



Report of the Third Annual Permanente Rheumatology Association Meeting

The Permanente Rheumatology Association (PRA), an organization representing Permanente Rheumatologists from around the Kaiser Permanente (KP) Program, met for its third annual meeting in Half Moon Bay, California, in May 2001. The association is dedicated to providing state-of-the-art, cost-effective, personalized care for patients with rheumatic disease. The annual conference is an effective way for rheumatologists in the Permanente Medical Group (PMG) to review the world medical literature and compare best practices within the KP system nationwide. In the three years of the PRA's existence, the nature of the annual meeting has changed from a simple didactic conference to a dynamic meeting exploring many facets of rheumatology at KP. This year's meeting included several topics: updates on vasculitis, osteoporosis, and fibromyalgia; treatment strategies in rheumatoid arthritis (RA), functional assessment of patients with rheumatic disease; and controversies with antiinflammatory agents (COX 2). A brief Executive Summary, written by the Section Chair from each group, follows (See Participants, Table 1).

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic, progressive inflammatory disease which is associated with clinically significant morbidity and mortality and imposes a large economic burden on both society and the Kaiser Permanente (KP) organization. In recent years, several new antirheumatic drugs have been developed which produce superior outcomes from conventional types of therapy. The high expense of these drugs and treatment regimens has prompted increased effort to identify outcome measures useful for monitoring disease progress, response to therapy, and cost-effectiveness of various treatment options.

After last year's discussion, the Rheumatoid Arthritis Study Group presented the most recent data on leflunomide, etanercept and infliximab, including postmarketing experience reported for adverse reactions. These drugs continue to show statistically significant benefit even in patients who have had poor clinical outcomes from traditional methotrexate therapy. With increased use of these new drugs, however, concern has grown regarding hepatotoxicity resulting from use of leflunomide (especially when combined with methotrexate) and infection resulting from etanercept. Use of anti-TNF (tumor necrosis

factor) therapy in treatment of juvenile rheumatoid arthritis to date has been disappointing. Initial information on two new therapeutic options—IL-1Ra plus etanercept; and CTLA4-Ig—was also presented.

The increasing use of these expensive therapeutic options was borne out by a review of the pharmacy purchase data for these three drugs from November 1998 through March 2000 and by results of the Rheumatoid Arthritis Study Group Questionnaire. In a published study in the October 2000 issue of *Arthritis and Rheumatism*,¹ cost-effectiveness of treatment options was analyzed for methotrexate-resistant RA. Therapy which combines either three drugs (methotrexate, sulfasalazine, and hydroxychloroquine) or two drugs (etanercept and methotrexate) is the most cost-effective type of therapy available today. The study had several limitations but provides an initial framework with which to analyze cost-effectiveness of various treatment options.

—Aileen Dillon, MD, *Rheumatology (Chair), San Francisco*

Osteoporosis

The Osteoporosis Study Group provided an up-to-date review of key concepts of

bone mineral density (BMD) measurement and treatment options. Glucocorticoid-induced osteoporosis (GIOP), an issue of particular importance for rheumatologists, also was covered.

Dr David Zelman reviewed indications and recommendations for BMD testing. Indications for testing vary among KP Regions, and no clear consensus has been established. BMD testing is recommended both for women over age 65 years and for postmenopausal women over age 55 years who have risk factors influencing a decision on hormone replacement therapy (HRT) and who have known or suspected causes of secondary osteoporosis and radiographic abnormalities suggestive of osteoporosis. Serial testing to determine efficacy of treatment is not currently recommended in all KP Regions. Providing a definitive opinion on this subject was outside the scope of the workgroup.

Dr Chee Chow described the process of evaluating a patient for secondary causes of osteoporosis. No consensus exists for a cost-effective strategy, but a reasonable option is to test selected patients who have recently been diagnosed with osteoporosis, women for whom the Z score is < -2.0, and all men. Initial evaluation includes obtaining a comprehensive medical history, administering a complete physical examination, and laboratory evaluation of erythrocyte sedimentation rate as well as levels of calcium, phosphorus, thyroid-stimulating hormone, liver function tests, blood urea nitrogen, and creatinine.

The study group recommends that all persons who have T scores < -2.5 be treated using bisphosphonates, synthetic estrogen replacement molecules (SERMs), or calcitonin—agents with antifracture efficacy demonstrated in clinical trials. For these persons, only observational and retrospective evidence suggests that HRT is beneficial for lowering the risk of fracture. The

GERALD LEVY, MD, MBA, (left), is an SCPMG Rheumatologist practicing at the Bellflower Medical Center. He chairs the annual Rheumatology for Primary Care Providers symposium and is a member of the steering committee of the Permanente Rheumatology Association. Dr Levy is active in several areas of research involving COX 2 anti-inflammatory agents. E-mail: Gerald.D.Levy@kp.org.

STANFORD SHOOR, MD, (not pictured), is a TMPG Rheumatologist at Santa Clara. He is Chairman of the Northern California Rheumatology Group and Chairman of the Permanente Rheumatology Association. E-mail: Stanford.Shoor@kp.org.



antifracture efficacy of available agents for persons with a T score between -1.5 and -2.5 has not yet been conclusively proven. Increased bone density in these persons has been shown, but a definitive answer regarding fracture benefit will require large studies conducted over many years. At present, HRT appears to be the most cost-effective strategy for treating osteoporotic women.

Dr Anthony Tay discussed combination treatment (bisphosphonate agents plus HRT) and use of parathyroid hormone. The latter therapy represents a new and promising development in the treatment of osteoporosis. Dr Tay reported that combination therapy has been shown to improve

bone density but has not yet proved to reduce rates of osteoporotic fracture. Therefore, use of combination treatment is not routinely recommended. Recent studies of parathyroid hormone therapy showed impressive changes in BMD as well as reduced rates of fracture due to osteoporosis. The US Food and Drug Administration (FDA) is reviewing appropriate indications for using parathyroid hormone to treat osteoporosis.

Dr Stephanie Chu discussed glucocorticoid-induced osteoporosis (GIOP) with emphasis on pathophysiology and management of this condition. Glucocorticoid agents' negative effects on bone are multifactorial and include suppression of gonadal hormone

production, induction of negative calcium balance, and direct suppression of osteoblast formation. Treatment and prevention of GIOP includes calcium plus vitamin D replacement and hormone replacement in male as well as female patients as appropriate. Use of bisphosphonate agents is recommended for treatment of patients at high risk. The American College of Rheumatology (ACR) was expected to release new guidelines some time after the PRA meeting.

—David J Zelman, MD, Rheumatology (Chair), Georgia

Fibromyalgia

The Fibromyalgia Syndrome (FMS) Study Group provided both a brief update on FMS programs within KP and a brief literature update. Jennifer Smith, RNP, presented findings from questionnaires distributed to patients receiving trigger-point injections in her clinic during a three-week period in March 2001. Sixty patients completed questionnaires asking about pain relief occurring in response to injection of lidocaine plus bupivacaine. Injections were administered at intervals ranging from every six weeks to semiannually. Of the 60 participants, 40 had received injections for more than one year. All participants felt that injections were of some benefit, and about two thirds of patients reported that pain relief lasted for more than a week.

Dr George Breth discussed a telephone follow-up study of 184 patients participating in KP Colorado's multidisciplinary FMS group clinic; results of the study were originally reported in the Summer 2000 issue of *The Permanente Journal*.² These patients completed a detailed initial electronic questionnaire that contained items about mental health comorbidity as well as intrusiveness and impact of fibromyalgia. Follow-up data were available for 99 patients who agreed to participate in the telephone survey. Statistically significant improvement of symptoms was seen for patients with anxiety and depression, and scores reflecting musculoskeletal stiffness as well as job interference improved in all patients. The group was stratified into patients with bipolar versus

Table 1. Participants of Third Annual Permanente Rheumatology Association (PRA) Meeting

Rheumatoid Arthritis: Aileen Dillon, MD, Rheumatology (Chair), San Francisco; Srisook Boonsue, MD, Rheumatology, Panorama City; Lloyd Ito, MD, Rheumatology, Sacramento; Paul Lambie, MD, Rheumatology, Roseville; Hui Pan, MD, Rheumatology, Stockton; Mark Roberts, MD, Rheumatology, Vallejo; Eric Schoen, MD, Rheumatology, Washington DC; Nina Schwartz, MD, Rheumatology, South San Francisco; Dinesh Shah, MD, Rheumatology, Los Angeles; Monica Stewart, MD, Rheumatology, Washington DC; Dennis Stobie, MD, Pediatrics, Sacramento; Mark Genovese, MD, Rheumatology, Stanford University (Faculty Advisor)

Osteoporosis: David J Zelman, MD, Rheumatology (Chair), Georgia; Anthony Tay, MD, Rheumatology, Woodland Hills; Chee Chow, MD, Rheumatology, Oakland; Eduardo Baetti, MD, Rheumatology, Atlanta; Stephanie Chu, MD, Rheumatology, Hayward; Nancy Lane, MD, Medicine-Rheumatology, University of California, San Francisco (Faculty Advisor)

Fibromyalgia: George Breth, MD, Rheumatology (Chair), Colorado; Jennifer Smith, RNP, Internal Medicine, Fontana; Souheil Habbal, MD, Allergy-Rheumatology, Baldwin Park

Clinical Information Service (CIS): George Breth, MD, Rheumatology, Colorado; Carole Rauchle, RN, Internal Medicine, Colorado

Vasculitis: Joji Kappes, MD, Rheumatology (Chair), Portland; Heidi Butcher, CRNP, Rheumatology, Bellflower; Alan Cohen, MD, Rheumatology, San Diego; Brian Huh, MD, Rheumatology, Baldwin Park; Charles D Kenyon, MD, Rheumatology, Bellflower; Maurice Kinsolving, MD, Rheumatology, Petaluma; Patrice Leonard, MD, Rheumatology, Bellflower; Michael Takehara, MD, Rheumatology, Fontana; Steven Orkand, MD, Rheumatology, Sacramento; Robert Wiskocil, MD, Rheumatology, Walnut Creek

COX 2 Controversies: Stanford Shoor, MD, Professional Education & Rheumatology, Santa Clara; David Campen, MD, Drug Information/Professional Services, Santa Clara

Functional Assessment in Rheumatic Diseases: Gerald Levy, MD, Rheumatology (Chair), Bellflower; Canagasund Balakrishana, MD, Rheumatology, Fontana; Jeffrey Biro, DO, Rheumatology, Ohio; David F Casey, MD, Rheumatology, Bellflower; Craig Cheetham, PharmD, Pharmacy Warehouse and Services, Downey Regional Pharmacy, Downey; Robert Goldfien, MD, Rheumatology, Richmond; Arthur Huberman, MD, Area Medical Director, Administration, West Los Angeles; David C Hurwitz, MD, Rheumatology, Woodland Hills; Donald Pierce, MD, Rheumatology, Novato; John F Scavulli, MD, Rheumatology, San Diego; Wayne Yee, MD, Rheumatology, Fontana; James F Fries, MD, Immunology & Rheumatology, Stanford University (Faculty Advisor)

nonbipolar fibromyalgia because bipolar illness was suspected in 59.2% of the original group of patients according to symptoms self-reported at baseline evaluation. In the group with bipolar fibromyalgia, scores for anxiety, depression, and job interference were statistically significantly decreased. Scores reflecting number of pain-free days, restful nights, missed work days, and days with pain and stiffness were also significantly improved. In patients with nonbipolar fibromyalgia, only scores for job interference improved; scores for all other items were unchanged or unimproved.

Dr Souheil Habbal summarized abstracts on FMS presented at the November ACR meeting. Of particular interest were abstracts describing neurologic abnormalities in FMS patients who had been treated with 5HT3 receptor antagonist plus a dopamine agonist and describing a controversial surgical intervention proposed for some fibromyalgia patients with spinal stenosis and Chiari malformation.

Dr George Breth reported that the rheumatology department at KP Bellflower started using electronic point-of-view questionnaires obtained from KP Colorado. KP Bellflower has established a multidisciplinary clinic under the direction of Patrice Leonard and with input from the mental health and social services departments. The KP Mid-Atlantic Region visited the KP Colorado FMS clinic and may be interested in future collaboration as well. Improvements made in the KP Colorado FMS program include an ongoing stress/psychodynamics focus group for the group session participants and prescreening for FMS (medical history and tender points) by the primary care department as a result of electronic medical record (CIS) referrals. Additionally, a pharmacist (PharmD) reviews pharmacologic pain and sleep management as well as alternative treatment and herbal medicines. Telephone follow-up of group session participants along with an opportunity for patients to return for further sessions on pain control, sleep, hygiene, and exercise review are planned.

—George Breth, MD, Rheumatology (Chair), Colorado

Clinical Information Service (CIS)

Dr Carole Rauchle discussed the KP Northern California CIS project, and Dr George Breth presented his view of the KP Colorado Region's experience with CIS system during the past two years. The vision for CIS is to facilitate immediate access to the patient's clinical record, centralized recording of orders and results, and seamless sharing of information among clinicians. The process is similar to the present flow of a patient visit except that records are not paper-based and are instead entered directly into the computer. The CIS system will include custom formularies and baselets (templates to assist in caring for patients with specific medical conditions).

The remaining discussion with the audience centered on the role of rheumatologists and development of rheumatology-specific content. The purposes of this effort are to facilitate documentation of commonly seen rheumatic syndromes and to establish baselets for care paths, both of which will lead to a more uniform and higher standard of rheumatology care. This result will have its greatest value in common diagnoses (eg, osteoarthritis) and high-cost treatments for RA (eg, biologic agents).

Consideration of an interregional approach to content development for rheumatology was tabled until implementation of the CIS becomes imminent. The audience and presenters believed that hands-on experience with CIS would be desirable for making decisions about clinical content in any medical specialty. The group agreed to revisit this topic at the next annual PRA meeting.

—George Breth, MD, Rheumatology, Colorado

Vasculitis

Vasculitis syndromes—which present diagnostic and therapeutic dilemmas—were discussed by the Vasculitis Study Group. Giant cell arteritis (temporal arteritis), Wegener's granulomatosis, and polyarteritis are classic examples of multisystem vasculitis. Hepatitis C syndromes with cryoglobulinemic vasculitis have added another dimension to an already complex and often confusing array of diseases. Evidence-based studies on both

giant cell arteritis and Wegener's granulomatosis have recently appeared and can help guide diagnosis and treatments. The new types of anticytokine therapy developed for rheumatoid arthritis, such as anti-TNF blockers, may add benefit medication regimens already established for treating these two conditions.

Diagnosis of giant cell arteritis remains predominantly clinical. Dr Steven Orkand discussed the noninvasive imaging studies that may help guide the clinician to an appropriate biopsy location or in diagnosis when biopsy is not feasible. No consensus currently exists for applying these methods. A major shortcoming of imaging studies is inability of these techniques to visualize smaller vessels, the most prominent location for ischemic events.

Dr Maurice Kinsolving discussed current glucocorticoid treatment, including some obscure and forgotten forms and promising treatments, such as dapsone therapy. Use of systemic corticosteroid drugs remains the standard of care, and undertreatment carries with it a risk of severe morbidity and mortality. Pulse steroid therapy does not appear to add any meaningful therapeutic advantage compared with standard daily oral drug administration. For patients whose condition is stable, treatment may be changed to alternate-day steroid therapy. Azathioprine therapy may be a useful adjunct. Methotrexate has a possible role for steroid-sparing immunosuppression. One recent report showed a steroid-sparing effect, whereas a second study did not.

Dr Patrice Leonard and Heidi Butcher reported that antineutrophil cytoplasmic antibodies arise not only in Wegener's granulomatosis and polyarteritis nodosa but also can be induced both by infection and by use of drugs. A secondary drug-induced vasculitis can develop. Dr Brian Huh discussed treatment for Wegener's granulomatosis: systemic corticosteroid therapy, cyclophosphamide therapy, and augmentation with cotrim. Methotrexate is an acceptable alternative to cyclophosphamide for treating non-life-threatening disease. Dr Robert Wiskocil contacted investigators who have



been using the TNF inhibitor, etanercept, and reported promising early results of Phase 2 studies. Caution is advised, however, because TNF inhibitors have not yet been rigorously tested and are not considered first-line therapy. Enrollment has been completed for a Phase 3 multicenter trial that is underway nationally.

Dr Charles Kenyon carefully reviewed the rheumatologic syndromes of hepatitis C virus biology. The broad topic of the viral role in rheumatic diseases deserves more time and attention and should be considered at future meetings of the PRA.

—*Joji Kappes, MD, Rheumatology (Chair), Portland*

COX 2 Controversies

In view of the recently released letter from the FDA Cardiovascular Safety Committee, Dr Stanford Shoor summarized the controversy surrounding use of COX 2 therapy:³

1. In randomized controlled trials, the risk of myocardial infarction with rofecoxib was shown to be three to five times that of nabumetone or naproxen.
2. The absolute risk of myocardial infarction with rofecoxib is 0.4% to 4.7%, and the number needed to treat is 200-250. Absolute risk is greatest in patients for whom aspirin is indicated.
3. Users of rofecoxib have no increased risk of stroke.
4. Adverse cardiovascular events associated with use of celecoxib and rofecoxib have not been compared.
5. Incidence of cardiovascular events among nonusers of aspirin ranges from 0.4% to 0.5% for naproxen, nabumetone, ibuprofen/diclofenac, or celecoxib; in these patients, a 0.8% incidence of cardiovascular events is associated with use of rofecoxib.
6. Whether the apparently increased risk of myocardial infarction associated with use of rofecoxib results from a prothrombotic effect of rofecoxib or from combining rofecoxib with naproxen (which may have an antithrombotic effect) is unclear. However, most secondary evidence favors the first explanation.

Key Points from the 2001 Permanente Rheumatology Association Meeting

1. The PRA is dedicated to providing state-of-the-art, cost-effective, personalized care for patients with rheumatic disease.
2. The high expense of new drugs and treatment regimens for rheumatoid arthritis has prompted increased effort to identify ways to monitor disease progress, response to therapy, and cost-effectiveness of treatment options.
3. The Osteoporosis Study Group recommends BMD testing in women over 65 and treatment in all persons with T scores < -2.5.
4. Fibromyalgia treatments are improving at KP due to ongoing research and innovative treatment models in pilot studies in a number of regions.
5. The vision for the KP CIS project is to facilitate immediate access to clinical records, centralized recording of orders and results, and seamless sharing of information among clinicians.
6. Members of the Vasculitis Study Group discussed diagnosis and treatment of vasculitis syndromes, including giant cell arteritis (temporal arteritis), Wegener's granulomatosis, polyarteritis, and hepatitis C syndromes with cryoglobulinemic vasculitis.
7. The use of COX 2 therapy remains controversial due to new information regarding possible increased risk of thrombotic events.
8. Disability associated with rheumatoid arthritis correlates better with functional assessment than with traditional clinical and laboratory measures of disease activity.

7. Until further data become available, the PRA recommends that rofecoxib be avoided when aspirin is indicated for antithrombotic prophylaxis. Moreover, the PRA recommends that potential harm should be disclosed to patients in whom aspirin therapy is not indicated.
8. The PRA recommends retrospective analysis of hospital data to verify or refute these risks.

—*Stanford Shoor, MD, Professional Education & Rheumatology, Santa Clara*

Functional Assessment in Rheumatic Diseases

Growing interest surrounds the question of whether the natural course of RA can be improved or arrested with introduction of newer, more effective antirheumatic medications. Long-term studies by Fred Wolfe^{4,6} and others have shown that RA is usually accompanied by progressive disability. Disability correlates better with functional assessment than with traditional measures of dis-

ease activity, including measurement of swollen and tender joints, radiographic studies of joint changes, and laboratory tests. Functional assessment can also be incorporated into clinical practice to monitor effectiveness of treatment. This determination of clinical effectiveness has become more relevant as introduction of biologic agents has dramatically increased the cost of medication.

The Rheumatology Practice Study Group evaluated common assessment instruments and their role in our clinical practice. To be clinically useful, the instrument must be simple to use, have only minimal impact on the physician's time, and be both validated and used outside KP. Ideally, every PMG rheumatologist would use the same instrument, thereby facilitating both sharing data and expanding research opportunities across the country. The committee examined the 20-year history of functional assessment and studied the most commonly used instruments in detail [Health Assessment Questionnaire (HAQ), Clinical-HAQ,

Modified-HAQ, SF-36, WOMAC, ALI, Paulus, FIQ, AIMS, RADAR, and RADAI].

The rheumatology community has basically accepted the HAQ for clinical studies,⁷ and the HAQ is a key component of the ACR comprehensive assessment tool, the ACR20. The MD-HAQ met the criteria established by a Rheumatology Practice Study Group subcommittee and was endorsed by the PRA as the preferred functional assessment tool. Actual implementation strategies for using the MD-HAQ will be left to the discretion of individual PMG rheumatologists. Each medical center that elects to use the HAQ should keep an accurate record of all patients completing the survey and should be prepared to share implementation experiences with the larger group. Attendees expressed the desire to be able to track patients individually, by specified physician, and by group. At the next annual PRA meeting, the Rheumatology Practice Subcommittee will present the experience

of clinicians who have used the HAQ.

—Gerald Levy, MD, Rheumatology (Chair), Bellflower ♦

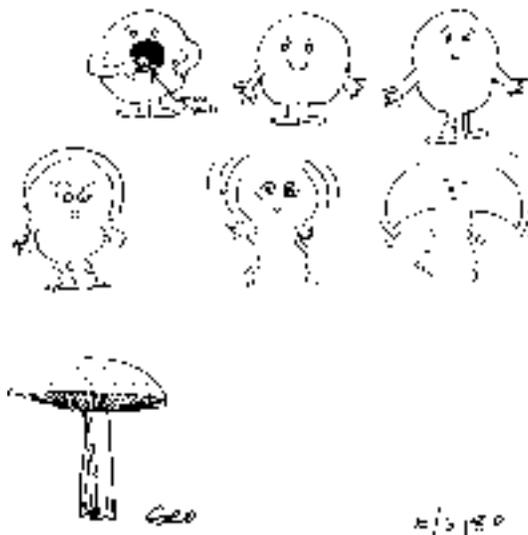
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Don't eat that green stuff!!



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