Impact factor’s influence on peer-reviewed journals—and authors—is on the rise

David G. Borenstein, MD

High-ranking journals list their impact factor (IF) with pride. In fact, Arthritis & Rheumatism (A&R), scientific journal of the ACR, just celebrated a jump in its IF, reinforcing its position as the preeminent journal in the field. (See “A&R, ACR Make an Impact,” p. 14.) But do you know what the IF actually means—and how it is affecting rheumatology research and careers?

Father of IF

In 1955, Eugene Garfield, PhD, came up with an idea to rate the importance of a scientific journal by how many times its articles were cited in other articles, and the IF concept was born. By 1961, the first Science Citation Index was published and IF was on its way to becoming a recognized tool.

T he epidemic is coming and its name is lumbar spinal stenosis. Among subspecialists most actively involved in the care of elderly individuals, rheumatologists will not only be taking care of patients with low back and associated leg pain, but they will be identifying these symptoms in colleagues and themselves. According to the United States Census Bureau, the baby boom generation (born between 1946 and 1964) encompasses approximately 78.2 million individuals or about 26% of the total population. Radiographic studies have documented the presence of anatomic lumbar stenosis in up to 25% of individuals older than 40. Simple arithmetic indicates that over the next two decades, almost 20 million individuals will be at risk of this disabling problem.

The last decade was a positive one for rheumatology training programs. According to the Workforce Study of Rheumatologists commissioned by the ACR in 2006, programs saw an increase in the number of adult and pediatric training positions filled and a high rate of fellowship completion. However, the demand for rheumatologists will only increase as the U.S. population ages, and the specialty will face many challenges meeting this demand.
Yes, that’s me with Senator Edward M. “Ted” Kennedy (D-Mass.) in Washington, D.C., this past May (at right). As we reported in The Rheumatologist last month, members of the ACR board of directors and I spent the morning of May 10 meeting with our members of Congress on Capitol Hill. Our visits were well received, and we met with representatives or their staff from over 60 offices. It was an opportunity to talk about the issues of importance to rheumatology, and yes, for a photo or two.

Access to a sitting senator, and one of such esteem and influence (whatever your politics may be), doesn’t always come easy. We were able to arrange this meeting because of a personal contact of mine who knows the senator’s former chief of staff. But our meeting with Sen. Kennedy was more than just a photo op: this 45-year veteran of politics spent more than thirty minutes with us, keenly aware of the issues facing medicine and the patients we treat. At the end of our meeting, he even asked for our opinion on the issue of follow-on biologics (aka generic biologics).

**Why I Care so Much**

In June, I spoke about why I still like being a rheumatologist—the “still” being in reference as much to the current environment of medicine and all of its hassles as it was to my three decades of being in practice. That column touched a chord with many of you, and you took time out of your day to write me and tell me why you still like being a rheumatologist. Many of you also touched on the hassles of practicing medicine today, and lamented that it didn’t seem like it was going to change any time soon.

I’m often asked why I spend time volunteering for the ACR and organized medicine. It’s enlightened self-interest more than anything; it is unlikely that anyone will look out for me better than I can look out for myself. I have to be a part of trying to make positive changes in medicine, for rheumatology and for our patients. I don’t see it as a choice, and it is not in me to abdicate this responsibility to others while I sit there offering nothing but Pollyanna rhetoric or harsh criticism against the efforts of others.

You see, the solution to these issues lie in our ability to effectively (and tirelessly) advocate. It’s an inescapable part of our existence in today’s world. The world is divided into two kinds of people: observers and participants. As a rheumatologist or a healthcare professional, if you’re complaining about the state of medicine today, you need to be a participant in the efforts to address and resolve these issues.

**How You Can Help**

We need you, now more than ever. Here are the top 11 ways you can get involved in advocating for yourself and for rheumatology:

1. Develop a personal relationship with your representatives in Congress and/or their staff. Visit them while you’re in Washington, D.C., or at their home offices in your state. ACR member Sharad Lakhanpal, MD, used his long political involvement to obtain Rep. Frank Pallone (D-N.J.), Chairman of the Energy and Commerce subcommittee on Health, as the keynote speaker for the ACR Board of Director’s meeting in Washington, D.C., this past May. Rep. Pallone’s committee has jurisdiction over general healthcare issues, including the Arthritis Prevention Control and Cure Act of 2007 (H.R. 1283).
2. Invite your Congressional representatives or a member of their staff to spend a day in your office. ACR member Al Denis, MD, demonstrated impressive leadership by inviting his Congresswoman, Rep. Thelma Drake (R-VA), to visit his office this year during Congress’ spring recess. During the visit, Rep. Drake witnessed DXA screenings and the value of having the procedure performed in an office as opposed to a hospital. She spoke to a patient receiving intravenous biologic therapy for RA. As a result of the visit, Rep. Drake signed on as a co-sponsor to the Arthritis Act and agreed to write a letter to Centers for Medicare and Medicaid Services regarding IV ibandronate. Allowing members of Congress to witness firsthand the daily routines within a rheumatology office gives them great perspective on the severity of the patients’ conditions, importance of the procedures, reimbursement needs of physicians, and necessity for research on arthritis and other rheumatic diseases.

3. Attend fundraising events for state and national candidates. Contribute if you are supportive of their efforts. Volunteer your time to election campaigns. All politics are local, and cultivating relationships at the inception of someone’s service (or at the time of reelection) is an invaluable opportunity. When asked to do so, write letters to Congress.

4. Go to www.rheumatology.org and click on our Legislative Action Center, www.capviz.org/acr. There you can read about the issues we’re currently advocating for as well as on behalf of the patients you treat. We offer tools you can use to easily find your members of Congress and send them your thoughts. We offer prepared letters on these issues, and encourage you to add your own personal story. You can always contact our Government Affairs department to assist you in your efforts; they are ready, willing, and able to help make your voice heard.

5. Display an ACR advocacy recruitment easel in your office. These tabletop easels contain pre-addressed postcards that patients can mail to the ACR to become involved with our advocacy efforts.

6. Subscribe to the ACR advocacy list serve. Again, go to www.rheumatology.org and select Networking List. Serves from the Practice menu. Join the conversation and hear about what others are doing in their communities and states to advance rheumatology’s agenda for better medicine.

7. Cultivate relationships with medical directors in the insurance companies your practice interacts with, and serve on insurance company advisory boards.

8. Serve as the rheumatology representative for Medicare’s rheumatology advisory committee when such positions become available. Join the American Medical Association.

9. Take a leadership role in your local or state rheumatology society. If there’s not a society for your community, start one.

10. Volunteer for the ACR. The Rheumatologic Care, Government Affairs, Research, and Quality Measures committees, as well as many ARHP committees, all have advocacy functions. Particularly if you’ve been in practice just 10 to 15 years, we invite you to serve to be sure the ACR effectively represents your perspective.

11. Engaging in advocacy efforts can take as little as a few minutes of your time, but you can reap so much in return. I ask that you join our other dedicated members in advocacy efforts. Engaging in advocacy efforts can take as little as a few minutes of your time, but you can reap so much in return. Do it for our patients, for our profession, and most of all, for yourself.

Dr. Binaubam is president of ACR. Contact him via e-mail at binaubam@rheumatology.org.
Rheumatinons  ❙ THOUGHTS FROM THE PHYSICIAN EDITOR

Rheumatology’s Chronic Crisis

How should we deal with a shrinking workforce and expanding patient pool? >> David S. Pisetsky, MD, PhD

Although, despite the necessity to expand the field of rheumatology, many training programs can’t fund all of their approved positions and there is difficulty in recruiting new chiefs and leaders of once distinguished programs.

At the recent EULAR congress in Barcelona, I sat down with a group of American rheumatologists for a late afternoon drink. We gathered in the lounge on the executive floor of the headquarters’ hotel. The hotel was a sleek high rise, Euro-modern in design, and the lounge adjoined a balcony overlooking the Mediterranean Sea. The day was warm and the water sparkled as a strong wind lifted white caps and propelled sail boats over the water like large fins.

The lounge was the perfect place for laughter and idle banter. Given the locale, the buoyant spirit of a beautiful city, and the sun that beamed down gloriously, our conversation should have bubbled and brimmed with optimism and excitement. Instead, the group seemed down. To a person, the Americans sitting in the lounge were reflective and sober as they expressed concern, even anxiety, about the landscape of rheumatology and the prospects for the future.

When I sauntered from my room to the lounge, my intention was to relax after a busy day at the congress. OK, OK. I didn’t go to as many sessions as I could have, but I stayed in the convention center the whole day and talked science and did the requisite networking that is the job (and the fun) of being the Editor of The Rheumatologist (TR). I promise you. I recruited several great articles at the meeting. The articles will be coming soon (Yes, my dear friends, the deadlines I gave you were real), and they will embody important research and innovations for practice. My day was busy even if low on CME credits.

Before sitting with my friends, I went to the bar and poured a glass of water called Vichy Catalan. Somewhat, I could not believe that a product called Vichy water still existed, but it fizzed nicely and was very refreshing. At the table, my American colleagues, instead of engaging in the usual gossip of academic comings and goings, were deep into a discussion of what many think of the crisis in rheumatology.

Rheumatology’s Paradox

Crisis is not my favorite word for a situation that seems chronic. The term, however, gives weight and seriousness to any discussion and certainly focuses attention. This crisis, which has been the subject of many important ACR initiatives and has been discussed in TR, reflects the collision of two ominous trends: the gap in the workforce as the supply of rheumatologists fails to meet the demand, and the increasingly troubled state of academic rheumatology. According to predictions, in the coming years, more people will leave the field than will enter it and training programs can’t keep pace.

These trends are, of course, paradoxical because at present there is every reason for rheumatology to expand and prosper. With the increasing sophistication and complexity in patient care and the arrival of the baby boomers in drives at the doctors’ offices, the demand for rheumatology service will soar. Further, future improvements in care will likely involve more aggressive treatment approaches that will necessitate more visits and more intensive monitoring.

The past years have witnessed impressive treatment advances especially of inflammatory disease. Patient outcomes are continuously improving, with the development of new drugs and strategies making remission in RA, for example, a realistic goal. To explore fully the array of possibilities in RA alone afforded by existing agents, we would need a dramatic boost in investigators. To test the panoply of new agents in the pipeline, a veritable army would be needed. Similar issues pertain to the workforce needs to explore new treatments of osteoarthritis, osteoporosis, and the autoimmune diseases.

Nevertheless, despite the necessity to expand the field of rheumatology, many training programs can’t fund all of their approved positions and there is difficulty in recruiting new chiefs and leaders of once distinguished programs. In the setting of large academic medical centers, the training programs are often beleaguered as they are forced to downsize, hamstring by financial models that are as harmful as they are baroque.

My thirst quenched with the Vichy water, I was about to switch to cava to get a jump on the festivities of the evening ahead. With my colleagues engrossed in a serious powwow, however, I wanted to stay sharp and participate with them to come up with ideas for lessening our crises. I poured another glass of Vichy water.

Our conversation ebbed and flowed as we sent up trial balloon after trial balloon for finding solutions. Many of the suggestions were expected: Lobby Congress to increase NIH spending, convince the medical school deans of the importance of rheumatology services; develop new financial models that are as harmful of the downstream revenues rheumatologists generate.

While the expected ideas all have value, somehow, none seemed particularly compelling or likely to succeed in the future. Indeed, as the sun shone brilliant silver-gold in the afternoon sky over the white buildings of Barcelona, the world seemed a bit darker.

Crisis Solved?

In situations like this one, the simplest thing to say is, “Think outside the box.” Along with crisis, this is another phrase that I resist. Frankly, I abhor the idea that I inhabit a box and the phrase “think outside the box” is one of the most trite and overused of all exhortations for a group. Nevertheless, original thought is good and I will relate an outside-the-box idea that our stalwart group in the executive lounge advanced just prior to our expedition to the Parc Guell for EULAR’s 60th birthday party.

The idea is a product of collective thought and has corporate ownership. I doubt, however, that any of us will put our name on this product despite its merit. If we did, the authorship would have some heavy hitters in the lineup.

Instead of giving the answer away now, though, I’m going to wait until next month to reveal our solution. Look for our chronic crisis solution in September’s “Rheuminations” column.

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

Civic duties may soon be too burdensome for even willing public servants  >> By Bruce N. Cronstein, MD

From jury duty to hospital committees, our institutions depend on the people of this country for community and public service. Although trying and often time consuming, this service is usually provided in good humor and with the best of intentions. Unfortunately, community service has recently earned a less lofty reputation. As punishment for miscreants, community service follows right after sincere regrets and rehabilitation for substance abuse in the “stations of the celebrity.” As documented in the news reports, for students applying for admission to top colleges, “voluntary” community service can be onerous but I often take pleasure in jury duty despite the time imposition. The joy is not due to the proximity of Chinatown and its delight-ful restaurants to the courts in Manhattan. It is interesting to see professionals of a different sort work and take part in a process that is critical to the proper functioning of civil society. Similarly, the drudgery of committee work at my medical center has its gratifications: the satisfaction of a job well done and the sense that the common-weal has been served are their own form of re-ward. During the following few weeks as I was being vetted for service, it became apparent that Merck was going to sponsor subscriptions for a review journal that I edit. I told the FDA of this sponsor-ship and was promptly told that this was an insol-uble conflict as my “employer” would benefit from the approval of the drug. Would that I could ben-eftit too, but I never heard any mention of sharing in the profits that would result from the increase in paid subscriptions.

Despite the flattering notion that my opinion of a new NSAID might matter enough to make a difference as to whether or not this drug was li-censed and administered to millions of patients, I was actually relieved that I would not have to serve on this FDA Advisory Committee. Going into these deliberations, it was clear that this drug stood little chance of approval; the mention of the name of Merck and COX2 inhibitor in the same sentence is to the watchdogs of the pharmaceuti-cal world what Enron is to Sarbanes and Oxley. Indeed, one of the non-physician members of that panel (who was on the losing side of that vote) has subsequently been called by the institution for service on any committee where decisions must be made. The committees on which I have served for which lia-bility is a possibility have included investigations of scientific misconduct and personal misconduct of individual physicians as well as promotion and tenure committees. Being confronted with the foibles and imperfections of my fellow scientists and physicians is not only distasteful but potentially financially ru-inous if I find myself charged with libel as a result. Service on an advisory panel of the FDA is not lu-mentious if I find myself charged with libel as a result. To Serve or Not To Serve?

I often find myself asking for written reassurance that I will not be held liable or that my legal costs will be covered by the institution for service on any committee where decisions must be made. The committees on which I have served for which liability is a possibility have included investigations of scientific misconduct and personal misconduct of individual physicians as well as promotion and tenure committees. Being confronted with the foibles and imperfections of my fellow scientists and physicians is not only distasteful but potentially financially ruinous if I find myself charged with libel as a result. Service on an advisory panel of the FDA is not lucrative if I find myself charged with libel as a result. The cost of public service may soon become too onerous for most people to participate. In addition to the time taken from other pursuits, the cost of public service now includes the potential for legal action. The cost of community service may soon become too onerous for most people to participate. In addition to the time taken from other pursuits, community service will be the exclusive domain of the criminal celebrity and all decisions will devolve upon those least likely to offer wise opinion. This regression to the minimum seems to have occurred, to a great extent, in the political world and it is unfortunate, but inevitable, that the divisions and vindictiveness have spread to the rest of us. Although I am not nearly as accurate a shoe tosser as the supermodel Naomi Campbell nor blessed with the looks of the rock singer Boy George, I would like to take my turn at serving the public. Nonetheless, I do not wish to serve my community while wearing a reflective vest and pushing a broom through the streets of New York. It might be nice, however, to have a safe, non-GI toxic NSAID to treat the inevitable aches and pains resulting from such unusual exertions. Dr. Cronstein is Paul R. Ecserner professor of medicine at NYU School of Medicine in New York.
**Medicare Reimburses for Discarded Single-use Drugs**

Medicare will now reimburse for a single-use vial or single-package of a drug or biological that was discarded along with the amount of that single-use vial or package that was administered to the Medicare patient. The policy applies to both average sales price (ASP) and competitive acquisition program (CAP) drugs, and states:

- Medicare contractors with a policy on drug or biological wastage for billing purposes (JW modifier) may continue to use it for CAPs.
- Medicare contractors should use J1 (no payor) and J3 (flush as written) modifiers along with the JW modifier for unused CAP drugs; and
- There is no payment for discarded multi-use vials.

Here are two examples to clarify Medicare’s reimbursement policy on discarded single-use drugs and biologicals:

**Scenario #1:** A provider schedules three Medicare patients to receive infliximab infusions on the same day and orders several vials for the upcoming office visits. The provider administers infliximab to the first and second patient, but the last patient has a home emergency after the infliximab is mixed and leaves before the infusion. The last medication mixture cannot be used, so the remaining infliximab must be discarded and can be billed to Medicare.

**Scenario #2:** A provider administers infliximab to a Medicare patient who has an allergic reaction to the medication. Two vials were mixed and the medication cannot be used for another patient and must be discarded. The provider bills Medicare for the infliximab.

Because there is no payment for discarded multi-use vials, control any waste by scheduling patients efficiently to provide the most use of the medication.

Contact Reasee Freeman, CPC, at rfreeman@rheumatology.org or (404) 633-3777 ext. 819, with questions on this or other reimbursement issues.
New ACR Strategic Plan Approved

On May 11, the ACR leadership approved a revised strategic plan for 2007–2009 that will guide the College’s work and determine the path the organization will take. The plan has a direct effect on the way the organization serves its members because ACR committees develop and implement programs and services based on the priorities it outlines.

In February, the ACR Board of Directors, standing committee chairs, and several invited guests met to define the College’s direction for the next two years. The result was a plan with greater emphasis on meeting the needs of all ACR members in the current rheumatology environment. Notable revisions were made in nearly all areas including:

Practice Support: The new plan includes strategies to help increase practice efficiency, with a particular emphasis on practices.

Education: Improved communication to define the priority.

Research: The ACR’s workforce study helped identify the challenges rheumatology will face over the next several years. With demand for rheumatology expected to exceed supply in the near future, the ACR is working to number of qualified professionals attracted to the field.

The results of the revision committee goals were also revised to better facilitate communication with members and ensure the necessary organizational capabilities and resources to support the ACR’s mission.

To view the revised ACR Strategic Plan 2007–2009, go to www.rheumatology.org and click on “About the ACR.”

CODING CORNER!

August’s coding challenge:

A 61-year-old established patient with severe RA comes in for a scheduled methotrexate injection and infliximab infusion; 600 mg of infliximab was set aside and mixed. The patient was injected with 15 mg of methotrexate. The patient also had a detailed problem history, a detailed examination, and a medical decision-making of moderate complexity due to a complaint of fatigue and joint pain. Thirty-five minutes into the infusion, the patient had a reaction to the infliximab. The infusion was discontinued after 200 mg of infliximab was infused, and an intravenous injection of methylprednisolone sodium succinate, 40 mg, was given. IV hydration of saline is continued for forty minutes to flush out the infliximab. All documentation was noted appropriately. How do you code for correct reimbursement? See page 13 for the answer.

ARHP Angle

Evidence-Based Practice: Making it a Reality

By Karen L. Kerr, MSN, NP, CPNP, APRN-BC

Evidence-based practice has become the standard of care in the 21st century. Evidence-based practice is “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.”1 It requires the integration of a health professional’s clinical expertise with the best available scientific evidence, and patient values and preferences to guide clinical decisions for individual patients.2

According to “Measuring the Quality of Healthcare,” a 1999 Institute of Medicine report, “Current professional knowledge emphasizes that health professionals must stay current in the rapidly expanding and changing knowledge base and use such knowledge appropriately.”3 But how can busy health professionals keep current with the ever-expanding body of scientific knowledge and integrate relevant research findings into their everyday clinical practice? Other rheumatology researchers have made significant contributions to improving the evaluation and management of persons with rheumatic diseases. The ARHP is committed to advancing the knowledge and skills of health professionals in order to improve health outcomes for people with rheumatic and musculoskeletal diseases. Through its publications and educational programs, ARHP disseminates relevant research findings to health professionals around the world.

The ARHP’s peer-reviewed journal, Arthritis Care & Research, publishes original research and review articles and evidence-based practice guidelines relevant to the care of individuals with rheumatic and musculoskeletal diseases. This publication is a primary source for rheumatology health professionals to review current clinical research relating to their practice. Research on healthcare disparities in rheumatic diseases was the focus of the May 2007 issue of Arthritis Care & Research.

Another way to keep abreast of current scientific evidence is by attending the ARHP Annual Scientific Meeting, where rheumatology researchers from around the world present their scientific findings. This year’s meeting promises to be outstanding. The sessions on “What’s New and Noteworthy in 2007: A Review of Rheumatology Research for Health Professionals” and “Arthritis and Manual Therapy: What is the Evidence?” are just two of many sessions presenting current research findings of interest to health professionals from various disciplines. In addition, mentored research poster tours are offered to help clinicians learn to critically analyze research reports.

These are just a few of the ways the ARHP is working to disseminate the best scientific evidence to rheumatology health professionals in order to promote evidence-based practice and improve health outcomes for persons with rheumatic and musculoskeletal diseases.

Karen Kerr is president of the ARHP and a pediatric nurse practitioner at Children’s Hospital of Michigan in Detroit. Contact her via e-mail at arhp@rheumatology.org.

References
MEMBER UPDATES

Dr. Engleman Receives Gold Medal from Columbia University

Ephraim P. Engleman, MD, clinical professor of medicine at the University of California, San Francisco (UCSF) and an ACR Master, was awarded the Columbia University College of Physicians and Surgeons’ Gold Medal for excellence in clinical medicine. It is the highest honor the school’s Alumni Association can bestow.

Dr. Engleman is also founding director of the Rosalind Russell Medical Research Center for Arthritis at UCSF.

He earned his bachelor’s degree from Stanford University (Calif.). After attending medical school at Columbia University in New York City and holding a fellowship at Massachusetts General Hospital in Boston, he went into private practice as the first rheumatologist in the San Francisco Bay Area. He joined the UCSF clinical faculty in 1947.

Among the many major honors that Dr. Engleman has received over his 60-year career are the Presidential Gold Medal of the American College of Rheumatology; visiting lecturer and visiting professor of medicine at Mayo Clinic and at Harvard’s Robert Brigham Hospital in Boston; honorary membership in the Chinese Medical Association and the rheumatology societies of Australia, France, Japan, Spain, and Uruguay; creation of the Ephraim P. Engleman Distinguished Professorship in Rheumatology at UCSF, and the UCSF Medal, the University’s highest honor.

REF NEWS

“Within Our Reach” RA Grant Recipients Announced

Because so much is still unknown about RA—what causes it, why it affects people differently, how to cure it—and because research is underfunded (see Table 1, right), the ACR Research and Education Foundation (REF) launched “Within Our Reach: Finding a Cure for Rheumatoid Arthritis.”

“Within Our Reach” is a multi-year fundraising campaign seeking to advance rheumatologic research by supporting RA research not normally funded by the National Institutes of Health or other peer-reviewed funding sources. Please join us in congratulating the first round of “Within Our Reach” RA grant recipients, who began their funding term in July.

Dr. Paul Anderson, MD, PhD, K. Frank Austen professor of medicine, Brigham and Women’s Hospital, “Post-transcriptional Regulation of TNF alpha Production”

Dr. Joan M. Bathon, MD, professor of medicine, Johns Hopkins Arthritis Center, “Rheumatoid Arthritis and Body Composition”

Dr. S. Louis Bridges, Jr., MD, PhD, associate professor of medicine and microbiology, University of Alabama at Birmingham, “Genetics and Ethnic Differences in C-Reactive Protein as a Biomarker of Radiographic Severity in Rheumatoid Arthritis”

Dr. Robert H. Carter, MD, professor of medicine and microbiology, director, division clinical immunology and rheumatology, University of Alabama at Birmingham, “Autoantigen-specific B cells in Rheumatoid Arthritis”

Dr. Gary S. Firestein, MD, professor of medicine, chief of rheumatology, allergy and immunology, director, UCSD Clinical Investigation Institute, University of California, San Diego, School of Medicine, “Neural Regulation of Synovial Inflammation”

Dr. Richard A. Flavell, PhD, FRS, sterling professor and chair, investigator, Howard Hughes Medical Institute, Yale University School of Medicine, “Regulation of T cell Function in Collagen-induced Arthritis by IL-10”

Dr. Gary Gilkeson, MD, professor of medicine and vice chair for research, Medical University of South Carolina, “Role of Sphingosine Kinase I in Inflammatory Arthritis”

Dr. Joseph Holoshitz, MD, associate professor of internal medicine, University of Michigan, Ann Arbor, “Functional Characterization of the Rheumatoid Arthritis Shared Epitope Binding Receptor”

Dr. David M. Lee, MD, PhD, assistant professor of medicine, Brigham and Women’s Hospital, “IgG Glycosylation and Rheumatoid Arthritis”

Dr. Elizabeth D. Mellins, MD, professor of medicine, Stanford University School of Medicine, “MHC Association in Rheumatoid Arthritis: A Novel Hypothesis”

Dr. John D. Moutz, MD, PhD, professor of medicine, University of Alabama at Birmingham, “Novel IL-17 Induced Germinal Center Formation and Arthritis-inducing Autoantibodies”

Dr. Harold E. Paulus, MD, professor emeritus, University of California, Los Angeles, “Joint MRI to Validate Clinical Remission Criteria in Early Rheumatoid Arthritis”

Dr. Antony Rosen, MD, Mary Betty Stevens professor of medicine, professor of cell biology and pathology, director, division of rheumatology, Johns Hopkins University School of Medicine, “Anti-PAD4

TABLE 1: RA Research Funding

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<tr>
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PATIENT FACT SHEET

Wegener’s Granulomatosis

Wegener’s granulomatosis (WG) is a rare and complex blood-vessel disease known, it can be treated and managed effectively. Although the cause of the disease is unknown, it can affect men and women equally. According to the fact sheet by Carol A. Langford, MD, MHS, director of the Center for Vasculitis Care and Research at the Cleveland Clinic, “Most patients with WG report systemic symptoms that cause fatigue, fever, weight loss, night sweats, and numbness or loss of movement in the fingers, toes, or limbs.

Well-studied therapies have proven effective in treating WG. Although the disease is permanent, they can reduce the potential for organ injury in many instances.

The fact sheet also notes that, “The impact of WG varies greatly between individuals. It is influenced by the severity of their illness, the organs involved, and the response to treatment.”

Even with effective treatment, relapses are common. Relapses can improve or even resolve organ injury in many instances.

For more details on diagnosing, treating, and living with WG, or to download this and other ACR patient-education fact sheets, visit the Rheumatology.org and follow the links to patient education from the Practice Support menu.

PHOTOGRAPHY PHOTODISC

PHOTOGRAPHY PHOTODISC
Immune Responses in Rheumatoid Arthritis: Markers of Disease Propagation

> Cornelia M. Weyand, MD, PhD, David Lowance professor of medicine, director, Lowance Center for Human Immunology, Emory University, “Defects of Hematopoietic Stem Cell Function in Rheumatoid Arthritis”

> Edward Yelin, PhD, professor of medicine and health policy, University of California, San Francisco, “Disparities in Healthcare Utilization and Outcomes in Rheumatoid Arthritis”

Complete information about “Within Our Reach,” current research, and future research can be found online at www.WithinOurReach.info.

REF Preceptorship Award Recipients

O

If the numerous training and research opportunities the REF offers, it is the Preceptorship Awards that best illustrate its commitment to ensuring the future of rheumatology.

By connecting a medical student with a mentor (preceptor) for a hands-on, real-world learning experience focused on rheumatology, the REF Preceptorship Awards give rheumatology professionals and medical students an opportunity to improve rheumatology’s future. Visit www.rheumatology.org/ref/awards for information about REF award and grant opportunities.

Please join in congratulating the 2007-2008 Preceptorship Award Recipients, who began their award terms in July.

Medical Student Research Preceptorship

> Aimee K. Angle-Zahn, Preceptor: Jane E. Salmon, MD, Hospital of Special Surgery

> Christopher P. Deibert, Preceptor: Joseph M. Ahearn, MD, University of Pittsburgh

> James M. Kelley, Preceptor: Robert P. Kimberly, MD, University of Alabama at Birmingham

> Robert W. Koschik II, Preceptor: Thomas A. Medger, Jr, University of Pittsburgh

> Eleni Nackos, Preceptor: John M. Von Feldt, MD, University of Pennsylvania

> Thomas M. Penoyer, Preceptor: Peter A. Simkin, MD, University of Washington, School of Medicine

> Balvinder Rehal, Preceptor: Nancy E. Lane, MD, University of California at Davis

> Robert Lee Salazar, Preceptor: Barry L. Myones, MD, Texas Children’s Hospital, Baylor

> Xueyuan Shelly Wang, Preceptor: Joan M. Von Feldt, MD, University of Pennsylvania

> Daniel M. Wells, Preceptor: Leonard L. Dragone, MD, PhD, National Jewish Medical & Research Center

> Robert L. Woolston, Preceptor: David Sherry, MD, Children’s Hospital of Philadelphia

> Daniel C. Windels, Preceptor: Susan A. Boackle, MD, University of Colorado HSC

> Jeremy J. Zimmermann, Preceptor: Calvin B. Williams, MD, Midwestern University

Medical Student Clinical Preceptorship

> David R. Carrier, Preceptor: David George, MD, Reading Hospital and Medical Center

> Jennifer C. Cooper, PharmD, Preceptor: Robert J. Janos, MD, Denver VA Medical Center

> Brandi D. Eastman, Preceptor: Marcy Bolster, MD, Medical University of South Carolina

> Brian H. Horner, Preceptor: David H. Collier, MD, University of Colorado School of Medicine

> Erin E. Meschter, Preceptor: Thomas M. Harrington, MD, Geisinger Medical Center

> Marisa C. Mizus, Preceptor: Joan M. Bathon, MD, Johns Hopkins University

> Elizabeth G. Riccardi, Preceptor: Hom Neupane, Upstate Medical Center

> Megan L. Shrapo, Preceptor: Reaver Collins, Jr., MD, Arthritis Associates of MS

> An T. Tran, Preceptor: Daniel George Arkfeld, MD, University of Southern California

Health Professional Graduate Student Preceptorship

> Stefanny Haaz, MFA, Preceptor: Susan J. Bartlett, PhD, Johns Hopkins University

> Cynthia W. Karlson, Preceptor: Michael Rapoff, PhD, University of Kansas

> Deepak Kumar, PT, Preceptor: Katherine T. Rudolph, PhD, University of Delaware

> Mei Yang, MA, Preceptor: Yuqing Zhang, DSc, MPH, Boston University School of Medicine

> Haoyang Zhang, Preceptor: Westley H. Reever, MD, University of Florida

Resident Research Preceptorship

> Shannon M. Rylee, MD, Preceptor: Ram Raj Singh, MD, University of California, Los Angeles

> Korey L. Ulrich, MD, Preceptor: John D. Reveille, MD, University of Texas HSC, Houston

Preceptorship Award Recipient Becomes Published Researcher

Noa Schwartz

Ever since Noa Schwartz was a child growing up in Israel, she knew that she wanted to help people. “I always had an affinity to be there for people, to help when I saw someone in need,” she recalls. When it came time to decide on a career path, Schwartz knew immediately that the healthcare industry would allow her to help in extraordinary ways. She discovered the field of rheumatology while attending Hebrew University Medical School in Israel. “It was the first lecture series on rheumatologic diseases and I attended a lecture on periodic fevers,” Schwartz recalls. “It was an unbelievable lecture where the professor spoke about the research, the multitude of symptoms, the difficulties of diagnosis, and so on. Because these diseases involve the entire body and manifest in a variety of ways, it is like putting together a puzzle. I was hooked on the science.”

While on leave from medical school and living in New York, Schwartz volunteered at the rheumatology research lab at the Albert Einstein College of Medicine. Under the direction of Chaim Putterman, MD, chief of the rheumatology division there, Schwartz began to show a great aptitude for research, despite having no prior experience. After three months in the lab, Dr. Putterman told Schwartz about the ACR REF/Abbott Medical Student Research Preceptorship. “I had no idea that awards like this existed, and I was excited about the opportunity,” says Schwartz. Schwartz and Dr. Putterman applied for and were selected to participate in the Medical Student Research Preceptorship. During her Preceptorship, she remained under the direction of Dr. Putterman and became closely involved on a project studying TWEAK, a relatively new cytokind discovered in 1997. “We believe TWEAK incites lupus nephritis,” Schwartz says. “It works on a project studying TWEAK, a relatively new cytokind discovered in 1997. “We believe TWEAK incites lupus nephritis,” Schwartz says. “It is a crucial player in the lupus nephritis process.” Schwartz has been studying the role of TWEAK in the context of lupus nephritis. She has published several papers on this topic, including a recent one in the Journal of Autoimmunity (2006;27(4):242-250). “Because of the Preceptorship and the support of everyone working on the project, I was able to make the project a priority among my work at the lab and now I’m published,” says Schwartz. “This amazing experience has affirmed in my mind that I want to be both a clinician and a researcher.”

Schwartz will eventually complete medical school when she returns to Israel, but for now, she is committed to the TWEAK project and will remain at the lab to conduct further research. “The paper was just the beginning,” she says. “We want to show that over time, the amount of TWEAK levels change with respect to the disease activity and treatment that would be helpful in the clinical management of patients with systemic lupus erythematosus.”

The ACR REF/Abbott Medical Student Research Preceptorship, part of the REF awards portfolio, is designed for students who are between the first and second year of medical school. The award introduces students to rheumatology by supporting a full-time, three-month research experience. Recipients also receive travel funds to attend the ACR/ARHP Annual Scientific Meeting. Funding for this award is made possible through the Abbott Endowment for Rheumatology Development. For more information, visit www.rheumatology.org/ref.
by Francine Kaplan

Originally conceived to help libraries and researchers be selective in journal management, the influence of IF has grown and spread significantly, raising issues about the process of the calculation and its current uses and abuses.

According to Thomson Scientific, which computes journal IFs, the number is “a measure of the frequency with which the ‘average article’ in a journal has been cited in a particular year or period.” (See Figure 1, below.)

In 2004, the fully automated system applied its algorithms to 27 million citations in 5,968 science journals and 1,712 social science journals. Originally, IF was intended as a practical quantitative tool to rank, evaluate, categorize, and compare journals worldwide. Now it is seen as a measure of the quality of a journal, its contents, and its authors. Recently, however, IFs have been used, or abused according to Dr. Garfield, as a dynamic in hiring decisions and in awarding grants and tenure. “It never occurred to me that ‘impact’ would become so controversial,” says Dr. Garfield.

Over the past 10 years, IF has come to routinely be applied in ways that Dr. Garfield never imagined. “The term ‘impact factor’ has gradually evolved, especially in Europe, to describe both journal and author impact,” he says.

Computing Impact Factor
The IF for a journal is calculated based on a three-year period, and is the average number of times published papers are cited up to two years after publication. For example, A&R’s 2006 IF was calculated as follows:

- Number of “citable” articles published in A&R in 2004 and 2005
- Citations in 2006 to A&R's articles published in 2004 and 2005

A&R's 2006 IF = 

Repercussions of Rank
According to Michael D. Lockshin, MD, editor of A&R, in countries such as England, Germany, France, and China, laboratory space, promotions, and budgets can be based on the IF of an author. “Academics in these countries are desperate to be in high-impact factor journals,” says Dr. Lockshin, who is professor of medicine and OB-GYN at Weill Medical College and an attending physician at the Hospital for Special Surgery in New York City. In Spain, researchers have a legal right to publish two articles in high-impact journals before the final calculation. Clinical studies, clinical definitions, consensus reports, and review articles are highly desirable because they generate the most citations. A single sensational article can increase IF more than several well-regarded basic science papers, so editors can be tempted to alter their publication mix to raise their IF. Consideration as to which authors and articles will contribute the most to IF could affect the information that ultimately gets to the readership.

Letters to the editor, news articles, editorials, book reviews, and abstracts of meetings are not counted as citable articles, but can raise the IF by lowering the equation’s denominator. In June 2006, the Public Library of Science (PLoS) issued this editorial opinion: “We conclude that science is currently rated by a process that is itself unscientific, subjective, and secretive.”

Although, according to Dr. Lockshin, the definition of “citable” is arbitrary, because journals are not uniform in article structure, he takes exception to the PLoS view. “Allowing for the many variations of journal and citation style, we judge that [the Thomson process] is an honest and fair attempt, and as sound as any we could devise, to rate journals by an open and explicable metric,” he says.

Perhaps the most resonant argument is that IF does not take into account the quality of the work in individual articles or the utility of a journal to readers. Citations may come from controversy, retractions, and authors who refute the findings of an article. Antony Rosen, MD, director of the rheumatology division at Johns Hopkins University in Baltimore and chair of the ACR Journal Publications Committee, views IF in a pragmatic light. “In terms of relevance, quality, and importance, there are lots of useful articles that never get cited,” Dr. Rosen says. “Impact factor is just one measure of a journal, nothing more.”

The allegations against this system run from claims that IF reporting can be artificially manipulated by editors who are trying to raise their numbers to complaints that while academics vie for limited space in reaching the community in the most timely fashion.

European critics say there is an English-language bias to the reporting. With American journals overwhelmingly citing research reported in English, the mean journal impact of American science is 30% above the world average. This puts pressure on authors around the world to eschew low-IF national journals in favor of a chance to appear in high-IF English-language publications. Papers that do appear in low-IF national journals are often undervalued by the scientific community and policy makers.

The ability of pharmaceutical companies and other potential advertisers to employ IF in their buying decisions ups the ante. Anecdotal reports of self-citations have editors, eager to boost their reputation, citing their own publication in editorials and suggesting that authors add citations from their journal to upcoming articles. Fortunately, according to Dr. Lockshin, Thomson Scientific sees these efforts as transparent and seeks to discount self-citations.

Controversial Calculation
Another issue is the mix of articles in a publication and manner in which Thomson Scientific arrives at the final calculation. Citations, clinical definitions, consensus reports, and review articles are highly desirable because they generate the most citations. A single sensational article can increase IF more than several well-regarded basic science papers, so editors can be tempted to alter their publication mix to raise their IF. Consideration as to which authors and articles will contribute the most to IF could affect the information that ultimately gets to the readership.

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Francine Kaplan is a medical journalist based in Atlanta.

References
3. The Impact Factor Game. It is time to find a better way to access the scientific literature. PLoS Med 2006;3(6):e291.
RHEUMATOLOGY ATTRACTS TOP FELLOWS

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Workforce study shows positive trends in rheumatology training >> By Terry Hartnett

**TABLE 1:**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Accredited fellowship programs</td>
<td>114</td>
<td>107</td>
<td>-7%</td>
</tr>
<tr>
<td>Total positions</td>
<td>329</td>
<td>378</td>
<td>13%</td>
</tr>
<tr>
<td>Total positions filled</td>
<td>266</td>
<td>333</td>
<td>20%</td>
</tr>
<tr>
<td>First year positions</td>
<td>154</td>
<td>177</td>
<td>13%</td>
</tr>
<tr>
<td>First year positions filled</td>
<td>120</td>
<td>149</td>
<td>20%</td>
</tr>
<tr>
<td>Residencies completed</td>
<td>116</td>
<td>161</td>
<td>28%</td>
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</tbody>
</table>

Source: ACGME

**Rheumatology’s Supply Side**

The most important factor affecting the supply of rheumatologists in practice today and in the future is the number completing fellowships each year. The workforce study therefore examined data from adult and pediatric rheumatology fellowships for the past 10 years. Both the number of positions and the number of applicants have increased during this period, and rheumatology has a high rate of fellowship completion overall. There are still a number of existing fellowship positions not filled each year, however, and the overall numbers of fellows completing programs needs to be even higher to meet the predicted demand.

In the official ACR response to the Workforce Study, Neal S. Birnbaum, MD, president of ACR said, “The expansion of current training capacity in rheumatology would require not only an increase in salary support for fellows but also meaningful growth in training resources including academic faculty, dedicated space for academic endeavors, and increased clinical opportunities.” In addition, “the Accreditation Council for Graduate Medical Education [ACGME] has created rigorous program requirements that help ensure the quality of training programs to overcome at start-up,” he notes. “In the face of all of these substantial challenges it seems unlikely that we will see any significant growth of rheumatologists entering the workforce anytime soon.”

The specialty has made good use of available training positions. “Our ability to recruit rheumatologists is better than it was 10 years ago and the number of applicants has gone up significantly,” says Walter G. Barr, MD, immediate past chair of the ACR Committee on Training and Workforce Issues, which spearheaded the workforce study advisory group. “There has been a major increase in the quality of those applying.” Dr. Barr contends that managed care’s gatekeeper model was in large part the cause of a move away from rheumatology and other specialties in the last decade. “Students were told by their deans until the late 1990s that managed care would limit their salary abilities,” he says, but the influence of managed care is waning.

Money is certainly an issue for upcoming medical students who have a large debt to repay after graduation, says Christy Park, MD, a young rheumatologist at Northwestern University in Chicago, and a member of the ACR’s young investigators subcommittee. It is also clear, she says, that there are limitations to the expansion of fellowship programs and that one in particular is the challenge of maintaining research funding to establish or support an academic research career. But Dr. Park and other young investigators see a brighter picture for their profession, if not five years out, then seven to 10 years from now.

“There are big sacrifices in the beginning, but overall I am happy with what I am doing and hope in a few years I will catch up financially,” says Giovanni Franchin, MD, who recently completed his rheumatology fellowship at Columbia University in New York City.

A recent survey of rheumatology fellows across the country shows that these young physicians are happy with their choice but have lingering concerns about financial issues that may arise, says survey author John Fitzgerald, MD, an adult rheumatologist at UCLA Medical Center in Los Angeles, and a member of the young investigator subcommittee.

**Residency and Fellowship Trends**

The workforce study takes a retrospective review of adult and pediatric rheumatology positions for the past 10 years, beginning in 1996. See Tables 1 (above) and 2 (p. 16) for a summary of rheumatology training trends.

“In our supply model, our baseline assumption is that rheumatology fellowship positions and fill rates will remain constant at the 2004–2005 levels,” Dr. Birnbaum notes.
Rheumatology attracts top fellows

Continuing from page 15

Rheumatology attracts top fellows

According to the workforce study report, "Comparing the number of first-year fellows to the number completing the program between 1996 and 2005 suggests that adult and pediatric rheumatology have a high completion rate, approaching 100%," says Dr. Birnbaum. "These data indicate that about 161 fellows in adult rheumatology and nine fellows in pediatric rheumatology entered the market in 2006.

Dr. Birnbaum notes that another important supply issue is the number of international medical school graduates (IMGs) who fill these fellowship programs. The study report shows that the percentage of IMGs has decreased significantly in both adult and pediatric rheumatology from 1997 to 2005, from 52% to 33% among adult fellowships and from 33% to 20% in pediatrics. IMGs represented a high percentage of first-year fellows in pediatric rheumatology from 1997 to 2005, so that about 80% of IMGs practice in the United States, the report said.

Based on our discussions with experts at the Bureau of Health Professions and elsewhere, we estimate that about 70% of IMGs practice in the United States, the report said. "Given the current funding environment, there will be more attention at this stage than before, with additional support or measures to protect this group, who will need to be responsible for training future rheumatologists," says Dr. Park.

Younger investigators are at a disadvantage when it comes to obtaining financial support for research. "In the current funding environment, the money has to go to retain the senior people," Dr. Park says, "but this means that the junior people get shut out."

However, upcoming doctors who choose rheumatology for a specialty will have exciting and rewarding work, says Dr. Park and her colleagues. "We are working to make rheumatology in the curriculum." New rheumatologists share similar reasons for making this their life's work, and two stand out: great scientific questions that intrigued them and wonderful mentors. "We are joining with the University of Arizona to work on a fellowship opportunities and about transitioning into rheumatology practice," says Dr. Cron. "This is a good time to be a rheumatologist," says Dr. Park. "We are a valuable commodity, with all of the new treatments and the complexity of new drugs."

As for the need for continuing emphasis on training for the specialty, senior rheumatologists can also increase their commitment, says Paul Caldwell, DO, a rheumatologist in community practice in Paradise Valley, Ariz., who served on the ACR Workforce Study Advisory Group. "Community practices are an excellent base for training," he says. "We are joining with the University of Arizona to begin fellowship training and we encourage more private practices and academic medical centers to do the same."

Terry Hartnett is writing the workforce study series.
Limited evidence and diagnostic options make this increasing condition difficult to treat

A
lthough lumbar spinal stenosis will have a major effect on public health, the numbers of studies on appropriate diagnostic and therapeutic choices are surprisingly few. Despite this lack of evidence-based options, clinicians need to make the best choices with available evidence and clinical acumen to alleviate the physical limitations of their patients. In this article, I will provide my approach to this challenging clinical disorder based upon the available medical literature and my experience of 29 years in practice.

**Definition and Pathogenesis**

Spinal stenosis is a disorder characterized by insufficient room in the spinal canal for the neural elements. Most commonly, acquired degeneration of the anatomic structures of the lumbar spine results in narrowing of the central spinal canal, lateral recesses, or the neural foramina. Acquired or secondary stenosis will be the focus of this article. Other major categories of spinal stenosis include other forms of acquired stenosis as well as congenital and developmental disorders. (See Table 1, p. 19.)

A basic understanding of the pathogenesis of this disorder is essential for making therapeutic decisions for the corresponding form of spinal stenosis. What might be appropriate for an intervertebral disc herniation (a form of acutely acquired spinal stenosis) will not necessarily be effective for spinal narrowing that has been decades in the making.

The earliest changes occur in the intervertebral discs that lose their structural integrity and start to flatten. The resulting biomechanical insufficiency results in transfer of stresses posteriorly to the ligaments and facet joints. The response to the added weight results in the development of osteophytes on facet joints, and vertebral endplates, as well as the redundancy and thickening of the ligamentum flavum. Depending on a number of physical factors including the central anterioposterior diameter of the canal, trefoil canal shape, and the height of the neural foramina, stenosis may occur in different areas of the spinal canal with attendant clinical syndromes corresponding to the location of compression. For example, more severe central stenosis may cause urinary retention symptoms. Persistent radicular pain that is unrelieved with a change in position is more indicative of lateral recess stenosis.

The mechanism of radicular pain production in spinal stenosis is incompletely understood. Individuals with similar degrees of canal narrowing experience different intensities and locations of pain. Mechanical compression of nerve roots may cause electrophysiological alterations in nerve conduction. However, slow, persistent compression is associated with neural adaptation that does not lead to symptoms. Simple compression of the neural elements alone does not fully explain the generation of radicular pain. Vascular compromise associated with arterial, capillary, and venous obstruction plays a substantial role in the development of neurogenic claudication. Standing in an extended posture decreases the room in the spinal canal while flexion increases the space.

The rapid reversibility of the clinical symptom of leg pain with a change in posture is strong evidence for the important role of vascular obstruction as a primary component of the pathogenesis of neurogenic claudication. The longer the duration of the vascular compromise, the more persistent and total becomes the neural dysfunction. The clinical correlate would be radicular pain followed by numbness and muscular weakness. Alleviation of vascular congestion can normalize the function of the sciatic nerve and diminish leg pain. Therefore, the goal of therapy is maximize neural blood flow and restore nerve function.

**Clinical History**

Neurogenic or pseudoclaudication is the most common symptom associated with spinal stenosis. Pain that is associated with standing or walking occurs in the buttock, thigh, or lower leg. The patterns of back and/or leg pain are as different as the patients who have the disorder. Most patients will complain of low back and leg pain. A smaller proportion will have leg pain alone. Many patients will have bilateral leg pain. The extent of the leg pain may be different in the extremities. Multiple dermatomes may be affected. The widespread distribution of symptoms makes it difficult to ascribe compression to a single nerve root lesion. In addition to pain, patients may also have numbness, paresthesias, and weakness in the lower extremities. Less commonly, similar symptoms can occur while patients are lying down and are relieved by getting out of bed. Neurogenic claudication is relieved by lying down, sitting, or flexing at the waist. Many elderly patients enjoy going to the grocery store so that they can flex over the shopping carts.

Some of my most perplexing patients have been those with spinal stenosis. One was an executive with the chief complaint of medial knee pain. This man wanted me to diagnose his problem so that I could save his marriage. He had knee pain for about a year that was exacerbated by standing and relieved by lying down, sitting, or flexing at the waist. The pattern of back and/or leg pain are as different as the patients who have the disorder. Most patients will complain of low back and leg pain. A smaller proportion will have leg pain alone. Many patients will have bilateral leg pain.
by sitting. He had been evaluated with knee radiographs and magnetic resonance (MR) demonstrating asymmetric reflexes, sensory loss, or motor weakness—radiculopathy associated with an intervertebral disc caused by lumbar spinal stenosis is distinct from radiculopathy associated with neural foraminal or lateral recess stenosis. Patients with compression associated with neural foraminal or lateral recess stenosis may not obtain relief by lying supine in bed. These are patients with compression associated with neural foraminal or lateral recess stenosis.

Other patients describe persistent leg pain that does not change significantly with assuming a flexed posture. They may not obtain relief by lying supine in bed. These patients with compression associated with neural foraminal or lateral recess stenosis.

Physical Examination
Patients with spinal stenosis may have no physical abnormalities when examined in the seated position, and abnormalities may appear only after the patient is stressed by walking until leg pain appears. Sciatica caused by lumbar spinal stenosis is distinct from radiculopathy associated with an intervertebral disc herniation. Objective neurologic findings—including asymmetric reflexes, sensory loss, or motor weakness—are found in a majority of stenosis patients.4 In many circumstances, the complete physical examination to be sure that no other findings indicate an alternate diagnosis. For example, an essential portion of the examination is internal and external rotation of the hips. On more than one occasion, I have diagnosed severe hip osteoarthrosis in someone with leg pain with lumbar root configurations and MRI scan demonstrating minimal narrowing with a presumptive diagnosis of lumbar spinal stenosis. I also palpate the feet for the presence of dorsal pedis and posterior or tibial pulses to eliminate the possibility of vascular claudication.

Radiographic Tests
Many radiographic techniques are available to evaluate the spinal stenosis patient.5 The least sensitive but most available is a set of plain roentgenograms of the lumbar spine. I order anteroposterior and lateral views as my initial test in most individuals. I may order oblique views if I am concerned about facet joint osteoarthrosis and foraminal stenosis. I obtain flexion and extension views to observe abnormal motion if I am concerned about instability of the spine. This method is helpful in identifying potential candidates with significant lumbar spondylosis, foraminal narrowing, short pedicles, facet joint arthritis, or degenerative spondylolisthesis. However, it is important to remember that these features are common findings among asymptomatic individuals of a similar age. Roentgenographic abnormalities are compatible, but not diagnostic, of spinal stenosis.

Magnetic resonance is the next radiographic test I order when further delineation of the osseous and soft tissue elements in both the sagittal and axial planes of the lumbar spine is necessary. This technique can visualize the areas of neural compression in the central canal, the lateral recess, and the neural foramen without contrast exposure. I look for abnormalities at levels of the lumbar spine that correlate with the clinical symptoms of the patient. However, it is a rare circumstance when an abnormality at a level of the lumbar spine is stenotic with only mild spondylosis at other levels. Not uncommonly, more than one level has some degree of stenosis with the greatest narrowing on the opposite side to the one that is most symptomatic. MR abnormalities are compatible with, but not diagnostic of, spinal stenosis.

MR techniques are constantly advancing. For example, there are now MR scanners that allow subject positioning during the examination. One of the reasons that an intact correlation exists between MR findings and clinical symptoms may be the supine position of patients in the MR tube, because the lying position minimizes canal narrowing. Recreating the most symptomatic position for the MR evaluation may maximize the anatomic abnormalities that cause compression. I predict that studies in the upright position will become the preferred diagnostic method for spinal stenosis as the technology improves and the scanners are readily available.

Computed tomography (CT) is an excellent technique to identify the osseous structures crowding the spinal canal. Myelographic dye enhances the resolution. I rarely order CT myelograms because I see this type of evaluation as a pre-operative test and expect the surgical surgeon to order one once a decision involving decompression surgery has been made.

Electrodiagnostic Tests
Electromyography (EMG) and nerve conduction tests (NCTs) are not routinely used in the evaluation of spinal stenosis. EMG and NCTs are abnormal in a proportion of spinal stenosis patients with persistent radicular symptoms, and the most common finding is bilateral multilevel radiculopathy. EMG cannot consistently predict the specific level of nerve compression associated with leg pain. The greater utility of EMG lies in determining the presence or absence of peripheral neuropathy and peripheral nerve entrapment syndromes that may be present simultaneously in an elderly population. It is in this circumstance that I utilize these tests. Somatosensory potentials (SSPs) may have sensitivity to identify levels of nerve root compression, however, they may be affected by processes that affect the peripheral nerves, nerve roots, the dorsal columns of the spinal cord, and the brain. Abnormalities are not specific for lesions in the spinal canal.

Differential Diagnosis
A recent systematic review examined the accuracy of diagnostic tests for lumbar spinal stenosis.10 The review of 41 studies concluded that no clinical, radiographic, or interventional injection method was the “gold standard” for the diagnosis of spinal stenosis.

With our current inadequacy of evidence-based studies to identify definitive tests for its diagnosis, lumbar spinal stenosis remains a clinical diagnosis characterized by specific historical and physical findings and confirmed, but not diagnosed, by radiographic techniques documenting compression of neural elements.

Leg pain is caused by a number of ailments in the elderly population. Vascular claudication is manifested by leg pain associated with physical activity that radiates from the foot or calf, proximally. Vascular insufficiency causing lower leg pain associated with activity is a common finding in differentiating between the two forms of claudication. Hip arthritis will cause pain with walking but rarely below the knee. Peripheral neuropathy will cause lower leg dysesthesias that are prominent at night when the individual is supine.

Facet joint syndrome may cause symptoms that mimic lumbar spinal stenosis. These patients have back pain with extension of the spine. Pain in the buttock and posterior thigh may develop with prolonged compression associated with standing. Patients may walk in the flexed posture for extended distances without pain. Facet syndrome is unassociated with any neurologic abnormalities.

Management
Lumbar spinal stenosis management requires judgment that matches the severity of functional impairment with benefits and risks of the interventions.11 The options range from education, to weight loss, to exercises, to drugs, to injections, to surgical decompression. No one therapy works for all patients. Some therapies are not worth the risks. Other patients have no choice but surgical decompression if genitourinary or gastrointestinal dysfunction is imminent.

When advising the elderly spinal stenosis patient, I try to gauge the impact of their functional impairment in standing and walking with their general medical condition. I tell my patients, “You are only as young as your oldest part.” For example, most patients have co-morbidities, including cardiovascular disease, pulmonary insufficiency, and diabetes. In many of these individuals, spinal stenosis does not limit their function. Instead, they are limited because of angina after walking two blocks, or dyspnea after three blocks. These individuals have cardiovascular or pulmonary disease that limits activity before leg pain causes them to take a seat. The non-musculoskeletal systems are their oldest parts. In these patients, I attempt to relieve pain with the simplest of therapies. In other patients, spinal stenosis is their only major health problem. These individuals are treated intensively to reverse neurogenic claudication. In these individuals, the spine is their oldest part.

Non-surgical
The recommendations I make for patients with spinal stenosis are based upon the few outcomes trials that are in the literature and the knowledge of the pathologic basis of the disease. Spinal-occupying tissues compress the neural elements when the volume in the canal is diminished. The goal of therapy is to maximize the space in the canal by flexing the spine and reversing swelling of any of the soft tissues that have

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TABLE 1: Classification of Lumbar Spinal Stenosis

<table>
<thead>
<tr>
<th>A. Congenital/Developmental</th>
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<tbody>
<tr>
<td>1. Idiopathic</td>
</tr>
<tr>
<td>2. Metabolic/Genetic</td>
</tr>
<tr>
<td>3. Other</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Degenerative</td>
</tr>
<tr>
<td>2. Metabolic/Endocrine</td>
</tr>
<tr>
<td>3. Postoperative</td>
</tr>
<tr>
<td>4. Traumatic</td>
</tr>
<tr>
<td>5. Miscellaneous</td>
</tr>
</tbody>
</table>

---

A. Congenital/Developmental

1. Idiopathic
   - Achondroplasia
   - Morquio’s syndrome
   - Hyppophosphatemic vitamin D-resistant rickets

2. Metabolic/Genetic
   - Osteoporosis with fracture
   - Acromegaly
   - CPPD disease
   - Renal osteodystrophy
   - Etiopathic lipomatosis

3. Postoperative
   - Postdisectomy
   - Postfusion
   - Postlaminectomy

4. Traumatic
   - Fracture

5. Miscellaneous
   - Paget’s disease
   - DISH
   - Fluorosis
   - Amyloid
   - Conjoined origin of lumbarosacral nerve roots

---
TABLE 2: Surgical Procedures for Lumbar Spinal Stenosis

Stable Spine:
1. Wide laminectomy: Decompression of the central canal (removal of the spinous process, midline laminae, and ligamentum flavum), lateral recess (partial medial facetectomy), and neural foramina (ostectomy removal).
4. Expansive laminoplasty: Use of bone grafts to enlarge the volume of the spinal canal.

Unstable Spine: Degenerative Spondylolisthesis/Scoliosis Without Fusion:
5. Laminitomy alone: Similar to wide laminectomy with specific preservation of facet integrity.

With Fusion
7. Laminectomy with instrumented fusion: Wide laminectomy with bone grafts and pedicle screw fixation.
8. Laminectomy with scoliosis segmental correction with fusion and stabilization with instrumentation: Wide laminectomy with stabilization of sagittal or coronal scoliosis.

Therapeutic Outcomes

Very few studies have looked at the outcome of similar patients treated non-surgically or surgically over a similar time period. Investigators have described small groups of non-surgical spinal stenosis patients with stable symptoms for extended periods of time. Others have described a natural history of slow but steady decrease in function measured in years. Surgical decompression offers better short-term outcomes than medical therapy. Patients with fewer co-morbid conditions have better outcomes. However, the difference in benefit diminishes over time. Debate is ongoing on the fate of surrounding intervertebral disc spaces and the risk of stenosis.

Conclusions

Lumbar spinal stenosis is an important medical disorder with an increasing effect on the aging population. Unfortunately, there have been few investigations into its pathogenesis, natural history, diagnostic criteria, and therapeutic options, resulting in a predilection of little evidence-based proof of diagnostic accuracy of tests or the clinical benefits of therapies. While unresolved issues should form the basis of an exciting research agenda (as shown in Table 3, below left), clinicians cannot wait until this evidence is available to choose a therapy to lessen the pain and improve the function of their patients.

Spinal stenosis is one of those disorders where clinical judgment is essential in achieving the best outcome for the patient. Our understanding of the illness suggests that initial non-surgical therapy is appropriate. Delayed surgery does not diminish the possibility of a favorable outcome, particularly in patients who believe their health is good and who do not have any cardiovascular co-morbidities.

With the coming epidemic of spinal stenosis, therapeutic choices will become more frequent, challenging rheumatologists and other specialists treating this prevalent and debilitating condition.
This April, two of immunology’s premier investigators joined the prestigious ranks of the National Academy of Sciences (NAS). What’s remarkable about this year’s newly elected immunologists is that both are also rheumatologists. Michael B. Brenner, MD, Theodore B. Bayles professor of medicine at Harvard Medical School and chief of rheumatology, immunology, and allergy at Brigham and Women’s Hospital in Boston, and Wayne M. Yokoyama, MD, investigator at the Howard Hughes Medical Institute and Sam and Audrey Loew Levin professor of medicine, professor of pathology and immunology, and chief of rheumatology at Washington University School of Medicine in St. Louis, Mo., thus join other notable rheumatologists (see “Other NAS Rheumatologists,” below).

Election to the NAS is considered one of the highest honors accorded a scientist. The multi-stage election process begins with nomination of a scientist by an NAS member, with the NAS Council determining the number of members that can be elected each year from each of six classes (from physical and mathematical sciences to biomedical sciences) that represent all of science. Class IV, the Biomedical Sciences class, comprises sections for immunology, medical genetics, hematology, and oncology; medical physiology and metabolism; and microbial biology.1 Although the NAS keeps no data on percentages of elected members by specialty, it appears that immunology/rheumatology has a healthy representation, despite the small size of the subspecialty.

The Most Fundamental Experience in Science

Although they were recognized for different discoveries in immunological research, the two investigators share common threads in their scientific development. Drs. Brenner and Yokoyama were both drawn to laboratory research following clinical fellowships; acquired extensive post-doctorate training in fundamental techniques of molecular biology and biochemistry; and were unafraid to take risks in their investigatory career paths.

While a rheumatology fellow at the University of California, Los Angeles (UCLA), Dr. Brenner became fascinated by the fact that “immunological mechanisms produced such a vast array of devastating pathology.” To understand these mechanisms, he chose to do post-doctoral work in the laboratory of David Yu, MD, professor of medicine (rheumatology) at UCLA. Following that, he decided to take a hiatus from clinical medicine, and moved to Harvard to work with the famed biochemist Jack Strominger, MD, Higgins professor of biochemistry, who did much of the pioneering work on the major histocompatibility complex (MHC). Dr. Brenner recalls that he was the only MD in the Strominger lab at the time. “Many of his other trainees were wonderful scientists who taught me an approach to addressing significant questions in the field rather than conducting incremental analyses.” Immersing himself in the fundamentals of basic science, Dr. Brenner was able to define his own style of research, which was to take on problems that were technically challenging and highly risky.

For Dr. Brenner, this has been a fruitful approach. Following his discovery of a new T-cell receptor—the gamma delta T-cell receptor—he found himself in the fundamentals of basic science, Dr. Brenner was able to define his own style of research, which was to take on problems that were technically challenging and highly risky.

For Dr. Brenner, this has been a fruitful approach. Following his discovery of a new T-cell receptor—the gamma delta T-cell receptor—he found unique insights into the synovium to the joints in RA. These discoveries have been acknowledged by his interest in fundamental biochemistry and cellular immunology with clinical disease, especially rheumatic diseases.

Making the Leap

When Dr. Yokoyama established his first laboratory at University of California, San Francisco (UCSF), he decided to focus his investigations on the Ly49 molecule, which he first studied while working at the National Institutes of Health in the laboratory of Ethan Shevach, MD, head of the cellular immunology section at the National Institute of Allergy and Infectious Diseases. Ly49 (now known as Ly49A), originally identified on a T-cell tumor, appeared to belong to a polymorphic family of molecules and was expressed on a natural killer (NK) cell subset. At the time, says Dr. Yokoyama, he chose to deviate from other active areas, particularly investigation of T cells, to work on the NK cell. “I think a lot of people had difficulty understanding why we would do that,” he reflects. “But I was trained and exposed, in Ethan’s lab, to follow where the data take you. We wanted to figure out the function of this putative receptor. When we first began working on NK cells, almost everyone thought the cells had something to do with tumor surveillance. Yet buried in the literature were results from a number of people clearly pointing out that NK cells were important in innate immune control, particularly of viral infections.”

Dr. Yokoyama acquired extensive research experience through a series of post-doctoral fellowships, first in the lab of Robert Ashman, MD, professor of rheumatology at the University of Iowa, then in Dr. Shevach’s lab at the NIH.

Part of the “aha!” moment for Dr. Yokoyama’s team occurred when they cloned the mouse NKR-P1 form and realized that the NKR-P1 and Ly49 families of molecules had a super-family type of relationship. When they then mapped the genes for NKR-P1, using the same techniques they had for the Ly49s, the

A pair of rheumatologists among this year’s NAS inductees

>> By Gretchen Henkel

by CD11), which activates cell immunity. Later, he discovered cadherin 11, which plays a role in the damage caused by the synovium to the joints in RA. These discoveries have been informed, he says, by both his immersion in basic science and his time in the clinic. When he was recruited (1991) and became chief of rheumatology, immunology, and allergy at Brigham and Women’s Hospital (1995), it became possible for him to combine his interest in fundamental biochemistry and molecular immunology with clinical disease, especially rheumatic diseases.

We, as scientists, should be doing a better job of educating the public about the way in which science is conducted.—Wayne M. Yokoyama, MD

K. Frank Austen, MD, director of the inflammation and allergic diseases research section, Brigham and Women’s Hospital in Boston

Dennis A. Carson, MD, professor of medicine at the University of California, San Diego

Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases

Douglas T. Fearon, MD, PhD, professor of immunology at the University of Cambridge (UK)

Laurie H. Glomcher, MD, professor of medicine and immunology at Harvard

Hugh O. McDevitt, MD, professor of medicine (immunology and rheumatology), Stanford University (Calif.)

Arthur Weiss, MD, PhD, chief of rheumatology at the University of California, San Francisco (UCSF)

James B. Wyngaarden, MD, professor of medicine emeritus at Duke University in Durham, N.C. and former director of the National Institutes of Health

Other NAS Immunologists

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team realized that the receptors were encoded in the same genomic region, now known as the NK gene complex. Dr. Yokoyama’s laboratory revealed that Ly49 receptors on NK cells were intrinsically involved in recognition of MHC Class I molecules which then turned off the NK cell, one of the first examples of inhibitory receptors on immune cells.

Dr. Yokoyama, along with Klas Karre, MD, PhD, professor of microbiology at the Karolinska Institute in Stockholm, Sweden, and Lorenzo Moretta, professor of medicine at the Università degli Studi di Genova in Genoa, Italy, was awarded the Novartis Prize for Immunology in 2001. His lab today continues with threads emanating from the Ly49 work, identifying Ly49H as the activation receptor responsible for resistance to murine cytomegalovirus (CMV) infection and the role of Ly49 inhibitory receptors in the development of NK self-tolerance.

Dr. Yokoyama conceded that there is a certain irony about his discoveries’ indirect connection to rheumatology. “In a sense,” he says, “I divorced the scientific investigation part of my job from my clinical responsibilities. One could try to force the issue, and try to find a reason for studying NK cells in rheumatic illnesses. But I have been fortunate enough to work for Shevach, [Ira Goldstein, MD, a former ACR president], and others, whose premise was just do good scientific work and see where it takes you. It’s of course not clear if [our discoveries] will make an impact in the rheumatology clinic, but they may end up having a big impact in HIV or CMV infection. And there is some emerging data that NK cell receptors could play a role in RA, so who knows?”

A Public Service Role

Now having 2,025 members, the NAS was established in 1863 under President Abraham Lincoln. Its mission is to foster the furtherance of science and its use for the general welfare. The NAS has a powerful opportunity “to bring the most logical, scientific, and insightful appreciation to problems in a way that is honest, transparent, and not influenced by a political orientation or special interest,” says Dr. Brenner.

Dr. Yokoyama anticipates the challenges of NAS membership to include his concerns about the current level of scientific literacy. “As a rheumatologist, it is appalling to me how many people believe a testimonial is equal to a placebo-controlled, double-blind trial as evidence for efficacy of a drug,” he says. “We, as scientists, should be doing a better job of educating the public about the way in which science is conducted.”

Advice for Young Investigators

Asked how young rheumatologists might prepare themselves for the next generation of important discoveries, Dr. Brenner recommends they include “a very deep, intense, research-focused experience” in their training at some point. For laboratory-oriented physicians, that would include the “most fundamental research that will teach you the principles of science,” he notes. Similarly, clinical researchers should also seek out immersion in the fundamental approaches to discovery. “A very nice way to approach one’s post-doctoral training,” Dr. Brenner says, “is to make one experience very fundamental and the other more applied. Then, some combination of the two can give you a broad appreciation for disease as well as the basic scientific method to approach it in a very substantial and original way.”

Dr. Brenner tells to trainees in his program that, “It’s much more important to pick a mentor who can teach you and allow you to develop strong research methodology than it is to pick a particular topic to work on.”

Amid these challenges, Dr. Brenner tells his trainees, “It’s much more important to pick a mentor who can teach you and allow you to develop strong research methodology than it is to pick a particular topic to work on.” Indeed, young investigators might do well to follow the examples set by these two distinguished and intrepid scientists.

References:

Gretchen Henkel is a medical journalist based in Los Osos, Calif.
Rituximab for Neuropsychiatric Lupus

By Robyn Domsic, MD


Abstract

Aim: Neuropsychiatric systemic lupus erythematosus (NPSLE) is a serious treatment-resistant phenotype of systemic lupus erythematosus. A standard treatment for NPSLE is not available. This report describes the clinical and laboratory tests of 10 patients with NPSLE before and after rituximab treatment, including changes in lymphocyte phenotypes.

Methods: Rituximab was administered at different doses in 10 patients with refractory NPSLE, despite intensive treatment.

Results: Treatment with rituximab resulted in rapid improvement of central nervous system (CNS)-related manifestations, particularly acute confusional state. Rituximab also improved cognitive dysfunction, psychosis, and seizure, and reduced the SLE Disease Activity Index Score at day 28 in all 10 patients. These effects lasted for more than one year in five patients. Flow cytometric analysis showed that rituximab down-regulated CD40 and CD80 on B cells and CD40L, CD69, and inducible costimulator on CD4+ T cells.

Conclusions: Rituximab rapidly improved refractory NPSLE, as evident by resolution of various clinical signs and symptoms and improvement of radiographic findings. The down-regulation of functional molecules on B and T cells suggests that rituximab modulates the interaction of activated B and T cells through costimulatory molecules. These results warrant further analysis of rituximab as treatment for NPSLE.

Commentary

This study is the first case series reporting the outcomes with rituximab for CNS manifestations of lupus. Prior series have included patients with CNS involvement as one of their lupus manifestations, but improvement in CNS symptoms has not been the focus of these studies and received little more than a few sentences in the discussion. Interestingly, this article received the fourth highest number of hits in the month of April on the Annals of Rheumatic Disease Web site. This is not surprising since the use of rituximab in the treatment of rheumatic disease, particularly lupus, is a hot topic.

From the abstract, the study sounded convincing and I was excited about the use of rituximab for CNS manifestations of lupus. Once I delved into the methods section, however, concerns began to arise. Allow me to review the inclusion criteria of the study: 1) highly active disease; and 2) CNS lesions resistant to conventional treatment. If the latter criterion is strictly followed, then it is not clear how one individual with a headache and normal MRI and a second with mood disorder and a normal MRI qualify as two of the ten patients.

Another of my concerns relates to standardization of treatment regimen. In fact, there were four different regimens of rituximab given, and seven steroid treatments (consisting of three preparations) at the time of study entry. Whether these differences influenced outcome is unknown, although a more uniform regimen would have simplified interpretation of the study. With respect to laboratory studies, the assessment appears to be extensive and includes the IgG index and IL-6 from cerebrospinal fluid, MRI, SPECT scan, and FTG–positron emission tomography. The analysis of costimulatory molecule expression also appears complete, with a reduction in functional molecule expression and high recurrence of depressive state of one reported modality. (See Table 1, above.) The results are certainly intriguing. However, because of the manner in which results are reported and the differences in the treatment regimens, it is difficult to draw firm conclusions about the value of rituximab in this setting.

For now, I think I’ll keep rituximab in my back pocket for my patients with CNS lupus who are either unable to tolerate or in whom I would like to minimize use of other cytotoxic therapies, and in those patients not responding to more traditional therapies.

Clearly, the rheumatology community needs a well-conceived and executed study to examine the clinical effects of rituximab for lupus CNS manifestations. I hope that either a large center or group of centers take on this challenge and provide a prospective study with well-defined patient groups, standardized imaging protocols, pre-defined follow-up criteria, and a control group. One possible protocol could randomize patients with severe CNS manifestations (seizures, coma, ophthalmic neuritis, transverse myelitis) to pulse steroids plus IV cytoxan therapy versus pulse steroids plus rituximab. Immunologic studies could also be performed so that we gain knowledge not only on clinical outcomes, but immunologic mechanisms and effects of this drug in lupus patients.

TABLE 1: Clinical outcomes of NPSLE after rituximab treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>CNS manifestations before</th>
<th>CNS manifestations after</th>
<th>Objective measure improved after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Consciousness disorder, seizure, psychosis</td>
<td>Complete recovery</td>
<td>SPECT</td>
</tr>
<tr>
<td>2</td>
<td>Consciousness disorder</td>
<td>Improved consciousness</td>
<td>No follow-up data</td>
</tr>
<tr>
<td>3</td>
<td>Consciousness disorder, seizure</td>
<td>Complete recovery</td>
<td>No improvement in MRI or SPECT</td>
</tr>
<tr>
<td>4</td>
<td>Headache</td>
<td>Resolution of headache</td>
<td>IgG index</td>
</tr>
<tr>
<td>5</td>
<td>Paresthesia of fingers, toes, and left precondial-back</td>
<td>Resolution of paresthesia</td>
<td>Neck MRI</td>
</tr>
<tr>
<td>6</td>
<td>Depressive state, insomnia</td>
<td>Improvement of depressive state</td>
<td>Neck MRI</td>
</tr>
<tr>
<td>7</td>
<td>Parestis of both lower limbs, muscle weakness, depressive state</td>
<td>Reduction of parest, improvement of depressive state</td>
<td>SPECT and IgG index</td>
</tr>
<tr>
<td>8</td>
<td>Psychosis, cognitive dysfunction</td>
<td>Improvement of psychosis</td>
<td>SPECT</td>
</tr>
<tr>
<td>9</td>
<td>Consciousness disorder, psychosis, parestis of both lower limbs, neurological bladder</td>
<td>Complete recovery</td>
<td>PET, MRI, and IgG index</td>
</tr>
<tr>
<td>10</td>
<td>Consciousness disorder, hallucination, cataplexy</td>
<td>Complete recovery</td>
<td>No significant improvement</td>
</tr>
</tbody>
</table>


Back Pain

Timing of Herniated Disc Surgery

By David G. Borenstein, MD


Abstract

Background: Lumbar-disk surgery often is performed in patients who have sciatica that does not resolve within six weeks, but the optimal timing of surgery is not known.

Methods: We randomly assigned 283 patients who had had severe sciatica for six to 12 weeks to early surgery or to prolonged conservative treatment with surgery if needed. The primary outcomes were the score on the Roland Disability Questionnaire, the score on the visual-analogue scale for leg pain, and the patient’s report of perceived recovery during the first year after randomization. Repeated-measures analysis according to the intention-to-treat principle was used to estimate the outcome curves for both groups.

Results: Of 141 patients assigned to undergo early surgery, 125 (89%) underwent microdiscectomy after a mean of 2.2 weeks. Of 142 patients designated for conservative treatment, 55 (39%) were treated surgically after a mean of 18.7 weeks. There was no significant overall difference in disability scores during the first year (p=0.13). Relief of leg pain was faster for patients assigned to early surgery (p<0.001). Patients assigned to early surgery also reported a faster rate of perceived recovery (hazard ratio 1.97, 95% confidence interval 1.72 to 2.22; p<0.001). In both groups, however, the probability of perceived recovery after one year of follow-up was 95%.

Conclusions: The one-year outcomes were similar in both groups.
By David Isenberg, MD

Today the British Isles Lupus Assessment Group (BILAG) Index is commonly used to chart multi-system progression of lupus from year to year, but just three decades ago there was no system in place to track this complex condition.

By the early 1980s there was a dawn of recognition in the lupus research community that the formal assessment of patients with lupus was hopelessly in disarray. As Matthew Liang, MD, MPH, professor of medicine at the Harvard Medical School in Boston, was later to point out, around 60 different activity indices for lupus had been published between the mid 1950s and mid 1980s, and they were all inadequate.1 There were attempts by many individual clinicians to capture lupus activity in ways that were never validated or shown to be reliable; all were global score indices.

The 1980s saw a considerable improvement in the situation. At the University of Toronto, Dafna Gladman, MD, and Murray Urowitz, MD, devised the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), although it is a global score, it was shown to be reliable, valid, and sensitive to change.1 Dr. Liang also developed the Systemic Lupus Activity Measure (SLAM).2

Different Concept of Measurement

In the United Kingdom, the relatively small number of rheumatologists interested in lupus began to think along different lines. It seemed in particular to Paul Bacon, MD, professor of rheumatology at the University of Birmingham, and Michael Snuth, MD, a senior lecturer in rheumatology at the University of Sheffield Medical School, that the notion of capturing disease activity with a single score, however thoughtfully derived and validated, was a suboptimal way to capture the reality of a multisystem disease like lupus. In particular, these investigators balked at the idea that severe disease in a single system that caused a patient fighting for her life in hospital could, at least theoretically, have the same score as a patient who had little activity in five or six systems and who might still be working. In 1984, during a discussion in Dr. Bacon’s Birmingham garden, they decided a better approach would be an index that:

1. Showed the level of activity in different organs and/or systems;
2. Captured an element of change in activity over time;
3. Was based upon the principle of the physician’s intention to treat; and
4. Recognized that disease activity was one part of a larger equation. To determine the total activity of the effect of lupus on a patient as well as disease activity, you needed a patient self-assessment index and a damage index.

Birth of BILAG

Realizing that developing this index was going to require a great effort, Drs. Snuth and Bacon decided to summon help. At that time I was working as Dr. Snuth’s senior registrar at University College Hospital. Others who were drafted and the group began meeting approximately every three to four months (which it still does) to work through the principles and development of the index.

In brief, we agreed that activity should be assessed in terms of constitutional features, mucocutaneous, central nervous system, musculoskeletal, cardiovascular respiratory, vasculitis, renal, and hematological organs or systems. In some instances, we asked outside experts to help us. Original renal criteria were drawn up with the help of J. Stewart Cameron, MD, now emeritus professor of nephrology at Guy’s Hospital of King’s College in London.3 In abiding by the intention to treat principle, we had to agree which particular signs and symptoms in each of these organs or systems, if present, would lead us to treat patients with a significant dose of corticosteroids (more than 25 mg prednisolone per day) with or without additional immunosuppressive drugs. This would then constitute the most Active form of disease (in that organ or system) and would be characterized as a grade A.

The B grade in each organ or system—in effect, a “Be aware” grade—envisaged a patient with active disease, also carefully defined, who required continuing steroid or immunosuppressive therapy but at a lower level, a C grade in each organ or system would imply “Contentment” meaning low-grade disease activity only, which might require just symptomatic therapy. The D grade implied inactivity in the respective organ or system. This was later divided into two grades: D for “Discount,” meaning the disease had once been active in this organ or system but was no longer active, and the E grade implying that the disease had never “Ever” been active in that organ or system.

Test of the System

An advantage of the system we established was that it provided a testable hypothesis. With a grant from the Arthritis Research Campaign, Dr. Hay visited five different rheumatology units around the United Kingdom to review the notes of patients to determine whether patients with grade A symptoms or signs were actually treated with the large doses of steroids or immunosuppression. As part of a concurrent reliability assessment, we also determined whether Dr. Hay’s assessment of the patients agreed with that of the local physician.

We were greatly encouraged by the results of Dr. Hay’s study, which showed strong correlations in seven out of eight of the systems.4 Only for the central nervous system was it difficult to obtain satisfactory agreement. By 1988, BILAG felt able to “go public” by presenting a poster at the 1st International Lupus Meeting in Calgary, Alberta. The organizers of this meeting placed this poster (which was defended by myself and Dr. Maddison) next to a poster describing the origins of the SLEDAI (defended by Drs. Urowitz and Gladman). The four of us felt that the issue of disease activity assessment was something that ought to be agreed globally. With the help of a grant from NATO three meetings were held between 1988 and 1991 to explore these indices and Dr. Liang’s SLAM index. Both real and paper patient exten-cases were undertaken with the support of other interested parties including Gunnar Sturfelt, MD, PhD, adjunct professor of rheumatology, and Ola Nived, MD, PhD, associate professor of rheumatology, both at Lund University in Sweden, and Keneth Kalunian, MD, professor of clinical medicine at the University of California, San Diego.

In practice, the BILAG index requires few blood or urine tests and, in most cases, the bulk of the form can be completed either on paper or a computer in three or four minutes. The form asks the clinician to determine if a clinical feature, which must be due to lupus, is absent or present. If present, is it better, worse, or the same as a month ago or a new or recurrent problem, and these data are converted into A–E scores for each organ or system.

Although somewhat antithetical the concept, the BILAG letter scores were assigned numbers so that they could be converted into a global score and thus compared more easily with SLEDAI and SLAM. In spite of their varying origins, there is a strong correlation among these three indices and also, as shown in later studies, with the European Community Lupus Activity Measure (ECLAM), which was devised by Stephano Bombardieri, MD, and colleagues.5 The choice of the A=9, B=3, C=1, D/E=0 point notation, while widely used now, was a rather spur-of-the-moment decision. The BILAG group is currently performing more objective modelling studies to determine how valid this numbering system is. It is likely that the C score will be downgraded.

By 1991, most of the necessary comparisons had been undertaken and the NATO group developed a damage index and selected the patient self-assessment index.6 The group was named the Systemic Lupus International Collaborating Clinics (SLICC) and enlarged for the first time in 1991, when Dr. Gladman was appointed its first chair. During the 1990s, a number of distinguished rheumatologists joined.

FBA and Tech Boosts

The turning point for the BILAG Index came in 2003.
lupus. One ‘glitch’ that has emerged is the tendency in some organs/systems in the classic BILAG Index to allow an improvement in a grade A feature to become a C on the next assessment a month later, which then remains the same and can score a B at the third assessment—giving the false impression of an extra flare. The new BILAG 2004 makes this jump unlikely to occur, firmly establishing the more natural progression from grade A to B to C.

Next Generation: BILAG 2004

An updated version—BILAG 2004—has been published and is now being tested for reliability and validity in large studies. The revised index has removed the vasculitis section, placing individual clinical features more appropriately within the other organs/systems. It now incorporates sections on gastrointestinal disease and has an ophthalmology section, both missing from the original. Furthermore, some items, which were damage items, have been removed. A software version of the new index will be available soon.

Dr. Isenberg is ARC Diamond Jubilee professor of rheumatology at the University College London. He would like to thank the other current members of the BILAG group.

References

TTHHEE  RRHHEEUUMMAATTOOLLOOGGIISSTT

Dr. Bacon, Snath, and Isenberg (shown left to right) at in Dr. Bacon’s garden, where—in 1984—he and Dr. Snath developed the initial concept for the BILAG Index.

References