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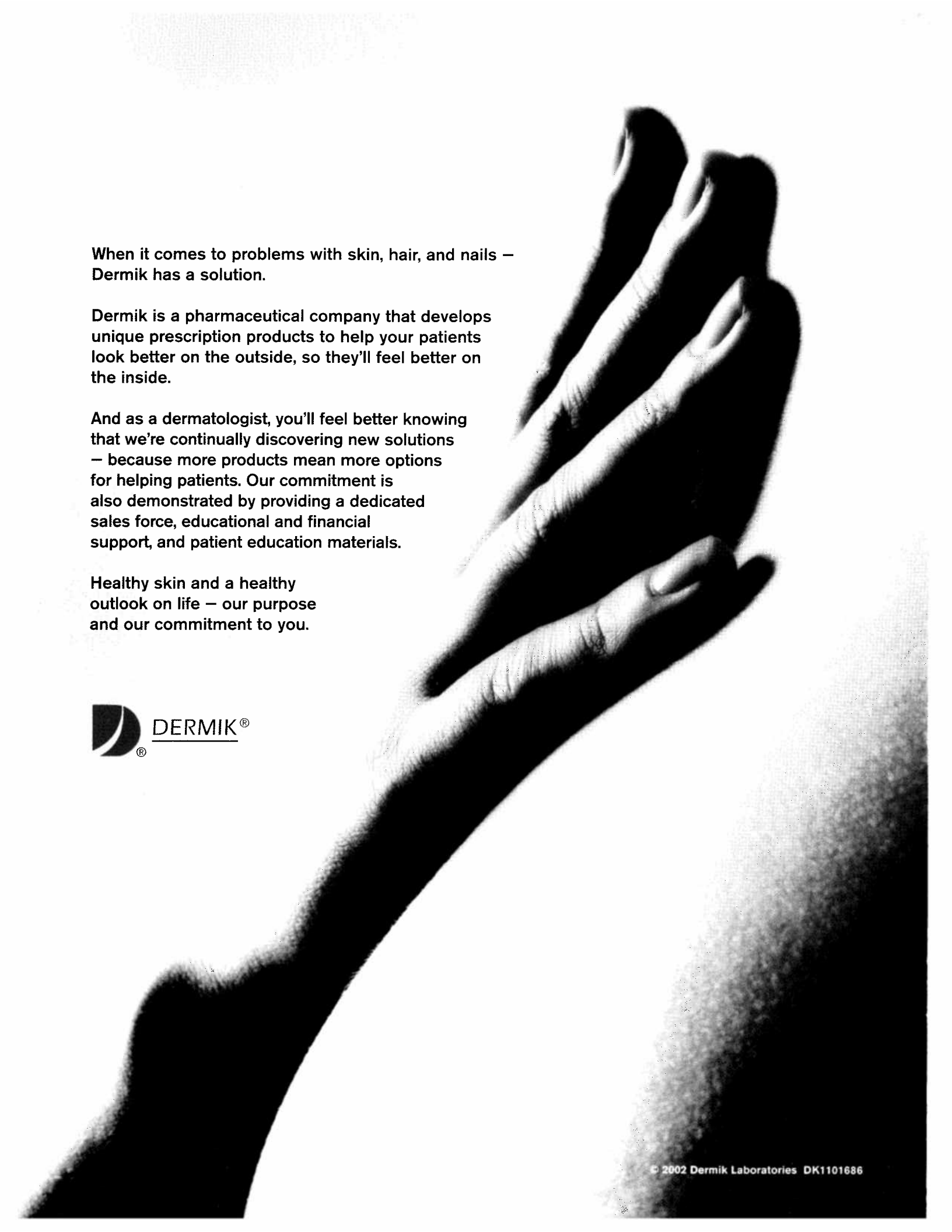
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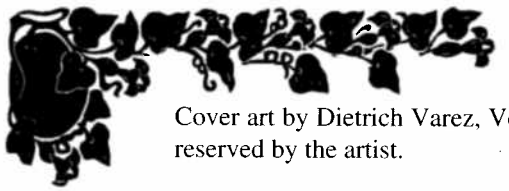
Contents



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Laka

Laka is the goddess of the hula.

Editorial

Norman Goldstein MD
Editor, Hawaii Medical Journal

Report to the Hawaii Medical Association Hawaii Medical Journal Annual Meeting October 2002

The Journal has had its best year in 2001. Despite an economic downturn, in part because of the events of 9/11, our published manuscripts as well as our advertising revenue have been excellent. Many thanks to our national advertisers, their local representatives and Michael Roth, the Journal advertising executive.

We published 35 manuscripts and two Special Issues on Alternative Medicine (October and November 2001). Mahalo to the staff of the Hawaii Medical Journal for once again preparing our yearly index.

In addition to our regular columns, *News and Notes* by Henry Yokoyama MD, and *The Weather Vane* by Russell Stodd MD, we added the *Cancer Research Center Hotline* and the *Medical School Hotline*. Sincere appreciation is extended to Doctors Ann Catts, Drake Will, and Al Morris for editing the manuscripts; to Dietrich Varez, our cover artist for keeping us looking so good; to Drake Chinen, our editorial assistant for keeping us on time; and to my wife, Ramsay, for keeping my editorials on point.

The Hawaii Medical Journal continues to be the main source of information about medical, clinical, epidemiological and research activities in our state, including coverage of the University of Hawaii Cancer Research Center, and our exciting, expanding Medical School.

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FAMILY MEDICINE

Dr. Aaron Kauhane's special interests include preventive medicine for all family members, native Hawaiian health, integrative medicine and sports medicine. Received Doctorate of Medicine from Western University of Health Sciences, College of Osteopathic Medicine of the Pacific, Pomona, Calif. Residency at University of Massachusetts Medical School, Worcester, Mass. (Straub Lanai Clinic)

HOSPITALIST

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Evidence Based Complementary Intervention for Insomnia

Hassan H. López PhD, Adam S. Bracha BA, and H. Stefan Bracha MD

Abstract

Increasing scientific evidence point to a non-pharmacological complementary treatment for insomnia: white noise. Its presentation has been shown to induce sleep in human neonates and adults, probably by reducing the signal-to-noise ratio of ambient sound. White noise may be a simple, safe, cost-effective alternative to hypnotic medication in many psychiatric disorders, especially acute stress disorder and PTSD.

Sleep dysfunction is common among people with acute stress disorder, posttraumatic stress disorder (PTSD), as well as most other mood and anxiety spectrum disorders, both in the primary care setting and in specialty clinics. Patients report difficulty falling asleep, are easily awakened, and may suffer from disturbing, unpleasant nightmares.[1] Indeed, two of the major symptom criteria for PTSD, re-experiencing and hyperarousal, are negatively related to sleep regulation.[2] Re-experiencing phenomenon may include intrusive thoughts and images of the traumatic event that prevent individuals from falling asleep and distressing nightmares that wake them. Similarly, enhanced arousal may lead to difficulty in falling asleep (perhaps due to hypervigilance), as well as increase the probability of nighttime awakenings provoked by an exaggerated startle response to external stimuli that do not penetrate the consciousness of normal individuals.

Primary care clinicians often prescribe hypnotics such as benzodiazepines, in addition to the pharmaceutical regimen directed at the underlying disorder, to psychiatric patients who suffer from insomnia. The difficulties and harm that can ensue from benzodiazepine administration are well documented. As such, there is growing interest in adjunctive and integrative biological approaches in medicine, and there may be safer alternatives that deserve greater research and clinical attention.

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One intriguing possibility is the controlled presentation of white noise, which may possess hypnotic properties. To date, only a few controlled experiments have tested the sleep utility of low-intensity, consistent auditory stimulation. White noise has been shown to effectively induce sleep in human neonates between the ages of two and seven days.[3] Eighty percent of those neonates exposed to white noise fell asleep within five minutes, compared to a spontaneous rate of 25%. Simulated music composed of white noise also induces sleepiness and higher delta component power densities (measured via EEG) in adult subjects, suggesting that it has the capacity to alter overall level of arousal and state of consciousness.[4] Another study tested the clinical effectiveness of white noise in a sample of postoperative coronary artery bypass graft (CABG) patients, following their transfer from an intensive care unit.[5] Subjects exposed to ocean sounds (composed of white noise) for three nights reported experiencing significantly better sleep, in terms of sleep depth, number of awakenings, ease of return to sleep, quality of sleep, and total sleep, when compared to subjects not given white noise treatment.

Presumably, white noise functions to reduce signal-to-noise ratio, and thus promote decreased arousal and prevent sleep interruption. Very simply, invariable, low-intensity auditory stimulation could mask the perception of normally disrupting nighttime noises, such as wind, car-alarms or voices. This could be particularly useful for victims of acute stress disorder and PTSD, by serving as an effective startle-prevention tactic. Interestingly, it has been shown that the presentation of white noise reduces norepinephrine concentration in the auditory pathways of rats.[6] Given this neurotransmitter's involvement in arousal, stress and the etiology of PTSD,[7] it is possible that white noise may have a direct therapeutic effect on certain stress-mediated disorders. For several years now, many PTSD experts in the VA healthcare system have been advising their patients to sleep with a fan on to induce sleep, and unpublished anecdotal reports from patients in the VA regarding the effectiveness of this simple suggestion have been encouraging. A more precise strategy would be the use of standardized, wide-spectrum white noise, currently available in CD format (www.whitenoisecd.com) as a complementary intervention for insomnia.[8]

Clearly, a prescription of white noise possesses strong advantages over benzodiazepines in terms of both safety and cost. We would like to suggest that more research be conducted on the effectiveness of white noise as a sleep-aid for psychiatric patients, as well as on the neurophysiological mechanism behind its potential function.

Continues on p. 213

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Report of the First Annual Hawaii Asthma Research Consortium

Debora S. Chan PharmD, Charles W. Callahan DO, Sheila Beckham RD, Gregg Kishaba, Kara Yamamoto MD, Francis J. Malone MD, Rodney Boychuk MD, Elizabeth Tam MD, Claude Jourdan-Lesaux PhD, George Underwood MD, Thomas M. Vogt MD, and Ernest Takafuji MD

The first Hawaii Asthma Research Consortium was held on 7 May 2001 at Tripler Army Medical Center. Researchers investigating asthma-related problems and program directors of asthma projects were solicited statewide to present their projects. Ten lecturers focused on research and asthma projects in Hawaii in 20-minute presentations. An informal ten-minute discussion followed each presentation to encourage audience questions about the project and to discuss possible collaboration efforts between institutions. The institutions that were represented include: American Lung Association-Hawaii, Kaiser Permanente Center for Health Research Hawaii, Kapiolani Medical Center, Tripler Army Medical Center, University of Hawaii at Manoa, and Waianae Coast Comprehensive Health Center.

Introduction

COL Ernest Takafuji, Tripler AMC

Presenters and attendees were thanked for their interest in the consortium. An interest to combine resources to better address asthma research in Hawaii was expressed.

Asthma in Hawaii: What are the Questions?

COL Charles Callahan, DO, Tripler AMC

How many people with asthma are there in Hawaii? Using the 2000 State population census report and a national asthma prevalence model the number of people with asthma in Hawaii was estimated at 101,000. Using a similar model 27,800 people were estimated to have mild intermittent asthma, 26,800 to have mild persistent, 45,400 have moderate, and 1,100 have severe asthma. This estimate puts over 73,000 people in Hawaii in need of chronic "controller" therapy.

How much does asthma cost in Hawaii? Cost estimates ranged from 127 to 296 million dollars per year and include both direct and indirect costs. The asthma admission rate for children has significantly decreased from 3.2/1000 in 1996 to 1.3/1000 in 2000 ($p<0.01$) at Tripler Army Medical Center (TAMC). This decrease is thought to be due to the focused asthma education provided to patients and health care providers using National Heart, Lung, and Blood Institute (NHLBI) Guidelines and increased patient access to a pediatric pulmonologist. Asthma education was primarily provided at TAMC via a pediatric asthma education service titled Military Community Asthma Program that was initiated in 1997 using a multi-disciplinary team that consisted of a pediatric nurse case manager, a clinical pharmacist, pulmonologists, and allergists.

Do primary care physicians use guidelines? In a survey of 244 primary care physicians in Chicago 88% reported that they had heard of The National Asthma Education and Prevention Program (NAEPP), 55% used spirometry in initial evaluation, 47% follow peak flows in patient, 24% referred for formal asthma education, and 48% provided written treatment plans.

Do asthma specialists adhere to guidelines? A survey of 113 allergists and pulmonologists revealed that 86% used inhaled corticosteroids in children less than 5 years old, 71% of patients with moderate/severe asthma received written asthma treatment and management plans (78% of allergists, 59% of pulmonologists), and patient home peak flow monitoring was utilized in 80% of patients of allergists and 58% of pulmonologists.

Which patients know about asthma? In an asthma survey of 568 Chicago residents women had more correct responses than men and younger respondents scored higher than older ones. Other factors that influenced scores of the survey were higher educational level, racial differences, zip code and income.

Why gather together? The purpose of meeting today is to determine what questions are being answered, or need to be answered, what resources are available in the community, and what funds are available. Other relevant issues include the advantages of partnerships and deciding where do we need to go from here.

Electronic Children's Hospital of the Pacific (ECHO-Pac): Asthma Intervention Initiative

COL Charles Callahan, DO and Francis Malone, MD , Tripler AMC

ECHO-Pac is a transpacific teleconsultation project for pediatricians from sites in Guam, Okinawa, Korea, and Japan to subspecialists in Hawaii. Asthma management was used as a model to demonstrate the effectiveness and cost-efficiency of the telemedicine consulta-

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HOSPITALIST

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INTERNAL MEDICINE

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Dr. Robert Y. Shaw is Board Certified in Internal Medicine. His special interests include screenings and preventive medicine for both men and women, sports medicine, tendinitis and bursitis injections and dementia consultations. Dr. Shaw received Doctorate of Medicine from Albany Medical College, Albany, N.Y. Residency at University of Hawaii John A. Burns School of Medicine. Fellowship in Geriatric Medicine from Oregon Health Sciences University, Portland, Ore. Bachelor of Arts in Anthropology from Stanford University. (Straub King Street Clinic)

ONCOLOGY/HEMATOLOGY

Dr. Galen Choy is Board Certified in Hematology / Oncology and Internal Medicine. Received Doctorate of Medicine from St. Louis University, St. Louis, Mo. Residency at University of Texas, Southwestern Medical Center, Dallas, Texas. Fellowship in Hematology / Oncology at Memorial Sloan-Kettering Cancer Center, New York, N.Y. (Straub King Street Clinic)

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tion service. It is a web-based, store and forward consultation system. The consultant has a combination of free text and pull down menus to complete the history and physical, and demographic sections. There is also the capability to attach radiographs (if indicated), spirometry and a video clip of the patient's metered-dose inhaler (MDI) + spacer technique. The completed consult is reviewed by a pediatric pulmonologist and feedback given to the referring provider via the e-mail option built into ECHO-Pac. Of the 28 patients enrolled: one patient had mild intermittent, nine had mild persistent, fifteen had moderate persistent, and three had severe persistent. Patients are seen at pre-assigned intervals (initiation, 2, 6- weeks, 3-, 6-, and 12-months). At each visit an assessment of skills and knowledge is performed and a personalized asthma action plan is distributed to the family. Quality of life surveys are performed by the patients virtually via the web site at all visits except for the 2-week visit and a satisfaction survey is performed at the last visit. Outcome data are in the process of being analyzed.

In-Home Telemonitoring of Children with Asthma

Debora Chan, PharmD and COL Charles Callahan, DO, Tripler AMC

The purpose of Telemedicine In-Home Monitoring Evaluation-Pilot (TIME-P) project is to demonstrate the feasibility of in-home asthma monitoring for children with persistent asthma. Study objectives are to demonstrate the feasibility of in-home asthma monitoring for children with persistent asthma using Internet-based store and forward technology and to evaluate software, hardware, and cameras of commercially available computer systems.

All patients will be loaned identical computers, video cameras, and provided Internet access. Patients will videotape peak flow meter readings prior to medication use and metered dose inhaler use two times a week. This information will be recorded and forwarded to the clinical pharmacist case manager for review and response. All patients will be followed in-person in the Pediatric Clinic at intake, 2-, 6-weeks, 3- and 6-months after enrollment. The pharmacist will provide asthma education to five patients in-person in the Pediatric Clinic during their follow-up visits. The remaining five patients will receive their asthma follow-up education visits via the web site at the same intervals.

A variety of different outcome parameters will be assessed. These include measurements of adherence and disease control. Treatment regimen adherence was assessed by several aspects of therapeutic and diagnostic monitoring. Therapeutic monitoring includes controller medication use (by computerized prescription refill record) and adherence and technique score from the dry powder inhaler (DPI) or metered-dose inhaler (MDI) + spacer video. Diagnostic monitoring includes asthma symptom diary completion, adherence to video taping of peak flow use two times a week, and peak flow technique scores. Disease control measures include: peak flow values (percent of personal best), utilization of services (ED visits, hospitalizations, unscheduled acute clinic visits), rescue therapy use (beta-agonist use and refills, and steroid bursts), symptom control (symptom free days and diary symptom score).

TIME-P will serve as the first step for a larger trial of Internet case management of children with asthma. This project is supported by a grant from U.S. Army Medical Research Activity.

Asthma Programs in Our Community

Gregg Kishaba, American Lung Association-Hawaii

The Windward Oahu Asthma Coalition (WOAC) was first established in 1999 to improve asthma awareness among the windward community. WOAC was established as a result of efforts by the State Health Planning and Development Agency's data-driven health priorities for Windward Oahu. The main goal of the coalition is to improve the health of asthmatic windward-area school aged children (5-12 years old) through collaborative private-public agency program implementation, promotion and outcomes measurement. Meetings are held every second Monday of the month at 5:30 p.m. at the Castle Medical Center Auditorium.

Hanocare is an asthma management program of the Queens Physician Group, which is led by Carl Hallenborg, MD. The first meeting was held on January 13, 1998. Hanocare follows the National Heart, Lung, and Blood Institute treatment guidelines for the treatment of asthma and focuses on familiarizing physicians with these guidelines and provides ongoing continuous medical education programs. Hanocare also focuses on patient education programs. Last year Hanocare offered statewide spirometry testing and pulmonary function testing of high school seniors. The program was conducted at 12 high schools statewide in an effort to collect baseline PFT's in Hawaii.

Partners Against Asthma (PAA) was established in November 2001. The goal of the coalition is to reduce the negative consequences of asthma among Hawaii's children from birth to 12 years of age. The coalition is made up of four work teams: Data/Evaluation, Educational Materials, Educational Outreach, and Educational Training. The Advisory Council meets quarterly while the Working Teams meet monthly. The objectives of PAA include to: increase the early identification of childhood asthma through family education, particularly among the families of children who are poor and of Hawaiian heritage; reduce the severity of asthmatic episodes and its impact on overall child well being through the promotion of disease management education; and improve the data collection and reporting system relating to asthma among Hawaii's children.

Dyson Project: Asthma in Community Pediatrics

Kara Yamamoto, MD, University of Hawaii School of Medicine

The Dyson initiative is a five year grant awarded to the University of Hawaii School of Medicine's Department of Pediatrics under principal investigators Louise Iwaishi, MD and D. Christian Derauf, MD. The initiative allows for further development of the residency training curriculum in community pediatrics in the areas of: child welfare, mental health, children with special health care needs, school health and early childhood. The goals of the project are to equip pediatric residents with the tools and knowledge to become future professionals committed to improving the health of children in their community, expose pediatric residents to their communities using local community resources, provide didactic and experiential opportunities in advocacy and assessment of community goals, strengths and needs, develop meaningful partnerships between academic departments of pediatrics with community-based organizations in their regions, and enhance pediatric training through interdisciplinary collaborations with other schools and university departments.

The impact on pediatric resident training in the area of chronic

illness/CSHCN was identified as acquiring knowledge and skills necessary for comprehensive, interdisciplinary, and culturally effective primary care management for these children in the community setting both home and school. Management would include technical needs, e.g. tracheostomy and gastrostomy, interacting with important community based organizations and services they provide, gaining experience in assessing the needs of the community, and working with organizations and other health care professionals in the community.

Medically fragile children who may be technologically dependent (PICU, NICU), children with chronic illness in the ambulatory setting (asthma, rheumatic disease), and premature infants are potential beneficiaries of the program. Resident training experiences such as attending supervised home visits and rural outreach clinics, family-based interactions for identifying needs and challenges, developing culturally effective management and discharge plans with interdisciplinary team (includes hospital and community providers), presenting didactic sessions and writing handouts on specific management issues or conditions are coordinated by the faculty. The Community Based Organization (CBO) based training experiences include: home and school visits with public health nurse, assisting with coordination of care and communication with the child's primary care physician and other care providers in the community, and accessing specific resources in cross-cultural effectiveness for help with specific families. Asthma specific community based training experiences include: assessing school/community health center needs in asthma screening and education, providing educational program for CBO and the community, assisting with coordination of care and communication with the child's primary care physician and other care providers in the community, and developing culturally effective educational materials for families.

The value and benefits of the program are linkage of CBO to primary care providers and specialists, enhanced coordination and access to care, educative consultation, facilitated and coordinated linkages to other CBOs. The impact on child health were described as improved interdisciplinary coordination of care and communication in the community, increased support for CBOs, increased access to care for families, improved outcomes for all children with special needs/chronic illness, provide skilled and knowledgeable PCPs, maximize efforts of interdisciplinary, culturally competent approaches.

Clinical and Economic Outcomes (CEO): Asthma Management

George Underwood, MD, Tripler AMC

In the fall of 2000, the Clinical Economics Outcome (CEO) web-based computer program became available to the practitioners at Tripler Army Medical Center. This is a web-based interface to a Microsoft SQL Server data warehouse. The CEO is populated with data from Tripler Army Medical Center's major medical information system, the Composite Health Care System, and the Ambulatory Data System record of ICD9 and CPT4 coded outpatient visits. The specific capability for coding of patients with asthma by severity, performance of spirometry and analysis of medication use is made possible through these systems. In May 2001, the capability to generate provider specific reports was established. Sample reports presented include the ability for the Primary Care Manager (PCM) to quickly pull up a list of their asthmatic patients (based upon the patient's problem list), the identification of their persistent asthmatic patients who are not on controller medications, which of their patients have not had asthma education, and the cost of the standard asthma medications. PCMs can also look at the medication refill compliance of their patients. In addition, the Department Chief can review the data for all the PCMs within their clinics.

Genetics of Asthma in Hawaii

Elizabeth Tam, MD, University of Hawaii

Genetic determinants of asthma in Hawaii were evaluated by characterizing subjects and their families with asthma. Ethnicity of study population, ethnic distribution in Hawaii, skin test reactivity, serum tryptic activity, circulating eosinophils, bronchial obstruction at baseline, bronchial reactivity, and IgE level for asthma and non-asthma patients were reported.

Genetic determinants of asthma were also evaluated by studying genetic markers previously associated with asthma traits. Human airway epithelium and fibrosis were described as modulation by airway inflammatory proteases processes which include: inflammatory proteases hydrolyze collagen type IV and other proteins of the basement membrane, modulation of CGRP-mediated epithelial proliferation, and promoting lung and airway fibroblast proliferation and collagen deposition.

Immunogenetic diseases provide a mentoring milieu and support for hypothesis-driven projects which examine immunologic conditions that disproportionately affect Pacific Islanders; such as, asthma, systemic lupus erythematosus, and acute rheumatic fever. Also of consideration in Hawaii are the respiratory effects of volcanic air pollution. Future study efforts will develop community research infrastructure, estimate chronic exposure of school children using archival air monitoring data, historical weather patterns, volcano emission rates, and concentration of PM2.5 and SO2. Endpoints include cross-sectional analysis of school children and a longitudinal study of school children to determine differences in lung growth rates

The Progression from Allergic Inflammation to Airway Remodeling in Asthma

Claude Jourdan-Lesaux, PhD, University of Hawaii

The progression from allergy to airway remodeling begins with acute inflammation, then progresses to chronic inflammation, and finally to remodeling of the airways. The goals of the research are to identify immunologic mediators and genetic determinants of susceptibility in asthma and to identify extracellular matrix protein gene response, analyze fibrotic response, and characterize potential apoptotic effect in airway remodeling. Preliminary data suggests that symptoms of allergy are determined by skin test and IgE levels while symptoms of asthma are of obstructive and hyper responsiveness.

The research is supported by Hawaii Community Foundation Medical Funds, Clinical Research Center, National Institutes of Health (Research Centers in Minority Institutions Program, Selective Research Excellence in Biomedicine and Health), and the American Lung Association.

Community-Based Asthma Management

Sheila Beckham, RD, MPH, Waianae Coast Comprehensive Health Center

The Waianae Coast Comprehensive Health Center (WCCHC), located on the rural leeward coast on the island of Oahu, implemented a community-based asthma management project that improved health care utilization patterns and quality of life among asthmatic children between the ages of 3 and 14 years.

The WCCHC is the largest service provider to Native Hawaiians in the State, where the prevalence of asthma exceeds State rates. During 2000, 806 children under 14 years of age presented at WCCHC for medical care with a diagnosis of asthma. Seventy-four percent of these children were Medicaid/Medicaid Managed Care (QUEST), or uninsured. A review of utilization patterns among those managed care patients that incurred the most charges and most encounters over a period of 1 year revealed that less than 5% of total patients were responsible for 25% of the charges. Children with asthma represented a high percentage of these utilizers. The WCCHC piloted an integrated community-based asthma management project in an effort to reduce inappropriate medical utilization and improve quality of life, targeting 50 children between 3 and 14 years of age diagnosed with asthma. The objectives were to develop an electronic identification and tracking system, coordinating asthma management through team care, and obtaining consensus for evidence-based clinical decision guidelines among providers. The asthma management project was implemented primarily by community health workers through home visitation. During the home visit an assessment was made of the environment, knowledge, and self-management skills. Individual prevention and management education was provided during multiple visits.

After the first year of the project, emergency department utilization among the children participating in the project decreased from 57 to 11 visits. Total asthma related visits decreased from 83 prior to educational intervention to 20 after at least one educational encounter. Total asthma-related charges dropped, with 81% incurred prior to educational intervention and 19% after an educational encounter (46% of these charges were incurred by two individuals). Ninety-six percent reported fewer daytime symptoms and 72% fewer nighttime symptoms as a result of participation in the program.

The project has been well received and is being used as a model in a number of other community-based asthma projects and is supported by a grant from Hawaii Medical Service Association (HMSA) Foundation.

Asthma Demonstration Projects

Rodney Boychuk, Kapiolani Medical Center

Prior attempts in 1993 at collaborative approach to pediatric asthma management and problem identification in Hawaii were presented. Research funding possibilities with Robert Wood Johnson Foundation for managing pediatric asthma were discussed. Several published studies from Hawaii researchers were provided. The focus of these research projects was in pediatric patients with asthma receiving treatment in the emergency department. Study topics included: effect of environmental factors and/or dispensing of home nebulizers on asthma outcomes and problem identification via pulse oximetry in wheezing children.

Shared Decision-Making and Asthma Outcomes

Abstract submitted by Thomas M. Vogt, MD, MPH, Kaiser Permanente Center for Health Research Hawaii

Only about half of patients with persistent asthma adhere to prescribed long-term controller medications. One way the improve this record is to involve patients more in decisions about their treatment. This study is a 5-year project to develop and evaluate the effectiveness of a new model of clinician-patient interaction, shared decision-making, in improving outcomes in adults aged 18-70 years with suboptimally controlled, mild to moderate persistent asthma. The shared decision-making model will be compared in a randomized, controlled clinical trial to a model based on national asthma guidelines, and to usual care. Primary outcomes will be asthma control, adherence, symptom-free days, lung function, dispensing of asthma medications, satisfaction with asthma care, asthma-related costs, and total asthma-related health care utilization.

The project, directed by Sonia Buist, MD of the Oregon Health Sciences Center, will be carried out in three clinical sites–Kaiser Permanente Hawaii (T. Vogt, MD, Principle Investigator (PI), Christine Fukui, MD, Co-PI), Northwest Kaiser Permanente, Portland, OR (S. Buist, MD, PI), and Northern California Kaiser Permanente (S. Wilson, PhD, PI).

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Acute Myocardial Infarction and Friedreich's Ataxia

Arvind K. Sharma MBBS, Miki Kiyokawa MD, Edward T. Kim MD, MPH, David T. Lee DO, FACC, and Richard Kasuya MD

Abstract

While cardiac disease is noted in 90% of patients with Friedreich's ataxia (FRDA), the finding of coronary artery disesase is unusual. To the best of our knowledge only two cases of acute myocardial infarction (AMI) has been reported in patients with FRDA. Large vessel CAD has not been reported previously in patients with FRDA. We report a young patient with AMI and obstruction of large epicardial arteries.

Introduction

Friedreich's ataxia (FRDA) is an autosomal recessive neuromuscular disorder characterized by spinocerebeller ataxia, loss of tendon reflexes and skeletal deformities. Its association with heart disease has been known since Friedreich's first description in 1863 and is now believed to be present in 90% of patients.[1-3] The most common cardiac pathology is left ventricular hypertrophy.

Coronary artery disease (CAD) is distinctly unusual with autopsy studies demonstrating only small vessel abnormalities. The functional significance of these have been challenged.[3] To the best of our knowledge only two cases of acute myocardial infarction (AMI) have been reported in patients with FRDA,[4,5] though few reports have alluded to suspected cases.[2,5,6] Large vessel CAD has not been reported previously in patients with FRDA. We report a young patient with AMI and obstruction of large epicardial arteries.

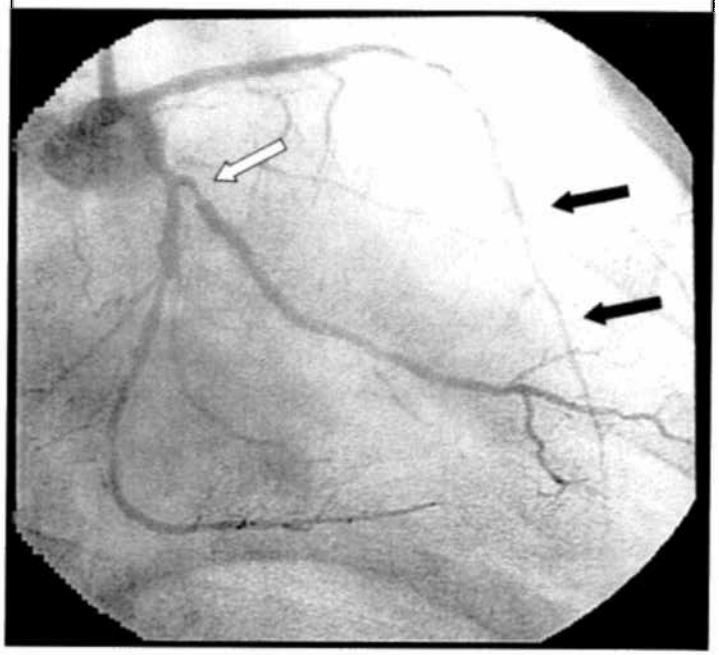
Case Report

A 35-year-old Caucasian male with FRDA presented for evaluation of chest pain. In childhood he was noted to be slow and clumsy in motor activities such as running and throwing. At age nine, he had bilateral pes cavus corrected surgically. As a teenager, he fell frequently and had difficulty ambulating. He has been wheelchair-bound since age 20. Over the past year, increased upper extremity weakness and incoordination has been noted. Genetic testing had confirmed him to be homozygous for FRDA.

Over the last two years, he experienced intermittent, retrosternal chest pain which was exacerbated markedly eight months prior to evaluation. He then presented to the emergency room with abrupt onset of severe, crushing retrosternal chest pain with radiation to left arm. This was associated with acute onset of dyspnea and diaphoresis. He did not have diabetes mellitus or hypertension and denied use of alcohol or smoking. Family history for premature coronary artery disease was negative. The most recent lipid profile was as follows: total cholesterol 156 mg/dl, triglyceride 238 mg/dl, HDL 26 mg/dl, and LDL 82 mg/dl. Homocysteine level was 19 μmol/L.

On physical examination, the patient was noted to be a well-developed, dysarthric caucasian male in no acute distress. Vital signs revealed blood pressure of 120/60, heart rate of 100, respiratory rate 18 and he was afebrile. Cardiovascular examination revealed normal heart sounds, a non-displaced PMI and no murmurs

Figure 1.— The right anterior oblique view of the left coronary artery angiogram showing a diffusely narrowed left anterior descending artery (black arrows) without focal abnormality and a small diagonal branch with a 60% proximal lesion. Circumflex artery had a 60% segmental occlusion and a large obtuse marginal branch (culprit vessel) with 90% proximal stenosis (white arrow).



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or features of heart failure. Musculoskeletal examination was significant for pes cavus, hammer toes, and feet inversion. He was areflexic and had loss of proprioception and vibration sensation in lower extremities. He had dysmetria with poor coordination bilaterally and Grade 2/5 lower extremity muscle strength with bilateral extensor plantar response.

EKG changes were consistent with acute infero-lateral MI and the cardiac injury markers confirmed this. His peak troponin I was 46 ng/ml (n<2.0). Echocardiogram done urgently showed apical and inferior hypokinesis and left ventricular hypertrophy (LVH) with wall thickness of 1.8 cm. Cardiac catheterization revealed a diffusely narrowed left anterior descending artery (LAD) without focal abnormality. The diagonal branch was small with a 60% proximal lesion. Circumflex artery had a 60% segmental stenosis and the large obtuse marginal branch with 90% proximal stenosis was believed to be the culprit vessel. A 40% stenosis of the distal right coronary artery was noted. Left ventriculogram showed severe hypokinesis of left ventricular apex and an ejection fraction of 40%. Percutaneous transluminal coronary angioplasty with stent placement of the obtuse marginal vessel was done successfully with TIMI grade III flow. Patient was placed on clopidogrel, aspirin, and metoprolol.

A month later, he was re-admitted for an acute non-Q wave MI with a peak troponin I of 47 ng/ml. Subsequent cardiac catheterization revealed acute occlusion of the stented vessel and the ejection fraction was 35%. Coronary artery bypass was then performed successfully using saphenous vein grafts to the two obtuse marginal branches sequentially, and to the diagonal branch of LAD. During the subsequent month, he developed recurrent chest pain with several hospitalizations necessitating a cardiac catheterization, which revealed complete occlusion of the obtuse marginal graft and 60% occlusion of the graft to the diagonal branch of LAD.

Stress thallium scan showed a large non-reversible perfusion defect involving the lateral, inferior wall and apex of the left ventricle. He was managed conservatively with aspirin, warfarin, metoprolol, quinapril, atorvastatin, folic acid and multivitamins.

Discussion

Cardiac involvement is noted in 90% [1-3] of patients with FRDA and has been studied extensively using EKG,[7,8] cardiac catheterization,[9] echocardiography,[10-12] radionuclide studies,[13] and autopsy series.[2,3,5,14]

The main feature of heart disease associated with FRDA is concentric LVH,[10-12] but asymmetrical septal hypertrophy and left ventricular outflow tract obstruction [9] may also occur. In some cases, cardiac features precede neurological manifestation.[15-17] Symptoms such as chest pain, palpitations and dizziness occur in the minority of patients. However, in Hewer's series 12% had angina and 73% had cardiac symptoms before death.[5] They often have arrhythmias, syncope and sudden death. For these reasons, coronary disease has been suspected for many years. However, most reviews and reports on this subject dismiss the coronary lesion as not functionally significant, largely on the basis of Hewer's interpretation.[3] He found that only 9% of the 900 arteries had a reduction in the luminal diameter by 50% and concluded that it was not responsible for the extensive muscle fibrosis that was observed. Rather, he believed these coronary lesions to be a secondary phenomena. The narrowing of coronary arteries is, however, not described in other muscular dystrophy with myocardial involvement and has not been observed in myocardial fibrosis of other etiology.[2] Though he reports on 27 cases, histological specimens were available in only 16 cases. Only three complete hearts were available to him and 100 sections each of 30um could not have examined the entire 100mm coronary artery. It is possible that the incomplete histopathologic study of the coronary arteries described in these studies may have obscured this finding from the investigator.

James et al. demonstrated small coronary artery occlusions caused by focal fibromuscular dysplasia, intimal proliferation, medial degeneration and fibrosis.[18] Positive acid-Schiff deposits are noted in the subintima and resemble amyloid. However, specific staining for amyloid, fat and fibrin has been consistently negative. Involvement of large coronary artery has been noted in few cases.[18-20] Nadas et al. went on to suggest that CAD might be responsible for myocardial damage in FRDA. A thallium stress imaging reported by Casazza et al. demonstrated perfusion defects in three of the thirteen asymptomatic FRDA patients with LVH.[21] Angiographic studies were limited by the use of non-selective coronary catheterization. Since the inception of selective coronary artery angiography in 1958,[22] no explicit reference has been made to coronary vessels in FRDA patients.

In Hewer's study of 82 fatal cases of FRDA, four patients were clinically diagnosed with MI, of these one had a confirmed diagnosis at autopsy. Calvo et al. reported a case of AMI involving microvascular disease and spasm of coronary arteries.[4] No other confirmed cases of MI in FRDA have since been reported. Our patient had an acute myocardial infarction and left ventricular hypertrophy. On coronary angiography the culprit lesion was determined to be a proximal stenosis of a large epicardial vessel. In view of the above deliberations we believe that the finding of acute myocardial infarction and large vessel coronary artery disease in our patient raises the possibility of cause and effect, however his lipid abnormality and hyperhomocysteinemia could be alternate explanations.

The pathogenetic mechanisms leading to myocardial infarction in our patient may be multifactorial. Multiple case reports [3,5,6,15,23] make reference to thrombus formation in the heart chambers. In Hewer's autopsy series, twelve out of twenty seven patients showed thrombus formation, of which four cases presented with thrombosis in the heart and in a major artery including the left middle cerebral and the superior mesenteric artery.[5] Our patient showed thrombosis of stent and later occlusion of the grafts. Thrombosis may have been the primary cause of the cardiac lesion in this patient, and certainly played a significant role once the endothelium was disrupted by these procedures. Vasospasm was reported as one of the mechanisms causing angina.[7] However, the role of this process in our patient is difficult to determine. His lipid abnormality and hyperhomocysteinemia could be added explanations as noted in the general population at large. There are no reports of homocysteine abnormalities in patients with FRDA. Diabetes mellitus is noted in 10-23% of the FRDA patient,[1,5] but was not present in our case.

Left ventricular hypertrophy is prevalent in FRDA patient and may have a direct or an indirect impact on mortality. LVH is independently associated with increased incidence of cardiovascular disease and cardiovascular mortality.[24] Diminished coronary vasodilator reserve, increased myocardial oxygen demand, subendocardial ischemia, lethal arrhythmias, and diminished ventricular

performance may explain the increased risk associated with left ventricular hypertrophy.[25] In a meta-analysis of 39 randomized double blind clinical trials performed through June 1995, the use of angiotensin-converting enzyme inhibitors, calcium-channel blockers, diuretics, or b-blockers was associated with respective reductions in left ventricular mass of 13%, 9%, 7%, and 6%.[26] This prominent effect of ACE inhibitors on left ventricular hypertrophy regression may reflect their action on local renin-angiotensin system in addition to the effective blood pressure control. This theory is further supported by the evidence that angiotensin II exerts direct trophic effect on myocardial cells [27]. Although the use of these agents and their impact in FRDA patients is not specifically reported, it is likely to be beneficial.

Recent advances have improved the understanding of FRDA at a molecular and genetic level. Chamberlain et al. localized the gene for FRDA to chromosome 9 q13 in 1988.[28] In 1996, Campuzano et al. discovered the FRDA gene, which is an intronic GAA triplet repeat expansion.[29] This led to an accurate genetic testing for this disease. Researchers showed that frataxin, the protein encoded by FRDA gene, [30] is an iron transporter protein in mitochondria.[31] Babock et al. found that the shortage of this protein in yeast cells led to a toxic build up of iron in the mitochondria. When excess iron reacted with oxygen, free radicals were produced leading to cell destruction.[31] This syndrome of ataxia and neuropathy, in association with diabetes, cardiomyopathy, deafness and optic atrophy, has all the hallmarks of a mitochondrial disease. Hence, FRDA may very well turn out to be the commonest mitochondrial disease.[1] Further investigation in this area may result in the development of an effective treatment for this condition.

Currently, there is no cure for FRDA, and cardiac disease remains the primary cause of death.[5,7,15] Median survival is 35 years.[5] Our patient, 35 years of age, presented with AMI involving large epicardial vessels. To our knowledge, this has been demonstrated for the first time angiographically in a patient with FRDA. Improved awareness and early intervention may significantly affect the outcome. With recent advances in diagnosis and possibly treatment of FRDA, we anticipate a larger number of patients to live longer. The impact of premature coronary artery disease may become more relevant; thus, it may be appropriate to evaluate for coronary artery disease in these patients. In addition, the role of left ventricular hypertrophy and thrombosis in these patients needs to be studied further.

Authors

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Continued on p. 212

Residents' Case Series

A 16-Year-Old Female Presenting With Coma and Hypertension

Christian Spies MD, Resident in Internal Medicine, University of Hawaii John A. Burns School of Medicine, Internal Medicine Residency Program and Shiuh-Feng Cheng MD, Assistant Professor of Medicine, Consultant in Nephrology, University of Hawaii John A. Burns School of Medicine, Department of Internal Medicine

A 16-year-old Vietnamese female was admitted to the hospital with new onset generalized tonic-clonic seizures and loss of consciousness. She was in her usual state of good health until the day prior to admission when she developed an acute severe occipital headache. The following night, she was found having generalized tonic-clonic seizure activity for three minutes. After she arrived in the emergency room, she had two further episodes of seizures which were terminated with diazepam. She was started on valproic acid intravenously and was intubated for airway protection. Hypertension required treatment with repetitive doses of intravenous labetalol.

The patient had no significant past medical history as she had no known illnesses and had never been hospitalized. Her past medical history was also unremarkable for surgeries, medications, and allergies. She was a high school student living with her parents and never smoked, drank alcohol, or used illicit drugs. Her father had hypertension and diabetes mellitus, but the family history was negative for any seizure disorders or congenital neurological disease.

Physical examination revealed a well developed female, who was comatose. She was intubated and supported on mechanical ventilation. She was afebrile, had a blood pressure of 200/110 mmHg, a heart rate of 120 beats per minute, and a respiratory rate of 14 breaths per minute by controlled ventilation. The skin showed no neurocutaneous stigmata, the heart was regular in rate, without murmurs, and the peripheral pulses were strong bilaterally. The neurological exam revealed a comatose patient withdrawing to painful stimuli and moving all extremities. The pupils were equal at 3mm and sluggish to direct light, the dolls eyes and corneal reflex was absent and there was no reaction to cold caloric testing. No posturing was noted. Reflexes were equal bilaterally 2+ and the Babinski reflex was present bilaterally.

Laboratory evaluation revealed a sodium of 136 mEq/L (135-145), potassium 3.2 mEq/L (3.5-4.5), Chloride 98 mEq/L (95-105), Bicarbonate 25 mEq/L (22-32), creatinine 0.5 mg/dl (0.6-1.4), and BUN 12 mg/dl (8-18). The CBC revealed a leucocyte count of 16.9×10^9/L with no left shift, a hemoglobin of 11.1 g/dL, and platelet count and coagulation studies were within normal limits. Drug screening and serum alcohol level were negative.

She immediately underwent CT scanning of her head which revealed a faint amount of blood within the right Sylvian fissure, consistent with a subarachnoid hemorrhage. A lumbar puncture was performed which revealed a slightly blood tinged cerebrospinal fluid with an opening pressure of 235 mm CSF fluid. The CSF cell count revealed a significant RBC count of 3820/µl (<1) and a WBC count of 3/µl (0-10). Glucose level in the CSF was 70 mg/dL (40-80) and total protein in the CSF was 27 mg/dL (15-45). Subsequently, she underwent cerebral angiography which demonstrated mild vasospasm of the branches of the right middle cerebral artery, but no aneurysm or arterio-venous malformation. She was transferred to the ICU, where she received supportive care and standard treatment for subarachnoid hemorrhage, including nimodipine and labetalol.

After a few hours she regained consiousness and became awake, alert, and cooperative. She was extubated on the day of admisson. She slowly recovered from the postictal state with a residual right sided nystagmus on left gaze which resolved within three days. She remained hypertensive despite regular dosing of an oral beta blocking agent with occasional symptomatic blood pressure peaks of 220/110 mmHg. Further evaluation consisted of an MRI and MRA of the head which confirmed the small subarachnoid hemorrhage and the abscence of an aneurysm. No stenotic lesions of the carotid or basilar arteries were seen and no residual vasospasm was noted. However, the MRI revealed evidence of hypertensive encephalopathy. Although the EKG fulfilled the Sokolow-Lyon voltage criteria for left-ventricular hypertrophy, an obtained echocardiogram showed a normal left ventricular wall thickness.

Workup for secondary hypertension was initiated. A 24 hour urine collection revealed normal metanephrine and urine vanillylmandelic acid levels. The renin plasma activity was elevated with a value of 35 ng/ml/hr (0.2-1.6). Aldosterone was 19.8 ng/L (10-160) while ANA, ANCA and RA factor were within normal limits. A radionuclide renal scan with captopril was performed. The scan showed a regular glomerular filtration rate (GFR) at 97.6 cc/minute (128.8 cc/minute/1.73 m^2) and a moderately diminished GFR after application of captopril at 57.2 cc/minute cc/min (75.5 cc/minute/1.73 m^2). A split-function analysis showed a right GFR of 45.7 and a left GFR of 11.5, suggesting left renal artery stenosis and a normal right renal function.

Consequently, a renal artery angiogram with standby balloon angioplasty was performed showing severe bilateral stenosis of the proximal renal arteries (figure 1). This was thought to be due to fibromuscular dysplasia. A bilateral balloon angioplasty was performed, resulting in unsatisfactory angiographic results with persistently elevated trans-stenotic pressure gradients in both renal arteries; thus, endoluminal stents were deployed resulting in satisfactory flow rates with residual trans-stenotic pressure gradients of 3 mmHg and 5 mmHg, respectively.

Anti-hypertensive treatment with metoprolol was stopped the evening before the procedure. Post-procedural systolic blood pressures were ranging between 120 to 135 mmHg and diastolic blood pressures were 62 to 80 mmHg. The patient had no further seizure activity and was discharged one day after the percutaneous revascularization procedure in stable condition and taking one aspirin daily. Follow up after hospital discharge revealed no further seizures, headaches or hypertension.

Discussion

The patient's initial presentation with sudden onset of severe head-

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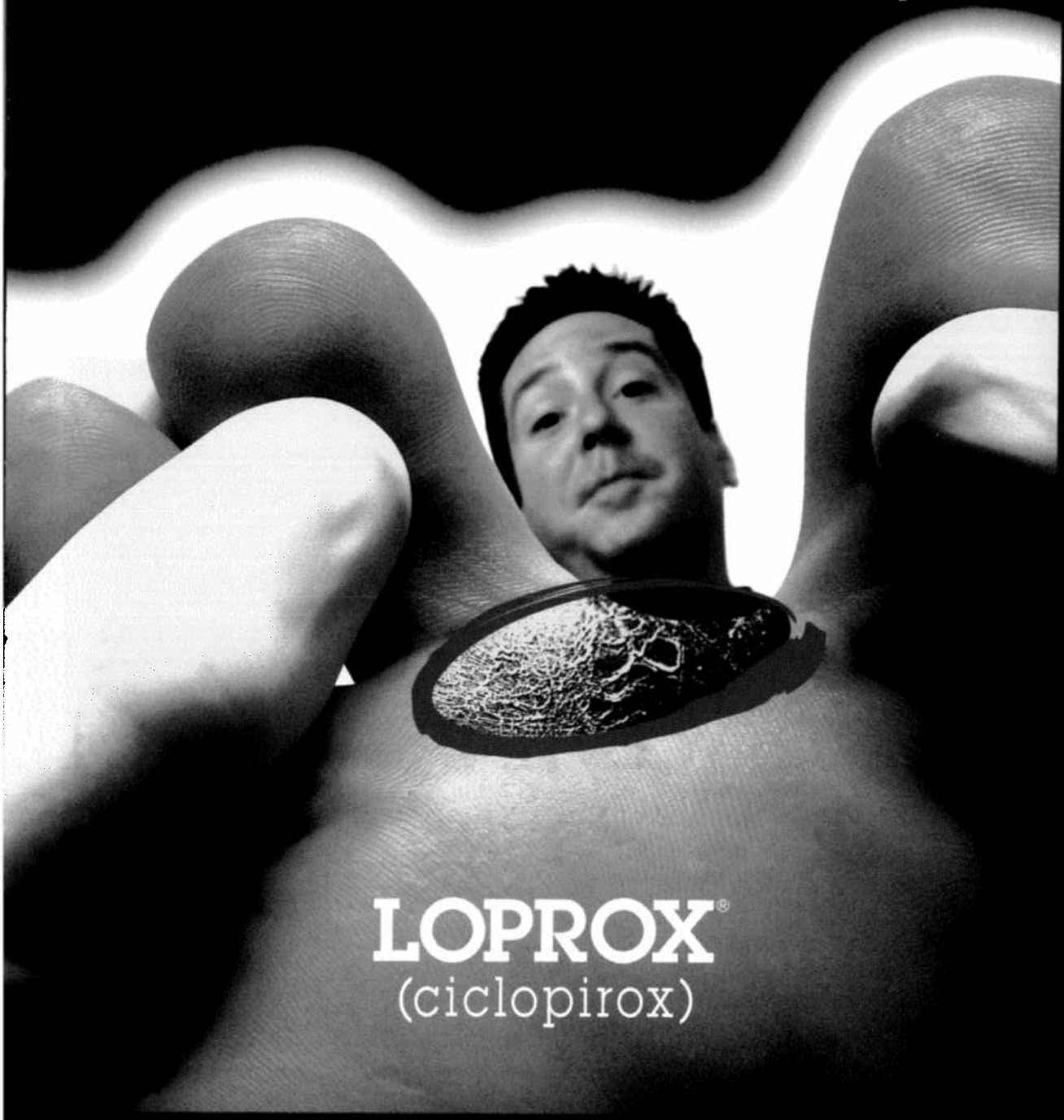

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Carcinogenesis, Mutagenesis, Impairment of Fertility: A carcinogenicity study in female mice dosed cutaneously twice per week for 50 weeks followed by a 6-month drug-free observation period prior to necropsy revealed no evidence of tumors at the application site. The following in vitro and in vivo genotoxicity tests have been conducted with ciclopirox olamine: studies to evaluate gene mutation in the Ames Salmonella/Mammalian Microsome Assay (negative) and Yeast Saccharomyces Cerevisiae Assay (negative) and studies to evaluate chromosome aberrations in vivo in the Mouse Dominant Lethal Assay and in the Mouse Micronucleus Assay at 500 mg/kg (negative). The following battery of in vitro genotoxicity tests were conducted with ciclopirox: a chromosome aberration assay in V79 Chinese Hamster Cells, with and without metabolic activation (positive); a gene mutation assay in the HGPRT-test with V79 Chinese Hamster Cells (negative); and a primary DNA damage assay (i.e., unscheduled DNA Synthesis Assay in A549 Human Cells (negative)). An in vitro Cell Transformation Assay in BALB/C3T3 Cells was negative for cell transformation. In an in vivo Chinese Hamster Bone Marrow Cytogenetic Assay, ciclopirox was negative for chromosome aberrations at 5000 mg/kg.

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WARNINGS: LOPROX Lotion is not for ophthalmic use. Keep out of reach of children.

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Information for Patients: The patient should be told to:

1. Use the medication for the full treatment time even though signs/symptoms may have improved and notify the physician if there is no improvement after four weeks.
2. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, oozing) indicative of possible sensitization.
3. Avoid the use of occlusive wrappings or dressings.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A carcinogenicity study in female mice dosed cutaneously twice per week for 50 weeks followed by a 6-month drug-free observation period prior to necropsy revealed no evidence of tumors at the application site. The following in vitro and in vivo genotoxicity tests have been conducted with ciclopirox olamine: studies to evaluate gene mutation in the Ames Salmonella/Mammalian Microsome Assay (negative) and Yeast Saccharomyces Cerevisiae Assay (negative) and studies to evaluate chromosome aberrations in vivo in the Mouse Dominant Lethal Assay and in the Mouse Micronucleus Assay at 500 mg/kg (negative). The following battery of in vitro genotoxicity tests were conducted with ciclopirox: a chromosome aberration assay in V79 Chinese Hamster Cells, with and without metabolic activation (positive); a gene mutation assay in the HGPRT-test with V79 Chinese Hamster Cells (negative); and a primary DNA damage assay (i.e., unscheduled DNA Synthesis Assay in A549 Human Cells (negative)). An in vitro Cell Transformation Assay in BALB/C3T3 Cells was negative for cell transformation. In an in vivo Chinese Hamster Bone Marrow Cytogenetic Assay, ciclopirox was negative for chromosome aberrations at 5000 mg/kg.

Pregnancy Category B: Reproduction studies have been performed in the mouse, rat, rabbit, and monkey, via various routes of administration, at doses 10 times or more the topical human dose and have revealed no significant evidence of impaired fertility or harm to the fetus due to ciclopirox. There are, however, no adequate or well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Caution should be exercised when LOPROX Lotion is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 10 years have not been established.

ADVERSE REACTIONS: In the controlled clinical trial with 89 patients using LOPROX Lotion and 89 patients using the vehicle, the incidence of adverse reactions was low. Those considered possibly related to treatment or occurring in more than one patient were pruritus, which occurred in two patients using ciclopirox lotion and one patient using the lotion vehicle, and burning, which occurred in one patient using ciclopirox lotion.

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CONTRAINDICATIONS: LOPROX Gel is contraindicated in individuals who have shown hypersensitivity to any of its components.

WARNINGS: LOPROX Gel is not for ophthalmic, oral, or intravaginal use. Keep out of reach of children.

PRECAUTIONS: If a reaction suggesting sensitivity or chemical irritation should occur with the use of LOPROX Gel, treatment should be discontinued and appropriate therapy instituted. A transient burning sensation may occur, especially after application to sensitive areas. Avoid contact with eyes. Efficacy of LOPROX Gel in immunosuppressed individuals has not been studied. Seborrheic dermatitis in association with acne, atopic dermatitis, Parkinsonism, psoriasis, and rosacea has not been studied with LOPROX Gel. Efficacy in the treatment of plantar and vesicular types of tinea pedis has not been established.

Information for Patients: The patient should be told the following:

1. Use LOPROX Gel as directed by the physician. Avoid contact with the eyes and mucous membranes. LOPROX Gel is for external use only.
2. Use the medication for fungal infections for the full treatment time even though symptoms may have improved, and notify the physician if there is no improvement after 4 weeks.
3. A transient burning/stinging sensation may be felt. This may occur in approximately 15% to 20% of cases, when LOPROX Gel is used to treat seborrheic dermatitis of the scalp.
4. Inform the physician if the area of application shows signs of increased irritation or possible sensitization (redness with itching, burning, blistering, swelling, and/or oozing).
5. Avoid the use of occlusive dressings.
6. Do not use this medication for any disorder other than that for which it is prescribed.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A carcinogenicity study of ciclopirox (1% and 5% solutions in polyethylene glycol 400) in female mice dosed cutaneously twice per week for 50 weeks followed by a 6-month drug-free observation period prior to necropsy revealed no evidence of tumors at the application site. The following battery of in vitro genotoxicity tests was conducted with ciclopirox: evaluation of gene mutation in the Ames Salmonella and E. coli assays (negative); chromosome aberration assays in V79 Chinese hamster cells, with and without metabolic activation (positive); gene mutation assays in the HGPRT-test with V79 Chinese hamster cells (negative); and a primary DNA damage assay (i.e., unscheduled DNA synthesis assay in A549 human cells) (negative). An in vitro cell transformation assay in BALB/c 3T3 cells was negative for cell transformation. In an in vivo Chinese hamster bone marrow cytogenetic assay, ciclopirox was negative for chromosome aberrations at 5000 mg/kg.

Pregnancy: Teratogenic effects: Pregnancy Category B: Reproduction studies of ciclopirox revealed no significant evidence of impaired fertility in rats exposed orally up to 5 mg/kg body weight (approximately 5 times the maximum recommended topical human dose based on surface area). No fetotoxicity was shown due to ciclopirox in the mouse, rat, rabbit, and monkey at oral doses up to 100, 30, 30, and 50 mg/kg body weight, respectively (approximately 37.5, 30, 44, and 77 times the maximum recommended topical human dose based on surface area). By the dermal route of administration, no fetotoxicity was shown due to ciclopirox in the rat and rabbit at doses up to 120 and 100 mg/kg body weight, respectively (approximately 121 and 147 times, respectively, the maximum recommended topical human dose based on surface area). There are no adequate or well-controlled studies of topically applied ciclopirox in pregnant women. LOPROX Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Since many drugs are excreted in human milk, caution should be exercised when LOPROX Gel is administered to a nursing woman.

Pediatric Use: The efficacy and safety of LOPROX Gel in pediatric patients below the age of 16 years have not been established.

ADVERSE REACTIONS: In clinical trials, 140 (39%) of 359 subjects treated with LOPROX Gel reported adverse experiences, irrespective of relationship to test materials, which resulted in 8 subjects discontinuing treatment. The most frequent experience reported was skin burning sensation upon application, which occurred in approximately 34% of seborrheic dermatitis patients and 7% of tinea pedis patients. Adverse experiences occurring between 1% to 5% were contact dermatitis and pruritus. Other reactions that occurred in less than 1% included dry skin, acne, rash, alopecia, pain upon application, eye pain, and facial edema.

DOSAGE AND ADMINISTRATION:

Superficial Dermatophyte Infections: Gently massage LOPROX Gel into the affected areas and surrounding skin twice daily, in the morning and evening immediately after cleaning or washing the areas to be treated. Interdigital tinea pedis and tinea corporis should be treated for 4 weeks. If a patient shows no clinical improvement after 4 weeks of treatment, the diagnosis should be reviewed.

Seborrheic Dermatitis of the Scalp: Apply LOPROX Gel to affected scalp areas twice daily, in the morning and evening for 4 weeks. Clinical improvement usually occurs within the first week with continuing resolution of signs and symptoms through the fourth week of treatment. If a patient shows no clinical improvement after 4 weeks of treatment, the diagnosis should be reviewed.

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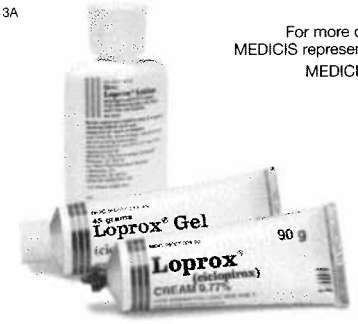

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Figure 1.— Digital Subtraction Angiogram of the Renal Arteries, Showing Bilateral Stenosis, Involving The Os.

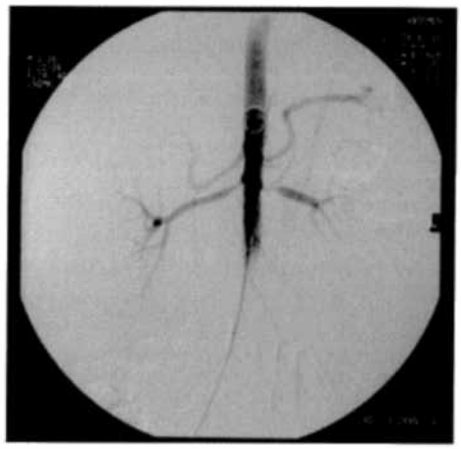
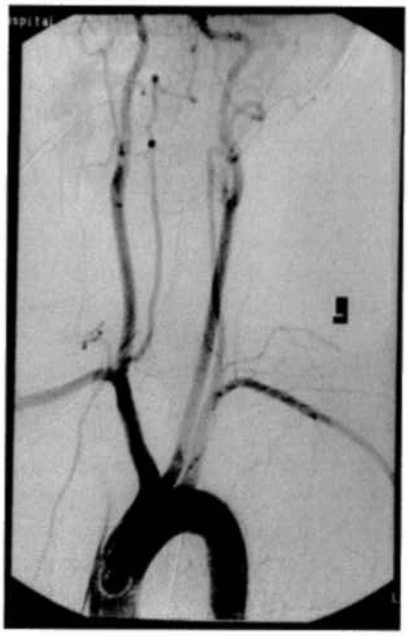


Figure 2.— Digital Subtraction Aortogram of the Aortic Arch, Showing Disease-Free Branches Without Stenotic Lesions, Including the Carotid Arteries.



ache, followed by new seizure activity and loss of consciousness, was highly suggestive of a subarachnoid bleed, which was confirmed by the initial CT scan of the head. Since no ruptured aneurysm or arteriovenous malformations as the cause of bleeding had been identified, other etiologies for the clinical presentation needed to be considered. Although subarachnoid hemorrhage is not typically seen as a complication of hypertension, the MRI was consistent with hypertensive encephalopathy.

Essential hypertension is uncommon in a 16 year old patient. In this setting, a work-up was initiated to identify causes of secondary hypertension, including hyperaldosteronism, pheochromocytoma, or renal artery stenosis. Renovascular hypertension accounts for only 1-2 percent of hypertension in the general population but is the most common cause of secondary hypertension. Certain features can be suggestive of renal artery stenosis, including hypokalemia, absence of family history, duration of hypertension less than one year, and the onset of hypertension before the age of 50 years.

In the general population, there are two different primary diseases causing renal artery stenosis. First, atherosclerotic renal artery stenosis, which typically accounts for about 90 percent of cases, and second, fibromuscular dysplasia, which tends to affect females between 15 and 50 years of age.[1] Fibromuscular dysplasia is considered to be the underlying etiology in the present case. In children, the spectrum of causes for hypertension associated with renovascular disease is different. Given the overall prevalence of this disease, there are only a few published articles addressing this situation. The largest series includes 54 children with hypertension secondary to renovascular disease.[2] Fibromuscular dysplasia was the most often underlying abnormality accounting for almost half of the cases, followed by neurofibromatosis (15%) and arteritic illnesses (9%).

The evaluation of a patient with suspected renal artery stenosis may, besides the standard tests such as serum creatinine or urine analysis, include more sophisticated, non-invasive studies. This includes functional tests, such as measurement of plasma renin activity, the captopril test, and captopril renal scintigraphy, as well as imaging studies, including duplex ultrasonography, magnetic resonance angiography (MRA), and computed tomography angiography (CTA).

Initial tests, including serum creatinine and creatinine clearance, were normal. The captopril renal scintigraphy was consistent with left renal artery stenosis. In addition, the twenty times greater than normal renin plasma activity was consistent with this presumed diagnosis. This finding is compatible with an acute stage of renal arterial constriction,[3] which later was confirmed by angiography of the renal arteries. A recently published meta-analysis suggests that CTA and gadolinium-enhanced MRA have better diagnostic accuracy than ultrasonography, captopril renal scinitigraphy, and the captopril test.[4]

Fibromuscular dysplasia is a non-atherosclerotic and non-inflammatory vascular disease that primarily affects the medium and small-sized arteries, especially the renal and carotid arteries.[5] In a significant number of patients, more than one vessel is affected. Thus, in this case, concomitant fibromuscular disease of the carotid artery needed to be ruled out by an aorto- and angiogram of the aortic arch branches (figure 2). Depending on the vessels involved, clinical manifestations range from renovascular hypertension to stroke, subarachnoid hemorrhage, abdominal angina, or claudication. The underlying etiology is unknown, despite several hypotheses having been proposed, including those involving humoral and mechanical factors, genetic predisposition, smoking, and conditions causing ischemia of the vessel wall.[1,5] Fibromuscular dysplasia is further sub-classified by the layer of the arterial wall primarily involved in the disease, namely intimal, medial, or periarterial fibrodysplasia. Of these subclasses, 90 percent involve the medial layer. This subtype presents with the typical "string-of-beads", aneurysmal angiographic appearance. If fibromuscular dysplasia involves the renal artery, the middle and distal segments of the renal artery are usually affected. However, in the subgroup of pediatric patients with fibromuscular dysplasia involving the renal arteries, the vast major-

ity is of the intimal, untypical medial, or periarterial fibrodysplastic type. These types are characterised by lack of the typical series of stenosis and intervening aneurysms, as usually seen in adults (figure 1).[6] Additionally, fibrodysplastic lesions in children or adolescent are most commonly ostial stenosis, as seen in this case. Even though fibromuscular dysplasia is a histologic diagnosis, it is mostly diagnosed in adults by the clinical presentation and the typical "string-of-beads" stenoses seen angiographically. In contrast, these angiographic features are usually not seen in children; thus, other causes of renal artery stenosis need to be taken in consideration since arteriosclerotic lesions are uncommon in this age group.

The differential diagnosis of fibromuscular dysplasia includes Takayasu's arteritis, and vascular lesions of neurofibromatosis. Similarly, Ehler-Danlos syndrome can angiographically mimic an aneurysmal type of fibromuscular dysplasia. However, Takayasu's arteritis may be the foremost consideration in the differential diagnosis of fibromuscular dysplasia. It is a vasculitis involving large- and medium-sized vessels affecting mostly women below the age of 40. This vasculitis is common in southern and eastern Asia. The aorta is almost always involved as well as the immediate branches of the aortic arch. There are rare reports regarding involvement of the renal arteries in Takayasu's arteritis, which affects the main and the intrarenal braches of the renal arteries.[7]

This patient does not fulfil the criteria for Takayasu's disease and the angiographic appearance does not support this diagnosis, either, since the braches of the aortic arch are free of stenotic lesions (figure 2). Finally, the patient had no stigmata on examination suggestive for Neurofibromatosis or Ehler-Danlos syndrome.

The natural history of renal artery stenosis caused by fibromuscular dysplasia is relatively benign. In contrast to atherosclerotic renal artery stenosis, patients with fibromuscular dysplasia rarely have impaired kidney function. It has been reported that renovasular disease tends to progress in about one third of patients with atherosclerosis, but in only 16% of those with fibromuscular dysplasia.[5]

Treatment options for renal artery stenosis consist of percutaneous or surgical revascularization or medical treatment. The preferred treatment is revascularization in fibrodysplastic renal artery stenosis. It has been shown that regardless of the type of revascularization, 60% of hypertensive patients with fibromuscular dysplasia are cured after revascularization.[1] Thus, percutaneous revascularization with conventional balloon angioplasty is the treatment of choice for patients with uncontrolled hypertension and fibromuscular dysplasia. The procedure has success rates of 82 to 100 percent. [8]

Re-stenosis occurs in only 10 to 11 percent. This is remarkable, considering the re-stenosis rate in atherosclerotic renal artery stenosis is up to 47 percent [1] and in non-stent PTCA procedures of the coronaries at least 42 percent.[9]

In general, conventional balloon angioplasty of the renal artery is sufficient for treatment of the stenotic lesion in fibromuscular dysplasia. Stent placement, as in this case, might be a sufficient procedure if the immediate post-dilatation result by balloon alone is suboptimal.[10] However, long-term results for balloon angioplasty with consecutive stent deployment in fibrodysplastic renal arteries are not available yet. Thus, the rate of re-stenosis remains uncertain. Given the young age of the patient, the stent was placed understanding that the patient may need bypass surgery in the future.

Acknowledgements

We are indebted to Dr. Sandra Loo and Dr. James Madison for their constructive comments.

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Medical School Hotline

Student Profile: Class of 2006 John A. Burns School of Medicine (JABSOM)

Satoru Izutsu PhD
Senior Associate Dean
Chair, Admissions Committee

One thousand sixty-six men and women applied for sixty-two positions in the 36th class at JABSOM. Of the total applicants, 881 were non-residents of the State of Hawaii and 185 were residents. Residency for application purposes is determined by a "kama`aina" screen that takes into consideration 5 factors: legal residency, birthplace, parents' residence, high school and college or professional school(s) attended. An applicant must have at least three of the five factors to be considered a "resident". Six of the total class are non-resident: one each from Guam, California, Montana, Washington, Marshall Islands, and Samoa.

Those candidates interviewed were selected on the basis of undergraduate Grade Point Averages (cumulative and science), scores on the Medical College Admission Test (MCAT), honor awards, extra-curricular activities and employment in health, medicine or human services, in general. For example, 10 or more points on the MCAT were given 2 points. Of the total of possible 22 points, a resident must score at least 7, a non-resident 14, and certified Western Interstate Commission of High Education and early decision candidates 10. Of the total number of candidates, 224 (141 residents and 83 non-residents) qualified to be interviewed by two of the 71 interviewers and the Chair of the Admissions Committee.

The eleven-member Admissions Committee, 5 men and 6 women, met 21 times between September, 2001 and May, 2002 to rate the 224 applicants. The Committee consisted of 8 clinicians, 2 basic scientists and 1 social scientist. The major ethnic groups and varied age groups were represented. The members examined the following documents of each applicant: academic transcript, MCAT scores, a biographical sketch (includes a chronological listing of extracurricular and work experiences) written by each candidate, letters of references, and three essays, "Describe succinctly the important experience (s) in your life which began the process that motivated you to enter the career of medicine", "Explain why you are applying to the University of Hawaii John A. Burns School of Medicine", and, ". . . describe your life and medical practice as you envision them ten years from now". After a period of deliberation by the committee, each member rated the applicant, by secret ballot, and submitted his/her rating to the Registrar who averaged the ratings for each applicant. The ratings were not discussed. In May, the 224 ratings were ranked and the top 52 candidates were notified of their acceptances. In June, 10 students in the Imi'Ho`ola Post Baccalaureate Program were confirmed to join the 52, thus adding to a total of 62 in the Class of 2006. The Office of the Dean decides upon waitlist. The numbers on this list varies each year.

The median scores of the entering class are: cumulative GPA, 3.52; Science GPA, 3.42; MCAT total, 29; Verbal Reasoning, 9; Physical Sciences, 10; Writing Sample, P; Biological Sciences, 10.

JABSOM remains the nation's most ethnically diverse School of Medicine. There are 16 Japanese, 8 Caucasians, 8 Chinese, 7 Hawaiians/Other, 6 Mixed/Other Asian, 3 Filipino, 3 Korean, 1 American Indian/White, 1 Asian/East Indian, 1 Chamorro, 1 Chamorro/Filipino, 1 Chamorro/Filipino/White, 1 Japanese/White, 1 Okinawan/White, 1 Persian, 1 Tongan, 1 Vietnamese, and 1 Vietnamese/Chinese.

Twenty-seven graduated from colleges in Hawaii, 34 came from mainland colleges and 1 from a foreign college. There were 24 from University of Hawaii at Manoa, 2 from Hilo and 1 from Hawaii Pacific University. Seven are graduates of University of Washington, 3 from University of California, Berkeley, 2 each from Oregon State, Stanford University, and University of California, San Diego. The following university/colleges are represented by one matriculate: Brandeis University, Claremont McKenna College, Colorado College, Creighton University, Harvard University, Hawaii Pacific University, Lewis and Clark College, Macalester College, Marquette University, Point Loma Nazarene College, Reed College, University of Montana, University of Guam, University of Portland, University of Puget Sound, University of California, Irvine, Santa Barbara, Los Angeles, Wellesley College, and Whitworth College.

One student is entering with a Doctor of Philosophy degree, 13 have Masters degrees and all have Baccalaureate degrees. Eighteen have their degrees in Biology; two each in Biology/Physiology, Cell & Molecular Biology, and Psychology; one in each of the following: Animal Physiology/Neuroscience, Anthropology, Biochemistry, Biochemistry/Chemistry, Public Health, Biochemistry; Biology/Education, Biology/Chemistry, Biology/English, Biology/Ethnic Studies, Biology/History; Genetic & Molecular Biology, Biology/Japanese, Biology/Microbiology/Bacteriology, Biology/Psychology, Biology; Cell & Molecular Biology, Biology; Maternal & Child Health, Biology; Public Health, Business, Chemistry/Math/Physics; Biomed Eng; Tele-Rehab, Chemistry; Physiology, Chinese Studies/Physics, Civil Engineering; Chemistry, Comparative literature, English, Exercise & Sports Science, Science General, Fine Arts; Business, Foreign Language, French, Hospital administration, Life Science, Mathematics; Public Health, Microbiology/Bacteriology, Molecular & Cell Biology, Molecular & Cell Biology, Immunology Emphasis, Pre-Medicine, Religion, Speech, and Zoology; Biomedical Science.

The admission committee has deemed that the 62 are the most likely candidates to succeed in JABSOM for the Medical Doctor (M.D.) degree. They were identified as having the best potential of becoming competent, culturally sensitive, humane physicians. The 26 men and 36 women whose median age is 24 are on a journey that will change their lives — as well as that of others — forever.

On August 2, 2002, at the "White Coat Ceremony"[1], each student received a white coat from the alumni of the Class of 1981, a stethoscope from the Hawaii Medical Association and Pacific Cardiology, a book, "On Doctoring" from the Robert Wood Johnson Foundation, "Bates' Guide to Physical Examination and History Taking", a gift from the Friends of the Medical School and a lapel

Continued on p. 213

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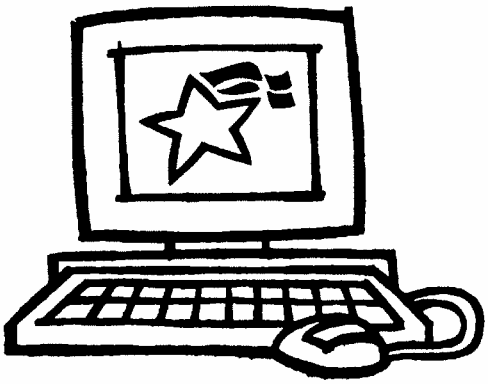

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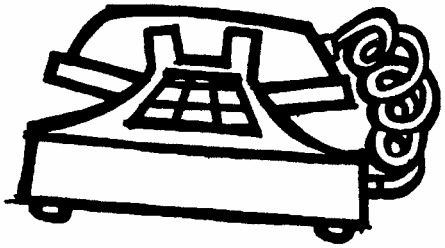

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Cancer Research Center Hotline

The Study of Tamoxifen and Raloxifene (STAR Trial) for the Prevention of Breast Cancer

Ann Kelminski, RN, MBA, Program Coordinator, STAR Trial
Cancer Research Center of Hawaii

The Study of Tamoxifen and Raloxifene (STAR) is designed to determine whether the drug used to treat and prevent osteoporosis, raloxifene (Evista®) is as effective as tamoxifen (Novaldex®) in reducing breast cancer in women who are at the greatest risk for the disease. The study has a five-year recruitment plan, which will enroll 22,000 women nationwide, making it one of the largest studies designed to find ways to prevent breast cancer. The study opened in Hawaii at the University of Hawaii's Cancer Research Center of Hawaii in July of 1999. The STAR Study has since recruited 114 of Hawaii's women, all of whom have an increased risk of developing breast cancer.

Tamoxifen was shown to reduce the chance of developing invasive breast cancer by 49% in the Breast Cancer Prevention Trial (BCPT), a study of over 13,000 premenopausal and postmenopausal women at high risk of breast cancer[1]. In the BCPT, half the women took tamoxifen and half took a placebo (an inactive pill that looked like tamoxifen). Participants taking tamoxifen also had fewer fractures of the hip, wrist, and spine than women taking the placebo.

Data regarding breast cancer incidence and raloxifene were obtained from the Multiple Outcomes of Raloxifene Evaluation (MORE) trial. The MORE trial was a multi-center osteoporosis trial that involved 7,705 postmenopausal women with osteoporosis entered at centers around the world. Women were randomized to receive either raloxifene at 60 or 120 mg/d or placebo. The 48 month results from the MORE trial showed a reduction in invasive breast cancer by 72% in women who took raloxifene daily for four years[2]. It is important to recognize that this study was designed as an osteoporosis study. Women were selected because of their pre-existing osteoporosis. Breast cancer risk was not considered. These results emphasize the value of the STAR which will compare the worth of raloxifene in women at increased risk for the disease, and will compare this with tamoxifen in a randomized clinical trial in which breast cancer incidence is a primary study end point.

While tamoxifen has been shown to reduce breast cancer risk in high risk women, the drug increased the women's chances of developing four potentially life-threatening health problems: uterine cancer, deep vein thrombosis, pulmonary embolism, and possibly stroke. Women taking tamoxifen have a two- to three-fold increased risk of uterine cancer. While previous data indicated that tamoxifen increased the risk of only endometrial cancer, recent case studies suggest that tamoxifen may also slightly increase the risk for uterine sarcoma[3]. In the BCPT there are about two cases of uterine sarcoma per 10,000 women taking tamoxifen each year[3,4]. Risk for vascular events are similar to those seen with hormone replacement therapy (HRT).

Information about the safety of raloxifene is limited compared to the data available on tamoxifen. Raloxifene was approved in December 1997 by the FDA to prevent osteoporosis and has been in clinical trials for about five years. Tamoxifen has been approved by the FDA to treat women with breast cancer for more than 20 years and has been in clinical trials for about 30 years. Women taking raloxifene in studies of osteoporosis have had an increased chance of developing a deep vein thrombosis or pulmonary embolism similar to the risk seen with tamoxifen. In these studies, raloxifene did not increase the risk of endometrial cancer. An important objective of STAR will be to compare the long-term safety of raloxifene and tamoxifen in women at increased risk for breast cancer.

Women who participate in STAR must be postmenopausal, at least age 35, and have an increased risk of breast cancer as determined by their age, family history of breast cancer, personal medical history, age at first menstrual period, and age at first live birth. They will also go through a process known as informed consent, during which they will learn about the potential benefits and risks of tamoxifen and raloxifene before deciding whether to participate in STAR. Information sessions for STAR are held monthly at the Cancer Research Center of Hawaii.

Once a woman chooses to participate, she will be randomly assigned to receive either 20 mg tamoxifen or 60 mg raloxifene daily for five years. She will be seen at the Cancer Research Center for follow-up every six months. At that time she will be interviewed regarding her health status and may also receive a clinical breast exam which is required every six months. Each woman will continue her health care with her regular physicians. Annual mammograms and lab tests to include CBC and liver and kidney function studies are required. Pelvic exams will be required annually for all women with the exception of those who have had a total hysterectomy and bilateral oophorectomy. Study drugs are provided without charge and a six months' supply will be given at the time of the follow-up visit. Throughout her participation, a woman will be closely monitored for any adverse events, and updated regarding any new findings.

The STAR presents an important option for women at high risk for breast cancer. Tamoxifen has been approved for this indication. In the recent "American Society of Clinical Oncology Technology Assessment on Breast Cancer Risk Reduction Strategies: Tamoxifen and Raloxifene"[5], it is stated, "It is premature to recommend raloxifene use to lower the risk of developing breast cancer outside of a clinical trial setting."

STAR is now into its fourth year with more than 60% of accrual achieved. Please consider this important trial when counseling women who are at high risk for breast cancer.

The University of Hawaii's Cancer Research Center of Hawaii is one of more that 400 sites participating in STAR. Dr. Nancy Furumoto is the Principal Investigator; Ann Kelminski, R.N. is Program Coordinator.

For more information about STAR, or to refer patients please call the Cancer Research Center at (808)586-2979 or visit the National Surgical Adjuvant Breast and Bowel Project (NSABP) web site at http://www.nsabp.pitt.edu, the NCI clinical trials web site at http://cancertrials.nci.nih.gov, or the Cancer Research Center of Hawaii web site at www.crch.org.

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New representative in Hawaii **David Higashiguchi**

- Graduate of University of Hawaii at Manoa and St. Louis High School
- Having been born and raised here in Hawaii, I appreciate the commitment a mainland-based company shows when creating a local sales/service position. Medicis sees Hawaii as a very important market that deserves a dedicated representative. A local presence translates into a local phone call to resolve questions and concerns, not to mention fast delivery of needed samples. I am very excited to represent the Medicis family of products and I look forward to building lasting relationships with the physicians of Hawaii.

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"Acute Myocardial...", Continued from p. 201

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"Evidenced Based...", Continued from p. 192

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"Medical School Hotline", Continued from p. 207

pin from the Foundation*. At the end of the ceremony, Dr. Ken Sarawatari, Class of 1981 led the class in restating the "Oath of Hippocrates". Each student will recall this ceremony as they challenge the years of training before them, remembering " . . . To honor all who have taught me this art and in the same spirit and dedication to impart a knowledge of medicine to others. I will continue with diligence to keep abreast of advances in medicine, and respect those who broaden our knowledge by research. . . . that caring for the patient will be my primary concern and while dong so I will honor the autonomy of the sick. I will recognize that such caring requires my being available, giving my time generously, communicating honestly, and comforting as well as treating . . . [2]"

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* The pin depicts a logo, a stethoscope in the shape of a heart, surrounded with the words, "Humanism in Medicine".

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The Weathervane Russell T. Stodd MD

How Many Times Do I Have To Tell You, She's Your Sister!
Over 200 years ago, a typhoon struck the remote Micronesian atoll of Pingelap and decimated the population. Famine followed and only 20 people remained, but one male survivor carried a rare recessive mutated gene for achromotopsia. This is a condition of absent retinal cone receptors characterized by light sensitivity, poor acuity, and complete absence of color perception. Recently a Johns Hopkins University group studied the isolated population of 3000 Pingelap people, and found that five to ten percent of the people are affected with the problem. At this geneticists paradise, scientists were able to trace the ancestry of each afflicted person to the single male typhoon survivor. Intermarriage of two of his descendants, each carrying the recessive gene, has resulted in the emergence of this rare disorder.

Seen It All. Done It All. Wish I Could Rememer It.
A study published in *Stroke: Journal of the American Heart Association* revealed that individuals with changes in the tiny branches of retinal vessels might serve as a predictor for the dementia associated with Alzheimer's Disease. A study of more than 8,000 middle-aged people who had not suffered a stroke, showed that those with impaired mental function were three times as likely to have abnormal retinal arterioles. According to Tien Y. Wong, M.D., M.P.H., this finding coincides with a previous hypothesis that some vascular cause beyond just aging, is associated with Alzheimer's and CVAs. Dr. Wong believes that this finding has the potential to provide a non-invasive, inexpensive way to screen for vascular dementia in the general population. And a recent study in the Journal of the American Medical Association, affirmed the benefit of anti-oxidant vitamins E and C in retarding the progress of Alzeheimer's.

No Good Deed Goes Unpunished - Even Forty Years Later!
In the 1950s and 1960s, William Sweet, M.D., was a world famous neurosurgeon, and chief of the department at Massachusetts General Hospital. In the early 60's he conducted a medical experiment study known as boron neutron capture therapy. The research was conducted with advance approval of the MGH executive committee, and the MGH Board of Trustees, and was partly funded by the federal government. The procedure was performed only on terminally ill patients with fast growing brain tumors. The boron injection was painful at times, and the radiation damaged healthy brain tissue as well as tumors. Ultimately, the experiment was a failure, and all the patients died. In 1995, the President's *Advisory Committee on Human Radiation Experiments* issued an analysis of radiation exposure going back 50 years, and the study was reported to the media. Now, a widow of one of the patients, and a son of another have sued Dr. Sweet, MGH, the United States Government, and several others, with the claim that the doctor was negligent in not telling the patients that the procedure was not FDA approved, and had no reasonable probability of success. After a 21 day trial, most of the defendants were dismissed or found not liable, but the jury found against Dr. Sweet and awarded $4,750,000 in damages, which was later reduced to $830,000 by the court. Both sides have appealed. Dr. Sweet was 89 years old at the time of the trial, suffering from Parkinson's Disease and could not testify. He has since died.

"Vegetarian" - Indian Word For Lousy Hunter.
Fast food giant McDonald's got caught with their lard laden ladle in the beef broth. Last year it was found that McDonald's was using beef flavoring in the tallow used for cooking fried potatoes. Previously, vegetarians had been led to believe that the potatoes were prepared in pure vegetarian oil. An apology has been placed on their web site, and the fast food company is donating $10 million to Hindu and other groups as partial settlement of litigation. Additionally, the company has created an advisory panel on vegetarian dietary practices to manage relevant restrictions and guidelines.

If You're Only Making Ends Meet, You're Running In Circles.
Frustrated and angry with manipulation, down-coding, payment delays, contract violations, and criminal profiteering, physician groups in Washington state have filed suits in state court against Regence Blue Shield and Premera Blue Cross. Similar law suits have been filed in state courts in Illinois, Connecticut, Texas and New York. Other lawsuits brought against HMOs have been in federal court which slowly wend their way through various pretrial motions. Now, according to counsel Debra Hayes in Washington state, "class certification is simpler in state court." Resorting to lawyers and courts is a distasteful route to go, but individual physician voices are ignored by the behemoths such as HMSA, which have overwhelmed the medical profession.

It's Silly To Keep Up With The Joneses. Drag Them Down To Your Level.
A study published in the April *Review of Ophthalmology* brought out some interesting data regarding cataract surgery. (Not discussed was how much longer surgeons can afford to perform the procedure considering the relentless decline in reimbursement.) While all the surgeons claimed excellent results, 60% prefer an incision in sclera or at the limbus, and 40% prefer the clear cornea. The primary issue has to do with patient discomfort and possible increased risk of infection in the clear cornea opening. It was stated that corneal incisions cause irritation and are more likely to leak. Also an interesting finding was that fewer surgeons are using retrobulbar anesthesia, down to 30% from 45% just three years ago, while topical drug use is going up. Contrarily, patient acceptance of topical is going down. Of those surgeons who prefer retrobulbar anesthesia, over 70% are unlikely, or very unlikely to change to topical. Safety and patient comfort were major issues. As one surgeon stated, "with my ethnically diverse population, you would have to be ready to shout 'don't move' in six different languages."

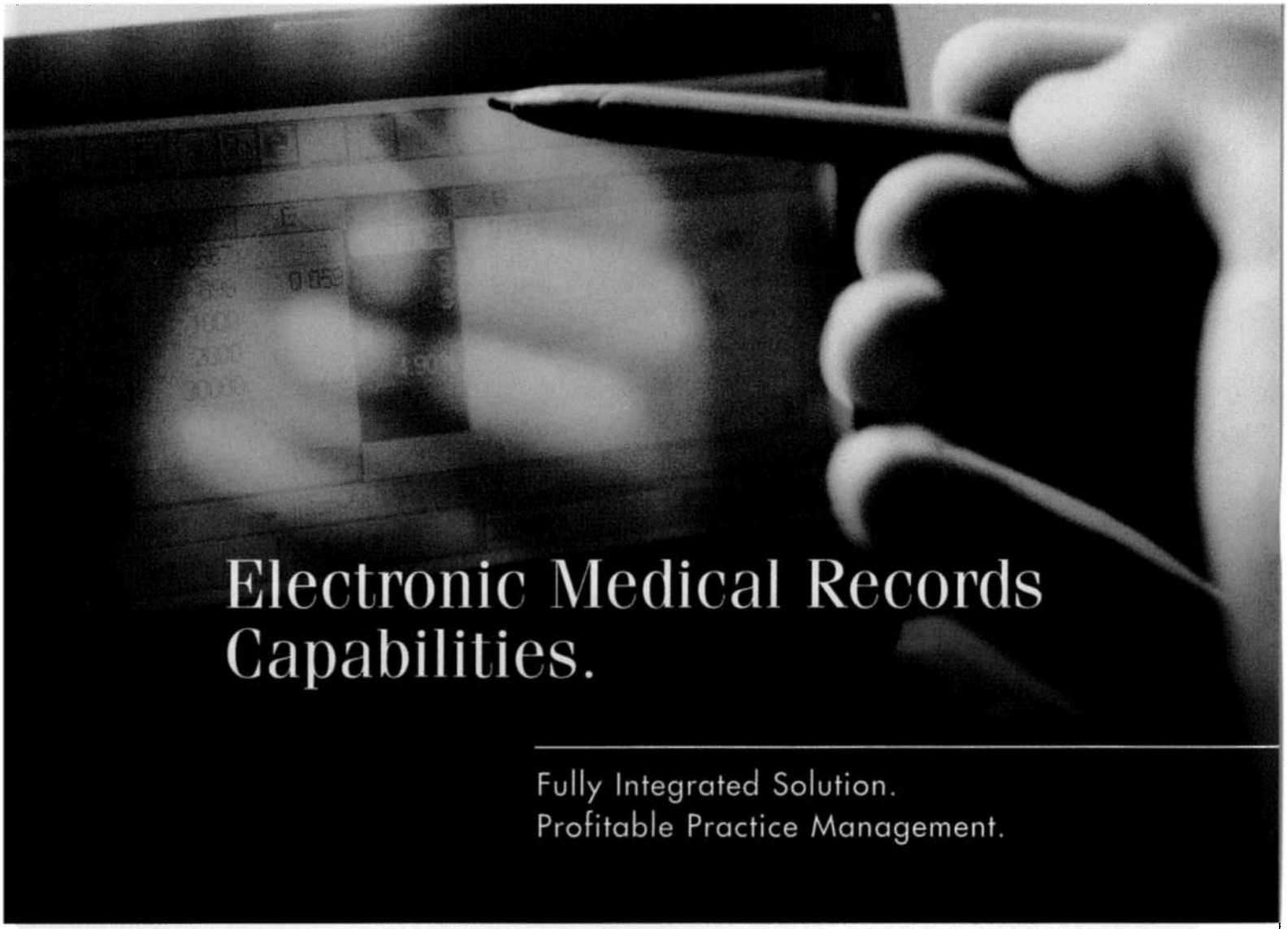
Forget The Organic Food. I Need All The Preservatives I Can Get.
Europe suffered an outbreak of mad-cow disease and hoof-and-mouth disease last year which sent the agriculture industry into a tailspin. Panicky people turned to *organic* products, and to encourage consumption, the German government established a certification seal on organic eggs, meat and other products. Now, consumers have been shaken up again with the finding of organic chicken feed contaminated with nitrofen, a carcinogen that was outlawed in West Germany 20 years ago. The pesticide was traced to feed that was stored in a warehouse in eastern Germany, and has been found in eggs, bread and even organic baby food. The organic label on food products has become a warning sign, and supermarket managers are pulling them from shelves. Around a quarter million hens were slaughtered, hundreds of farms have been temporarily shut down, and green growers are scrambling to determine if their stocks were unwittingly tainted. In one day sales dropped 20%. The organic food industry in Germany has been hit hard, and estimates are that half of those farms which were closed down will not survive.

In The War Of The Sexes, There Are No Conscientious Objectors.
In Stockholm, Sweden, a lesbian couple wanted to have children. They asked a man to donate sperm for procreation, which he did on three occasions. The couple had three children. Like so many other couples, sometime later the lesbian relationship ended, and the biological mother took custody of the children. She also took the man to court demanding child support. The court ruled that the sperm donor had to pay $280 per month. How's that for being Mr. Niceguy?

ADDENDA
❖ In the late 1800s and early 1900s it was fashionable for ladies to shave off their eyebrows and glue on artificial brows made of mouse fur.
❖ In Florida, a quadriplegic man has filed a complaint against a night club under the ADA for not providing wheel chair access for lap dancing.
❖ A London theater company has changed the name of their play to "The Bellringer of Notre Dame" from "The Hunchback of Notre Dame," to avoid offending people with scoliosis. .

Aloha and keep the faith —rts■

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



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