

the Rheumatologist

An official publication of the ACR and the ARHP serving rheumatologists and rheumatology health professionals

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OSTEOARTHRITIS, Quo Vadis

Our knowledge of OA has progressed far—
does a cure lie ahead?

>> By Roland W. Moskowitz, MD

When David Pisetsky, MD, PhD, physician editor of *The Rheumatologist*, asked me to contribute an article on osteoarthritis, I said yes without hesitation, looking forward to communicating all the exciting new advances taking place regarding osteoarthritis (OA). (Accepting the invitation had its risks. In addition to needing to meet the deadline—which always comes sooner than expected—my wife, Peta, keeps telling me to say no to new academic requests or to stop complaining about being busy!)

There were a number of alternatives—this could be a highly scientific article on everything we know about osteoarthritis (obviously this would be much too long) or a *New Yorker*-type article with interesting vignettes, a quasi-scientific rendition, or something in between.

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SYSTEMIC VASCULITIS

Low incidence makes research and diagnosis a challenge

>> By Virginia Hughes

BOSTON—The latest research on the pathophysiology and treatment of small- and large-vessel vasculitides was presented by three international experts at a clinical symposium called “Therapeutic Decisions in Systemic Vasculitis” at the ACR/ARHP Annual Scientific Meeting in Boston last November. Alexandra Villa-Forte, MD, of the rheumatic and immunologic disease department at the Cleveland Clinic, and Carol Langford, MD, MHS, director of the Center for Vasculitis Care and Research at the Cleveland Clinic, discussed treatment options for small-vessel vasculitides. Paul Bacon, MD, professor of rheumatology at the University of Birmingham, discussed the latest research on the pathophysiology and treatment of small- and large-vessel vasculitides.

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Pediatric BOOST

Many innovative programs aim to meet the increasing need for pediatric rheumatologists

>> By Terry Hartnett

This is the final part of a four-part series on the 2006 Rheumatology Workforce Study. (See Part 1 on page 1 of the January 2007 issue, Part 2 on page 1 of the April 2007 issue, and Part 3 on page 1 of the August 2007 issue.)

The small pediatric rheumatology subspecialty is growing, although demand is likely to increase faster than supply, according to the results of the Rheumatology Workforce Study commissioned by the ACR in 2006. However, a variety of efforts to support fellows interested in this field both during training and early in their careers offer rays of hope for the future. For example, the number of pediatric rheumatology fellowships is steadily increasing and both pediatric and adult rheumatologists are taking bold steps to change the practice model and become mentors for medical students.

“Exposure of the field is a major issue for pediatric rheumatology,” says Marisa Klein-Gitelman.

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Rheumatology's Architect



Help the REF lay foundations for our future >> By David A. Fox, MD

Most members of the ACR know something about the ACR Research and Education Foundation (REF). It's likely, however, that many don't know as much as they should, considering the scope of its programs, its recent dramatic growth in re-

sources, its ambitious agenda, and its critical role in creating a future for the profession of rheumatology.

This is the fifth consecutive year in which I've had the privilege of participating in the meetings of the REF's board of directors, in the course of filling

various roles for the REF and the ACR. The most recent board meeting, held January 18–19, 2008, encapsulated for me just how far the REF has come, and how much further it plans to go.

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Leslie Crofford, MD



James O'Dell, MD



Mike Weisman, MD

REF and ACR: Partners in Rheum

REF presidents serve two-year terms, and are members of the ACR's Executive Committee. ACR officers participate in the REF board as voting members (secretary and treasurer) or ex officio (ACR president and president-elect). In

this way, even though the REF is a distinct entity, it carries out its work in close coordination with the ACR. REF president Leslie Crofford, MD, recently succeeded James O'Dell, MD, who was preceded by Mike Weisman, MD. These three share a passion for the mission of the REF, and their leadership has been a remarkable blend of successful innovation while simultaneously strengthening the

existing core functions of the REF.

The staffs of the ACR and the REF are also structured to balance the independent role of the REF with the advantages of organizational support from the ACR. The REF staff, ably led by Steve Echard, CAE, includes specialists in grant review, grant management, and development, but shares staffing with the ACR in such areas as communications, accounting, and information technology. The REF is a lean organization—approximately 85% of its expenditures flow out the door as research grants, with the remaining expenses in the categories of fundraising, peer review, grant administration, and infrastructure. This puts the REF among the ranks of the most highly rated of charitable organizations, in terms of how effectively the donor's dollar is put to use.

Just as the ACR has standing committees in all key areas, the REF has a Scientific Advisory Council (SAC) that sets up the grant portfolio and supervises the study sections that review the grant applications, and a Development Advisory Council that figures out how to raise the money the SAC so eagerly spends. The Committees on Finance and Nominations are joint committees with the ACR. A variety of task forces are also hard at work on other functions of the REF. The REF's governance structure, which is modified every few years in a strategic planning process, has proven to be nimble and effective in serving the mission of a rapidly growing organization.

REF's Mission and Goals

The goals of the REF are to attract highly qualified individuals into rheumatology and the allied health professions, to foster academic career development, and—added more recently—to support targeted research in rheumatic disease. The portfolio of grants that are distributed by the REF to more than 100 recipients per year ranges from clinical or research preceptorships for medical students, to the Physician-Scientist Development Award for rheumatology fellows, to the grants awarded to established investigators for the most innovative research on RA, as our targeted research initiative, *Within Our Reach*, begins to bear fruit. And those are just a few examples of the more than 25 categories of grants that the REF now funds.

At its January 2008 meeting, the REF board voted to create a new grant category, the Rheumatology Investigator Award, which will provide substantial support for career development of rheumatology junior faculty who are launching their research programs. Although a thorough review and overhaul of all REF grant mechanisms is underway, the REF board saw an urgent need for this new grant mechanism and put it on the fast track; the first round of proposals will be due this summer and will be funded in 2009.

Progress in the *Within Our Reach* campaign was also reviewed at the meeting. Halfway through the campaign, the REF has raised nearly \$20 million dollars, more than 60% of its goal. Fifteen two-year grants were awarded in 2007, representing an expenditure of \$6 million dollars, and another round of applications has already been received for review. The REF is still building its base of patient-donors, a process in which all members of the ACR can participate. And the ACR's Committee on Research is beginning to develop the REF's next targeted research initiative, which is due to be presented to the combined boards of the ACR and REF in August 2009.

The decision to embark on large-scale targeted research was a bold step for the ACR and the REF, but it did not come at the expense of our training and career development programs. Indeed, the REF, blessed by assets fourfold greater than it had just five years ago, has created an endowment to guarantee permanent funding of its core missions, and is on target to build that endowment to \$25 million by 2010. New goals will be framed as we near that initial target. Don't be surprised if we set our sights on a \$100-million endowment by 2020 or sooner.

You might wonder why an endowment of such proportions is necessary. Con-

sider that much of the growth of the REF has been fueled by the pharmaceutical and biotechnology industries' interest in strengthening the field of rheumatology through participation in the REF Industry Roundtable. Becoming a roundtable member requires significant contributions to the REF. It's difficult to know how long these companies will be willing or able to provide this support, and it would be a serious error to assume that it will continue in perpetuity. Consider also that expenditures by the NIH and charitable foundations for rheumatologic research include only limited—and shrinking—funding for rheumatology trainees. And consider that our manpower projections (which the REF board studied carefully in January) compel us to create mechanisms to train more rheumatologists than we are currently. The issue is not whether we need an endowment, but how large we can make it.

Everyone Can Help

If you are one of the majority of ACR members who is engaged in clinical practice outside of an academic unit, you might wonder why the REF is important to you. The activities of the REF are essential to the health of the academic rheumatology units, which, in turn, is the key to sustaining our profession. In addition to guiding young physicians and health professionals towards a career in rheumatology and preparing them for clinical or academic practice, specialized disease-focused centers localized in academic institutions provide education, referral opportunities, and clinical research that defines best practices for our most challenging patients. Only a few years ago, barely more than 100 trainees per year were entering rheumatology fellowships, including few U.S. medical graduates. By developing new mechanisms to fund training

for clinical fellows and expanding research training support, the REF played a major role in addressing this crisis. Today, about 180 physicians enter rheumatology fellowship programs each year, most of whom are U.S. medical graduates, and the number of fellows training in pediatric rheumatology units has more than doubled. We all know that a significant workforce shortfall exists nonetheless, and will get worse unless we take further action—but just imagine how much worse this might be if not for the vision of the REF leaders, the aggressive implementation of new programs, and the generous support of those who have donated to the REF.

The REF's task is to build the future of rheumatology, and it is the responsibility of every member of the ACR to support and participate in the work of the REF. Go to the REF Web site, www.rheumatology.org/REF, and find out what the REF is up to. You can also become acquainted with individual REF success stories highlighted in the pages of *TR*. Donate every year, and consider increasing your donor level—you'll even get rewards, such as access to the donors' lounge at the ACR meeting. Let your students and residents know about the REF and its multiple mechanisms that help trainees enter rheumatology. Finally, consider becoming involved in patient-targeted fundraising for the *Within Our Reach* campaign or for the other programs of the REF. We have no shortage of challenges to deal with in the present, some of them frustrating and stubborn, but in the process of creating our future we transcend the present and leave an enduring legacy. | THE RHEUMATOLOGIST |

Dr. Fox is president of the ACR. Contact him via e-mail at fox@rheumatology.org.

the Rheumatologist

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EDITORIAL STAFF

David Pisetsky, MD, PhD
Physician Editor
Piset001@mc.duke.edu

Dawn Antoline
Editor
dantolin@wiley.com

Lisa Dionne
Editorial Director
ldionne@wiley.com

Art Director: Liliana Estep, alldesign@cox.net
Writers: Terry Hartnett, Virginia Hughes,
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VP and Publisher
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Bridget Seay
Associate Director, Advertising Sales

ADVERTISING STAFF

Display Advertising
Frank Cox, Valentin Torres
Pharmaceutical Media Inc.
30 East 33rd Street
New York, NY 10016
Phone: (212) 685-5010
Fax: (212) 685-6126
info@pminy.com

THE AMERICAN COLLEGE OF RHEUMATOLOGY

Phone: (404) 633-3777
Fax: (404) 633-1870
Web site: www.rheumatology.org

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February 1 – August 25, 2008

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- 2. Networking Opportunities** – A variety of ways to gain insight through professional interaction with others in various practice situations across the country and globe.
- 3. Rewards and Recognition** – The top two recruiters (one ACR and ARHP member) will win a \$500 gift certificate to the airline of their choice and will be recognized at the 2008 ACR/ARHP Annual Scientific Meeting in San Francisco, CA and in upcoming publications.

All applications must be postmarked by August 25, 2008 to be considered. To receive credit for your recruited members, your name and signature must appear as the sponsoring ARHP member.

>>> For additional information, visit www.rheumatology.org/arhp or contact Ramona Hilliard at (404) 633-3777 or rhilliard@rheumatology.org.



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If the Best You Can Do Is Zero

When we focus on loss, do we hurt our chances for gain? >> By David S. Pisetsky, MD, PhD

Leon Fleisher is one of the great pianists of our generation, but 30 years ago—at the height of his career—he was struck by a baffling illness that afflicted his right hand and drastically impeded his playing career. According to Fleisher's biography, the fingers of his hand weakened and became painful and numb, and they would curl uncontrollably. Exercise was of no avail and, indeed, seemed to worsen the condition. Fleisher sought the help of the best experts. Despite numerous workups, doctors could not make a diagnosis with confidence, meaning the treatments that Fleisher tried were—at best—empiric and—at worst—desperate, including dousing the hand with a bottle of whiskey.

agnosis. I think that when all of the signs and symptoms of RSD are present (the pain, the autonomic dysfunction, the washout of the bones by X-ray) I can be in the ballpark. Even a first-year medical student can make the diagnosis when a claw deformity is present. But in the early stage of the condition or the less classical cases, I usually feel in terra incognita when I put down RSD as a diagnosis.

Turn Losses to Gains

Without a diagnosis and with no improvement, Fleisher had to change his life. Fortunately for him, there is a repertoire of pieces for the left hand that allowed him to perform despite an otherwise great impairment. Fleisher's condition was ultimately diagnosed as focal dystonia and, with a variety of treatments, he regained the use of his right hand and has continued performing. He is now almost 80.

While a rheumatologist or any other physician may be stymied by diagnosing and treating a condition like Fleisher's, we nevertheless have a large armamentarium of measures that could define his disability using metrics that range from the SF-36 to my favorite, the Health Assessment Questionnaire (HAQ). The HAQ is a catalog of woe and provides a remarkably accurate assessment of loss through questions that probe the functioning of the upper and lower extremities.

If a physician or other provider wants to know what a patient has lost (i.e., cannot do), the HAQ is terrific. Consider its construction and the man-

ner in which points are awarded to the extent of limitation. For any given activity (e.g., opening a jar), full function gets a zero while full dysfunction gets 3 points. The best a person can do in life is a zero. The worst is 3. While I would have preferred a scaling system that gives function a positive number and dysfunction a negative one, the HAQ is enormously valuable and is one of bedrocks of modern rheumatology research.

While I occasionally do a HAQ in my clinic, usually I ask the patient a more direct question about function, especially if I am with a trainee: "What are things that you would like to do but cannot do because of your arthritis?" The array of answers is remarkable for its variety (and sadness) and, hopefully, impresses on the trainee the seriousness of arthritis and the need for better treatment. After 30 years of caring for arthritis patients, I am well aware of the monumental loss this disease causes.

The Goal: Less Loss

There are many reasons for providers and investigators to focus on loss and demonstrate its magnitude in quantitative ways. For the individual patient, a measure like the HAQ is an important way to characterize health status and measure outcomes. A change in the HAQ is often as good an indicator as a change in the joint count or sedimentation rate.

In a larger realm of health policy, a quantitative measure of loss provides a basis for advocating for patients to get more and better care and a greater share of the healthcare dollar. The greater the loss caused by a given type of illness, the greater the allocation of resources—whether by the NIH for research or the insurers for the provision of services. Certainly, the pharmaceutical industry is attuned to the burden of illness—as reflected in quality-adjusted life-years (QALYs)—and it is likely to invest in diseases where the unmet needs are high.

Whether the patient fills in a questionnaire like the HAQ or answers an open-ended question about function, the message is clear: Arthritis is about loss. Fortunately, medical therapy for inflammatory arthritis and improved surgical procedures are producing dramatic improvement in patient outcome, but the benchmark of success is really less loss, with gain only moving the HAQ back to zero.

We should all be thankful for these improvements in patient care, but this perspective can be narrow as it relates to how patients view the world and how we view our patients. I often fear that we are telling our patients that, in life, they are losers. Is there gain from arthritis or is there only loss? I will answer this question in a future column when I describe the Leon Fleisher concert I attended.

THE RHEUMATOLOGIST |

Dr. Pisetsky is physician editor of *The Rheumatologist* and professor of medicine and immunology at Duke University Medical Center in Durham, N.C.

I often fear that we are telling our patients that, in life, they are losers. Is there gain from arthritis or is there only loss?

A rheumatologist may have been one of the physicians who saw Fleisher, and I suspect that he would have diagnosed a repetitive strain injury or carpal tunnel syndrome. Had I been consulted, I might have added reflex sympathetic dystrophy (RSD) or complex regional pain syndrome type 1. RSD is one of those baffling conditions that rheumatologists see.

Certainly from my own experience, I am never sure that I am correct when I make that di-



Leon Fleisher

From the COLLEGE

NEWS FROM THE ACR AND THE ARHP

ACR ANNOUNCEMENT

Meet the Affiliate Society Council

The Affiliate Society Council (ASC), a subcommittee of the Committee on Rheumatologic Care, will replace the Regional Advisory Council

as a support mechanism for the ACR when working with rheumatology programs at the local and national level. It launched in January. The ASC and the ACR will work in conjunction with state and local societies on practice advocacy issues and create best practices for information sharing.

The first meeting of the ACR's newly formed

ASC was February 24–26, in conjunction with the ACR's "Advocates for Arthritis" advocacy visit. The meeting was well attended, with an agenda that included training on structure and strategic planning for affiliate delegates and training for Capitol Hill visits.

State and local societies that join the ASC will benefit from:

- > Yearly presentations from ACR-certified professional coders;
- > Yearly presentations from an ACR board member providing ACR updates;
- > Policy analysis from the ACR health policy department;
- > Information on federal legislation;
- > Access to current information on reimbursement and insurance issues;
- > Participating in discussions on the ACR list serve for societies;
- > Web site development using the ACR design template;
- > Bi-annual meetings held at the ACR's "Advocates for Arthritis" visit and Annual Scientific Meeting; and
- > Appointing one representative to attend the ASC meetings.

ACR director of practice management Antanya Chung, CPC, CCP, states that the ACR is looking forward to finding new ways to reach out to physicians at the local level through the ASC. "The ACR is excited to bring this new program to state and local societies," she says. "Strengthening communication with individual physicians and providing practice support is a top priority this year."

For more information regarding the ASC or to download an application, visit www.rheumatology.org/practice, or contact Antanya Chung at (404) 633-3777, ext. 818 or achung@rheumatology.org.

Sample Office Forms

During the last quarter of 2007, the practice support section of the ACR Web site was updated to include new sample forms.

These forms can help ACR members organize and streamline the daily activities in their practices. Members are encouraged to visit this section of the site to download useful forms, including:

- > Disease Activity Score Sheet;
- > Health Assessment Questionnaire; and
- > Super Bill.

You can also share forms that may be helpful to your fellow rheumatologists. If you have sample forms that could assist other offices, please fax them to the ACR office at (404) 633-1870, attention Melesia.

To download forms, visit www.rheumatology.org/practice and click on the Sample Office Forms link. If you have questions, contact Melesia Tillman, CPC, at (404) 633-3777 or mtillman@rheumatology.org.

Within Our Reach

Finding a Cure for Rheumatoid Arthritis

Research Funded by *Within Our Reach* Highlighted

Five *Within Our Reach* science investigators provided overviews and updates of their RA research projects to the newly formed *Within Our Reach* advisory board at its inaugural meeting, held November 8, 2007.

The meeting gave advisory board members an opportunity to interact with these award recipients, seeing just how their donor dollars have been used and appreciating the impact of financial support from the *Within Our Reach* campaign. Here are some highlights from the recipients' presentations.

> *Joan M. Bathon, MD, professor of medicine at Johns Hopkins Arthritis Center in Baltimore, discussed her research on rheumatoid arthritis and body composition:*

RA is highly inflammatory chronic disease that significantly diminishes physical function and causes premature mortality, primarily through accelerated cardiovascular disease. It has been shown that body composition is adversely affected in RA, as reflected by a reduction in lean (muscle) mass and in an increase in fat mass. Fat itself is a potent source of proinflammatory cytokines and adipokines, and increased fat mass is associated with insulin resistance and cardiovascular events in the general population.

Dr. Bathon's study will lay the groundwork for clinical recommendations and interventions to identify and reverse adverse body composition, and will set the stage for clinical trials to investigate the effect of modifying body composition on morbidity and mortality in RA.

> *Gary S. Firestein, MD, professor of medicine; chief of rheumatology, allergy, and immunology; and director of the Clinical Investigation Institute at the University of California, San Diego, School of Medicine, provided updates on his research on neural regulation of synovial inflammation:*

Many of the therapies currently available for RA focus on the role of the immune system and its regulation of synovial inflammation and joint destruction. Dr. Firestein's lab has discovered a novel pathway that allows the central nervous system to communicate with the immune system and decrease joint inflammation and destruction. His recent studies suggest that blocking a specific protein kinase in the central nervous system may enable regulation of the vagus nerve and release of certain acetylcholine receptors, which in turn can limit tumor necrosis factor (TNF) production and inflammation. If this hypothesis is correct, a new class of agents could be developed to regulate functions in the spinal cord and brain to decrease joint inflammation and joint destruction.

> *Antony Rosen, MD, Mary Betty Stevens professor of medicine, professor of cell biology and pathology, and director of the division of rheumatology at Johns Hopkins University School of Medicine in Baltimore, discussed his research on anti-PADI4 immune responses in RA:*

Recent discoveries have provided important new therapies for RA by identifying novel pathways that drive disease and

generate tissue damage. This study will focus on an important and previously unrecognized immune response in RA. PADI4 is one of the major proteins that create other common autoantigens in RA. Dr. Rosen hopes to define the use of new blood tests to monitor disease activity and outcome and investigate why the disease-associated form of PADI4 is chosen for immune attack. This information may help to define and monitor a critical event occurring in early RA that causes the disease to amplify.

> *Cornelia M. Weyand, MD, PhD, David Lowance professor of medicine and director of the Lowance Center for Human Immunology at Emory University in Atlanta, discussed her research on defects of hematopoietic stem cell function in RA:*

Although our ability to treat RA with potent antiinflammatory medications has increased enormously, the cause of this disabling syndrome remains unresolved. Dr. Weyand's study builds on prelimi-

nary data, which suggest that hematopoietic precursors cells are defective in frequency and function in most RA patients. She believes this identifies bone marrow as the primary site of RA pathology. Her research will examine precursor cell function in RA and focus on how these cells engraft and build the different types of blood and immune cells.

Dr. Weyand's team will investigate how treatment with methotrexate or TNF blockers affects bone marrow precursor cells to determine where the defects in these cells exist. The ultimate goal is to develop a totally novel approach to RA, aiming at regeneration of bone marrow precursor cells to improve function and tissue repair.

> *David M. Lee, MD, PhD, assistant professor of medicine at Brigham and Women's Hospital in Boston, discussed his research on immunoglobulin G (IgG) glycosylation and RA:*

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This project will investigate the usefulness of a new laboratory test measuring a natural modification of antibodies (glycosylation) in patients with rheumatoid arthritis. By employing a new methodology, Dr. Lee hopes to determine the utility of IgG glycosylation (a natural modification of antibodies) as a biomarker for diagnosis, prognosis, and prediction of response to therapy in RA. If measurement of IgG glycosylation proves a useful biomarker in patients with RA, the newly developed methodology is readily transferable to clinical practice. It could aid in early diagnosis of the disease, or help predict disease severity and which patients will respond to specific medications.

The *Within Our Reach* advisory board was created to provide a forum for interaction between lay and other campaign donors, leadership, and science investigators. This was of great importance to Dr. Lee, as he saw this as an opportunity to thank the advisory board for their support of the *Within Our Reach* campaign, which—according to Dr. Lee—has enabled work on a novel and exciting disease pathway in RA. “Because of the *Within Our Reach* campaign, we have been able to put together the resources and personnel to move forward,” says Dr. Lee. “It is quite likely this funding mechanism will enable RA-focused research projects that previously languished for lack of appropriate funding.”

Within Our Reach is a multi-year, \$30-million fundraising campaign seeking to advance the future of rheumatologic research by accelerating RA research not normally funded by the National Institutes of Health (NIH) or other peer-reviewed funding sources.

Launched by the ACR Research and Education Foundation (REF) in March 2006, *Within Our Reach* has the capacity to improve RA patients’ quality of life, alleviate long-term effects of RA, and, ultimately, ensure that future generations can enjoy life without RA.

For more information on the *Within Our Reach* campaign, visit www.WithinOurReach.info.

Within Our Reach Leadership Supporters

The REF gratefully acknowledges the following companies and individuals who have demonstrated leadership support for the *Within Our Reach* campaign. This information was current as of January 11:

Pinnacle (\$5 million+):

- > Abbot Immunology
- > ACR
- > Bristol-Myers Squibb

Partner (\$1 million+):

- > Genentech, Inc.

Milestone (\$250,000–\$499,999)

- > J. Peter Cahill (in memory of Carol K. Cahill)
- > Shirley and Hunter Enis
- > Betsy and John McLinden

Visionary (\$100,000–\$249,000):

- > Anonymous
- > The Hersh Foundation
- > Myles McDonough
- > Sandra and Alan Williams

PRACTICE UPDATES

Bring a New Partner Into Your Practice

The professional relationship between partners in a joint medical practice is sometimes compared with a marriage. The partners must work under the same roof, share the same goals, and strive to make the practice as successful as it can be. Here are some tips for adding a new partner to your practice.

Interviewing and Contracting

During the interview process, you must develop a well-rounded picture of the candidate. Could this doctor’s skills and expertise increase the range of services offered by the practice? Does the doctor’s personality fit well with the staff and the workplace culture? Are the candidate’s long-term goals compatible with that of the existing partners and their vision for the practice? Invest a lot of time in your top candidates, and do thorough reference and background checks. Someone who aims to become a partner of your practice will have a lot of questions for you—facilities available (e.g., onsite diagnostics), payer mix, benefits (e.g., malpractice, CME, relocation), workweek, call schedule, and so on. You may also want to provide top candidates with a general idea of the practice’s gross collections, overhead costs, owners’ net incomes, and perhaps even a ballpark figure for the buy-in cost. For interested parties who may be new to your community, providing information about cost of living, community growth rates, community amenities, and schools is also a good idea.

A practice will usually hire a new doctor as an associate first and, after several years, decide whether or not to offer a partnership. Some practices provide a letter of intent, which deals with issues related to a potential future partnership, such as the intended timing of partnership and the buy-in formula. The wording of the letter may be deliberately vague to allow for changes. A letter of intent is not legally binding, but it does demonstrate good faith on the part of the practice, and offers the new physician a measure of security.

Alternately, some large practices may stipulate in their employment contracts that a physician will be offered a partnership if he or she remains employed with them for a certain period of time or up to a certain date. Although a contract is a legally binding agreement, the practice could still fire an unsatisfactory physician before the completion of the period, thus eliminating the possibility of a partnership.

The “Engagement” Period

During this time, the new physician is employed as an associate, and receives a salary and possibly incentive bonuses. The engagement period is usually two to three years, but can last anywhere from one to four years.

This is the time for careful observation. Does the newcomer have excellent clinical skills and bedside manner? Does he or she generate a similar

amount of revenue as the existing partners? Is the doctor willing to accept constructive criticism and improve performance if needed? Does this person inspire your trust, respect, and confidence?

Compatibility and trust are crucial. Does the individual work well with the existing partners, staff, and patients? Does the new physician share a common vision with the other members of the clinic? Does this person offer helpful input during discussions and contribute to decisions that affect the clinic? If you were to retire tomorrow, would you feel confident leaving the practice—and your patients—in this person’s hands?

A potential partner needs to care deeply about the practice, and not just see it as a place of employment. Look for someone who is motivated and wants the clinic to thrive rather than simply maintaining the status quo. Someone who is “partner material” should put the best interests of the practice above their own self-interest—for example, making an investment in a new piece of diagnostic equipment, even though it will cut into profits.

Do not offer the new doctor a partnership if you have serious reservations at the end of the “engagement” period. Although you may feel obliged due to the doctor’s years of service, you should not add a partner who will not benefit the practice. Additionally, you want to avoid the possibility of a separation down the road, which is almost certain to cause financial and emotional damage, and potentially added legal problems and expenses.

The Partnership Agreement

Negotiations for partnership arrangements should begin as early as six months before the effective date. If negotiations last longer than expected, the partnership documents may be applied retroactively. In practices that already have two or more partners, the new partner will often be asked to accept the same terms as the existing partners. Key issues to consider when drafting a partnership agreement include:

- > **The buy-in:** How much the new partner should pay for his or her share of the practice will be based on the value of the practice’s tangible assets and its average earnings. The new partner may pay up front, over a period of time with interest, or by accepting a percentage reduction in income over a period of time. A combination of any of those payment approaches may also be used. Typically, the new partner buys into the practice over a period of three to five years. Structuring the new partner’s buy-in as a percentage of their income has several benefits. First, it avoids disputes about the exact value of the clinic’s assets. Second, it links the new partner’s buy-in price with the practice’s performance, because his or her income depends on the practice’s profits.
- > **Division of net income:** Most practices divide their net income among partners in one of three ways. The first approach is to divide all profits, based on what percentage of the practice each physician holds. The second is to divide the income based on each physician’s relative productivity, as measured by his or her fee collections. The third uses a combination of the two. For example, 50% of the clinic’s net income may be distributed equally, and the other 50% may be distributed based on relative productivity. Alternately, there may be an equal base salary for all partners, and bonuses based on relative productivity.
- > **Decision-making powers:** Some practices require a 70–80% supermajority, rather than a simple majority vote for major decisions. Examples of major decisions include adding a new partner, hiring or firing a physician, changing the practice’s location, large expen-

continued on page 12

CODING CORNER!

March’s coding challenge:

A 60-year-old female with severe RA presents for her third dosage of infliximab (the patient is currently on methotrexate and prednisone). A chest X-ray and tuberculosis skin test were ordered and reviewed prior to the day of the infusion. The patient’s rheumatologist is on vacation, so she has to see his partner (who has never treated the patient). The rheumatologist does a brief encounter to ensure that it is safe for the patient to have the infusion. The physician questions and examines the patient to make sure there is no active infection; he reviews the skin test and X-ray report. He recommends the patient go ahead and begin the infliximab infusion. The patient had no additional questions. An extended counseling session to review the risks and benefits of infliximab did not need to be repeated because the patient’s usual rheumatologist had done this during the last visit. A problem-focused history and examination are done. The medical decision-making is of low complexity. The patient is infused for two hours and 38 minutes with 600 mg of infliximab.

How would you code this? See page 23 for the answer.

ditures, and acquiring, selling, or merging a practice.

> **“Senior doctor right”:** In a two-partner practice, the senior partner may retain a “senior doctor right” for a mutually agreed-upon period. In the event of a separation, the senior partner would be entitled to keep the practice’s name, tangible assets, medical charts, and location. The senior partner may also have the power to break deadlocks on certain decisions.

> **Termination:** A partner should not be vulnerable to termination without cause. What constitutes justifiable cause for termination should be included in the partnership agreement. It should also stipulate how large a majority is needed to terminate a partner. For example, a practice with six physicians may require a unanimous vote to terminate, while a larger practice may only require a supermajority vote of 80%.

> **Losing a partner:** Partnership agreements should include provisions for a partner’s retirement, resignation, death, or inability to work. A buy-out agreement may be included or may be negotiated later.

> **Debts:** If a practice has existing debt, the new partner is usually asked to sign on as a guarantor along with existing partners. However, the agreement should absolve the new partner of responsibility for actions that occurred before he or she gained partnership status.

Deciding to add a partner to your practice is an exciting and potentially lucrative move. Understanding what goes into this type of agreement will protect you, your practice, and your future partner.



GIANT CELL ARTERITIS

Giant cell arteritis (GCA)—a type of vasculitis—is a group of diseases whose typical feature is inflammation of blood vessels. The blood vessels most commonly involved are the arteries of the scalp and head (especially the arteries over the temples), which is why another term for GCA is “temporal arteritis.” GCA can overlap with another rheumatic disease called polymyalgia rheumatica, and symptoms of the two conditions can occur at the same time or separately. The causes of GCA and polymyalgia rheumatica are unknown.

GCA affects older adults (usually older than age 60), females more than males, and Caucasians more than other races. The most common symptom of GCA is a new headache, usually in the area of the temples. Almost as common are more generalized symptoms, such as unusual fatigue, loss of appetite, weight loss, a flu-like feeling, or fevers. Occasionally, the only indication of GCA is a recurring, prolonged fever. Less common symptoms involve facial, tongue, or throat pain and pain in the jaw when chewing. If GCA spreads to the blood supply of the eye, vision can be affected. Visual symptoms include temporary blurring, double vision, or actual blindness.

GCA can be difficult to diagnose and requires prompt treatment to preserve vision. Rheumatologists are specialists in musculoskeletal disorders and, therefore, are more likely to make a proper diagnosis of GCA. Unfortunately, there is no noninvasive way to confirm the diagnosis. According to William Docken, MD, author of the patient fact-sheet, “It is common to recommend a biopsy of a small piece of the temporal artery, which is then examined under the microscope for evidence of inflammation. This outpatient procedure is done under local anesthesia and leaves only a small scar, which generally cannot be seen, at the hairline in front of the ear.”

When a patient is diagnosed with GCA, treatment should begin as soon as possible due to the risk of vision loss. High doses of corticosteroids are usually given for the treatment of GCA. A typical corticosteroid treatment for GCA would be 40 to 60 mg of prednisone per day.

For most patients with GCA, headaches and other symptoms subside quickly and the sedimentation rate declines to a normal range. High-dose corticosteroid treatment typically lasts one month and then is slowly decreased. After treatment, subsequent recurrences of GCA are rare.

Download the complete GCA fact sheet and other patient-education materials at www.rheumatology.org by following the links to patient education from the Practice Support menu.



Eye on the Election

Over the past two years, we have heard presidential candidates touting their messages to voters. Each candidate has crafted messages they believe will appeal to voters, and as campaigns continue to accelerate, these messages will saturate the radio, television, and the reading materials of the American public.

Leading up to the election, “From the College” will profile both Republican and Democratic candidates and their healthcare messages and plans. This nonpartisan look at the candidates will give the

rheumatology community an opportunity to see where candidates stand on issues that affect them and the patients they serve.

If you are not sure where to vote or if you need to register, please either call or visit the Web site of your state’s secretary of state.

If you have questions concerning any legislative or government affairs issues, contact Kristin Wormley, director of government affairs, at kwormley@rheumatology.org.

The ACR does not support any specific political candidates. This look at both Republican and Democratic nominees is a service of information, not an endorsement. | THE RHEUMATOLOGIST |

Legislative Issues Affecting the Rheumatology Community

The ACR government affairs staff works closely with members to lobby Congress on issues that affect rheumatologists, healthcare professionals, and the patients they serve. Below is a closer look at three of the issues on the ACR’s political radar:

> **Sustainable Growth Rate (SGR):** The SGR is part of the formula used to calculate physician reimbursement for Medicare. Unfortunately, the basic premise of the formula is flawed. Repairing the SGR formula is imperative to ensure that physicians will be fairly compensated and that patients will have access to appropriate care.

> **Dual energy X-Ray absorptiometry (DXA):** The Deficit Reduction Act of 2005 dealt a major blow to imaging studies—including DXA. DXA reimbursement will be cut by 75% by 2010 if Congress does not act now. The Deficit Reduction Act’s practice expense changes decrease the reimbursement for this important preventative service from

approximately \$140 to \$35.

> **NIH Funding:** The ACR advocates for an increase in funding for federal programs engaged in vital research to combat arthritis and related diseases. Support for these programs is essential to continuing the search for innovative treatments that can help millions of Americans live longer, healthier, and more productive lives, and is critical to developing more effective treatments, decreasing costs, and improving the quality of life for patients suffering from rheumatic diseases.

> **Arthritis Legislation:** The Arthritis, Prevention, Control and Cure Act would expand efforts to discover and implement new ways to prevent, treat, and care for patients with arthritis and related rheumatic diseases. This legislation would enhance rheumatic disease research and public awareness of these often debilitating diseases.

CALENDAR

2008

MARCH 18

> **Audiocconference:** Hypermobility Syndromes: The True Collagen Disorders

MARCH 26

> **Audiocconference:** Coding for Quality: Fact or Fiction?

MARCH 28

> **Deadline:** ACR State-of-the-Art Symposium Registration

APRIL 11

> **Deadline:** ARHP Merit Awards and Com-

mittee Volunteer Forms

> **Course:** Practice Management, Chicago

APRIL 12-13

> **Symposium:** ACR State-of-the-Art, Chicago

APRIL 15

> **Deadline:** Spring Applications for ACR/ARHP Membership

APRIL 17

> **Audiocconference:** The Pain Puzzle

APRIL 30

> **Webcast/Audiocconference:** Minimize Risks and Protect Your Practice!

MAY 1

> **Deadline:** Abstract submission for ACR, ARHP, ACR Basic Research Conference and, ACR Clinical Research Conference

MAY 15

> **Deadline:** ACR Awards of Distinction and ACR Masters nominations

MAY 19

> **Exam:** ABIM Maintenance of Rheumatology Certification

MAY 21

> **Audiocconference:** Non-Surgical Management of Lumbar Spinal Stenosis

MAY 28

> **Webcast/Audiocconference:** Incident-to-Coding and Supervision Rules

For more information about these or any other ACR, ARHP, or REF activities, visit www.rheumatology.org.

OSTEOARTHRITIS, Quo Vadis

Our knowledge of OA has progressed far—does a cure lie ahead?

>> By Roland W. Moskowitz, MD

After thinking about the content of the article, I decided to write about some of the prevailing quandaries and controversies in the field of osteoarthritis, with respect to etiopathology, guidelines for symptomatic therapy, and our quest for disease modification, the Holy Grail of our search.

I have been an investigator in the osteoarthritis field for almost four decades. I began at a time when the disease was ignored and the victim of a number of myths: it never cripples, it's an inevitable disease of aging, you can live with the pain without difficulty, and there's nothing in the way of treatment that really works anyway. Perhaps Sir William Osler was right when he said, "osteoarthritis is an easy disease to take care of—when the patient walks in the front door, I walk out the back door."

There was a time when, if I gave a lecture on osteoarthritis, five people would show up—three would be technicians in my lab and two would be family members. Now, I have seen 1,500 people attending a lecture on Gene Mutations in Osteoarthritis with a standing room-only audience. The fourth edition of our textbook *Osteoarthritis—Medical and Surgical Management*, is 750 pages long. We could have added another 750 pages, but the publisher thought that would make the book too costly to sell. Forty years ago, an osteoarthritis textbook would have done well to take up 100 pages. So, with this background, I would like to reflect on OA—what is and what might be.

Pathophysiology and Etiopathology

For many years, osteoarthritis was looked at purely as a degenerative disease. (See Figure 1, p. 15.) The analogy was a correlation to erosions that occur over the years as water falls on a rock. It has become obvious over the past decade that osteoarthritis is not only a disease of cartilage and is not only degenerative. Many tissues are involved in the process—subchondral bone characterized by eburnation; synovial involvement characterized by inflammation; bone marrow edema (uncertain pathology but has a relationship to pain); new bone and cartilage formation at the periphery of the joint in the form of osteophytes; inflammatory effusions; and ligamentous and muscle changes.¹

In osteoarthritis, inflammation appears to

begin early, progressing in parallel with disease worsening. (See Figure 2, p. 15.) Synovitis of involved joints is almost universally seen in patients coming to total joint replacement. The cause of the inflammation is multifold, involving release of inflammatory cytokine mediators, such as IL-1 and TNF- α , and prostaglandins; activation of inflammatory proteases targeted toward destruction of both collagen and proteoglycans; NF- κ B activation; and nitric oxide formation.²

Initiation of inflammatory mediator activation and release occurs early with an interplay of re-

sponses between synovium and cartilage. It has been hypothesized that suppression of inflammation has the potential to be disease modifying, slowing down disease progression. Perhaps daily intake of nonsteroidal anti-inflammatory agents, if tolerated safely over a prolonged period of time, could be structure modifying as well as pain relieving. Such a hypothesis has yet to be tested.

OA Risk Factor

Major risk factors for OA include age, gender, obesity, heredity, trauma (related to sports or occupa-

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tion), joint overuse (such as repetitive knee bending), and joint instability or malalignment.³ Does the increased incidence with age result from OA's asymptomatic early development at age 30 or 40, becoming clinically evident only after 10 or 20 years, or does the aging process itself play a role? There is a suggestion that aging per se may play a role in the form of advanced glycation end products that lead to formation of cross-links between sugars and proteins, making the cartilage more susceptible to injury from other risk factor inputs (obesity, chronic trauma, etc.). Osteoarthritis is more common in women after menopause, possibly relating to estrogen deficiency or (in the case of hand osteoarthritis) genetic predisposition.⁴

Obesity has a strong relationship to incident osteoarthritis but is even more likely to play a pathogenic role in the presence of joint instability or malalignment. A relationship of osteoarthritis to genetic mutations has been demonstrated, particularly as related to collagen abnormalities.⁵ Studies suggest that run-of-the-mill osteoarthritis has a hereditary component, with a number of genes under suspicion. Since the only risk factors you can really control at this time are body weight and over- or under-exercise, disease prevention is not easy. Perhaps we ought to be studying not who gets the disease, but who doesn't get the disease.

Symptomatic Treatment Approaches

There is an umbrella-like nonpharmacologic approach to management that all patients should receive. Pain in OA has both an inflammatory and

TABLE 1:
Sources of Pain in OA

- SYNOVIUM**
- > Inflammation
- BONE**
- > Medullary hypertension
- > Subchondral fracture
- OSTEOPHYTES**
- > Periosteal reaction
- > Nerve compression
- CAPSULE**
- > Distension
- > Instability
- MUSCLES/LIGAMENTS**
- > Spasm
- > Strain

non-inflammatory origin. (See Table 1, left.) Therapeutic approaches include weight reduction, appropriate exercise (both joint targeted and nontargeted), avoidance of joint overuse, and use of various orthotics. Unfortunately, most patients require additional analgesic or anti-inflammatory therapy. Guidelines, formulated by the ACR in 2000 (see Figure 3, below right),⁶ are being reformulated by several groups including the Osteoarthritis Research Society International (OARSI), the European League Against Rheumatism (EULAR), and the ACR. The OARSI recommendations were recently published.⁷

Recommendations in the ACR guidelines suggested that, after instituting appropriate nonpharmacologic programs, analgesics and anti-inflammatory agents should be considered. The use of acetaminophen in doses up to 4 g per day was recommended as initial therapy. However, in patients with evidence of inflammation or with severe pain, other initial therapeutic approaches, including nonsteroidal anti-inflammatory agents (NSAIDs) or intra-articular steroids, should be considered. Simple analgesics include acetaminophen followed by agents such as tramadol, propoxyphene, and—in appropriate cases—opioids.

Most patients with OA benefit to various degrees when administered NSAIDs, either traditional nonselective NSAIDs or COX-2 selective agents (called coxibs). COX-2 selective agents have a significant advantage over traditional NSAIDs; they cause fewer adverse gastrointestinal events such as peptic ulcers with associated bleeding, perforation, or obstruction. The observation that some coxibs were associated with an increased rate of cardiovascular events (particularly myocardial infarction) raised concern that increased cardiovascular risk might outweigh the gastrointestinal benefit of the coxibs.⁸ Coxibs are thought to increase CV risk by causing an imbalance between inhibition of thromboxane and prostacyclin. Coxibs would shift the tendency toward thrombosis by inhibiting prostacyclin, a thrombosis-inhibiting prostaglandin, while not inhibiting thrombosis-promoting thromboxane.

The relationship of nonselective NSAIDs, which effectively inhibit platelets and thromboxane, to CV events is less readily explained.⁹ Increased thrombotic CV events seen with nonselective NSAIDs may occur because effective inhibition of platelet aggregation requires sustained, over-80% inhibition of platelet COX-1, a level achieved by aspirin and high-dose naproxen. A second mechanism important as a potential cause of increased CV events with NSAIDs of all types, however, relates to increases in hypertension and edema seen to various degrees both with nonselective NSAIDs

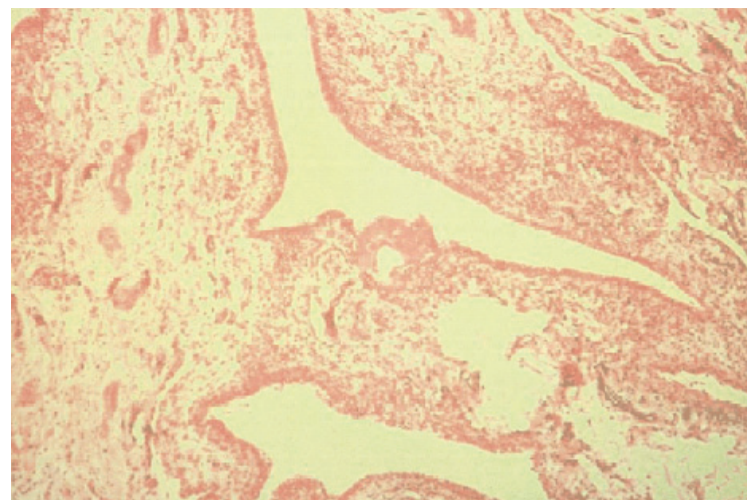


FIGURE 2: Synovitis associated with OA of the hip. Note increased inflammatory cells, edema, and vascularity.

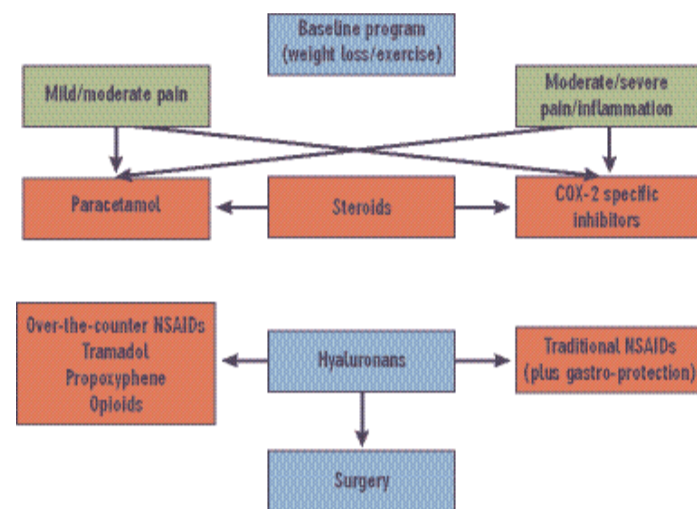


FIGURE 3: Nonpharmacologic, pharmacologic, and surgical approaches to OA pain.

Source: ACR Subcommittee on OA Guidelines. *Arthritis Rheum.* 2000; 43:1905-1915.



FIGURE 1: Standing X-ray of OA of the knee. Joint-space narrowing and osteophytes are hallmark pathologic changes.

and coxibs.

A recent statement regarding the treatment of OA by the American Heart Association described a stepped care approach to pharmacologic therapy for osteoarthritis.¹⁰ The suggestion was made that initial therapy should include acetaminophen, nonacetylated salicylates, and short-term narcotic analgesics. These recommendations are not evidence based in several respects. Firstly, nonacetylated salicylates (like coxibs) are COX-1 sparing and their potential for increased cardiovascular risk has not been defined. Narcotic analgesics, particularly in older individuals, are associated with significant side reactions, including constipation, cognitive impairment, and the risk of falling. Further, the suggestion that one can differentiate clinical responses to coxibs on the basis of their COX-2–COX-1 specificity ratio has not been clinically validated.

The cardiologists' suggestion that high-dose aspirin be administered alone as first-line therapy for patients with pain and arthritis might have been true as a recommendation 40 years ago, but I would venture to say that there are few—if any—rheumatologists today who use full doses of aspirin as primary therapy for osteoarthritis.

With respect to guidelines for treating OA, the importance of risk versus benefit is, without question, always an uppermost consideration. Unfortunately, pain itself is a cardiovascular risk factor related to increased blood pressure and pulse rate, so lack of pain relief can put the patient at increased risk. Treatment paralysis is not an attractive alternative. Risks of any type are not to be considered lightly, and need to be balanced against relief of pain and improved quality of life—not al-

continued on page 16

ways an easy decision. Judgment calls by both the patient and physician are important in determining eventual management in any given individual.

Other agents utilized in the symptomatic treatment of osteoarthritis include intra-articular corticosteroids and intra-articular hyaluronans.¹¹ These have the advantage of minimal systemic effects, and are of particular benefit when one or two joints do not respond adequately to other forms of management. At this time, hyaluronans are indicated only for use in osteoarthritis of the knee; they can be considered for use off-label in other joints if appropriate. I have used them in ankle OA with success, and efficacy in OA of the shoulder has been reported. Pre-approval for insurance coverage is recommended.

Glucosamine and chondroitin sulfate have been recommended in the treatment of OA, particularly the knee.¹²⁻¹⁴ A large study carried out under the auspices of the National Institute of Arthritis and Musculoskeletal and Skin diseases and the National Center for Complementary and Alternative Medicine showed that, in a post-hoc hypothesis-testing analysis, a combination of glucosamine and chondroitin sulfate appeared to be effective in individuals with higher degrees of OA pain.¹⁵ Based on clinical studies and experience with OA patients, I recommend use of glucosamine and chondroitin sulfate as adjunctive therapy in management.

Other modalities of therapy may be considered in the overall therapeutic approach. Acupuncture has been shown to be effective in the treatment of OA of the knee, although the effect size is low in most individuals. The increased interest in alternative therapies such as tai chi and yoga has led to increased research in evaluating these techniques. Although some studies support efficacy, investigations utilizing larger numbers of subjects in double-blinded studies would add to our knowledge in this arena.

Disease Modification

The elusive target of osteoarthritis management is disease modification with prevention of OA onset or (probably more achievable) retardation of disease progression. At this time, there are no specific agents approved for disease modification. Some studies do suggest that certain agents are associated with a slowing of disease progression, including glucosamine sulfate, chondroitin sulfate, sodium hyaluronan, soybean-avocado extract, and diacerrein.¹⁶ Identification of drugs as structure modifying is particularly challenging given that there is disagreement as to the best outcome measure for defining such structure modification. Classically, a slowing of joint-space narrowing (a measure of cartilage loss) has been the gold standard for demonstrating inhibition of disease progression. MRI will detect structural changes earlier and more comprehensively than radiologic study of joint-space narrowing alone.¹⁷

Using joint-space narrowing as a measure of structural change is dependent on the accuracy of X-ray measurement, not an easily achievable goal. In the past, standing X-rays have been routinely used in study performance. It

has been subsequently shown that more accurate definition of joint-space responses can be made using special positioning techniques which involve semiflexed knee positions.¹⁸ In an upright position, the joint space appears wider than when studied in a semiflexed position.

As noted, osteoarthritis is a disease not only of cartilage but also of other joint tissues. Accordingly, MRI measures which investigate the whole joint (so called WORMS) are important in designing structure-modification studies.¹⁷

Biomarkers

There is a great deal of interest in using biomarkers found in the serum and urine to provide earlier clues to structural disease changes, particularly as they relate to

therapeutic responses to disease-modifying agents.¹⁸ At this time, biomarkers have limited effectiveness for assessing disease modification. Biomarker assessment is complicated by the fact that osteoarthritis is frequently multi-articular. A given patient may have early as well as late osteoarthritis in various joints, so a biomarker to identify OA responses in one specific joint will be confounded by biomarker responses related to other joints with OA not being assessed. C-telopeptide-II, a biomarker measuring type-II collagen breakdown, seems to be the most promising of these biomarkers.

Markers of inflammation including hyaluronans and C-reactive protein may help identify patients more likely to have increased rates of disease progression, based on studies demonstrating a positive correlation. This may be because these are measures of inflamma-

tion, which is associated with more severe and rapid disease advancement.

Surgical Approaches

Partial or total joint replacement, particularly in the knee or hip, is recognized as a major advance in decreasing pain and increasing quality of life in patients with late-stage osteoarthritis. New procedures, including minimally invasive techniques and uni-compartmental replacement rather than total knee replacement, represent additional improvements offering faster rehabilitation and fewer complications. Surface replacement in the hip in carefully selected patients allows maintenance of bone stock and increases opportunities for additional therapeutic alternatives if future surgery is required.

Conclusion

We know a great deal more about OA etiopathogenesis and treatment than we did even a short time ago. The therapeutic advances have not, unfortunately, been as striking as those that have occurred over the past decade in the management of RA. Advances in our knowledge of disease pathophysiology, however, auger well that agents capable of better and safer symptomatic control and disease modification will be forthcoming.

Interest in OA from investigators, governmental agencies, nonprofit institutions, and pharmaceutical companies is at an all-time high—an appropriate response to the ever-increasing burden we can expect in the aging baby-boomer population over the next decade. I am hopeful that, down the line, when Dr. Pisetsky asks me to write an update on OA treatment,

we will have found “Dr. Ehrlich’s Magic Bullet” for OA.

THE RHEUMATOLOGIST

Dr. Moskowitz is professor of medicine at Case Western Reserve University and director of the Rheumatology Clinical Research Center at University Hospitals, both in Cleveland. The editorial assistance of Ann Awadalla, rheumatology clinical research center student intern, is appreciated.

References

1. Felson DT, Kim YJ. The futility of current approaches to chondroprotection. *Arthritis Rheum.* 2007;56(5):1378-1383.
2. Pelletier JP, Martel-Pelletier J, Abramson SB. Osteoarthritis, an inflammatory disease: potential implication for the selection of new therapeutic targets [review]. *Arthritis Rheum.* 2001;44:1237-1247.
3. Moskowitz RW, Altman, RD, Hochberg, M, Buckwalter, J, Goldberg, VM. *Osteoarthritis—Diagnosis and Management.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.
4. Abramson SB, Honig S. Antiresorptive agents and osteoarthritis: More than a bone to pick? *Arthritis Rheum.* 2007;56:2469-2473.
5. Holderbaum D, Haqqi TM, Moskowitz RW. Genetics of osteoarthritis: Exposing the iceberg. *Arthritis Rheum.* 1999;42:397-405.
6. ACR Subcommittee on Osteoarthritis Guidelines. Recommendations for the medical management of osteoarthritis of the hip and knee. *Arthritis Rheum.* 2000; 43:1905-1915.
7. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage.* 2008;16:137-162.
8. Moskowitz RW, Abramson SB, Berenbaum F, Simon LS, Hochberg M. COXibs and NSAIDs—Is the air any clearer? Perspectives from the OARSI international COX-2 workshop 2007. *Osteoarthritis Cartilage.* 2007;15(8):849-856.
9. Singh G, Mithal A, Triadafilopoulos G. Both selective COX-2 inhibitors and non-selective NSAIDs increase the risk of acute myocardial infarction in patients with arthritis: Selectivity is with the patient, not the drug class. *Ann Rheum Dis.* 2005;64:S85-S86.
10. Antman EM, Bennet JS, Daugherty A, et al. Use of nonsteroidal anti-inflammatory drugs: An update for clinicians. *Circulation.* 2007;115:1634-1642.
11. Altman RD, Moskowitz RW. Hyaluronate sodium injections for osteoarthritis. *Arch Intern Med.* 2002;162:2498-2499; author reply 2499-2500.
12. Reginster JY, Deroisy R, Rovati LC, et al. Long-term effect of glucosamine sulfate on osteoarthritis progression: a randomized placebo-controlled clinical trial. *Lancet.* 2001;27:251-265.
13. McAlindon TE, LaValley MP, Gulin JP, et al. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA.* 2000;283:1469-1475.
14. Leeb BF, Schweitzer H, Montag K, et al. A meta-analysis of chondroitin sulfate in the treatment of osteoarthritis. *J Rheumatol.* 2002;27:205-222.
15. Clegg D, Reda D, Harris H, et al. Efficacy of glucosamine, chondroitin sulfate, and the combination in painful knee osteoarthritis. *N Eng J Med.* 2006;354:797-808.
16. Moskowitz RW, Hooper M. State-of-the-art disease-modifying osteoarthritis drugs. *Curr Rheumatol Rep.* 2005;7:15-21.
17. Peterfy CG, Guermazi MD, Zaim MD, et al. Whole-organ magnetic resonance imaging score (WORMS) of the knee in osteoarthritis. *Osteoarthritis Cartilage.* 2004; 12:177-190.
18. Brandt KD, Mazucca SA, Conrozier T, et al. What is the best radiographic protocol for clinical trial of a structure modifying drug in patients with osteoarthritis. *J Rheumatol.* 2002;29:1308-1320.
19. Garnero P, Ayrat X, Rousseau JC, et al. Uncoupling of type II collagen synthesis and degradation predicts progression of joint damage in patients with knee osteoarthritis. *Arthritis Rheum.* 2002;46(10):2613-2624.

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PEDIATRIC BOOST

Many innovative programs aim to meet the increasing need for pediatric rheumatologists

>> By Terry Hartnett

man, MD, a pediatric rheumatologist in the division of pediatric immunology-rheumatology at Children's Memorial Hospital and assistant professor at Northwestern University in Chicago. "We hope that by taking steps to let rising medical students know about this field and to lessen the clinical burden for those who do choose to become pediatric rheumatologists, we will recharge the workforce over the next few years," she says. Dr. Klein-Gitelman served as a member of the ACR Workforce Study Advisory Group in 2005–2006. She adds that continuing efforts by the pediatric rheumatology executive committees at both the ACR and the American Academy of Pediatrics (AAP) are aimed at spreading this message.

One new idea to bolster the pediatric rheumatology workforce is a practice model in Arizona, which resulted in bringing a pediatric rheumatologist to the state for the first time. Other initiatives include a plan by a group of pediatric rheumatologists to do multicenter research in the United States and Canada, visiting professor programs, sponsoring residents to attend professional meetings, and increasing the number of fellowships and mentors for those who choose this specialty.

Survey Findings

The ACR's analysis shows that the supply and demand for the subspecialty will run in parallel during the next 20 years. Projected increases in demand stem from increases in the overall population as well as in real personal income per capita that enables consumers to purchase a greater level of healthcare services. The overall population of the United States is expected to rise in the next two decades with definitive increases in the population under age 18.

The study predicts that the baseline demand for pediatric rheumatologists will rise to 287 in 2025. Meanwhile, the supply will increase to only 254 in 2025, too little to meet the demand at that time.

The Lewin Group, which prepared the report for the ACR, says that, according to data from the American Medical Association (AMA) in 2005, the number of board-certified and/or fellowship-trained pediatric rheumatologists is 171. Supplementing the AMA list with ACR membership files, the total estimate rises to 256. This includes some physicians trained in both adult and pediatric rheumatology (46). The majority of pediatric rheumatologists are board certified (138) and 45 have both adult and pediatric board certification.

Because of the differential between supply of and demand for pediatric rheumatologists, many children are seen by adult rheumatologists. But this doesn't mean that there is always an available provider willing to take on a new pediatric patient. The survey asked adult rheumatologists the youngest age of patients they are willing to treat. The highest percentage (27.7%) said they would treat a patient between 16 and 17 years old; another 22.4% said they would treat patients between 12 and 15 years old. But the percentage that would treat younger patients drops dramatically: 9% would treat 7–11-year-olds; 7.1%, 4–6-year-olds; and 10.9%, children 4 and under. Respondents also were less likely to take on 18-year-olds (only 17.3%).

Pediatric rheumatologists are a little younger than their adult counterparts. While the median age for the adult rheumatologist is 51, the median age for pediatric rheumatologists is 47. Just under half (49%) are female. The median age for rheumatolo-

gists on the whole is older than some other medical specialties due in part to the fact that the normal path to this profession is a residency in internal medicine or pediatrics followed by a two- or three-year fellowship.

Even more striking is the age spread within pediatric rheumatology. The percentage of women varies considerably by age, with a majority of pediatric rheumatologists over age 55 being male and, in contrast, 67% of pediatric rheumatologists under 40 being female. Females account for 69% of new pediatric rheumatology fellows. The survey analysis speculates that retirement will pose less of a factor in the future because females tend to stay in practice longer than their male counterparts. However, averaged over their careers, women tend to work fewer hours than men, which will affect the number of pediatric rheumatologists needed to meet annual demand.

Pediatric rheumatologists practice mostly in academia and in large urban settings. The highest concentration (28) is found in the New York–Northern New Jersey–Long Island, N.Y.–N.J.–Pa. metropolitan statistical area (MSA). The highest percentage per one million population is 2.7 in the Boston–Cambridge–Quincy, Mass.–N.H. metropolitan area. There are nine states that had no pediatric rheumatologist (Alaska, Idaho, Maine, North Dakota, Nevada, South Dakota, West Virginia, Wyoming, and Vermont). Only recently has Arizona come off this list, with a specialist for these children in the Phoenix–Mesa–Scottsdale, Ariz., area of 3.6 million.

Pediatric rheumatology fellowships have increased from 25 total positions in 1997–1998 to 58 in 2004–2005, although some are unfilled. The number of first-year positions available in 2004–2005 was 24; 12 (53%) were filled, and nine (39%) had completed their program at the time of the survey. The percentage of international medical graduates in these fellowships went from 33% in 1997–1998 to 20% in 2004–2005.

These numbers are on the rise despite the fact that salaries for pediatric rheumatologists are in the low range for specialists. Most physicians who chose pediatric rheumatology instead of adult rheumatology end up working in academic medical centers where they can do clinic research and see patients but make less in salary than those in private practice. The median total compensation for academic faculty in pediatric rheumatology in 1998 was \$106,844. That rose 9.2% during a four-year period to \$116,723 in 2002. As a comparison, physicians who go into internal medicine, endocrinology, allergy/immunology, and geriatrics tend to have higher salaries than pediatric rheumatologists.

Many Avenues to Meet Pediatric Need

"Choosing to go into pediatric rheumatology is daunting," says Patience White, MD, chief public health officer for the Arthritis Foundation, professor of medicine/rheumatology at George Washington University in Washington, D.C., and a member of the Workforce Study Advisory Group. "The reasons for the shortage are complex and there are many factors that make the earning potential less attractive than in other subspecialties," she says. "In the academic setting, there are limited numbers of good mentors and great teachers who motivate the students with exposure to exciting cases in pediatric rheumatology."

The Arthritis Foundation is working with the ACR on getting a bill passed by the U.S. Congress to help students who are interested in this field pay for their medical education. The Arthritis Prevention, Control, and Cure Act has been introduced in both the U.S. Senate (S626) and the House (HR 1283). A hopeful sign for this authorizing bill (with no exact funding caps) is the lead taken by Senator Edward Kennedy (D-Mass.) who is a sponsor and chair of the Health Education Labor and Pensions (HELP) Committee.

continued on page 20 →

Dr. Klein-Gitelman says that the ACR and the AAP have both had positive feedback for a visiting professor program that will fund a pediatric rheumatologist to work with residents and fellows and spend two days each week teaching pediatric rheumatology. The first of these visiting professorships was completed at the University of Alabama, Birmingham. Alabama has historically had a severe shortage of pediatric rheumatologists.

In 2002, the ACR established the Pediatric Residents Program to provide a travel grant, complimentary registration, and a networking breakfast to 25 Pediatric Residents to the ACR Annual Scientific Meeting. Since its inception the program has funded 100 pediatric residents to ACR Annual Scientific Meeting of the participants 29% have entered a pediatric rheumatology fellowship program.

A major need is for all medical school curricula to include pediatric rheumatology, say Drs. Klein-Gitelman and White. The ACR has taken a keen interest in pushing for this commitment from all medical schools in the U.S., she says. "We need to teach everyone who will listen about the benefits of this field of medicine," says Dr. White. "We have been successful in increasing the number of fellowships and raising funds to support our fellows," she says.

Drs. White and Klein-Gitelman know what it is like to be the lone specialist in a practice and say that a new generation of mentors to guide future pediatric rheumatologists is also critical to meeting long-term goals.

Sharing the Load: A New Model

One unique mentoring effort is taking place in Ari-

zona. "It had become the accepted norm that children are seen by adult rheumatologists," says Paul Caldron, DO, head of Arizona Arthritis and Rheumatology Associates, Paradise Valley, AZ. Until recently, Arizona had no pediatric rheumatologists. "Most adult rheumatologists have some training in pediatrics, but it is fragmented," he says. "New physicians are afraid to go solo because it is tough to make a living, they have no training in business, and above all there are no mentors to help in the practice with patient load and on-call schedules."

His practice is the largest for rheumatology in Arizona and the surrounding states. In the past he has seen as many as four to five pediatric patients each day. "It was 25% of my practice," he says. But that is now down to approximately 5%.

Dr. Caldron spearheaded an effort that resulted in a formal collaboration between his practice and the Children's Hospital of Phoenix. The two developed a single contract that pays for the salary of a pediatric rheumatologist who splits his time three ways—two afternoons a week at the community clinic (office space and support staff provided), three afternoons at the hospital's pediatric rheumatology clinic, and mornings on rounds seeing patients in the hospital.

"We split call coverage so that our new pediatric partner has on-call duty one night a week and one weekend a month," says Dr. Caldron. "We seek his input. We have to be open to listen and understand the problems that our new colleague will have."

Michael Shishov, MD, is the pediatric rheumatologist who joined the Arizona group, and so far he has been pleased with the outcome. "When I came out of training in 2003, many people told me it wouldn't be a good idea to look at taking this position in Arizona," he says. "But some like Dr. Caldron were really encouraging me to go for it." One of the main things that attracted him to the position was the network of practice support that would alleviate some of the burdens of private practice. "My fellow doctors like Dr. Caldron share on-call duty with me and I have medical assistants and infusion nurses to help in the practice. We borrow ideas and help each other."

Dr. Shishov says he knows that there is room to grow this collaborative program and looks forward to working to achieve that. "When my schedule is full and we can no longer see children within a good time frame, then we might look at adding a nurse practitioner," he explains. "The hospital has really allowed me to ramp up slowly. I am sure I could see as many as 50 kids a week in the clinic, but that would be too much to handle right now," he says. "This program has allowed me to go at my own speed and do things I could not do if I had chosen to take a job at an academic medical center," says Dr. Shishov. "There is no doubt that I had many reservations when I decided to come here. But I definitely have never regretted it. Now if we can just get the word out to others to create similar practice models and entice residents to take a chance, I think we may change the field of pediatric rheumatology for the future."

Others interviewed for this article have a similar optimism for the future of pediatric rheumatology. "Working in a group practice as a pediatric rheumatologist is a good lifestyle and a rewarding profession," says Dr. White. | THE RHEUMATOLOGIST |

Terry Hartnett wrote the Workforce Study series.

Reading RHEUM

HANDPICKED REVIEWS OF CONTEMPORARY LITERATURE

OSTEOPOROSIS

Which Bone Agent Is Best in High-risk Osteoporosis?

>> By Eric S. Schned, MD

Saag KG, Shane E, Boonen S, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med.* 2007;357:2028-2039.

Abstract

Background: Bisphosphonate therapy is the current standard of care for the prevention and treatment of glucocorticoid-induced osteoporosis (GIO). Studies of anabolic therapy in patients who are receiving long-term glucocorticoids (GCs) and are at high risk for fracture are lacking.

Methods: In an 18-month randomized, double-blind, controlled trial, we compared teriparatide with alendronate in 428 women and men with osteoporosis (ages 22 to 89) who had received GCs for at least three months (prednisone equivalent, 5 mg daily or more). A total of 214 patients received 20 µg of teriparatide once daily, and 214 received 10 mg of alendronate once daily. The primary outcome was the change in bone mineral density at the lumbar spine (LS). Secondary outcomes included changes in

bone mineral density at the total hip and in markers of bone turnover, the time to changes in bone mineral density, the incidence of fractures, and safety.

Results: At the last measurement, the mean (±SE) bone mineral density at the LS had increased more in the teriparatide group than in the alendronate group (7.2±0.7% versus 3.4±0.7%, $p<0.001$). A significant difference between the groups was reached by six months ($p<0.001$). At 12 months, bone mineral density at the total hip had increased more in the teriparatide group. Fewer new vertebral fractures occurred in the teriparatide group than in the alendronate group (0.6% versus 6.1%, $p=0.004$); the incidence of nonvertebral fractures was similar in the two groups (5.6% versus 3.7%, $p=0.36$). Significantly more patients in the teriparatide group had at least one elevated measure of serum calcium.

Conclusions: Among patients with osteoporosis who were at high risk for fracture, bone mineral density increased more in patients receiving teriparatide than in those receiving alendronate.

Commentary

Rheumatologists know intimately the hazards of long-term GC therapy. GIO and resultant fractures are especially vexing problems since some patients in whom we use GCs are already at high risk for these complications. These patients include postmenopausal women with long-standing RA or lupus and elderly patients with polymyalgia rheumatica (PMR) and giant cell arteritis (GCA).

Bisphosphonate therapy is the current standard of care for patients who already have—or are at risk for developing—GIO.¹ Bisphosphonates act primarily on bone resorption, however, while teriparatide directly stimulates osteogenesis and inhibits osteoblast apoptosis, two key mechanisms in bone affected by GCs.² These actions make teriparatide a good candidate for treating or preventing GIO.

Saag and colleagues undertook trial comparing teriparatide and alendronate in patients with GIO. All patients also received 1000 mg of calcium carbonate and 800 IU of vitamin D. The primary outcome was change in bone density at the LS.

Patients had a history of sustained GC therapy and a T-score at the LS or total hip of either -2.0 or less or -1.0 or less plus at least one fragility fracture while receiving GCs.

Four hundred twenty-eight patients were randomized, and 75% were being treated for rheumatologic disorders (almost half with RA). The median daily prednisone dose was 7.6 mg and the median duration of therapy was 1.3 years. Almost 70% had

prevalent fragility fractures and the mean baseline LS T-score was -2.5.

At 18 months, patients in the teriparatide group had a significantly greater increase in mean bone mineral density (BMD) at the LS than those in the alendronate group. Similarly, at the total hip, the teriparatide group's increase in BMD from baseline (3.8±0.6%) was significantly greater than the alendronate group (2.4±0.6%, $p=0.005$).

Ten patients in the alendronate group ($n=165$) had new radiographic vertebral fractures while only one in the teriparatide group ($n=171$) did ($p=0.004$). Markers of bone formation and resorption both showed increases in the teriparatide group and decreases in the alendronate group.

There were no significant differences in the overall incidence of adverse events between the two groups, although more patients treated with teriparatide had one or more serum calcium values greater than 10.5; there were no instances of sustained elevation.

I think this paper should encourage rheumatologists to be more aggressive in evaluating patients on sustained GCs and considering the various therapeutic options. For many individuals on GCs who are at relatively low risk for immediate GIO or fracture—such as younger individuals starting GCs, individuals with only mildly or moderately low BMD, or those with relatively mild osteoporosis—I'll undoubtedly continue to use oral bisphosphonates.

However, this study's patient population, which clearly was at high risk for fracture (over two-thirds had prevalent GC-induced fractures at baseline), benefited significantly from teriparatide compared with alendronate. Less than 5% of the patients in this study had PMR and the mean age of the patients was 57. It seems likely that for patient populations which are enriched in PMR, GCA, and other diseases in older individuals, benefits of teriparatide might be even more striking.

At least two practical issues could limit the use of teriparatide: daily injections and cost. In particular, when Fosamax becomes available generically in 2008 and cost is reduced, resistance from payers to use of teriparatide can be expected. Cost-effectiveness analyses may be necessary to demonstrate the magnitude of fracture risk needed to justify teriparatide use. In the meantime, this study should reinforce the value of performing routine fracture assessments on postmenopausal women and men over age 60 who are on chronic GCs in order to help identify patients at particularly high risk.

References

1. ACR Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. *Arthritis Rheum.* 2001;44:1496-1503.
2. Jilka RL, Weinstein RS, Bellido T, et al. Increased bone formation by prevention of osteoblast apoptosis with parathyroid hormone. *J Clin Invest.* 1999;104:439-446.

IN BRIEF

Trauma and Fractures

>> By Daniel H, Solomon, MD, MPH

Mackey DC, Lui LY, Cawthon PM, et al. High-trauma fractures and low bone mineral density in older women and men. *JAMA.* 2007;298:2381-2388.

“I support the REF financially by donating in honor of esteemed colleagues or in memory of my patients. What better way to honor these individuals while also doing my small part to ensure that there will always be rheumatologists to care for future generations of patients?”

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Abstract

Context: It is widely believed that fractures resulting from high trauma are not osteoporotic; however, this assumption has not been studied prospectively.

Objective: To examine the association between BMD and high-trauma fracture and between high-trauma fracture and subsequent fracture in older women and men.

Design, setting, and participants: Two prospective U.S. cohort studies in community-dwelling adults 65 or older from geographically diverse sites. The Study of Osteoporotic Fractures followed up 8,022 women for 9.1 years (1988–2006). The Osteoporotic Fractures in Men Study followed up 5,995 men for 5.1 years (2000–2007).

Main outcome measures: Hip and spine BMD were assessed by dual-energy X-ray absorptiometry. Incident nonspine fractures were confirmed by radiographic report. Fractures were classified, without knowledge of BMD, as high trauma (due to motor vehicle crashes and falls from greater than standing height) or as low trauma (due to falls from standing height and less severe trauma).

Results: Overall, 264 women and 94 men sustained an initial high-trauma fracture and 3,211 women and 346 men sustained an initial low-trauma fracture. For women, each 1-SD reduction in total hip BMD was similarly associated with an increased risk of high-trauma fracture (multivariate relative hazard [RH], 1.45; 95% confidence interval [CI], 1.23–1.72) and low-trauma fracture (RH, 1.49; 95% CI, 1.42–1.57). Results were consistent in men (high-trauma fracture RH, 1.54; 95% CI, 1.20–1.96; low-trauma fracture RH, 1.69; 95% CI, 1.49–1.91). Risk of subsequent fracture was 34% (95% CI, 7%–67%) greater among women with an initial high-trauma fracture and 31% (95% CI, 20%–43%) greater among women with an initial low-trauma fracture, compared with women having no high- or low-trauma fracture, respectively. Risk of subsequent fracture was not modeled for men.

Conclusions: Similar to low-trauma nonspine fractures, high-trauma nonspine fractures are associated with low BMD and increased risk of subsequent fracture in older adults. High-trauma nonspine fractures should be included as outcomes in osteoporosis trials and observational studies.

Commentary

Many clinicians have long suspected that even fractures occurring after high trauma (such as in a motor vehicle accident) might be related to osteoporosis in a given individual. Mackey and colleagues used data from several large prospective cohorts to prove that this is the case. They found that high-trauma fractures had a similar relationship with bone mineral density as did low-trauma fractures and that high-trauma fractures predicted future fractures equally as well as their low-trauma counterparts. These findings should spur physicians to consider any prior fracture (low- or high-trauma) as a marker of patients that need vigorous screening and possible treatment for osteoporosis. | THE RHEUMATOLOGIST |

CORRECTION

In the article "Difficult Gout" (July 2007 issue, p. 1), regarding statements that oxypurinol does not effectively inhibit the oxidized form of xanthine oxidase, the statements should read as follows:

Oxypurinol can slowly dissociate from the enzyme. Moreover, oxypurinol can fail to completely inhibit the oxidized form of xanthine oxidase in certain biologic milieus (as opposed to enzyme inhibition in simple solution), as shown by the recent work of Kelley et al (Kelley EE, Trostchansky A, Rubbo H, et al. Binding of xanthine oxidase to glycosaminoglycans limits inhibition by oxypurinol. *J Biol Chem.* 2004;279:37231-37234).

Please visit www.The-Rheumatologist.org to download a corrected version of the July issue under the "Download Issues" tab.

CODING CORNER!

Coding Corner answer (question on p. 10):

March's coding answer: 99212-25, 96413, 96415 x 2, J1745 x 60, Diagnosis 714.0

The visit would be considered established even though the patient has not seen this rheumatologist before; he is a partner to her physician. A patient is considered as an established patient if he or she is seen by anyone in the practice within three years. The visit would be considered as 99212 because the history and exam were problem focused and the medical decision making was of low complexity. You only need two out of three components for an established visit. A modifier -25 is needed on the office visit because it was separate and significant to the infusion.

The infusion of infliximab would be coded as 96413 one unit and 96415x2 because the infusion was two hours and thirty-eight minutes. The first hour is coded 96413, the second hour is coded as 96415, and, because the third hour was more than 31 minutes, it is qualified as a third hour and would be coded as 96415. The drug would be coded as J1745 with 60 units because this code is for 10 mg.

SYSTEMIC VASCULITIS

Low incidence makes research and diagnosis a challenge

>> By Virginia Hughes

ingham (U.K.), discussed large-vessel vasculitis.

For Treatment, Severity is Key

"The most important message," for practitioners, said Dr. Villa-Forte, is that the treatment approach should be "decided according to the severity of clinical manifestations" and the rate of change of disease progression.

Vasculitides are a diverse group of diseases the result from inflammation of the arteries, veins, capillaries, or other blood vessels. Depending on the extent and duration of vessel involvement, vasculitis can be very serious because it ultimately impedes blood flow to vital organ systems. It affects patients of all ages, can be chronic or acute, and often flares up after long periods of remission.

Each year, only about 500 Americans are diagnosed with Wegener's granulomatosis—a type of small-vessel vasculitis that eventually causes damage to the lungs and kidneys. The same low incidence is true for large-vessel vasculitis, like Takayasu's arteri-

tis. Not surprisingly, practicing rheumatologists may not have extensive experience with the management of this family of diseases, and treatment options have been limited.

Vasculitic disease can be difficult to diagnose because they share symptoms—like fatigue, abdominal pain, hypertension, renal insufficiency, and neurologic dysfunction—with many other diseases. A firm diagnosis usually requires a tissue biopsy of one of the organs that has been affected.

Small- and Medium-Vessel Vasculitides

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides are among the most common forms of vasculitis. Until recently, the standard treatment of ANCA-associated systemic vasculitis was cyclophosphamide (CYC)

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Arteriogram showing arteritis in the lower limbs.

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and prednisolone. However, both of these drugs can have serious side effects.

"The initial protocols for CYC came with high rates of infection, bone marrow suppression and other prolonged types of toxicity," said Dr. Villa-Forte. Since then, combination therapy of CYC, prednisolone, and methotrexate (MTX) "has made a marked impact on the treatment of the disease. Otherwise it would be mostly fatal."

The first study to directly compare CYC and MTX was conducted by nephrologist Kirsten de Groot and colleagues at the Hannover Medical School in Germany in 2005 (*Arthritis Rheum.* 2005;52(8):2237-2242). The 100-patient study found that, at six months, the remission rate in patients treated with MTX was 89.8%, just slightly less than the 93.5% remission rate of patients treated with CYC. At the same time, 34% of patients treated with MTX experienced adverse events, while 74% of CYC patients experienced adverse events.

The MTX regimen was not as effective in patients with extensive disease, however, and was associated with more relapses than CYC after the initial treatment period. Also, Dr. Villa-Forte noted, patients whose vasculitis involved the kidney should not be given MTX because it accumulates in patients with renal insufficiency. "I don't think we have enough data to support that [MTX] should be started as a first-line agent" for patients with extensive disease, said Dr. Villa-Forte. Instead, practitioners "should always be thinking of a staged therapy," she said. Her two-step approach for patients with severe disease is to first begin treatment for a short period with CYC, and then switch to a less toxic treatment like MTX for maintenance treatment. For mild to moderate disease, she advised treatment with MTX alone.

Dr. Villa-Forte has evidence for the efficacy of two-step staged approach because of her experience with 82 Wegener granulomatosis patients over 12 years, with a 4.5-year follow-up. As published in *Medicine* in September 2007 (86(5):269-277), patients on the staged treatment all improved. Fifty percent of patients achieved remission within six months and 72% within a year. Sustained remission was ultimately achieved in 78% of patients. However, relapse rates were high. Of the 75 patients who had any kind of remission, 45% relapsed within a year and 66% within two years. "No matter which current standard therapy we decide to use, we still have high relapse rates. We need to better understand the physiology of this disease," she said.

Dr. Langford agreed: "In reality there's very little data focused specifically on the issue of relapse. Ultimately, when we face how to manage, a lot comes down to what's best for our individual patient. A lot comes down to opinion."

Large-Vessel Vasculitides

When Dr. Bacon discussed Takayasu's arteritis, a vasculitis disease that affects the aorta, one of the first things he stressed was that it "is not in any sense a sister disease to the small vessel vasculitides" that were discussed by Drs. Villa-Forte and Langford. "And that's important when you try to extrapolate treatment," he continued. "This clinical course is different and the pathology is different."

Patients with Takayasu's arteritis will generally complain of symptoms related to reduced blood flow in the upper neck and

head, he said. Takayasu's arteritis is sometimes referred to as "pulseless disease" because it's difficult to take the pulse of many patients with Takayasu's arteritis. Unlike the small-vessel vasculitides previously described, Takayasu's arteritis has a nine-to-one ratio of females to males. It usually occurs in women under 40, and is more common among Asians.

Takayasu's arteritis is like the other vasculitides, though, in that it is very uncommon—Dr. Bacon said there is only one case per million population in the U.K.—and in that it's extremely challenging to diagnose. The inflammation can exist for many years, producing mild or non-specific symptoms, arthralgia or myalgias until there is a evidence of serious vascular insufficiency such as claudication, angina or a major complication, such as stroke; aortic regurgitation may also occur because of valve involvement. The vast majority of patients with Takayasu's arteritis are

treated with prednisone.

Dr. Bacon discussed various factors to look for when diagnosing Takayasu's arteritis. "The major factor, unfortunately, is pulse loss," he said, though the disease can be detected using other tests before it progresses that far. Angiograms, which show narrowing or occlusion of the blood vessels, are currently the standard diagnostic test. But an angiogram "doesn't tell you anything about what's going on in the blood vessel wall, so it can't distinguish disease activity from scars and is therefore a poor guide to therapy," he explained. Recent studies have shown that advanced MRI can show wall thickening both in the aorta and in all the major arterial segments. "Therefore, this is a clear advance in assessing the degree of activity of the disease," he said. ■ THE RHEUMATOLOGIST ■

Virginia Hughes is a medical writer based in New York City.