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Editorial

Norman Goldstein MD
Editor, Hawaii Medical Journal

May is Melanoma Month

Governor Ben Cayetano has proclaimed May as "Melanoma Month in Hawaii" (page 113)

The American Academy of Dermatology has sponsored Skin Cancer Screening Clinics for more than 15 years. Dermatologists nationally have screened over one million people. Detecting over 91,000 suspected lesions, including approximately 12,000 suspect melanomas. Our Hawaii Dermatological Society, working with the Cancer Center of Hawaii and the Hawaii State Department of Health, has screened thousands of Hawaii's skins at Liberty House locations, churches, schools and Longs Drug Stores on all islands.

Last year, in Hawaii, we screened 762 people and found nine suspect melanomas as well as 49 basal and squamous cell carcinomas and 376 keratoses. The Hawaii Dermatologists will again be doing these volunteer services this month May 12, at Longs Drug Stores on all islands.

On Friday, May 14, The Straub Foundation and HMSA will sponsor a major program for professionals on the good and bad features of sun exposure in Hawaii. Screening for skin cancer will be held after the special Straub Foundation public symposium on "Sun and Skin in Paradise". These exams will be conducted at the end of the public program to be held at the Ilikai Hotel on Saturday afternoon May 15th. Call 524-6755 for further information.

This Month—Food for Thought

The Waianae Diet

Theresa Danao-Camara MD, and Terry Shintani MD, present a preliminary study of the use of the Waianae Diet in the treatment of two patients with seropositive inflammatory arthropathies — presumably systemic lupus erythematosus. The Waianae Diet was first reported by Shintani and his associates in the American Journal of Clinical Nutrition in 19911 and after in the Hawaii Medical Journal in 1994.2

While this is a very limited study, the authors present an excellent review of diets and the effect of fasting on arthritis.

In the second manuscript, Terry Shintani continues his studies of the Waianae Diet, reporting on the long-term follow-up of the diet. Terry and his associates studied 173 obese subjects and were able to evaluate 82 of them at the end of the study, eight years after initiation of the project.

Their study does have some limitations, notably in the interpretation of the results but the ad libitum Waianae diet seems to be a practical method for some weight control in native Hawaiians. Food for thought.

Proclamation

WHEREAS, skin cancer represents the most common of all cancers in the United States, accounting for thirty to forty percent of all malignancies reported; and

WHEREAS, the Centers for Disease Control and Prevention reports that for the period from 1973 through 1997 the incidence of melanoma, a deadly form of skin cancer, increased faster than any other form of cancer in the United States; and

WHEREAS, while melanoma may be lethal if not properly treated at an early stage, melanoma and other forms of skin cancer are easily prevented through reducing exposure to sunlight; and

WHEREAS, in addition to those who are at high risk for genetic or biological reasons, and those who pursue high risk activities that are likely to cause overexposure, research shows that childhood overexposure to sunlight may increase a person’s risk of skin cancer; and

WHEREAS, protecting skin from the sun during childhood and adolescence is very important in reducing the risk of skin cancer in later years; and

WHEREAS, about eighty percent of skin cancers could be prevented by protecting skin from the sun’s rays; and

WHEREAS, the State Department of Health, Hawaii Skin Cancer Coalition, Hawaii Dermatological Society, American Cancer Society, Cancer Information Service of Hawaii, and Sun Protection-Hawaii, Inc.—working with other organizations in Hawaii—have planned activities for the month of May that will focus on the importance of early detection and prevention of skin cancer;

NOW, THEREFORE, I, BENJAMIN J. CAYETANO, Governor of the State of Hawaii, do hereby proclaim the month of May, 1999, to be

MELANOMA AND SKIN CANCER DETECTION AND PREVENTION MONTH

in Hawaii, and encourage all citizens to participate in planned activities this month that focus on the importance of early detection and prevention of skin cancer.

DONE at the State Capitol, in the Executive Chambers, Honolulu, State of Hawaii, this twelfth day of April, 1999.

[Signature]
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Continuing medical education (CME) is a distinct and definable professional activity. It encompasses all of the learning experiences that physicians engage in with the conscious intent of continuously improving the performance of their professional duties and meeting their professional responsibilities. As an essential element in the continuum of medical education, CME shapes the professional development of physicians regardless of the nature and scope of their duties and responsibilities. CME is integral to practice throughout all stages of a career beginning with the completion of graduate medical education.1

The Hawaii Consortium for Continuing Medical Education (HCCME), a joint venture between the Hawaii Medical Association (HMA) and the John A. Burns School of Medicine (JABSOM), University of Hawaii, is a CME provider and is accredited by the Accreditation Council for Continuing Medical Education (ACCME). As a state medical society, the HMA serves a dual role as a CME provider in joint venture with the JABSOM and as a CME accreditor. As a CME accreditor, the HMA has the authority to accredit local CME sponsors such as community hospitals and state specialty societies.

The ACCME is a cooperative effort of seven national medical organizations: American Board of Medical Specialties, American Hospital Association, American Medical Association, Association for Hospital Medical Education, Association of American Medical Colleges, Council of Medical Specialty Societies, and Federation of State Medical Boards. Today, the accreditation system involving the ACCME and state medical societies accredits more than 2,500 organizations that offer CME programs.

The major purposes of accreditation are to ensure quality and integrity of accredited providers by: establishing criteria for evaluation of educational programs and their activities, assessing whether accredited organizations meet and maintain standards, promoting organizational self-assessment and improvement, and recognizing excellence.2

In the U.S., accreditation of providers of continuing education for physicians is voluntary. Accreditation is not a governmental function, is not a rating system, and does not deal with credit. It is not a stamp of approval for individual courses or activities — although it is often mistakenly perceived as such. Accreditation is a process that consists of guided self-evaluation and self-improvement.3

To obtain accreditation, the HCCME submitted an application to the ACCME requesting accreditation. The application was a self-evaluation instrument of the process by which CME activities were planned and implemented, and included documentation of each step of the process. Representatives of the HCCME were interviewed in Chicago by a survey team. During this interview, the team gathered additional information regarding the HCCME’s program of CME. A report of the interview was then forwarded to the Accreditation Review Committee (ARC) for review and action. In April of 1996, the ACCME approved reaccreditation of the HCCME for four years. The HCCME was found to be in substantial compliance of all essentials.

The HCCME sponsorship committee, comprised of representatives of the HMA and JABSOM clinical departments, was initially co-chaired by HMA members. Under the leadership of Drs. S. Kalani Brady and Paul DeMare, JABSOM faculty received on-the-job training on the CME process. For the past three years, HMA and JABSOM have shared the chairmanship.

In addition to sponsoring CME activities, the HCCME has jointly sponsored individual activities with groups that are not accredited. In the joint sponsorship relationship, the HCCME “lends” its accreditation status to an unaccredited body and the HCCME accepts the responsibility to ensure that the ACCME requirements are met. The HCCME has jointly sponsored activities with the Straub Foundation; HUMSA Foundation; Pacific Association of Pediatric Surgeons, Rehabilitation Hospital of the Pacific; March of Dimes, Chapter of the Pacific; University of Hawaii College of Business Administration; and the American Cancer Society, Hawaii Pacific Division.

At the national level, the Association of American Medical Colleges (AAMC), Division of Medical Education (DME) has constituted the CME Advisory Group for the purpose of developing an action plan for the AAMC in CME. The action plan, currently under review by the CME section of the Group of Educational Affairs (GEA), addresses the role of CME in the continuum of medical education; appropriate settings for CME; barriers and bridges to the continuum; and models to facilitate CME in the continuum.

In coming months the HCCME will complete a self-evaluation survey and will apply for reaccreditation. In response to changes in the way physicians practice, rapid advances in biomedical knowledge and its application to the practice of medicine, and incorporation of evidence-based medicine, new ways of thinking about CME will be required. The HCCME recognizes the challenges they will face as they strive to provide meaningful learning opportunities for Hawaii’s practicing physicians.

References
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Waianae Diet Program: Long-Term Follow-up

Terry Shintani MD, MPH, Sheila Beckham MPH, RD, Jon Tang BS, Helen Kanawaliwali O’Connor CHW, Claire Hughes DrPH, RD

Abstract
A long-term follow-up was conducted on 82 participants from prior programs based on ad libitum feeding of a traditional Hawaiian diet. Follow-up period ranged from 72 months to 90 months and averaged 33.67 months. An average weight loss of 15.1 pounds was maintained over 7.5 years of follow-up (p<0.0005) even when stratified over two year intervals, suggesting that this type of program may be an effective long-term weight loss intervention.

Introduction
Obesity is a serious health problem in America; the national prevalence is approximately 31% in men and 34% in women and it has been rising over the past 30 years. It is associated with higher risks of a number of chronic diseases, such as cardiovascular disease, cancer, hypertension, and diet-induced diabetes. Obesity is of special concern among Native Hawaiians, as this ethnic population has one of the highest prevalences of obesity at approximately 64%. Furthermore, Native Hawaiians have among the highest age adjusted mortality rates in the Nation from disease associated with obesity, such as cardiovascular disease, diabetes, and stroke.

Over the years, numerous approaches to the problem of obesity have been attempted using calorie restriction, exercise, meal substitution, surgical correction, medication, self-imposed fasting, and behavior modification. Unfortunately, while all of these approaches have demonstrated initial success, practically none of these interventions have shown any long-term efficacy in retained weight loss.

Recently traditional diets, such as a traditional Mediterranean diet and traditional Asian diet, have been discussed as a viable approach to health risk factors and obesity intervention. The ad libitum use of a traditional Native Hawaiian diet coupled with a whole person approach, including lifestyle changes unique to the ancient culture and perspective has been previously evaluated in the Waianae Diet Program for its short term efficacy. However, the long term effectiveness of this approach has not been evaluated.

This article presents an analysis of a long term follow-up of individuals who have participated in an obesity and cardiovascular risk reduction program employing ad libitum feeding of a traditional Hawaiian diet known as the Waianae Diet Program.

Methods

The Original Intervention/Study
The original intervention evaluated was a 21 day dietary and lifestyle change program. A number of these programs were conducted over a 9 year period since the first intervention. Groups of approximately 20-25 men and women aged 24-64 years were fed an ad libitum, whole meal diet of traditional foods available in Hawaii before Western contact, such as taro, poi, sweet potato, yams, breadfruit, and greens (fern shoots and leaves of taro), fruit, seaweed, fish, and chicken. These staples were prepared in a manner that approximated ancient styles of cooking. To approximate the diet of the ancient Hawaiians, which was estimated to contain <10% fat, the amounts of fish and chicken were limited to a total of 142-198 g/d. As a part of the intervention, a whole-person oriented education component perspective was also provided in this program. In the evenings, during the dinner portion of the program, everyone met for cultural or health education sessions. Details of the intervention are described in previous publications.

After-program Follow-up
After each twenty-one day program, the participants organized follow-up for themselves usually in the form of weekly pot-lucks or monthly gatherings for support and the sharing of meals. This fellowship, most often, was undertaken enthusiastically shortly after the program, however, interest dwindled within a few months of each program. Thus, organized follow-up was not consistent. Nevertheless, participants in general, continued to apply the principles of the diet and lifestyle to the extent that they could on their own without much professional support.

Long-term Follow-up Study
Eight years after the first program was conducted, a formal survey was undertaken in order to track the long-term results and efficacy of the program. In order to ensure that the follow-up period was of sufficient length, only those participants who had completed their respective programs one-year or more prior to this survey were included in the pool of eligible participants. An attempt was made to contact each participant in each of the 8 programs who were closely monitored and who completed one year or more prior to the
of follow-up or longer. All participants in these programs with a known phone number or address were called and letters sent in an attempt to schedule them for a physical measurement of their weight.

Each participant who came in for follow-up was weighed on a balance scale similar to that which had been used in all prior programs. In addition, each participant was interviewed as to their knowledge, attitudes and behavior, and a health assessment was conducted. Encouragement and additional health and nutrition education were provided at this interview. The date of each interview was recorded so that the duration since the original diet could be calculated.

**Statistical Analysis**

The statistical significance of the results of the program was analyzed using a paired, two-tailed test, and a 95% confidence interval for the difference between the means was calculated.

**Results**

Of the 173 participants in the 8 groups eligible for this follow-up study, we were able to contact and make appointments for 82 individuals for follow-up and weigh-in at the Waianae Coast Comprehensive Health Center. The follow-up period ranged from 12 months to 90 months with an average follow-up time of 33.67 months. As the time of follow-up became greater, a smaller percentage of the participants could be contacted. The attrition rate was due to a number of factors. The most difficult factor was out-migration from the community and inability to locate a current phone number or address. Another factor included the fact that follow-ups were done during working hours and many of the participants were unable to come in for a follow-up due to their employment commitment which contributed further to the attrition rate. Six of the participants of the original programs who would have otherwise been eligible for this survey were deceased.

The original weight loss over the initial three week program in these participants who completed the survey was an average of 13.9 pounds. The overall mean weight loss over all periods of follow-up of the 82 individuals surveyed was 15.1 pounds or 6.85 kg. The greatest amount of weight loss was 174 pounds, 78.9 kg, and the second greatest amount was 117 pounds, 53.1 kg. The greatest amount of weight gained was 31 pounds, 14.1 kg. Of the 82 individuals, fifty-five (67%) individuals weighed less than they did when they started and 27 remained the same or weighed more. Among these 55 individuals, 43 (72.4%) weighed 10 or more pounds less than when they started; 24 (42.3%) weighed 20 or more pounds less; 15 (18.3%) weighed 30 or more pounds less.

Retained weight loss stratified over time was also examined in figure 1. One would expect the weight loss to diminish with time, especially in light of the studies that indicate that most diet programs see their participants gain their weight lost back in only a few years.27,28 Remarkably, however, the retained reduction of weight remained fairly constant over time, when participants are stratified into periods of follow-up at two-year intervals.

Of the 82 individuals surveyed, 36 of them were surveyed one to two years after their participation in the program and they weighed a mean 15.02 lb or 6.81 kg (p < 0.0133) less than they did when they started. There were 28 participants who were in the two to four year follow-up period and they weighed a mean of 15.38 lb or 6.98 kg (p < 0.0098) less than that of when they had started. There were 10 participants surveyed in the four to six year time period and their mean weight was 12.12 lb, 5.49 kg (p < 0.1960) less than their beginning weight. The remaining 8 individuals were surveyed six to eight years from time of completion of the WDP. They weighed a mean of 18.31 lb or 8.31 kg (p < 0.0789) less than what they did at the start of the intervention.

**Discussion**

The use of an ad libitum, low fat, traditional Hawaiian diet has been shown to induce short-term weight loss in obese adults. This phenomenon may be due, primarily, to its high bulk, low caloric content. Epidemiological studies have positively correlated obesity with high amounts of dietary fat. One reason may be that the high bulk of the diet increases satiety and its low energy density causes a reduction in caloric intake despite an increase in the total amount of food consumed. Other studies of ad libitum diets have shown that subjects spontaneously consume less calories on high carbohydrate diets.22,23,24 In addition, a low fat diet has a positive correlation with leanness and weight loss independent of caloric intake. This suggests that there are other factors aside from caloric intake that contribute to obesity.

**Short term analysis**

While the average weight loss of some other weight reduction programs is greater than in this study, those results cannot be compared directly to the results of this program as treatment usually spanned several months longer than this three week program. Therefore, comparisons were made using the rate of weight loss, calculated from the results of original research by dividing the total average weight loss by the duration of treatment. Over the 21 d treatment period, the mean weight loss for all subjects was 2.1 kg/week. Other studies using the low fat approach had substantially lower rates of weight loss than ours.25,26,27 Studies using the behavior modification approach also had relatively modest rates of weight loss in comparison.22,23,24 One study using the "very low calorie diet" (VLCD) approach had results that were the most similar to our findings,25 but another showed rates similar to those.
found using behavior modification alone. Our rate even exceeded the rate of weight loss in a study using the combination of VLCD and behavior modification.

**Long term analysis**

The success of any obesity treatment program must be measured in terms of weight loss maintenance because obesity is a chronic condition. Atkinson asserts that “life-long follow-up by health professionals... is needed. Maintenance of weight loss or improvement in complications for 6 months is a minimum standard; lesser periods have little meaning.” In fact, “full success,” defined by Atkinson, “is a 5-year period of weight maintenance [for patients with chronic obesity].”

Again, due to the relatively short period of the initial program, 21 days, data taken from original research had to be reanalyzed for comparison purposes. Percent weight regain was chosen as a good guideline for comparison as well as a measure of weight cycling. Studies have found that fluctuations in body weight may result in increased long term health risks.

After 8 years of follow-up, on the average, none of the weight lost while on the Waianae Diet Program was regained. While individual weight loss or weight regain varied widely from each individual, the overall average weight loss remained at about 15 pounds. A significant constancy in the amount of weight loss retained through the first four years of follow-up and then at the six to eight year follow-up interval demonstrates that this approach appears to limit the dangers of weight cycling due to the relatively slow rate of weight regain. Continuity of weight loss was maintained over the four to six year interval of follow-up as well, though the level of significance was somewhat marginal.

Few studies have been conducted that demonstrate the success of weight loss programs after two or more years. One behavior modification program conducted by Lavery, et al. yielded similar results to ours, though the amount of weight loss maintained was noticeably less than our results. Participants demonstrated a net weight loss of 5.8 kg at time of a 2 year follow-up. Percentage weight regain of three other weight loss programs was significantly higher than ours: Kramer, et al., showed a weight regain two years after a behavior modification program of 62% in group A and 65% in group B. The study by Wadden, et al., long term evaluation of VLCD, behavior therapy, and their combination yielded weight regains of 84%, 75%, and 73%, respectively, in a three year follow-up. In a successive study with a 5 year follow-up, Wadden et al., demonstrated similar results. Only 11.1% of subjects following a VLCD maintained a weight loss of 5 kg or more and 10 kg or more. 13.3% of subjects on behavior therapy maintained a weight loss of 5 kg or more, whereas 0% could maintain a weight loss of 10 kg or more. Combination therapy allowed 27.3% and 9.1% of subjects to maintain a weight loss of 5 kg more and 10 kg or more. Hovell, et al., presented subjects who lost a mean of 83.9% of their excess weight, only to regain an average of 59% to 82% of their initial excess weight by 30 months of follow-up.

Other studies examining the efficacy of an ad libitum, low fat, high carbohydrate diet have confirmed its greater effectiveness in promoting sustained weight loss, though their follow-up period was not as exhaustive: In one such weight maintenance program by Toubro and Astrupin which an ad libitum diet or a fixed energy regimen was administered, 65% of those subjects following the ad libitum diet maintained a weight loss greater than 5 kg after one year of follow-up. Comparatively, only 40% of those subjects on a fixed energy intake were able to maintain a weight loss greater than 5 kg at time of follow-up. The ad libitum group also maintained 13.2 kg of the initial weight loss of 13.5 kg, whereas the fixed energy intake group maintained 9.7 kg of the initial 13.8 kg weight loss. This clinical study and a successive review by Astrup, et al., concluded that “after a major weight loss, an ad libitum, low fat, [high carbohydrate] diet program, appears to be superior to caloric counting in maintaining weight loss 2 years later [from initial treatment].” Fitzwater, et al., also showed additional average weight loss at two years follow-up: 53% of subjects maintained their weight loss or continued to lose weight; 24% regained some weight, but below that of their pretreatment weight, whereas 23% incurred full weight rebound.

The steady maintenance of weight during the 90 month period was remarkable in that the mean weight reduction remained at 15 pounds. While these figures are very promising, they do need to be read with some caution. First it should be noted that as may be expected, as time elapsed, there were fewer participants who could be reached. Thus, the groups with a longer follow-up period had fewer participants: The 4-6 year follow-up group had only 10 participants who were measured in this survey, whereas the 6-8 year group had only 8 participants. This decrease in “n” had a commensurate effect on the significance of the survey results. There may also be some measure of selection bias as some of the individuals may have declined to participate if they had not retained much of their healthy lifestyle and weight control habits. Finally, the individual weight and amount of weight loss varied fairly broadly from individual to individual, especially in the later follow-up intervals. This wide variation had a consequential effect on the associated confidence indexes per time interval, as some participants lost a remarkable amount of weight, while a few gained in weight. Again, the corresponding p-values from the 4-6 year and 6-8 year marks are only moderately reliable as they are not significant. With these cautions in mind, a complete survey of the long-term weight loss of the ad libitum feeding of traditional Hawaiian diet reveals a remarkable consistency that suggests an effective long-term dietary intervention.

Assuming the results are real we can at least speculate about what is it about this program that yields these relatively good results. As with other ad libitum feeding diets, we experienced results that were superior to simple calorie restriction diets. It appears that an approach to weight loss that features ad libitum feeding of foods high in mass to energy ratio yet are low in mass to energy density is an easier approach to maintain than other diets. It may be that a whole person approach, which includes modifications based on traditional Hawaiian diet had a long-term impact on diet and lifestyle changes even without consistent follow-up or support. This has important implications in hard to reach populations such as those with lowered socio-economic status and in minority groups who may be alienated from white-middle class level health education.

**Conclusion**

In this long-term follow-up survey, the traditional Hawaiian diet administered ad libitum is a comparatively effective approach to the
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treatment of obesity in terms of rate of weight loss and extended maintenance. Utilizing a whole person approach, including lifestyle behavioral modification, culture-sensitive education, and ad libitum feeding of traditional foods, participants on average were able to maintain a consistent weight loss over the course of eight years following the cessation of the initial program.

Some discretion should be exercised however, when interpreting these results. Over the course of follow-up, contact with many of the participants could not be established or maintained for various reasons. Ideally, the number of participants in successive follow-up years should be maintained so as to strengthen the significance of the results. Future studies should also add a control group and provide for closer long-term follow-up so that a larger percentage of the participants from the original interventions may be included in the long-term analysis. It is also suggested that the subjects should be reevaluated at least annually with blood analysis for serum lipids, glucose and other health risk factors to provide an even more detailed survey. Nevertheless, a positive overall performance from this three week, whole person, ad libitum program may be an effective long-term weight loss intervention and warrants further study.

Acknowledgements

The authors wish to thank the generous support of the Waianae Coast Comprehensive Health Center and the Office of Hawaiian Affairs without which this study could have been completed.

References

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The Dietary Treatment of Inflammatory Arthritis: Case Reports and Review of the Literature

Theresa C. Danao-Camara MD, FACP, FACR and Terry T. Shintani MD, MPH, JD

Abstract

Two patients with seropositive inflammatory arthropathies who experienced clinical improvement on the Waianae Diet are presented.

The scientific literature validates the usefulness of fasting in the control of joint inflammation. Elimination diets are variably successful. Fasting followed by a vegetarian diet can produce a sustained positive response measured clinically and by laboratory variables of inflammation; the efficacy of such an approach appears to hinge on the alteration of oral flora. Swinging the balance of dietary fats in favor of the omega 3 and omega 6 fatty acids has an antiinflammatory effect but does not appear to correct the basic immunologic processes involved in the development of the arthropathies. Practical guidelines for the application of this information are offered.

Introduction: The Hawaii Diet Program

The Hawaii Diet is a multi-cultural version of the Waianae Diet which is based on traditional Hawaiian foods. The Waianae diet program was developed at the Waianae Coast Comprehensive Health Center in response to the high rates of obesity and chronic disease in the native Hawaiian population. The selection of food consists of items eaten in Hawaii before the onset of Western influence, including such items as taro (a native potato), poi, sweet potatoes, yams, breadfruit, rootcrop greens, fruit, seaweed, fish and chicken. All items are served raw or steamed. The diet contains less than 10% fat, 12 to 15% protein and 75 to 78% carbohydrate. The Hawaii diet is based on the same macronutrient composition but with multi-cultural foods replacing many of the traditional Hawaiian meals. The Hawaii Diet includes as its staples in addition to poi and taro, whole starches such as brown rice, pasta, vegetables, fruit, legumes and a small amount of seafood or poultry.

Both diets have been shown to be effective in the control of high blood pressure, diabetes and hypercholesterolemia. It has not heretofore been reported to positively influence the activity of the inflammatory arthritides.

Case Reports

Case 1. LS, a 38 year old Japanese female presented with fevers, 20 pound weight loss, joint pain and polyarticular synovitis in the metacarpophalangeal joints and ankles. Antinuclear antibody titer was 1:80 with a speckled pattern, sedimentation rate 53 mm/hr; antibodies to ribonucleoprotein and SSA were present. A presumptive diagnosis of systemic lupus erythematosus (SLE) was made, and the patient was started on low-dose oral prednisone (10 mg/day) supplemented with indomethacin for the control of fever. Hydroxychloroquine 200 mg/day was eventually added as a steroid-sparing agent.

Two years into the disease course, the patient went on the Hawaii Diet. The sedimentation rate dropped from the 70 to 90 mm/hr range to 39 mm/hr. The platelet count, which had been elevated, normalized. The patient lost 10 pounds over 3 months. She reported increased energy, and was able to discontinue indomethacin without recurrence of the fevers. Synovitis disappeared.

The diet was discontinued after three months. Within a month, fatigue, rashes, fevers and joint pain had recurred.

Case 2. HS, a 44 year old female of mixed Hawaiian-European ancestry presented with synovitis in the metacarpophalangeal and proximal interphalangeal joints. She had an antinuclear antibody titer of 1:256, and antibody to DNA of 217 IU/ml (normal < 100 IU/ml). A presumptive diagnosis of systemic lupus erythematosus was made, and the patient was started on prednisone 10 mg/day, hydroxychloroquine 200mg BID and ketoprofen 200 mg/day. The response to oral hydroxychloroquine was less than optimal; this agent was discontinued. Steroid side effects (hyperglycemia, weight gain, fluid retention and Cushigoid facies) prompted the addition of oral methotrexate 10 and then 12.5 mg/week. Prednisone was tapered to 5 mg every other day; doses less than this resulted in disabling synovitis in the small joints of the hands.

The patient went on the Waianae diet program two years into the disease course. Within two months, the patient had discontinued the prednisone. On her own, she also went off the methotrexate a month later. She remained free of pain and synovitis for another month after she went off the diet, at which point both the prednisone and methotrexate had to be restarted.

Neither of these two patients meet strict classification criteria for SLE, but both clearly had an inflammatory arthropathy accompanied by significant serologic markers of autoimmune activity.

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Honolulu, HI 96813
The Dietary Treatment of Arthritis

Interest in the impact of nutrition on disease causation, activity and cure is universal among patients with arthritis. The great majority will attempt some form of dietary manipulation, in large part unsupervised by and even unknown to their physician.2

Clearly, in gout and saturnine gout, dietary forces have a well-defined role, the first being a disorder of purine metabolism and elimination, and the second a lead intoxication state. Obesity is a risk factor for osteoarthritis, especially in the weight-bearing joints. Reiter’s syndrome is a reactive arthropathy triggered in some cases by food pathogens. Beyond these well-defined circumstances, however, the role of food in the arthropathies is controversial.

Arthritis as a Food Allergy

The literature is replete with case reports of arthritis and synovitis being temporally associated with the ingestion of certain foods—dairy products 3,4 gluten5 and azo dyes6. The behavior of the arthropathy in these situations satisfies classical medical criteria for causation—ie. exacerbation with challenge, remission with dechallenge, and reactivation with rechallenge. By and large, however, these cases are seronegative and nonerosive. More importantly, they are sporadic and fairly rare.

Elemental hypoallergenic diets have been studied in patients with rheumatoid arthritis (RA).7,8,9 As a group, patients on these diets tend to do better subjectively, but objective improvements in the laboratory measures of inflammation do not improve significantly. Certain individuals respond better than others, but the magnitude of the response and the number of patients affected favorably are too small to produce statistical significance. The responders tend to be heavier at outset, and tend to have greater disease activity than the non-responders. Van de Laar et al have obtained synovial membrane and small intestinal biopsies on some of these responders. Mast cells and IgE bearing cells are decreased at these sites during dietary manipulation.7 The authors postulate that these histologic changes suggest an allergological mechanism underlying the observed arthritis response.

Kavanagh et al9 have attempted to sustain improvement by reinstituting feeding selectively. After an elemental diet, patients were refed with one food group at a time. Those food groups followed by a disease flare were eliminated from each individual’s maintenance regimen. Even such an individualized approach, however, failed to sustain improvement at 24 weeks.

The Effects of Fasting

Fasting—that is, the voluntary abstention from food for a limited period of time—has been validated as an effective short-term suppressor of inflammation in the arthritides.10,11,12 Subjective improvement in pain and stiffness starts within three to five days of the initiation of the fast, and is sustained for its duration. Joint inflammation indices as well as acute phase reactants (sedimentation rate, orosomucoid, haptoglobins) decrease. Return to pretreatment disease activity occurs on the day after the fast is discontinued. In the hands of most investigators, no maintenance diet can sustain the benefits of the fast. (An exception to this observation has been reported, and is reviewed below.)

While almost universal relapse at the termination of the fast makes fasting an untenable treatment for RA, understanding the mechanisms underlying the clinical response is instructive.

Lymphocytes are affected by fasting. Antigen-specific B cell responses improve.13 Suppressor cell activity, usually depressed in RA patients, normalizes with fasting.14

Neutrophilic functions are also influenced by food deprivation. Release of the pro-inflammatory chemical leukotriene B4 from neutrophils goes down, as does the ability to generate cytokotisons in vitro.15 Levels of linoleic and alpha linolenic acids are unchanged; their metabolites, arachidonic and eicosapentaenoic acid increase. Such a profile can be produced by impaired activity of phospholipase and 5-lipoxygenase, enzymes involved in the metabolism of arachidonic acid to leukotriene B4. From these data, Hafstrom et al have postulated stimulus-response decoupling of neutrophil metabolism reduced ability to generate cytokotisons, reduced leukotriene formation) as mechanisms of the antiinflammatory effect of food deprivation.

Fasting also alters intestinal permeability.16 Polyethylene glycol molecules penetrate intestinal mucosa less well during fasting; this reverses with refeeding of a lactovegetarian diet. If indeed inflammatory arthritis is an allergic or hyperimmune reaction to foreign antigens, the decreased penetration of immunostimulants may explain the temporary relief experienced by patients on a fast.

The Oslo Cohort

In the late 1980s, investigators in Oslo entered a group of 53 patients with RA in a single-blind controlled trial of diet therapy. Twenty-seven patients were randomized in a four-week stay at a health farm. The control group stayed for four weeks at a convalescent home, but ate an ordinary diet throughout the study period.

Treatment started with a 7 to 10 day subtotal fast. After the fast, one new food item was introduced every second day. If this was followed by an exacerbation in symptoms, the offending food was withdrawn for one week. If a similar exacerbation occurred with later rechallenge, then that food item was permanently removed from the maintenance diet. During the first 14 months, patients were kept on a strict gluten-free vegan diet (ie no meat, fish, eggs, dairy products or food containing gluten). After this period, dairy and gluten were reintroduced. Foods producing a flare in disease activity were recorded in a personal journal. Clinical and laboratory assessments were performed at 1, 4, 7, 10 and 13 months. One year after conclusion of the study (ie 25 months after the initiation of the diet), patients were contacted for follow-up examinations.

The results of this study have been published in a series of related articles covering the clinical, biological, psychosociological and immunologic sequela of the intervention.16, 17, 18, 19, 20, 21, 22

After four weeks at the health farm, the diet group showed significant improvements in the number of tender, swollen joints, pain, morning stiffness, grip strength, sedimentation rate, C reactive protein, and Health Assessment Questionnaire score (HAQ; a standardized instrument measuring the ease with which one performs the activities of daily living). Rest at a health farm did positively influence disease activity; the control group also demonstrated improved pain scores. Subjective improvement was accompanied by statistically significant drops in platelet counts, total IgG, IgM rheumatoid factor, C3 activation products, and complement compo-
nents C3 and C4, all of which are consistent with an amelioration of immunologic hyperactivity.

A little less than half of the experimental group (10 of the 24 evaluable subjects) could be classified as good responders, defined as having a 2-grade improvement on a subjective global assessment scale plus a 20% or better decrease in joint count, pain score, HAQ, and sedimentation rate. These good responders maintained their improvement at the one-year and two-year evaluation points.

Was there anything unique about these responders—ie are there characteristics that can identify which patients are likely to benefit from dietary intervention prior to the fact? The investigators did determine that:

a. diet responders tended to have had their disease for a shorter time (mean of 6 years versus 14 years for the nonresponders); this is consistent with the response to pharmacologic interventions, implying a more malleable situation in the early inflammatory phases of the disease, before chronic damage is in place,

b. diet responders were more likely to be seronegative (30% versus 58% for the nonresponders); this is reminiscent of the data for RA and food allergies, vide supra,

c. diet responders had a significantly lower belief in the effect of ordinary medical treatment compared with the nonresponders.

The investigators tried to identify laboratory variables that correlated with clinical response. They found that neither immunoglobulin levels nor phospholipid profiles covaried with clinical disease activity. While RA patients were found to have elevated levels of antibodies to food allergens (consistent with generalized B cell hyperactivity), the activity of these immunoglobulins did not correlate with the disease course. Plasma arachidonic acid levels dropped initially and returned to baseline with the lactovegetarian diet; eicosapentaenoic acid levels stayed low throughout the diet. Contrary to findings from the omega fatty acid literature (vide infra), plasma phospholipid profiles did not covary with disease activity.

What did appear to be consistently predictive of clinical improvement was a change in fecal flora. Gas-liquid chromatography (GLC) of bacterial cellular fatty acids obtained from stool samples indicated that the microbial profile changes significantly in patients responding to diet therapy. Nonresponders do not exhibit this variability. Unfortunately, GLC is a sensitive measure of quantitative changes in cell wall profiles, but is unable to determine specifically which bacterial species are decreasing or increasing.

Other Diet Programs

A calorie-optimized diet enhanced with fish meals and antioxidants has been tested in a single-blind 6 month study in Norway. Compliance was monitored through a diet diary. While the study is confounded by a 26% drop-out rate, those able to follow the diet demonstrated less morning stiffness, fewer swollen joints, less pain, and reduced medication cost. Objective laboratory data, however, did not change.

The Dong diet has also been put forward as a therapeutic diet for arthritis. This diet was designed by a southern California dermatologist, Dr. Colin Dong. He came down with RA and cured himself by returning to the traditional Chinese diet of his childhood. The diet consists of fish, little meat and occasional fowl, no fruit, herbs or spices, no dairy products, no alcohol, and no additives or preservatives. The diet was tested by the group of Dr. Richard Panush at the University of Florida in a 10-week randomized double-blind study involving patients. There were no statistically significant differences between the two groups at any point in the study. Interestingly, however, two individuals in the experimental group achieved noteworthy disease control, and elected to remain on the diet after termination of the study. Both had strong personal and family histories of atopy—other than this one observation, nothing else distinguished these remarkable responders from the rest of the subjects.

The Role of Dietary Fats

Fatty acids seem to have some effect on the inflammatory process possibly as a result of their role as precursors to prostaglandins and leukotrienes. N-3 (the designation refers to the location of the first double bond in the carbon chain, counting from the amino terminus) fatty acids are antiinflammatory. The 20-carbon n-6 and n-3 fatty acids arachidonic acid (AA) and eicosapentaenoic acid (EPA) are biosynthetic precursors for n-6 and n-3 eicosanoids of the leukotriene (LT) and prostaglandin (PG) families. The n-6 eicosanoids LTB4 and PGE2 are pro-inflammatory, causing neutrophil chemotaxis and activation as well as increased vascular permeability. The n-3 homologs are either less active (LTB5) or poorly synthesized from

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Table 1.—Sources, relationships and inflammatory effects of some metabolically important unsaturated fatty acids (adapted from 32).

<table>
<thead>
<tr>
<th></th>
<th>n-6</th>
<th>n-3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>18 Carbon Fatty Acids</strong></td>
<td>Linoleic Acid C18:2</td>
<td>Linolenic Acid C18:3</td>
</tr>
<tr>
<td><strong>Sources</strong></td>
<td>Soybean, sunflower and corn oil</td>
<td>Flaxseed, canola oil</td>
</tr>
<tr>
<td><strong>20 Carbon Fatty Acids</strong></td>
<td>Arachidonic Acid C20:4</td>
<td>Eicosapentaenoic Acid C20:5</td>
</tr>
<tr>
<td><strong>Sources</strong></td>
<td>From meat and ingested linoleic acid</td>
<td>From ingested linolenic acid, and from fish and fish oil</td>
</tr>
<tr>
<td><strong>Metabolized to</strong></td>
<td>Proinflammatory n-6 PGs and LTs</td>
<td>Competitive inhibitors of n-6 PGs and LT synthesis</td>
</tr>
<tr>
<td><strong>Effect on cytokines</strong></td>
<td>Unknown</td>
<td>Suppression of TNFa and IL1b production</td>
</tr>
</tbody>
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Abbreviations used: PG - prostaglandin, LT - leukotriene, TNF - tumor necrosis factor, IL - interleukin.
EPA (PGE3). Dietary n-3 fatty acids can increase cellular n-3 content and decrease n-6 eicosanoid synthesis. Dietary n-3 fats also suppress production of the peptide cytokines interleukin 1 beta (IL1B) and tumor necrosis factor alpha (TNFa). These cytokines stimulate PGE2 synthesis and collagenase production, and increase expression of adhesion molecules that allow leukocyte extravasation.  

Epidemiologic studies suggest a role for N-3 supplementation in RA. The consumption of baked or broiled fish appears to protect against rheumatoid arthritis, and the use of olive oil seems to have the same effect. At least 13 prospective studies on the role of fish oils in the symptomatic control of RA have been published in the English-language literature. These are summarized in Table 2.

Table 2.—Experimental studies of n-3 fatty acids in RA. Abbreviations used: EPA - eicosapentaenoic acid, DHA - docosahexaenoic acid, PUFA - polyunsaturated fatty acids, gel - morning stiffness, NSAID - nonsteroidal antiinflammatory drug, LT - leukotriene, IL - interleukin, TNF - tumor necrosis factor.

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Subjects, Study Period</th>
<th>Intervention</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kremer, 1985 (35)</td>
<td>37 12 weeks</td>
<td>1.8 gm EPA; diet high in PUFA, low in saturated fats</td>
<td>less pain and joint swelling, but rebound at the end</td>
</tr>
<tr>
<td>Kremer, 1987 (36)</td>
<td>40 32 weeks</td>
<td>2.7 gm EPA 1.8 gm DHA</td>
<td>less fatigue and joint swelling, decreased LTB4</td>
</tr>
<tr>
<td>Magaro, 1988 (37)</td>
<td>12 30 days</td>
<td>1.6 gm EPA 1.1 gm DHA</td>
<td>less disease activity; less neutrophil chemiluminescence</td>
</tr>
<tr>
<td>Van der Tempel, 1990 (38)</td>
<td>16 24 weeks</td>
<td>2.04 gm 20:5 n-3 1.32 gm 22:6 n-3</td>
<td>less gel and joint swelling, decreased LTB4, increased LTB5</td>
</tr>
<tr>
<td>Tulleken, 1990 (39)</td>
<td>27 12 weeks</td>
<td>2.0 gm EPA 1.3 gm DHA</td>
<td>less pain and fewer swollen joints</td>
</tr>
<tr>
<td>Kremer, 1990 (40)</td>
<td>49 24 weeks</td>
<td>27 mg/kg EPA 18 mg/kg DHA, vs 54 mg/kg EPA 36 mg/kg DHA vs 6.8 gm oleic acid (olive oil)</td>
<td>more improvement with high dose fish oils; decreased LTB4 and IL1; olive oil also helped</td>
</tr>
<tr>
<td>Nielsen, 1992 (41)</td>
<td>51 12 weeks</td>
<td>3.6 gm n-3 PUFA</td>
<td>less gel, less tenderness</td>
</tr>
<tr>
<td>Skoldstam, 1992 (42)</td>
<td>43 6 months</td>
<td>fish oil 10 gm/day</td>
<td>decreased NSAID consumption</td>
</tr>
<tr>
<td>Espersen, 1992 (43)</td>
<td>32 12 weeks</td>
<td>3.6 gm n-3 PUFA</td>
<td>improved Ritchie's index; drop in IL1; TNF and complement activation products unchanged</td>
</tr>
<tr>
<td>Kjeldsen-Kragh, 1992 (44)</td>
<td>67 16 weeks</td>
<td>3.8 gm EPA 2.0 gm DHA with doses of naproxen</td>
<td>fish oils mitigated impact of naproxen withdrawal</td>
</tr>
<tr>
<td>Lau, 1993 (45)</td>
<td>64 12 months</td>
<td>10 MaxEPA caps/day</td>
<td>decreased NSAID use</td>
</tr>
<tr>
<td>Geusens, 1994 (46)</td>
<td>90 12 months</td>
<td>2.6 gm n-3 vs 6 gm olive oil</td>
<td>decreased medication use only in n-3 group</td>
</tr>
<tr>
<td>Kremer, 1995 (47)</td>
<td>66 30 weeks</td>
<td>4.6 gm EPA 2.5 gm DHA diclofenac withdrawal</td>
<td>diclofenac could be stopped without a flare</td>
</tr>
</tbody>
</table>
N-3 fatty acids suppress joint swelling and decrease pain in a dose-dependent fashion. Inflammatory eicosanoid levels go down. The more traditional laboratory measures of RA activity, such as the sedimentation rate and complement degradation products, as well as the titer of rheumatoid factor, are by and large untouched. The clinical effect lasts no longer than four weeks after the supplements are stopped. The magnitude of the response is not impressive—at best, n-3 supplementation may have some drug-sparing properties, allowing the patient to use lower doses of a antiinflammatory or disease-modifier.

The plasma lipid alterations necessary to achieve clinically significant effects require 10 to 15 MaxEPA capsules a day. The same levels can be achieved by including 4 to 6 meals with fish per week.

Some Practical Advice

What should the practitioner say to a patient who asks about the relationship between non-gout inflammatory arthritis and his or her diet? Data support these guidelines:

1. Inflammatory arthritis is a true food intolerance only in a very small number of patients. These people tend to have seronegative, nonerosive disease.

2. No foods or food groups have been consistently identified as a cause, trigger or aggravating factor in unselected patients. However, if one clearly experiences disease worsening with a particular dietary item, then that item ought to be avoided. Some items that have produced such worsening in a few individuals are dairy products, nitrates, alcohol, simple sugars and azo dyes. Since the ability of these foods and additives to cause disease flares is far from universal, testing one’s reaction to each in turn makes better sense than avoiding everything indiscriminately.

3. Fasting clearly suppresses inflammation in the joints. Fasting should not be undertaken without medical supervision for longer than five days. Fasting may be dangerous in the setting of previous or ongoing medication intake, and should be discussed with the medical practitioner. The benefits of fasting are very difficult to sustain, but in some situations can be made to last by switching to a vegan diet. The people who tend to respond favorably to such dietary manipulation tend to be those who have had their disease for a shorter period of time. End-stage, burnt-out disease with severe joint destruction is unlikely to be helped by these measures.

4. Based on the work of Dr. Panush and this current report, reasonable diets to try are the Dong diet and the Hawaii/Waianae diet. Books on both remain widely available in popular bookstores. The responses reported are evident by 10 weeks; there is no data to support staying on these diets longer than that period in the hope of getting a delayed response. It must also be borne in mind that the evidence that these diets work is limited and anecdotal.

5. Omega 3 fatty acids (fish oils) can help suppress joint inflammation. The desired blood levels of the necessary fatty acids can be obtained by eating six fatty fish meal a week. Fish oils are about as effective as an NSAID. They do not reverse the basic immunologic processes underlying RA.

6. The use of olive oil may be of some benefit.

7. While diet can be a useful adjunct in the treatment of the inflammatory arthropathies, there is no reliable and consistent way to use it as monotherapy. It should be part of an integrated approach that pays attention to proper rest and exercise, work modification, family support, stress management and judiciously selected pharmacotherapy.

References


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The National Cancer Institute has free booklets about breast cancer screening. To order these publications, call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). Persons with TTY equipment, dial 1-800-332-8615.

http://rex.nci.nih.gov
Life in These Parts... Retired Doctor Lives Aloha

Soft spoken ‘Native Hawaiian’, Charman Akina grew up in Honolulu, graduated from Punahou and Stanford and practiced plush medicine with the Honolulu Medical Group for 30 years...

Answering an inner call, Charman retired 6 years ago joined the Waimanalo Health Center as an unpaid volunteer who even made house calls. "I thought it was time to practice medicine in a predominantly Hawaiian community, because we’re always hearing about the poor health statistics on Hawaiians. I wanted to come to a place that wasn’t a “squeaky wheel” – some place that had needs in terms of medical staff and medical care...Coming from a big clinic environment to a rural environment is a real change, but it really rounds out my career and it’s been very educational."

Mabel Spencer, one of the clinic founders says, "Charman’s patients love him and many followed him from the Honolulu Medical Group. He’s the only doctor I know who lets them call him at home — and that’s too much, if you ask me."

(Dear Lord... Please make more of us in the image of Charman Akina...)

Life In These Parts... Myron Shirasu ran into former fellow QMC resident Joe Bautista several years ago and they exchanged news about their families...

Myron: "My daughter is now in Yale."
Joe: "Oh my! What did she do?"
Myron elucidated: "Yale — not Jail."

Only in Hawaii, eh?

“One of my new medical assistant students took a very nice history on a patient and wrote: "The patient received KIMO THERAPY two years ago.""

(Norman Goldstein)

Potpourri... (From Isaac Asimov’s Treasury of Humor)

Mrs. Moskowitz and Mrs. Finkelstein met for the first time after a long separation, and inquiries as to status and health at once arose.

"Tell me, Mrs. Finkelstein," said Mrs. Moskowitz, "How is your sister Sadie?"
"Oh Sadie, poor Sadie," moaned Mrs. Finkelstein, "She has cancer."

Whereupon Mrs. Moskowitz said consolingly, "Listen, Cancer, shamaner – as long as you’re healthy."

It was rough ocean crossing and Mr. James was suffering the tortures of the damned. He was leaning over the rail, retching miserably, when a kindly steward patted him on the shoulder.

"I know sir," said the steward, "that it seems awful, but remember, no one ever died of seasickness."

Mr. Jones lifted his green countenance to the steward’s concerned face and said, “For Heaven’s sake, man. Don’t say that. It’s only the wonderful hope of dying that’s keeping me alive.”

Smith met Jones in the clubhouse one day and said, “I understand you experienced great tragedy last week.”
Jones sipped his drink and nodded, his eyes growing dark with the memory.

“I was playing a threesome with Brown,” he said, “and the poor fellow dropped dead on the 9th hole.”

Smith said, “I understand you carried him back to the clubhouse. That must have been difficult, considering he weighed two hundred pounds.”

James said, “Oh, it wasn’t the carrying that was so hard. It was putting him down at every stroke and picking him up again.”

Three buddies died in a car crash and went to Heaven for orientation. St. Peter asked, “When you’re in your caskets and friends and family are mourning you, what would you like to hear them say about you?”

“I would like to hear them say that I was a fine doctor and a great family man,” the first one replied.

“I would like to hear that I was a wonderful school teacher who made a difference in children’s lives,” said the second.

“And I, the last fellow said, “would like to hear them say, “Look he’s moving!” (From Playboy Apr '99)

Medical Tid Bits... Re Colon Cancer Prevention?

Physicians from St. Luke’s Roosevelt Hospital Center in New York reported at the American Association for Cancer Research annual scientific meeting in April that ASA with Statins may cut down colon cancer risk...

Re Pancreatic Cancer Therapy

Virulizin (an immune system booster derived from cow bile) shows promise in early testing against pancreatic cancer. Dr. Channan Liu of the University of Nebraska presented data on preliminary testing of Virulizin on 26 patients who had failed to respond to Eli Lilly’s Gemzar. Their average survival was just over six months, but there were some interesting glimmers. One patient is still alive 22 months later and in another patient, tumor that had spread to the liver completely disappeared, though the patient eventually died of cancer in the lung.

Potpourri II... (Milton Berle’s humor)

The rural doctor came out to the farm to check on the farmer’s wife. Upon arrival, the doctor felt thirsty. He walked over to the well to bring up some cool water, but slipped and fell in. The moral is that the doctor should take care of the sick and leave the well alone.

Doctor: You should live to be eighty.
Patient: I’m eighty five.
Doctor: See - what did I tell you.

An elderly lady fills out the registration form in the doctor’s office. After the address, the form asks for “Zip.” She writes, “Not bad for my age.”

Q: What do fishermen and hypochondriacs have in common?
A: They don’t really have to catch anything to be happy.
Q: What’s the difference between an English actuary and a Sicilian actuary?
A: The English actuary can tell how many people are going to die next year. A Sicilian actuary can give you their names.

Condensation of the medical article: “Vulnerable Plaque: The Future of Heart Disease” by Associated Press reporter, Daniel Haney... (Star-Bulletin Jan 12, 1999)

*Obstructed channels account for 15% of MI’s while vulnerable plaques account for 50%. Vulnerable plaques are soft and squishy. The plaques break off and form clots which block one of the three main coronary arteries...This explains a. Why MI’s occur in people in peak health b. Why CABB and angioplasty do not prevent MI’s and c. Why STATINS decrease the risk of MI’s without improving coronary flow.

The vulnerable plaque is an unseen danger (angiograms only show blockage and not the plaque.) Plaques usually grow outward into the arterial wall instead of into the arterial lumen. “By the time you see an irregularity on angiogram (i.e. the first little 25% narrowing, over 85% of the artery is atherosclerotic”) (Cleveland Clinic’s Steven Nissen)”Not all plaques are alike” (Frank Kologe – Armed Forces Institute of Path) Soft plaques: cholesterol ester; Hard plaque: crystalline cholesterol.

The Process: Soft plaques are caused by injury to the arterial wall (i.e HTN, smoking, high cholesterol) The body confuses this cholesterol plaque with infection and sends WBC’s which in turn produce tissue factor and generates a large clot. The clot comes in contact with blood and metalloproteinase which eat away at the fibrous cap. Our hormonal surge needed to face the day can break the vulnerable plaque. Mechanical forces can easily disrupt this plaque. While a rupturing plaque can lead to a heart attack, most of the time nothing happens. It seems that plaques break all the time and those that trigger heart attacks are the unlucky exception.

Statins have already proven to be a true breakthrough in cardiac protection. For people at high risk, statins reduce the chance of heart attack and death by more than 50% and even in healthy people with normal cholesterol by 20%. The statins probably draw out the soft cholesterol leaving the plaque firmer, more stable and less inflamed, but not necessarily smaller.
Introduction:
a. Depression among elderly wide spread
b. Serious illness in its own right
c. Occurs in context of medical illness
d. Frequently under diagnosed
e. Eminently treatable.

Prevalence of Depression:
a. 10% of individuals in elderly community
b. 17-37% of primary care elderly
c. 50-60% of elderly in nursing homes

Medical Conditions a/c Depression:
- Medications: steroids, cetimadine, anti-hypertensives, NSAID’s, sedatives, digitalis, alcohol, opiates, cocain
- CNS Disease: neurodegenerative disease, CVA
c. Heart Disease: Post MI, CHF
d. Collagen-Vascular: RA, SLE, TA
e. Endocrine: Hypothyroidism, Cushings
f. Neoplasm: pancreas, lung, breast
g. Renal Disease: dialysis

Causes & Effects of Late Life Depression:

**Depression**
- Suicide
- Anxiety, etch
- Cognitive Impairment
- Disability
- Medical sxs
- Healthcare utilization
- Mortality

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**Diagnosis:** DSM IV Subtype
- Major Depression: Uncomplicated; Melancholic; Psychotic; single episode/recurrent
- Dysthymia
- Minor Depression
- Brief & Recurrent
- Mixed anxiety-depression

Major Depression (5 or more of the following symptoms over 2 weeks):
- Depressed mood or loss of pleasure or interest
- Lost interest or pleasure in activities
- Changes in appetite or wtg
- Insomnia or hypersomnia
- Psychomotor retardation or agitation
- Feeling of worthlessness or guilt
- Difficulty thinking, concentrating or deciding
- Recurrent death thoughts or suicidal feelings

**Causes & Effects of Late Life Depression**

**Clues to Depression:**
1. In Primary Care: a. Help seeking complaints b. Frequent calls & visits c. High utilization of service
2. In-Hospital Patients: a. CABG, hip Fx, MI, Stroke b. Delayed recovery c. Treatment refused d. Discharge problem

**Barriers to Dx:**
a. Disorder itself
b. The patient
c. The provider
d. Health care system

**Improve Recognition:**
a. High index suspicion
b. Follow up clues with screening questions: Are you sad? Sleeping poorly? Do you worry too much? What have you enjoyed doing lately?
c. Talk to relatives & other professionals
d. Use screening instruments: eg CES-D, GDS

**Treatment:**
a. Pharmacologic
b. Psycho therapy
c. Electroconvulsive therapy
d. Combination

**Goals of Treatment:**
a. Decrease & resolve depressive Sys
b. Restore psychosocial function
c. Prevent relapse or recurrence
d. Relieve excess disability
e. Help patients accept medical therapies
f. Ease adaptation to irreversible loss

**STEPS:**
(Factors to consider in antidepressant selection)
- Safety - Drug interaction
- Tolerability - Acute and long term
- Efficiency - Onset, action, therapy & prophylaxis, activity in sub population
- Payment - Cost effectiveness, e. Simplicity

**Side Effects of Antidepressive therapy:**
1. CNS Effects a. Activation b. Sedation
2. GI Side Effects: Weight gain, Weight loss
3. Sexual dysfunction
4. Cardiovascular: HTN
5. Others: Dry mouth, Sweating

**Pharmacotherapy: Agents relevant to elderly:**
1. Tryptamines: Nortriptyline (Desipramine)
2. Trazodopyridines: Trazodone (Desyrel)
3. MAOIs: Nardil Parnate
4. SSRIs: Prozac, Paxil, Zoloft, Celexa
5. SNRIs/SDRIs: Effexor, Wellbutin

**Prozac:** 1987... anxiety & insomnia; appetite suppression

**Paxel:** sedating (esp nursing home pts); xx sedation in frail pts; sexual dysfunction

**Zoloft:** less sedating

**Celexa:** 10 yr experience in Europe; esp geriatric pts; safe agent; well tolerated by geriatric pts; doesn’t block liver enzymes

**Dosing:**
- Tricycles: Nortriptyline: Start 10 - 25 mg hs
- Trazodopyridines: Start 50-150 mg/72 h
- MAOIs: 10-25 mg bid
- SSRIs: Start 10-25 mg hs
- SNRIs: Start 115 mg cc

**Common Errors in Primary Care:**
- Use of anxiolytics as primary or sole drug
- Use of amitryptiline, imipramine or doxapine
- Failure to monitor outcome
- Underdosing
- Failure to consider drug interactions
- Early discontinuation
- Polypharmacy

**Pharmacokinetics:**
- Absorption
- Distribution
- Clearance — metabolism

**Referral:**
1. Problem in DX
2. Problems in Therapy

**Conclusions:**
- Late life depression is widespread
- Strongly a/c mental illness
- It is a serious illness
- It is eminently treatable
- Proper treatment and management require time and skill

**Potpourri III...**
A man walked into a drug store and asked the pharmacist if he had something to cure hiccups. The pharmacist promptly reached out and slapped the fellow’s face.

“What did you do that for?” the man asked.

“Well, you don’t have the hiccups anymore, do you?”

“No, but out in the car my wife still does.”

Two guys sat down for lunch in the office cafeteria.

“Hey, what happened to Pete in payroll?” one asked.

“He got this harebrained notion he was going to build new car of car” his co-worker replied.

“How was he going to do it?”

“He took an engine from a Pontiac, tires from a Chevy, seats from a Lincoln, hub caps from a Caddy and well, you get the idea.”

“So what did he end up with?”

“Ten years to life.”

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**Hawaii Medical Journal, Vol 58, May 1999**
**Women and Heart Disease**

**Why coronary heart disease is a major health problem for women:**

- As women approach menopause, their risk of heart disease increases and continues to rise with aging.
- Women with diabetes have 3 to 7 times the risk of heart disease as men.
- Fewer women than men are quitting smoking.
- About 44% of women 55 to 64 have high blood pressure.

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**Classified Notices**

To place a classified notice:

- HMA members.—Please send a signed and typewritten ad to the HMA office. As a benefit of membership, HMA members may place a complimentary one-time classified ad in HMJ as space is available.
- Nonmembers.—Please call 536-7702 for a non-member form. Rates are $1.50 a word with a minimum of 20 words or $30. Not commissionable. Payment must accompany written order.

### Office Space

- **Pearl City Business Plaza.**—Tenant Improvement Allowances for Long Leases; 880+ sq ft; 24-hr security; free tenant/customer pkg; Gifford Chang 581-8853 DP, 593-9776, 531-3526.

- **Ala Moana Bldg.—** PHYSICIANS WANTED to share space and support services. Interest in physical rehab. preferred. We have unique time-share arrangements starting at one half-day per week. Run your practice with no fixed overhead. Contact Dr. Speers, REHABILITATION ASSOCIATES, 955-7244.

### Locum Tenens

- **Locum Tenens Available.—** BOARD CERTIFIED FAMILY PRACTICE, 15 years caring clinical experience in Hawaii. Office coverage. Own MIEC policy. Fee flexible. Please call Deborah C. Love MD: Home Oahu: (808) 637-8611; Cell Ph: (808) 295-2770.

### Part-Time


- **Part-Time Physician.—** THE HONOLULU MILITARY ENTRANCE PROCESSING STATION needs a physician to do medical examinations on applicants for the Armed Forces. MD or DO any specialty. Must have a valid current medical license. NO MALPRACTICE INSURANCE NEEDED. IDEAL FOR A RETIRED PHYSICIAN. Call John Kustermann MD at 471-8725, Ext. 228.

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**wwwAMA-assn.org**

Home Page to the world of medicine.

**hma-assn@aloha.net**

E-mail the Hawaii Medical Association
Join us in the quest for continued medical excellence.

Join your Straub colleagues as we strive for continuing medical excellence.

Straub Clinic & Hospital, Inc. is accredited by the Hawaii Medical Association to sponsor continuing medical education for physicians.

Straub designates this educational activity for a maximum of one credit hour in Category 1 of the Physician’s Recognition Award of the American Medical Association. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

You are invited to attend...

- Patient Care Conference –
  **Herbal Psychotropics**
  Enrico G. Camara, MD, FAPM
  May 4, 1999  4:30 – 5:30 p.m.
  Doctors Dining Room

  **LEARNING OBJECTIVES**
  At the conclusion, participants should be able to:
  - Understand the basic biochemistry of valerian, kava, and St. John’s wort as it relates to their psychoactive properties.
  - Identify those patients for whom these agents may have a therapeutic role in clinical management.
  - Describe risks, side effects and possible interactions with each other and with prescription drugs.

- Ophthalmology Conference –
  **Unusual Retinal Vein Occlusions**
  Sherman Valero, MD
  May 20, 1999  5:00 – 6:00 p.m.
  Queen’s Medical Center Imaging Classroom

  **LEARNING OBJECTIVES**
  At the conclusion, participants should be able to:
  - Describe branch and central vein occlusions.
  - Evaluate and measure unusual causes for these disease processes.
  - Manage vein occlusions medically and surgically.

- Friday Noon Conference –
  **Latex Allergy As It Affects Health Care Providers**
  Carl W. Lehman, MD
  May 21, 1999  12:30 – 1:30 p.m.
  Doctors Dining Room

  **LEARNING OBJECTIVES**
  At the conclusion, participants should be able to:
  - Describe the epidemic increase of natural rubber latex allergy during the past 12 years and how to reverse the trend.
  - Manage a hospital to be safe for personnel and patients with latex allergy.
  - Recognize the seriousness of natural rubber latex allergy to personnel and patients.

- Patient Care Conference –
  **An Update on Medicine in Hawaii**
  Jared Acoba; Rudy de Alday, MD; Dan Canete, MD; Fort Elizaga, MD; Reuben Guerrero, MD; Keith Kamita; Robert Pang, & Vince Wong
  May 29-30, 1999  1:30 – 5:00 p.m.
  Turtle Bay Hilton

  **LEARNING OBJECTIVES**
  At the conclusion, participants should be able to:
  - Understand practice guidelines for routine health maintenance screening.
  - Summarize the regulatory issues surrounding the proper and legitimate prescribing of opioids for the management of pain.
  - Recognize the role of cosmetic pharmaceuticals in improving the appearance of aging skin.
  - Review the clinical uses or indications of low molecular weight heparin.

Please call Fran Smith at 522-4471 for more information.
Nothing is So Deceptive of a Man's Statistics, Expect a Woman's Figure.

Most eye surgeons consider it the standard of practice to advise patients not to wear their contact lenses overnight. Corneal infections from that virulent, ugly bug *Pseudomonas aeruginosa* occur not rarely in patients who wear their lenses constantly. Now Bausch & Lomb has claimed a breakthrough with a lens called PureVision that is safe to wear to bed. B&L claims the lens is the result of 10 years research to produce a soft lens of new material that allows more oxygen to reach the cornea while absorbing water. The lens is more comfortable and is approved by the Food and Drug Administration for one-week nonstop wear. “It’s certainly going to be much safer than existing products,” according to the B&L director of clinical research. However, after just two weeks of promotion, B&L was sued by Johnson & Johnson who alleges that the lens superiority claims were not substantiated. J&J claims that the clinical trial demonstrated “no statistically significant differences” from their own AcuVue lens. Sounds like another make-work project for the attorneys.

A Moralist is One Who Wants You to Live Life His Way.

The anti-abortion website called “The Nuremberg Files” was successfully sued for the sum of $109 million by various plaintiffs, including Planned Parenthood. A Federal jury decided that calling doctors baby butchers, posting pictures of physicians, providing their home addresses, information about their children, and even phone numbers, incited people to violence. By their action the jury limited the scope of constitutionally protected free speech, but the jury saw the posted messages on the website as a “hit list.” The message is that physicians should not have to live in fear of violence. Three doctors on the list have been killed by anti-abortion terrorists.

If God had not Meant for us to Procrastinate, He Wouldn’t Have Created Infinity.

Our fearless (feckless?) Republican leaders should jump on the bipartisan Congressional report to fix Medicare proposed by Breaux (D.La.) and Thomas (R.Ca.Li.f.). The plan would save money by gradually raising the eligibility age from 65 to 67. Also, it would allow people to join the existing Medicare plan or they could use a premium allowance to purchase private coverage. It would provide prescription drug coverage for those who cannot afford their medications. The report is less than perfect (latest news is the plan is dead), but much better than the Clinton/Gore intent of merely dumping an additional $700 billion in taxes into a program that isn’t working. The Breaux proposal would fold Parts A and B into one plan (YES!), offer targeted premium allowances to the poorest seniors and encourage purchase of private insurance. The key to saving Medicare is to create a genuine health care market in which people can decide where, whether and how much to spend on their own medical care.

What Really Hurt Humpty Dumpty was not the Fall, but his HMO Said the Surgical Care was not Medically Necessary.

The American Medical Association is pushing for legislative language that will protect patients from the arbitrary decision of insurers to deny payment based upon “not medically necessary.” The AMA claims that patients must be given the right to appeal such decisions to an independent reviewer with clinical expertise of the proposed treatment. The scoundrels who lobby for the insurance industry are fighting the language claiming that it will raise health care costs, reduce quality and lead to increases in health care fraud! Doctors are being painted as black-hat types and “fraud and abuse would increase in the private sector if significant deference were to be conferred upon providers.” Take a few minutes and contact our Washington people in support of the AMA in this pure patient protection issue.

Nothing is so Bad that It Can’t Get Worse.

And yet another insurance insult — The Supreme Court recently supported a Pennsylvania court which ruled that workers-compensation medical payments may be withheld during a review to determine if they involve reasonable and necessary medical treatment. Every medical care provider knows that insurance companies find any excuse to lengthen the “float” and avoid paying their bills in a timely manner. If a claim isn’t perfectly clean it will be delayed or returned for additional data, or faulted for improper numbers, or challenged for whatever. Doctors and hospitals must provide emergency care in a prompt and comprehensive manner or be subject to penalty, but no similar time constraint applies to insurance providers. Business and insurance interests claim the Supreme Court decision will help control health-care costs. Yeah, right! Thunks a lot, Judge.

Some People Smoke Between Meals, Others Eat Between Smokes.

Patricia Henley began smoking at age 15, and now at age 53 she suffers from inoperable lung cancer. Her suit against Philip Morris (Marlboro) blames the tobacco company because she became addicted before there was any warning about health risks. The California jury awarded her $1.5 million for medical costs, pain and suffering, and ordered Philip Morris to cough up ($exhale?) $50 million in punitive damages. Legal experts consider the case as a marker for additional individual lawsuits despite the settlement of state Medicaid cases. For personal injury attorneys the tobacco industry must appear like a giant mother lode.

There are Two Things that Never Live Up to the Ads—Sin and Circuses.

Those creative advertising people who bring you slick offerings for Viagra the impotence drug and Claritin for allergy, have embarked on a campaign to sell cataract surgery. Allergan will place ads for six months in Time, Newsweek, Reader’s Digest and Modern Maturity, among others, to inform seniors about the benefits of cataract surgery, but specifically the implant maker wants to plug into that market with their new multifocal device. The American Academy of Ophthalmology estimates that about 13 million Americans have age-related lens opacities, but as every ophthalmologist knows that doesn’t mean they all need or would accept an operation. Moreover, the ads come at a time when HCFA is increasing scrutiny of high volume procedures and Medicare contractors and HMOs are cooling toward requests for cataract surgery.

I Have Nothing to Say, and I’m Going to Say it Just Once.

In the private practice of medicine, a day’s loss of income cannot be regained. Not merely is there loss of several hundred dollars income, but employee benefits and wages, rent, utilities, security and answering services all go on. In a solo medical practice, a holiday costs at least $900, which explains why the median for medical practices is six paid holidays per year. Some doctors offer as many as eleven, and even holidays a year costs a solo practitioner about $10,000 per annum.

We’re not Attempting to Circumcise the Rules. (Professional football coach)

Worried about when to conceive your child? Get on-line with Babycenter.com The website lists dates of the Super Bowl, the World Series, the Final Four, NBA finals, the NASCAR and Indy 500, etc., and then provides information on how to plan the conception of your offspring so you will not fear missing some special event. The idea was originally pitch as a joke, but sports nuts took it seriously. During Super Bowl week, the site attracted over 1,000 visitors per day.

Addenda

- DUI history - On September 10, 1897, the world’s first drunk driver drove his electric car through the entrance of a building in London.
- NASA spent $200,000 for a sanitary napkin disposal for women astronauts in 1992, and it’s money well spent.
- It is easy to enjoy opera – everything but the music.
- Aloha and keep the faith — rts
**BRIEF SUMMARY**

Before prescribing, please see full Prescribing Information for ATACAND.

**USE IN PREGNANCY**

When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, ATACAND should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

**CONTRAINDICATIONS:** ATACAND is contraindicated in patients who are hypersensitive to any component of this product.

**WARNINGS:**

Fetal/Neonatal Morbidity and Mortality: Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin converting enzyme inhibitors. When pregnancy is detected, ATACAND should be discontinued as soon as possible.

Use of drugs that act directly on the renin-angiotensin system during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypocalcemia, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Observational data has also been reanalyzed and resulting in decreased fetal renal function. Olilygomyelins in this setting has been associated with fetal limb contracture, craniofacial deformation, and hypoplastic lung development. Promptly, intratreatment growth retardation, and patient ductus arteriosus have also been reported, although it is not clear whether these observations are due to exposure to the drug itself or other factors. These adverse effects do not appear to have resulted from intratreatment drug exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are at risk to an angiotensin II receptor antagonist only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should have the patient discontinue the use of ATACAND as soon as possible. Rarely (probably less often than once in every thousand pregnancies), rena adverse effects occur to the mother and fetus, and/or ultrasound examinations should be performed to assess the extra-embryonic environment.

ATACAND should be discontinued unless it is considered life saving for the mother. Contraction stress testing (CST), a nonstress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetuses has sustained irreversible damage. Infants with oligohydramnios at birth have had neonatal renal impairment, pulmonary hypoplasia, and in some instances have died. The babies should be observed for oligohydramnios and serial ultrasonography examinations should be performed to assess the extra-embryonic environment.

In the newborn period, oligohydramnios can be associated with respiratory distress syndrome, and oliguria. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing oliguria and/or substituting for diminished renal function.

There is no clinical experience with the use of ATACAND in pregnant women. Oral doses of 30 mg of candesartan cilexetil/kg/day administered in pregnant rats during the period of organogenesis was associated with increased survival and an increased incidence of hydrocephalus in the offspring. The 10 mg/kg/day dose of rats is approximately 2.8 times the maximum recommended daily human dose (MRHD) of 30 mg on a mg/m² basis (comparison assumes human body weight of 50 kg). Candesartan cilexetil given to pregnant rats at oral doses of 0.5 and 3 mg/kg/day (approximately 1.7 times the MRHD on a mg/m² basis) caused maternal toxicity (decreased body weight and death) but, in surviving dams, had no adverse effect on fertility, fetal body weight, weight of organs external, visceral, or skeletal development. No maternal toxicity or adverse effects on fetal development were observed when oral doses of 1 mg/kg/day (approximately 0.3 times the MRHD on a mg/m² basis) were administered to pregnant mice.

**Hypertension in Volume-Depleted Patients:** In hypertensive patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (e.g., those being treated with diuretics), symptomatic hypotension may occur. These conditions should be corrected prior to administration of ATACAND, or the treatment should start under close medical supervision. If hypotension occurs, the patient should be placed in the supine position and, if necessary, given intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment which usually can be continued without difficulty once the blood pressure has stabilized.

**PRECAUTIONS:**

General: Impaired Renal Function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals treated with ATACAND. Patients in whose renal function may depend upon the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors and angiotensin receptor antagonists has been associated with oliguria and acute renal failure and death. Similar results may be anticipated in patients treated with ATACAND. In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. There has been no long-term use of ATACAND in patients with unilateral or bilateral renal artery stenosis, but similar results may be expected. Information for Patients: Pregnancy: Female patients of childbearing age should be told about the consequences of ACE inhibitors and angiotensin receptor antagonists and to discontinue treatment if they plan to become pregnant. Patients should be advised to report pregnancies to their physicians as soon as possible.

Drug Interactions: No significant drug interactions have been reported in studies of candesartan cilexetil given with other drugs such as glyburide, nipecitone, digoxin, warfarin, hydrochlorothiazide, and oral contraceptives in healthy volunteers. Because candesartan is not metabolized by the cytochrome P450 system and has no effects on P450 enzymes, interactions with drugs that inhibit, or are metabolized by, these enzymes would not be expected.

**ADVERSE REACTIONS:**

ATACAND has been evaluated for safety in more than 3000 patients/skies, including more than 3000 patients treated with ATACAND. The overall incidence of adverse events reported with ATACAND was similar to placebo. The rate of withdraws due to adverse events in all trials in patients (78%) is 3% or less of patients treated. These events occurred at an incidence of more than 2% in patients treated with ATACAND and 3% (3% of 108) of patients treated with placebo. The most common reasons for discontinuation of therapy with ATACAND were headache (0.6%) and rash (0.3%). These adverse events were observed in patients treated in clinical trials at least 5% of patients treated with ATACAND or placebo. The incidence of each of these adverse events was similar to placebo.

**NEW ATACAND CANDESARTAN CILEXETIL**

- Powerful BP reduction @ the starting dose
- First line for hypertensive patients
- Convenient once-daily dosing for 24-hour BP reduction
- Usually starting dose: 16 mg once daily
INTRODUCING ATACAND.
A NEW SIGN OF POWER IN BP REDUCTION.

A new angiotensin II receptor blocker (ARB) with power @ every dose
- New once-daily ATACAND has significant power to reduce blood pressure (BP) at the 16-mg starting dose. And a dosage increase to 32 mg leads to an even greater reduction in BP.
- ATACAND delivers effective BP reduction when compared to amlodipine at the starting doses and to enalapril (at doses of 10 mg enalapril, 8 mg ATACAND).
- The most common adverse events that occurred with ATACAND in placebo-controlled clinical trials with an incidence greater than placebo were URI (6% vs 4%), dizziness (4% vs 3%), and back pain (3% vs 2%).

Exhibits a potent and long-lasting effect @ the AT, receptor site*
- ATACAND gets @ the site where angiotensin II causes vasoconstriction.
- ATACAND stays @ the site, where its antihypertensive effect is not overcome by angiotensin II.

Prescribe new ATACAND tablets—and Get the Power!

Use in Pregnancy: When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, ATACAND should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

Volume and/or salt depletion should be corrected prior to administering ATACAND or symptomatic hypotension may occur.

*The relationship between receptor site affinity and clinical effect is unknown.

Please see accompanying brief summary of Prescribing Information on adjacent page, including boxed WARNING regarding use in pregnancy.

To contact your local Professional Representative please call 1-800-523-3255
Deborah Luckett X4648
Pam Tsuzaki X4647
Mike Ocasek X5216

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