they need to withstand many of these real-world challenges.

Community Partners' Collective Experience and Perspectives

For the 5 community partners, the primary purpose for engaging in a CBPR initiative was to build capacity and resources to engage in future health disparities research, and sustain the programs and services developed in their respective communities, both independently and with academic partners. Communities are no longer accepting roles that minimize their abilities in research studies. The 5 community partners in the PILI 'Ohana Project had a fundamental commitment to contribute to research in a meaningful manner, and as a result, became key stakeholders in the design and implementation of this research project. Despite the experiences of the PILI 'Ohana Project's 5 communities, there still were some critics, both community and academic, who questioned the motives of researchers and also whether community groups have the capacity to participate in research projects as equal partners. The CBPR approach undertaken by the PILI 'Ohana partnership encouraged the communities to actively contribute to the research process from developing the research question to how the research is conducted, managed, and eventually, interpreted and disseminated in their respective communities.

Evident in the CBPR approach used throughout this project was the sharing of power that was evident in study resources as well as decision making and an established understanding of unrestricted exchange of knowledge and expertise. This multi-relationship dynamic involved not only community and academic partners but also involved community-to-community relationships. Although this was the first time that 4 of the 5 community partners were involved in an RCT, the community groups were continuously asked for their feedback and suggestions, and were never excluded from the conversation or decision-making process to improve not only the study implementation but also the CBPR process throughout the entire project. In fact, the 5 community partners felt they had more of a vested interest in this project because of the co-sharing of resources and the sense that for the project to succeed all had to succeed individually. Involvement in a co-sharing and co-learning partnership also resulted in the communities' willingness to participate in and work hard to achieve the goals of the research project. For all the community partners, the knowledge acquired and shared became intellectually, physically, personally enriching, and relevant to everyone involved.¹⁰

All 5 community partners faced similar challenges around the recruitment and retention of participants from their respective communities. The recruitment of participants took longer than expected, but there was an increase in recruitment and retention rates among participants who were already active in other programs or services offered by the community organizations. Most of the community partners found that participants with pre-existing service-providing relationships (i.e., church and family groups) with the community organizations were more likley to participate and remain in the study than those who had no pre-existing relationship. The other community partners found that the *PILI 'Ohana* Project allowed the opportunity to reach others who were in need of services, but had never visited their community organizations.

Because of their involvement in the PILI 'Ohana Project, the community partners have been enabled to seek more creative and innovative paths that can be used to continue programs and services that improve health outcomes for their communities separate from this specific research project. All 5 community partners now have more staff who are familiar with research skills (i.e. research development, implementation, and outcome data collection), which may be helpful with future community research and service projects. The transferablity of knowledge and opportunity to build the reputation of their organizations heightened the communities' regard for the integrity and accountability of their work. Each organization has staff who feel they increased their professional capacity in a manner that would allow them to participate in or implement other research projects. Despite the challenges endured, all the communities are confident that the PILI 'Ohana Project has the key components for a successful and sustainable CBPR partnership.

Conclusion

The intention of this article was to share the learned experiences of all partners in the *PILI 'Ohana* Project in forming a CBPR community-academic partnership and to describe the extent of the

communities' involvement in the major aspects (i.e., research focus, design and methods, and implementation of research protocols) of a scientific research project. It is the authors' hope that the reflections and collective experiences provided offer some insight into forming and sustaining CBPR partnerships to others who are seeking an opportunity to work with the diverse communities in Hawai'i and elsewhere in the Pacific to eliminate health disparities. In keeping with the spirit of CBPR, this article was conceived and written with meaningful and ongoing involvement from all partners, both academic and community.

Acknowledgements

We would like to thank all of the Native Hawaiian, Filipino, Samoan, and Chuukese people of O'ahu and Maui who have participated in the PILI 'Ohana Project. We also would like to thank the staff and administration of the five partnering community organizations of Hawai'i Maoli - The Association of Hawaiian Civic Clubs, Ke Ola Mamo, Kula no nā Po'e Hawai'i, Kalihi-Pālama Health Center, and Kōkua Kalihi Valley Comprehensive Family Services for their support of this project. The investigators and staff of the PILI 'Ohana Project are as follow: Marjorie Mau, M.D. (Principal Investigator and Academic Co-Director) and Charles Rose (Community Co-Director): Henry Gomes, MS, Sheryl R. Yoshimura, RD, Anne Leake, PhD, APRN-Rx, B. Puni Kekauoha, Adrienne Dillard, Donna Palakiko, RN, MS (community investigators); Andrea Siu,, BA, JoHsi Wang, Andrea Macabeo, Alohanani Jamais, OTD candidate, Keali'i Lum, OTD candidate, and Melaia Patu (community coordinators and staff); Joseph Keawe'aimoku Kaholokula, PhD, Margaret West, MPH, Andrea Nacapov, MA, Hanalei Abbott, Sean Mosier, BA, Sheri Kent, Jimmy Thomas Efird, PhD, Pollie Bith-Melander, PhD, Chieko Kimata, RN, MPH and Ka'ohimanu Dang, BA (academic investigators and staff). Finally, we would like to express our gratitude to Kaimi Sinclair, PhD, Erin Saito, PhD, Kanani Texeira, MD for reviewing drafts of this article.

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Conjunctival Pain at Termination of Cataract Surgery

Yong S. Goh MD



Yong S. Goh MD

Abstract

An explanation is proposed for the conjunctival pain at the conclusion of cataract surgery.

Pain associated with injection of antibiotics under the conjunctiva is sometimes observed at the end of cataract surgery performed under retrobulbar block.

Partial block of the sensory nerves of the eye has been proposed as a reason for this. Failure to block orbital-ciliary nerves, branches of the maxillary branch of the fifth cranial nerve is put forward as an additional explanation for the pain.

Injection of antibiotics under the inferior bulbar conjunctiva, at the end of cataract surgery and intraocular lens implantation by an apparently adequate retrobulbar block can sometimes produce severe pain. This mars what would have been a pleasant amnesic experience for the patient. Most patients, when questioned say that this pain was what they remembered of the procedure was the pain. In these patients the anesthetic had up to this point been adequate, the patient tolerating the eye cleansing, insertion of the lid speculum, incision of the scleral corneal junction and closing of the conjunctival incision.

Standard texts of anesthesia and operative ophthalmology do not comment on this minor albeit distressing phenomenon. 1.2 Hamilton³ in a review of 12,000 cases performed by retrobulbar and peribulbar techniques, does not mention this terminal pain. Wong⁴ reviewing regional anesthesia for intraocular surgery, says that "despite an otherwise satisfactory block the patient may feel pinching at the beginning or antibiotic injection at the end of surgery."

Sensory input from the eye is transmitted through the ophthalmic and to a slight extent the maxillary division of the trigeminal (5th) nerve. The bulbar conjunctiva is supplied by the ophthalmic division of the trigeminal nerve, ⁵ In greater detail, Wong states that the sensory supply to the conjunctiva is from 1) the frontal nerve supplying the superior conjunctiva by way of its supratrochlear; 2) the lacrimal nerve, which supplies the lateral conjunctiva; and 3) the nasociliary nerve, which enters the ciliary ganglion and reemerges as the infratrochlear and then supplies the medial conjunctiva, all these nerves being branches of the ophthalmic division. The maxillary division, through its infraorbital

nerve, supplies the inferior conjunctiva ⁴. (Fig 1).

A pain-free eye implies successful blockade of these branches of the ophthalmic division and the ciliary ganglion, as well as the infraorbital nerve of the maxillary. As these nerves and ganglion lie within or around the muscle cone they are usually blocked in a technically well administered retrobulbar block. Hamilton³ recorded that breakthrough pain at the beginning of surgery occurred with an incidence of 2% to 0.1% with various techniques of retrobulbar and peribulbar blocks. This was in spite of routine instillation of the topical anesthetic, proparacaine into the inferior fornix of the eye. Wong4 ascribes the pinching at the beginning and the pain at the end with antibiotic injection to the "sensory supply of the conjunctiva arising from the supraorbital, lacrimal, infratrocheal, and infraorbital nerves, most of which run outside the muscle cone and may not be totally blocked." While this explanation has some merit, it is based on the outdated concept that the muscle cone is a watertight seal. Ropo ⁶ documented spread of anesthetic outside the cone as early as 3 minutes after a retrobulbar injection. Zahl⁷ was also able to demonstrate intraconal spread of dye in a simulated periconal (peribulbar) blocking technique. This explains why peribulbar block, in which the anesthetic is placed outside the cone, is effective. It must also be noted that anesthesia in the distribution of the infraorbital nerve is of slower onset because of its greater diameter and seclusion in a groove and canal in the floor of the orbit.3

This distressing terminal pain might possibly be explained by a little known anatomical fact elucidated by Ruskell⁸ in 1974. He demonstrated in primates orbital branches of the maxillary nerve called orbital-ciliary nerves leaving the maxillary nerve in the pterygopalatine fossa, crossing the inferior orbital fissure and reaching the eyeball through the ciliary ganglion or the retro-orbital plexus (Fig 2). In an earlier study, he had defined this plexus as a loose plexus of fine autonomic nerves formed by the junction of internal carotid nerve branches and rami orbitales (orbital branches) of the pterygopalatine ganglion within and anterior to the cavernous sinus in monkeys and man. 9 The oculomotor, ophthalmic, trochlear, and abducens nerves pass through this plexus before entering the orbit through the superior orbital fissure. These orbital-ciliary fibers

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Correspondence to: Yong S. Goh MD P.O. Box 11779 Honolulu, HI 96828 Ph: (808) 428-5743 are predominantly sensory in nature. Possibilities of maxillary fibers passing to the eyeball in man had been noted by Beauvieux and Dupes in 1926 and Tanaka in 1932.

Two reasons are here given as an explanation for the terminal pain of cataract surgery:

- 1)inadequate blockade of the infraorbital nerve because of its location;
- 2) presence of the orbital-ciliary nerves described by Ruskell. Failure to block these, because of their very posterior location outside the cone and their occasional lack of connection to the ciliary ganglion would explain the pain when injection is made into the inferior bulbar conjunctiva.

While it is not possible to predict which patient will react to the injection, routine instillation of 1-2 drops of tetracaine prior to injection may prevent the pain.

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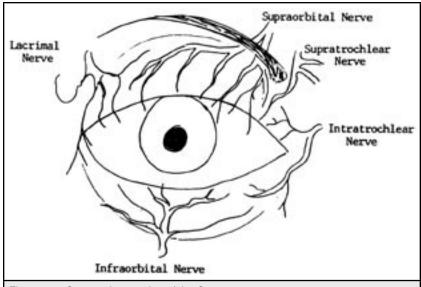


Figure 1.— Sensory Innervation of the Cornea

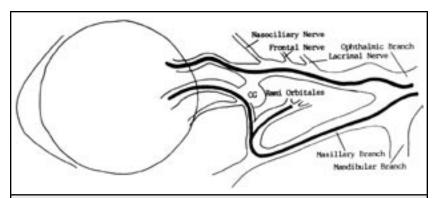


Figure 2.— Distribution of the Maxillary Nerve Fibers to the Eyeball. OG, ciliary ganglion. Modification of Illustration by G.L. Ruskell.





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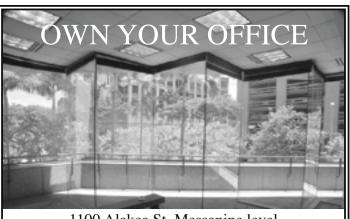
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PACIFIC PROPERTIES

At the Crossroads: Past, Current, and Future of the University of Hawai'i John A. Burns School of Medicine-Okinawa Chubu Hospital Partnership

Bruce Shiramizu MD, John A. Burns School of Medicine, University of Hawai'i; Masao Maeshiro MD, University of Hawai'i Postgraduate Medical Training Program, Okinawa Prefectural Chubu Hospital

Over 40 years ago, a program between the University of Hawai'i and Okinawa Chubu Hospital began training physicians through the efforts of the United States Civil Administration of the Ryukyu (USCAR). Prior to this collaborative effort, the physician supply and medical demands in Okinawa were constrained due to war-related issues (World War II; 1941-45).

Currently in Okinawa, there are approximately 200 physicians per 100,000. In the 1950's, the ratio was 18.7 physicians per 100,000. The increase in the number of physicians in Okinawa occurred through various mechanisms. Initially, in 1949 the USCAR administrator arranged for students from Okinawa to complete medical programs in Japan through financial assistance and a requirement that they return to Okinawa to practice medicine. Within 3 years, funds to support the program were exhausted. Since 1952, scholarships were provided by the Japanese government. In 1950, a program was started whereby examinations were administered to graduates of Okinawan high schools with select students sent to mainland Japan for higher education in the liberal arts, science, engineering, and medicine. Students agreed to return after graduation to serve at locations designated by the government. Over the next few years, the number of physicians in Okinawa increased. Since 1952, a few select physicians were sent to the United States each year to observe medical care practices. By 1963, over 15 physicians traveled abroad to countries that included the United States, England, and Denmark. A few completed master's degrees or graduated from established medical residency programs. As part of its mission, USCAR medical training focused on medicine, surgery, pediatrics, and dermatology. In 1967, USCAR appointed Dr. Lorne Phillips, interim director of the University of Hawai'i Postgraduate Medical Training Program, when the University of Hawai'i responded to a request from the US Army and State Department to send a teaching staff to a newly constructed hospital in Okinawa.

This formal rotating internship training was initiated in accordance with the Medical Act of Japan and the first program director, Dr. Neal L. Gault, was officially appointed to direct the Postgraduate Medical Training Program of University of Hawai'i at Okinawa Central Hospital (later became Prefectural Okinawa Chubu Hospital). The program differed from the Japanese traditional training and education by instituting a rotating clinical clerkship with an infrastructure to support stipends for room and board, a wide range of pathology related to patient care, 24-hour service medical library, and dedicated faculty staff members for teaching. The teaching staff consisted of 14 University of Hawai'i faculty members: 3 in medicine, 2 in surgery, 1 each of pediatrics, anesthesia, ob-gyn, psychiatry, pathology, radiology, laboratory medicine, nursing, and hospital administration. Over the next few years as the number of

trainees increased, a select number were sent to the United States to become competent teachers. Most of them returned and joined the Okinawa Chubu Hospital teaching staff. Through 1971, the training program was supported by the faculty of University of Hawai'i, but with funding cutbacks by the US government, the University of Hawai'i ceased training for an interim period. However with the support of the Japanese government, a new contract with the University of Hawai'i was generated when the Ryukyu Islands were reverted to Japan. The program has continued since then, with the contract renewed bi-annually.

The Postgraduate Medical Training Program through the UH JABSOM-Okinawa Chubu Hospital differs from training programs at institutions in Japan in many aspects. Compared to other programs in Japan, Okinawa Chubu interns and residents have broad experiences across major disciplines in the medical field. First year trainees rotate through medicine, surgery, ob-gyn, pediatrics, emergency room, and anesthesia, rather than being limited to a single area, which is the traditional method in Japanese programs. In the second year, the trainee experiences broad areas of major specialties such as in medicine, cardiology, gastroenterology, pulmonology, nephrology, neurology, and hematology. In surgery, the trainees are exposed to orthopedics, neurosurgery, genitourinary surgery, and anesthesia. These first two years are in contrast to traditional medical training programs in Japan in which trainees are confined to a single, narrow subspecialty.

The success of the program lies in the principles established, which are similar to medical education in the United States, in contrast to traditional medical education in Japan. Additional differences include responsibility for daily patient care that belongs to trainees with oversight by the full-time staff. The staff supervises the trainee as consultants and advisors. Trainees are encouraged to participate in patient-care rounds to discuss progress and plans for medical care and/or hospital discharge. Trainees are exposed to emergency care. University of Hawai'i teaching staff provide trainees with exposure to English language skill development. The Okinawa Chubu Hospital medical library is accessible to trainees 24/7, which is in contrast to Japanese University libraries, which are closed at night. Many Okinawa Chubu Hospital physicians have had formal, additional clinical training in the United States, after completion of the training at Chubu Hospital.

To date, over 750 trainees have completed the post graduate medical education program of which over 70% remain in Okinawa to practice medicine. The staff and trainees at Okinawa Chubu Hospital have recognized that the knowledge, experience, and pathology seen at their institution could benefit the medical community at

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Proteasome Inhibitors in Pediatric Cancer Treatment

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Abstract

The 26S proteasome regulates the degradation of many proteins involved in cell cycle control, apoptosis, and tumor growth. The inhibition of the proteasome by specific inhibitors is a viable target for anti-tumor therapy. Most prominently, the proteasome inhibitor bortezomib (Velcade®) was approved by the US Food and Drug Administration (FDA) for the treatment of relapsed or refractory multiple myeloma in adults, and is presently considered for several other types of cancer including pediatric malignancies. The first clinical trials by the Children's Oncology Group (COG) were conducted with bortezomib for the treatment of refractory solid tumors and refractory leukemia. Proteasome inhibitors are a promising new class of therapeutics that should be further explored in combination with other chemotherapeutic agents for the treatment of pediatric cancer patients.

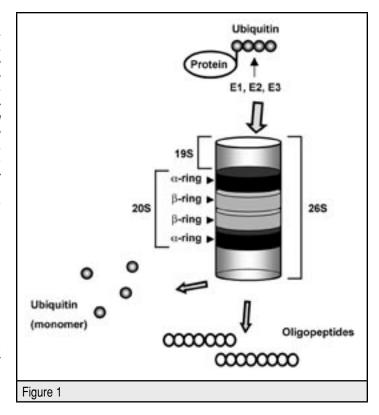
1. The Proteasome - Structure and Function

The 26S proteasome is a large multi-subunit protein complex that degrades a large number of cellular proteins, including regulatory proteins that control cell cycle progression, transcriptional activation, and programmed cell death (apoptosis). The proteasome also eliminates unneeded, damaged, and mutated or incorrectly folded proteins. Before the destruction process begins, the protein is marked for degradation by poly-ubiquitination (Fig. 1). The formation of the ubiquitin chain consists of 4 or more ubiquitin molecules, and this poly-ubiquitin attachment is catalyzed by a multi-step process involving the concerted action of enzymes E1, E2, and E3.^{1,2}

The 26S proteasome is a highly-structured cylinder-shaped complex containing a core of 4 stacked rings around a central pore (20S core). Each ring consists of 7 individual proteins. The inner two rings are composed of β -subunits that contain a total of 6 protease active sites (protease-like, trypsin-like, and chymotrypsin-like activities) (Fig. 1). The outer two rings contain 7 α -subunits that form the channel through which the protein substrates enter the cylinder-like barrel. The α -subunits are controlled by regulatory particles of the 19S proteasome including receptors Rpn10 and Rpn13, both of which recognize the poly-ubiquitin chain and initiate protein degradation. 1,2 The degradation process produces small peptides of about 7 to 8 amino acids long, which then are further degraded into individual amino acids outside of the proteasome. Amino acids and ubiquitin molecules are recycled to synthesize and label new proteins.

2. The Proteasome - A Target for Cancer Therapy

While the precise mechanisms of action of proteasome inhibitors are still unclear, it has been shown in many studies that transformed, malignant cells are more susceptible to proteasome inhibition than normal cells, thus suggesting that the proteasome is a viable target for cancer therapy. These findings were supported by convincing preclinical studies in cancer models, confirming that proteasome



[Figure 1]: The Structure and function of the 26S proteasome. The proteasome is a cylinder-like barrel that functions like a cellular garbage disposal unit and thereby regulates a large number of proteins important in cell division and apoptosis. Specific enzymes (E1, E2, and E3) mark proteins for degradation by attaching several molecules of ubiquitin. Small peptide chains and free ubiquitin monomers are released upon protein degradation in the catalytic core of the two β -ring systems.

inhibitors exhibit anti-tumor activity and induce apoptosis.³⁻⁶ Interestingly, proteasome inhibitors also sensitize tumors to the effects of well-established chemotherapeutic agents, therefore suggesting that drug combination cocktails may be formulated at lower doses, still giving a comparable therapeutic outcome, as well as reduced side-effects.

A plethora of molecular studies have been conducted that examine the cell signaling pathways activated by proteasome inhibition. Since a large number of different cellular proteins are degraded through the proteasome, it is maybe not unexpected that many cellular pathways are affected by proteasome inhibition. Especially the nuclear factor- κB (NF- κB) signaling pathway is impacted by proteasome inhibitors through down-regulation of NF- κB . This occurs by preventing the proteasomal degradation (and thus stabilization) of I κB , which binds NF- κB and prevents its nuclear translocation. The decreased NF-

κB activity leads in turn to reduced NF-κB-dependent transcription of genes important in tumor cell survival, proliferation, invasion, metastasis, and angiogenesis. Other pathways that are affected by proteasome inhibitors include the modulation of cell cycle regulatory proteins (for example cyclin-dependent kinase inhibitors p21 and p27) and apoptotic pathways (for example, tumor suppressor protein p53, and the pro-apoptotic proteins Bcl-2 and Bax). Finally, proteasome inhibitors also affect the p44/42 mitogen-activated protein kinase (MAPK) signaling pathway, which promotes tumorigenesis.

3. Proteasome Inhibitors in the Clinic

Due to these promising therapeutic advantages, proteasome inhibitors have created a considerable interest and have recently been introduced into the clinic as a new class of chemotherapeutic agents. The most prominent and relatively well-tolerated proteasome inhibitor in use today is bortezomib (Velcade[®], previously referred to as PS-341), which was approved by the US Food and Drug Administration (FDA) for the treatment of relapsed or refractory multiple myeloma in adult patients. In multiple myeloma, the adhesion of myeloma cells to bone marrow stroma leads to the activation of NF-κB-dependent production of anti-apoptotic factors and interleukin-6 (IL-6),8 This presents a strong rationale for targeting the NF-κB pathway in this cancer type with the proteasome inhibitor bortezomib. Bortezomib has also been successfully used for the treatment of patients with mantle cell lymphoma and other non-Hodgkin lymphomas.⁹⁻¹³ In addition to bortezomib, other proteasome inhibitors are currently in clinical trials, like carfilzomib, NPI-0052, and CEP-18770. However, as depicted in Table 1, the large majority of clinical cancer trials with proteasome inhibitors were or are conducted with bortezomib (336) trials), either alone or in combination with other chemotherapeutic agents. Only a small number of trials included carfilzomib (2 trials), NPI-0052 (4 trials), and CEP-18770 (1 trial).

4. Pediatric Cancer Treatment using Proteasome Inhibitors

Unlike the large number of clinical trials with adult patients, only a small number of proteasome inhibitor-based clinical cancer trials have been conducted or are in progress with pediatric patients (Table 1). Of 336 clinical trials with bortezomib, only 37 trials involve the treatment of pediatric patients with bortezomib. Two Phase I pediatric clinical trial studies that included patients with refractory solid tumors¹⁴ and leukemia¹⁵ were recently published by the Children's Oncology Group (COG). Both studies reported that bortezomib was well tolerated in children with refractory solid tumors. The dose recommendation for children with solid tumors and leukemia was very low, with 1.2 and 1.3 mg/m²/dose, respectively, administered twice weekly for 2 weeks followed by a 1-week break. ^{14,15} Bortezomib treatment was indeed shown to inhibit NF-κB activity, but the drug had little activity as a single agent in the tested populations. This suggests a need for future drug combination trials.

5. Proteasome Inhibitors and Neuroblastoma

Our research focuses on the identification of alternative therapeutics that improve the overall survival rate of pediatric patients with high-risk neuroblastoma (NB). ¹⁶⁻¹⁸ Despite intensive treatment of NB patients with high-dose chemotherapy, autologous peripheral stem cell transplantation, and radiation therapy, the long-term sur-

| Table 1.– Clinical Trials Including Proteasome Inhibitors | | | | | |
|---|---------------|-----------------------|--|--|--|
| Search terms | Studies (all) | Studies (open/closed) | | | |
| Bortezomib | 337 | 184/153 | | | |
| Bortezomib + Cancer | 336 | 183/153 | | | |
| Bortezomib + Children | 37 | 18/19 | | | |
| Neuroblastoma | 240 | 99/141 | | | |
| Bortezomib + Neuroblastoma | 1 | 1/0 | | | |
| Carfilzomib | 2 | 1/1 | | | |
| Carfilzomib + Children | 0 | 0/0 | | | |
| NPI-0052 | 4 | 4/0 | | | |
| NPI-0052 + Children | 0 | 0/0 | | | |
| CEP-18770 | 1 | 1/0 | | | |
| CEP-18870 + Children | 0 | 0/0 | | | |

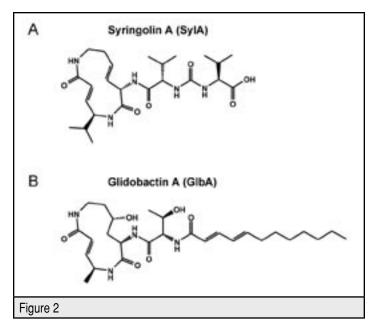
Data obtained on 6/27/2008 using the search engine at www.ClinicalTrials.gov, a service of the US National Institutes of Health. ClinicalTrials.gov currently has 58,167 trials with locations in 157 countries. All study types were considered including interventional, observational, and expanded access. Searching for PS-341 or Velcade® in place of bortezomib, and PR-171 in place of carfilzomib resulted in the same number of clinical trials.

vival of patients with high-risk NB remains poor. The response of patients that relapse or do not achieve complete remission is even worse, thus demanding the development of novel drugs that exhibit alternative mechanisms of action.

Considerable evidence exists in literature that proteasome inhibitors like bortezomib are also effective in NB, based on data from both *in vitro* and preclinical studies. 11,19-25 While a database search for completed or active clinical trials with NB patients revealed a total number of 240 clinical trials, only one Phase I trial concerned the treatment of recurrent or refractory NB patients with bortezomib. This is a presently on-going combination trial of bortezomib with the topoisomerase I inhibitor irinotecan (at the University of Michigan Cancer Center). Clearly, the use of proteasome inhibitors in combination with other drug therapeutics is warranted for more NB clinical trials and the outcome of the bortezomib/irinotecan NB trial at the University of Michigan shall be of great interest.

6. Syrbactins, a Novel Class of Proteasome Inhibitors

Despite the great advances made with bortezomib, other types of proteasome inhibitors with improved specificities and different modes of action are needed to provide a broader inhibitor platform for future combination trials. As part of our on-going search for natural products with anti-cancer activities, the Bachmann laboratory in collaboration with several international groups has recently identified a new structural class of proteasome inhibitors that we named syrbactins. This new class includes the *Pseudomonas syringae* plant pathogen-produced natural product syringolin A (SylA) and the structurally-related *Burkholderiales*-produced glidobactin A (GlbA) (Fig. 2).



[Figure 2]: Chemical structures of two new proteasome inhibitors, (A) syringolin A (Syl A) and (B) glidobactin A (GlbA). A, SylA is produced and secreted by the plant pathogen Pseudomonas syringae pv. syringae. B, GlbA is produced and secreted by Burkholderiales strain K481-B101 (ATCC 53080). SylA and GlbA are structurally related except for a single lipophilic tail in GlbA which is absent in SylA. The two molecules bind the 20S proteasome through a novel mechanism and form a new class of proteasome inhibitors, the syrbactins.

Most intriguingly, we found that syrbactins bind the catalytic center of the eukaryotic 20S proteasome by a novel mechanism.²⁶ Syrbactins form a new structural class of proteasome inhibitors and thus expand the growing list of existing proteasome inhibitors (Table 2).²⁷

We have also shown that SylA inhibits cell proliferation and induces apoptosis in NB and ovarian cancer cells. ^{26,28} A detailed molecular analysis of cell signaling pathways that are activated in NB by syrbactins is currently in progress in the Bachmann laboratory. Syrbactins will be further explored in preclinical studies that include NB and other tumor models.

7. Conclusions

Proteasome inhibitors hold promise as novel therapeutics for the treatment of cancer. Thus far, proteasome inhibitors have mainly been explored in adult cancer, for example, in the treatment of multiple myeloma. This class of inhibitors is now further explored in the treatment of pediatric patients, and one NB clinical trial with bortezomib combined with irinotecan is currently underway. A new proteasome inhibitor class (syrbactins) was recently identified in our laboratory, and is further developed into a new proteasome inhibitor-based drug. Evidence suggests that combination therapies, not single drug-based therapies, will most likely be required to successfully treat cancer patients with proteasome inhibitors.

Acknowledgments

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| Table 2.— Major Classes of Proteasomal Inhibitors | | | | |
|---|--|--|--|--|
| Class | Examples | | | |
| - Peptide aldehydes | Calpain inhibitor I/II, MG132 | | | |
| - Peptide boronates | Bortezomib (Velcade®), CEP-18770 | | | |
| - β-lactone | Lactacystin, Salinosporamide A/B, NPI-0052 | | | |
| - Peptide vinyl sulfones | NLVS, YLVS, ZLVS | | | |
| - Peptide epoxyketones | Epoxomycin, TMC, Carfilzomib | | | |
| - Syrbactins (new) | Syringolin A, Glidobactin A | | | |

For more information about the Cancer Research Center of Hawai'i, visit www.crch.org.

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Issues in Medical Malpractice XXVII

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

Question: You are treating a patient, a school-bus driver, for cirrhosis and alcoholism. He continues to drink heavily, so you report his condition to the employer. As a result, he is fired from his job and he now sues you for breach of confidentiality. Which of the following (more than one) are correct?

- A. You may be liable for having breached patient confidentiality.
- B. You do not normally have a legal duty to report a patient's medical condition to anyone.
- C. There is a public safety issue here that may require the doctor to breach confidentiality.
- D. The patient will probably win the lawsuit if he is an office clerk instead of a school-bus driver.
- E. If this is a sick-leave note, you should simply write "off work for medical reasons".

Answer: All are correct.

Breach of patient confidentiality is both a legal and ethical wrong. Privileged medical information cannot be disclosed except under well defined circumstances. Unconsented reporting of a patient's condition to the employer is not allowed, unless the law requires disclosure, e.g., where there is a substantial risk to an individual or the public. In this case, alcohol abuse in a school-bus driver can reasonably be said to constitute a potential risk of serious harm to the young passengers, so disclosure may be preferable to confidentiality. The physician should first warn the patient (bring in the family if possible) that unless he abstains from further drinking and enters a rehabilitation program, the physician will have no choice but to report to the employer in the name of public safety. The patient can always file a lawsuit, but he is much less likely to win under the circumstances. On the other hand, if the patient works as an office clerk instead of being a bus driver, then the doctor may no longer have as compelling a reason to disclose. Another approach is to consider reporting to the department of motor vehicles if the patient remains recalcitrant, especially if there is a past history of drunk driving or accidents.

For the usual sick-leave note, the doctor should simply write "off work for medical reasons," avoid specifying the diagnosis, and give the note directly to the patient.

Disclosure to Third Parties

The professional duty of protecting the confidences of a patient is not an absolute one, and there are circumstances provided by law where limited disclosure of patient secrets is not only permissible but obligatory. An obvious exception is a state law requiring the disclosure of communicable diseases. Other examples are the mandatory reporting of suspected child abuse and gunshot wounds.

A more difficult situation arises where there is no statute on point, but the public welfare is at stake. The well-known case of <u>Tarasoff</u>

v. Regents of University of California established that where there is threatened harm to a named third party, the practitioner is required to reveal the information to the intended victim. In Tarasoff, a jilted patient confided in the University psychologist his intention to kill his ex-girlfriend. The information, though shared with campus security, was not released to the intended victim, the girlfriend, who was stabbed to death by the patient two months later. The Court found the psychologist and the University of California (under respondeat superior) liable, and explained that in this case the protection of public safety was more important than the sanctity of the doctorpatient confidentiality relationship:

"... In this risk-infested society, we can hardly tolerate the further exposure to danger that would result from a concealed knowledge of the therapist that his patient was lethal. If the exercise of reasonable care to protect the threatened victim requires the therapist to warn the endangered party or those who can reasonably be expected to notify him, we see no sufficient societal interest that would protect and justify concealment. The containment of such risks lies in the public interest."

Disclosure to third parties of incorrect patient information such as having a contagious disease may constitute defamation, which is defined as harming a person's reputation through communicating to others a verbal or written falsehood. However, there may be a qualified privilege to such disclosure where there is a public health interest. For example, in *Simonsen v. Swenson*, a physician disclosed a positive syphilis test result that turned out to be an error. In the defamation suit that followed, the court declined to impose liability on the doctor, finding that he was protected in discharging his duty to disclose.²

Many motor vehicle agencies have established a medical advisory board (MAB) to evaluate medical issues relating to driving and licensure. What if, in the interim period of licensure, a patient's health condition deteriorates to a degree that hinders safe driving? When are doctors legally or ethically obligated to report their patient's condition? In many states, physician reporting of medically impaired drivers is encouraged, and some states actually mandate reporting conditions such as epilepsy.³ Doctors in California are required to report patients with dementia. Texas, Utah, Florida and Arizona (not Hawaii) have implemented provisions to immunize health care professionals from liability for making judgments regarding patients' ability to drive safely.⁴ Other states may make it difficult to report, and doctors may be accused of violating confidentiality should they do so. Doctors should therefore look to their own state laws on this issue before acting, but may be guided by the following published opinion of the AMA's Council on Ethical and Judicial Affairs:⁵

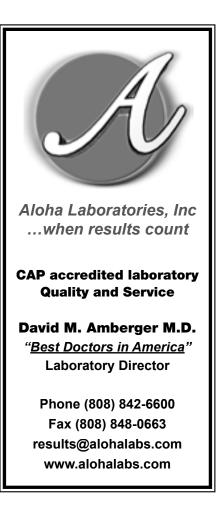
Continues on next page

"Physicians should use their best judgment when determining when to report impairments that could limit a patient's ability to drive safely. In situations where clear evidence of substantial driving impairment implies a strong threat to patient and public safety, and where the physician's advice to discontinue driving privileges is ignored, it is desirable and ethical to notify the Department of Motor Vehicles."

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

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large. As such, many find the resources to present and/or publish their experiences.² The UH-JABSOM-Okinawa Chubu collaboration continues to be regarded as a model program in Japan by the Ministry of Labor and Welfare.

Because of the structure of the training, the program has become highly competitive with applicants coming from throughout Japan. The University of Hawai'i JABSOM remains dedicated in its mission with the Okinawa Chubu Hospital to collaborate on the Postgraduate Medical Training Program. Each year, UH JABSOM faculty are hosted by the Okinawa Chubu Hospital Training Program through the Visiting Faculty/Scholar Program. Faculty members from UH JABSOM spend 1 week to 3 months with the Program's trainees and staff. Daily medical rounds are attended and pertinent lectures are provided. Although the initial objective of training to increase the number of physicians in Okinawa has been achieved, there remain locations throughout the region in which consistent medical care is still nonexistent because of the growing population of Okinawa and surrounding islands.

At the crossroads of the Program's 41st anniversary, its dedication and continuation remain paramount as it continues to supply physicians to isolated islands and train specialists such as obstetricians, gynecologists, and pediatricians whose numbers have decreased in Japan. As a successful training model, the scope and backbone of the training structure could be implemented in other regions throughout the world where more physicians are needed. At the crossroads of this collaborative effort, the past and current successes of the UH JABSOM-Okinawa Chubu Hospital Postgraduate Medical Training Program segues into an optimistic future as it continues to fulfill its mission by providing physicians to isolated areas and training specialists. Additionally, the program could be a role model for other places nationally and internationally to establish partnerships between resource-discordant institutions by coming together to benefit each other and respective communities.

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| 10/25-10/31 | PD | American Academy of Pediatrics, California Chapter & University Children's Medical | Grand Hyatt Kauaʻi | Aloha Update: Pediatrics 2008 | Tel: (808) 354-3263 Web: www.ucmg.org |
| | | Group | | | |
| 10/26-10/30 | OBG | University of California - Davis | Ritz Carlton, Kapalua | 25th Annual UC Davis Obstetrics and Gynecology Conference | Tel: (866) 263-4338 Web: www.ucdmc.ucdavis. edu/cme/ |
| 10/27-10/31 | AN | California Society of | The Mauna Lani Bay Hotel, | CSA Hawaiian Seminar | edu/cine/ |
| 10/27 10/01 | 7.11 | Anesthesiologists | Kohala Coast, Hawai'i | OO/TTIAWAIIAIT OCTIMILAI | l |
| 10/31-11/2 | ORS | Department of Surgery, John A. Burns School of Medicine, | Sheraton Kaanapali Hotel, Kaanapali, Maui | Wrist Injury Course Trauma to Reconstruction | Web: www.csahq.org Email: joann. sakuma@wristcourse.org |
| | | University of Hawaiʻi | | | Web: wristcourse.org/ maui08home.html |
| November 200 |)8 | | | | |
| 11/3-11/6 | Multi | Methodist Healthcare | Fairmont Orchid, Kona | Advances in Medicine | Tel: (901) 516-8933 |
| | | | | | Web: www.methodistmd.org |
| 11/4-11/7 | R | Duke University Medical School, | Hyatt Regency, Maui | Muskuloskeletal MRI in Maui | Tel: (800) 222-9984 |
| | | Department of Radiology | | | Web: www.dukeradiologycme. |
| 11/9-11/14 | RNR | Department of Radiology, Mayo | Fairmont Kea Lani, Maui | Neuroradiology: Practice to | Tel: (866) 242-1581 |
| | | Clinic | | Innovation | Web: www.mayo.edu/cme/radiology.html |
| 11/15 | Multi | Access Care Today | Queen's Conference Center | Hepatitis – Practical Clinical Concepts | Tel: (808) 373-3488 |
| | | | | | Email: alantice@idlinks.com |
| | | | | | Web: www.idlinks.com |

| December 2008 | | | | | | | | |
|---------------|--------------|---|--------------------------------------|---|---|--|--|--|
| 12/7-12/12 | EM | Institute for Emergency Medical Education, American College of Emergency Physicians | Wailea Marriott, Wailea, Maui | Annual Current Concepts in Emergency Care | Web: www.ieme.com | | | |
| January 2009 | January 2009 | | | | | | | |
| 1/10-1/13 | Multi | American Society for Reconstructive Microsurgery | Grand Wailea Resort, Wailea, Maui | 2009 Annual Meeting | Web: www.microsurg.org | | | |
| 1/25-1/30 | R | Department of Radiology, Mayo Clinic | Mauna Lani Resort | Tutorials in Diagnostic Radiology w/Advanced Radiology Life Support | Tel: (866) 242-1581 Web: www.mayo.edu/cme/radiology.html | | | |
| 1/28-1/31 | PMD | American Academy of Pain Medicine | Hilton Hawaiian Village, Honolulu | Annual & Scientific Meeting | Web: www.painmed.org | | | |

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General Membership/Opening Session: Oct. 31, 2008

10:00 AM - 3:00 PM, Queen's Conference Center lunch provided

Featured speakers: Edward L. Langston, MD - Immediate Past Chair, AMA Board of Trustees Arthur Lurvey, MD - Regional Medical Director, Palmetto GBA

Closing Session: Nov. 2, 2008

12:00 PM - 5:00 PM, Queen's Kamehameha Auditorium lunch provided

For more details, including resolutions and bylaws information, go to www.hmaonline.net

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Russell T. Stodd MD

AFTER THINGS HAVE GONE FROM BAD TO WORSE, THE CYCLE WILL REPEAT.

The Hawai'i Health Systems Corporation (HHSC) is the administrative organ created in the 1990s by the legislature to manage 13 state-owned incongruous health care facilities, including many of the neighbor island hospitals and extended care units. The system is like no other in the country if not the world, and the headaches are constant, multiple and varied. Many of the buildings are old and require repair and many others have been or must be modified to meet current medical requirements. Moreover, union contracts, the civil service system, and the employee retirement funding add to the

administrative burdens. However one describes it the HHSC is destined to fail financially, and the legislature must make annual appropriations to cover the multi-million dollar losses in order to prevent withdrawal or rationing of critical medical care. It follows that the legislature requires an accounting and explanation for the budget deficit and politicians want to find a pony somewhere in all this manure of red ink. As if this were not enough to challenge the HHSC leadership, in 2007 the legislature created regional boards to manage Maui, Hilo, Kaua'i, and Kona hospitals. As the Pacific Business News editorial noted, the legislature created another layer of bureaucracy to further confuse the management of inadequate resources. Now the HHSC is facing a huge financial deficit, and cannot even shift dollars to meet crises. One partial answer might be to spin off the neighbor island acute care hospitals Maui, Kona, Kaua'i Veterans, and Hilo, divorced from the state, to be locally managed as community non-profit institutions. This could provide financial avenues and opportunities not possible within the state system. In its present structure the HHSC is a garbled maelstrom of confused and conflicting demands.

❖ BRAIN CELLS COME AND GO, BUT FAT CELLS LIVE ON FOREVER.

Possibly the latest gimmick to lure patients into the doctor's office for up-front cash is the radio-wave cellulite reducer. The doctor or technician waves a hand held device delivering electromagnetic waves over the fatty area. The claim is that the waves can reduce the appearance of dimpled fat and even slightly shrink thighs, hips, buns, and belly. The waves supposedly work by heating the fat and tightening the collagen fibers so that the dimples flatten out to become less visible. Published data are limited, but some dermatologists claim the thermal rays are effective although they admit that the improvement is modest and temporary. The treatment takes from 20 minutes to 2 hours for a limited area and the cost varies from \$2500 to \$4000 usually not covered by insurance.

♦ DO YOU MIND IF I SMOKE? OF COURSE NOT. DO YOU MIND IF I FART? (STEVE MARTIN)

In 2005, Scotland passed a law banning smoking in all enclosed work places including public restaurants and bars. The purpose was to evaluate the number of hospital admissions for acute coronary syndrome (ACS). Data were collected from 9 hospitals serving a population of 3 million for a period of 10 months following the prohibition. The results recently published in the *New England Journal of Medicine* proved to be a profound indictment of the dangers of tobacco for all concerned. Overall, the number of admissions for ACS dropped by 17%. For smokers the number of ACS admissions dropped by 14%, for former smokers the drop was 19%, and for non-smokers the number was 21%. These heavy numbers serve as a serious reminder to those addicts who claim, "Hey, it's my life, man. What do you care?" Obviously, we all have a reason to care.

$\boldsymbol{\diamondsuit}$ established technology tends to persist in spite of New Technology.

While the Honolulu City Council and the Mayor continue to thrash and harangue over the perennial issue of building a rapid transit system, perhaps the answer lies in a different direction. In Texas, many people are turning to electric mini-cars about the size of golf carts, and parking the gas-guzzling sedan, SUV, or cross-over in the garage. The carts can be re-charged from a regular 110-volt house or garage outlet. In Texas they are legal only on streets with speed limits of 35 mph, but some owners have modified the car to travel much faster and even take them on the highway. Range is limited to 30 miles per charge which takes about 60 cents per fill-up. ZAP, a Santa Rosa, California, maker of small electric cars, saw their productivity jump

from 5 to 50 per day in the past 6 months. Chrysler LLC Global Electric Motorcars have increased sales by 30%, and some of its 150 dealerships around the country have tripled their sales. In Hawaii, why not give new electric car buyers a tax credit and modify or create parking areas, and measure the effect on traffic jams and gasoline prices. It is long past time for our political leaders to get their heads into the 21st century.

❖ CONFUSED? AMBIVALENT? WELL, YES AND NO.

In the Netherlands, July 1st brought a new law into effect that prohibits smoking tobacco in bars, cafes, restaurants, and clubs. The law conforms to similar statutes sweeping Europe since Ireland made pubs smoke-free in 2004. There is a problem, however, since Holland is famous for its 720 coffee shops that let people buy, light up, and puff away as much as 5 grams of cannabis each day. Moreover, the new law prohibits smoking marijuana mixed with tobacco, which is a popular practice in Europe. So, the Dutch health minister has the task of banning tobacco and tobacco-cannabis combos in coffee shops while not annoying those who are inhaling uncut weed. This appears to be a dopey unenforceable law.

$\mbox{\ensuremath{\diamondsuit}}$ research is what a scientist does when he doesn't know what he is doing.

Whoa! Now you can take a pill, sit on the sofa, and get in shape! Reporting in the journal Cell, research done at the Salk Institute for Biological Sciences at La Jolla, California, on lab mice yielded some startling results. With a combination of two drugs the ability of cells to burn fat and retain muscle mass improved substantially. Running endurance jumped by 44%, and some mice combined a month of exercise with long-distance running and increased performance by 70% when compared with untreated mice. One of the drugs is already in human trials and these experiments raise hopes for strategies to help control obesity, diabetes, and muscle-wasting disease such as muscle dystrophy. Interesting to note that unlike anabolic steroids, which enhance fast-twitch muscles, these are the first compounds shown to clearly improve slow-twitch cells and help endurance. Fast-twitch muscles burn sugar, but slow-twitchers primarily burn fat, which means they could help combat obesity. Of course, the drugs could easily be abused by competitive athletes to improve their performance, but a test has already been devised to detect them in blood and urine.

❖ SO MANY BUSH CHRISTIANS. SO FEW LIONS.

In the sunshine state of Florida lawmakers are considering changes to its sex-education curriculum. A survey of students revealed some bizarre beliefs being spread, including the myth that drinking a capful of bleach will prevent AIDS, and that drinking Mountain Dew sodas or smoking pot can prevent pregnancy. Critics of the state's abstinence-only education program say that such figments are a result of the head-in-the-sand approach. Planned Parenthood spokeswoman Jenna Cawley said that young people are getting STD and reproductive facts too little and too late.

❖ IF WE STOP VOTING, WILL THEY GO AWAY?

Texas Congresswoman Sheila Jackson Lee was addressing a group of scientists after the successful space probe landing on Mars. "At last we have finally gone back to the moon." Now she wants to name hurricanes with African-American monickers such as Chamiqua, Jamal, Tanisha, and Shaqueal and get away from caucasian sounding names. Would it be possible to establish some kind of IQ test for our elected officials?

❖ NO, MOM! YOU CAN'T HAVE THE CAR KEYS.

A 74-year-old woman was driving under the influence of alcohol when she crashed her Cadillac through the window of a convenience store. She got out of the car, walked to the fridge, got a six-pack of Bud and went to the cash register. The dumbfounded clerk refused to sell the beer, which aroused the woman's anger and she assaulted him. He called 911 and police cited the woman for driving under the influence (DUI).

ADDENDA

- ❖ In Naples, Florida, a woman visiting a bird sanctuary slipped on some bird droppings, was injured and sued the sanctuary for damages because there were no posted warnings. So, what are you guana do?
- ❖ A woman in Los Angeles, California, brought suit against Victoria's Secret for an eye injury which she claims resulted when a decorative metal piece fell off when she tried on a thong. Slipping it on over her head?
- ❖ "We are not attempting to circumcise the rules." (NFL coach)
- ❖ The Piper cub is the safest airplane in the world. It can just barely kill
- ❖ And remember, a closed mouth gathers no foot.

ALOHA AND KEEP THE FAITH — rts■

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



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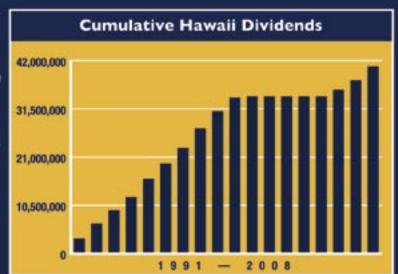


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