The Future for Anti-inflammatory Drugs

by Theodore R. Fields, MD, Associate Attending Physician, Hospital for Special Surgery

What are non-steroidal anti-inflammatory agents (NSAIDs) and COX-2 inhibitors?

NSAIDs and COX-2 inhibitors are medications that can decrease pain and inflammation and have a long history of use in various kinds of arthritis and other painful conditions. There are two enzymes (body chemicals) that these medications can block—COX-1 and COX-2. COX-2 is the chemical that causes arthritis inflammation. COX-1 protects the stomach from ulcers. Both of these enzymes have many more actions, but the aforementioned are especially important to understanding the excitement that surrounded the introduction of COX-2 inhibitors. While it was believed that COX-2 inhibitors could stop inflammation in the joints without causing ulcers, it was later discovered that COX-2 inhibitors still caused ulcers, though fewer than the older NSAIDs, which block both COX-1 and COX-2 (also called non-selective NSAIDs). These older, non-selective medications include naproxen (Naprosyn® and Aleve®), diclofenac (Voltaren®) and ibuprofen (Motrin®). The newer, COX-2 selective agents include rofecoxib (Vioxx®), celecoxib (Celebrex®) and valdecoxib (Bextra®).

Who ends up using these drugs and for how long? What are the benefits? What are the dangers?

Many people use these drugs relatively briefly after an injury, but those who use NSAIDs for the longest time are those with chronic arthritis. Recent studies raise concerns about the safety of COX-2 inhibitors, e.g., the study that led to Vioxx® coming off the market. These studies suggest cardiovascular issues only after long-term use, and in the Vioxx® study, the problem only showed up after 18 months of use. This creates a quandary; the people most likely to have a problem with these drugs are also the ones who need them the most—that is, people with chronic arthritis. When COX-2 inhibitors first came on the market, it was suggested that they be used for patients at higher risk for ulcer, such as those who had a prior ulcer. Over time, this use extended to people at lower ulcer risk, as 1) physicians believed these drugs might be safer for everyone and 2) several pharmaceutical manufacturers began large direct-to-consumer ad campaigns. New data has raised the question of whether these drugs should again be used in a more select group of people.

- continued on page 2
Why were Vioxx® and Bextra®, two of the COX-2 inhibitors, removed from the market? What has the FDA said about COX-2 inhibitors?

In a study to discover if Vioxx® reduced the development of polyps in the colon, an increased risk of heart attack and stroke was shown after 18 months in patients taking Vioxx®. A prior study had suggested more hypertension and edema in patients on Vioxx®, but that earlier study was felt by many physicians to actually reflect protection of the heart by naproxen, the drug being compared to Vioxx®. This is still a matter of some debate. In February of 2005, the FDA Arthritis Advisory Panel advised that all three COX-2 inhibitors might remain on the market, but with warnings about cardiovascular risk. However, on April 7, 2005, the FDA revised their earlier decision, deciding that Celebrex® could remain on the market, while requesting that the manufacturer voluntarily withdraw Bextra®. The FDA stated that it was concerned about both cardiovascular and skin toxicity with Bextra® and did not think there was sufficient data about its safety or effectiveness to justify its continued availability at the current time. For Celebrex®, the FDA will require a "black box" warning about cardiovascular risk. For Vioxx®, should the manufacturer wish to put it back on the market, a new public hearing would be required.

Are the older, non-selective, non-steroidal anti-inflammatory agents safer than the COX-2 inhibitors?

On April 7, 2005, the FDA recommended that all NSAIDs, including all over-the-counter agents except aspirin, carry the same "black box" warning about cardiovascular risk as Celebrex®. One previous study suggested that naproxen may increase risk of heart attack and stroke, but there is no conclusive evidence to show cardiac risk for this medication. However, all the NSAIDs, both selective and non-selective, can cause hypertension and fluid retention, which can lead to cardiac problems. Currently, the number of long-term studies of the older, non-selective medications is very limited, and this leads physicians to fear that if used long-term, these medications may not actually turn out to be safer than the COX-2 inhibitors—this was the basis for the FDA's broad "black box" requirement. It is important to note that there are a number of chronic arthritis sufferers who have very limited mobility without an NSAID, and in many of these cases, a decision may be made to use one of these medications. The decision would depend on which drugs helped them before, their risk of ulcer and cardiovascular disease and the alternatives to using NSAIDs, which are discussed in the next section. It is possible that some people may have success on smaller doses of a COX-2 inhibitor, such as Celebrex®, since studies to date have only shown cardiovascular problems when studying patients on higher doses.

What are the alternatives to both COX-2 inhibitors and older, non-steroidal anti-inflammatory agents?

A number of other choices are available. In people with rheumatoid arthritis (RA), treatment with a medication that alters the course of their disease, such as methotrexate, may allow them to come off an NSAID. For all kinds of arthritis, other ways to seek pain relief include physical and occupational therapy, local injection with steroids or viscosupplementation (fluids somewhat similar to natural joint lubricants which can decrease pain in osteoarthritis), local heat and ice, splinting, acupuncture, biofeedback and stress reduction. Pain killers such as acetaminophen (e.g., Tylenol®), codeine, tramadol (Ultram®), propoxyphene (Darvon®) and oxycodone (Percocet®) can often be taken on an “as needed” basis.

-continued on page 6
Walking: A Prescription for Good Health
by Robyn M. Stuhr, MA, Administrative Director & Exercise Physiologist, Women’s Sports Medicine Center
Hospital for Special Surgery

Walking is a terrific form of exercise. You do not have to learn complicated steps or buy expensive equipment. It is easy on the joints, and you can do it just about anywhere, anytime. Walking helps you burn calories, improve your heart and bone health, increase energy and improve your mood.

Recent studies published in the Journal of the American Medical Association (JAMA) have demonstrated that postmenopausal women can lower their risk of breast cancer by 18% if they walk 1.25-2.5 hours a week, significantly decrease total and intra-abdominal fat by walking three hours a week and lower their risk of hip fracture if they walk at least four hours a week! That is a pretty amazing return on a very reasonable investment. Walking just 30 minutes a day combined with less than 10 hours a week of television watching has been shown to reduce new cases of obesity and diabetes by 30 and 43% respectively.

Experts at the CDC and National Institutes of Health have published a recommendation that every American adult engage in 30 minutes or more of moderate-intensity physical activity just about every day of the week. One way to meet this standard is to walk two miles briskly (about four miles an hour). If this pace is too fast for you, start at a more comfortable pace. Begin with a 10-15 minute walk and add a couple of minutes each week. When you can walk 30-45 minutes easily, try to add some brisk walking intervals into your walk. One block fast, one block slow, etc. You can also combine 10-15 minute bouts of activity over the course of a day to equal 30 minutes. If you are interested in long-term weight control, the Institute of Medicine recommends a higher volume of activity: 60 minutes of moderate-intensity exercise five days a week. You will need to gradually work up to this level of exercise and then stick with it! Find a pleasant place to walk: a beautiful park or neighborhood or the shopping mall—without your wallet! Get a friend or family member to join you, and get in shape together.

The most important piece of equipment you will need for walking is a pair of comfortable and supportive athletic shoes. Select walking, running or cross-training shoes, depending on whether you will be using them for other forms of exercise. You do not need to pay $100 for a good pair, but the $19.99 budget model likely will not provide the support and performance you need. The shoe should fit comfortably right out of the box. Do not let a salesperson tell you to “break them in.” Make sure you have a little wiggle room between the end of your longest toe (1/2”) and the end of the shoe. Squeeze the heel area to make sure it is stiff and does not bend easily.

If you experience foot, knee, hip or back pain when walking, stop and check with your doctor to find out the cause. You may need special exercises or better shoes. If you have osteoarthritis and experience increased joint pain lasting an hour or two after walking, consider an alternate activity like stationery cycling or water exercise. Do not stop exercising altogether! Get guidance from your doctor or a physical therapist.

Regular aerobic, strength and flexibility training can help people with osteoarthritis maintain muscle function, manage weight to reduce stress on the joints and reduce pain.

In spring of 2003, Hospital for Special Surgery initiated an employee walking program called HSS on the Move, sponsored by the Women’s Sports Medicine Center. Employees walk during their lunch hour, along the East River walkway, and earn prizes each month for regular participation. Employees also receive health, fitness and nutrition information and win additional prizes for correctly answering fun quiz questions. In the first year, 133 employees were active in the program, with an average of 48 individuals walking each day.

-continued on page 4
Over a decade ago, the U.S. Department of Agriculture (USDA) developed the Food Guide Pyramid, based on the Dietary Guidelines for Americans, published by the USDA and Health and Human Services. The original pyramid was created to guide Americans in making healthy food choices. In the spring of 2005, a new, revised version of the Food Guide Pyramid, called MyPyramid, was created to reflect the new 2005 Dietary Guidelines and encourage regular physical activity in conjunction with healthy eating. As in the previous pyramid, eating plenty of fruits and vegetables is an essential element to a wholesome, well-balanced diet.

How much do you know about the fruits and vegetables you eat? Answer these True/False questions and find out! (See page 6 for the answers)

**True or False**
1. □ True or □ False
   A plain baked potato is almost 100 percent fat-free.

2. □ True or □ False
   Asparagus is not a good source of folic acid.

3. □ True or □ False
   Strawberries are part of the rose family.

4. □ True or □ False
   Sweet potatoes and yams are the same vegetable.

5. □ True or □ False
   Tomatoes and potatoes are in the same food family.

Walking: A Prescription for Good Health continued

Employees have improved their health in a variety of ways. They also value being able to take a break from the pressures of the day and return to work with more energy.

Whatever activity you choose, get off that couch and start moving. You can not afford to miss out on all the amazing benefits of a brisk walk.

**References**
For many years, it was thought that persons with arthritis should not exercise because it would damage their joints. Today, doctors and therapists know that exercise can improve your health without hurting your joints.

With this in mind, the Arthritis Foundation introduced People with Arthritis Can Exercise (PACE®). PACE® is an exercise-based program designed specifically for individuals with arthritis that uses gentle activities to help increase joint flexibility and range of motion, maintain muscle strength and increase overall stamina. The program is structured as hour-long classes generally held one to three times a week with a class series usually lasting eight weeks. The optimum class size is 10-20 people.

Any adult with arthritis may join the PACE® program. However, you must be able to walk independently with assistive devices, or if you are in a wheelchair, have the ability to transfer to a straight back chair. Individuals with osteoporosis, multiple or severe joint problems, a history of back or neck problems, or who have had joint surgery are encouraged to check with their doctor about the need for special precautions. Benefits of completing the PACE® program include:

- Increased joint flexibility
- Increased range of motion
- Increased overall stamina
- Maintenance of muscle strength

To learn more about the PACE® program, contact your local Arthritis Foundation chapter.

**Healthy Nutrition Tips for Arthritis**

In the media today, we are bombarded with diet and nutrition information. It may seem impossible to choose a diet that will help you reach optimal health. Even more important, where do you find the time and energy to stick to it?

What we do know is that anyone with arthritis can benefit from eating a healthy, well-balanced diet with foods rich in nutrients, antioxidants, vitamins and minerals. Follow these tips to help you start on the road to healthier eating:

- Eat a variety of foods
- Focus on fresh fruits, vegetables and whole grain products
- Include 2-3 servings of low-fat dairy foods daily
- Consume adequate protein with emphasis on fish, lean poultry, nuts and legumes
- Choose monounsaturated and polyunsaturated fats such as olive oil or canola oil
- Shop the perimeter of the store, where you find fresh foods with little or no added salt, fat or sugar
- Read the Nutrition Facts labels. Look out for saturated fats, transfats, added sugars and hydrogenated oils—all harmful to your health
- Keep chopped, fresh vegetables in your refrigerator with low-fat dip for a crunchy snack
- Have sliced fresh fruit and 1 cup of low-fat yogurt for a sweet and healthy dessert
- In recipes, cut the amount of meat or chicken in half and substitute vegetables or beans for an antioxidant boost
- Use unsaturated fats in recipes instead of butter

When you pay attention to what goes into your body, you can provide it with the nutrients needed for good health and weight maintenance, while reducing your risk of chronic disease.

---

**Errata**

We regret that an acknowledgement of Rheuminations, Inc. as the funder whose generous support make LupusLine, Charla de Lupus and LANtern possible was omitted from the article entitled “Finding the Right Connection for People with Lupus,” which appeared in the Winter 2004 edition of HealthConnection. The support of Rheuminations has been vitally important to the attainment of our academic mission at Hospital for Special Surgery in general and these programs specifically. We would like to take this opportunity to thank Katherine and Arnie Snider for their continued support.
The Future for Anti-inflammatory Drugs continued

There is also evidence that the supplements glucosamine and chondroitin sulfate may help with osteoarthritis stiffness and pain. In some patients, a surgical procedure, such as a total joint replacement, can dramatically reduce their susceptibility to ongoing pain once their post-operative pain resolves.

How may this issue become clearer in the future? What is the best course for someone with chronic pain right now?

To truly answer the key questions about COX-2 inhibitors, non-selective NSAIDs and the cardiovascular system, a large, government-sponsored study should be conducted to compare them over a two-year period. This is a difficult (and very expensive) study to do, but many support this option. It would also be very helpful to have smaller studies in arthritis patients at high risk of cardiovascular disease—at lower doses of the medications—to monitor the safety of their medications over a two-year period.

For now, however, it is clear that each person with chronic arthritis pain needs to discuss the pros and cons of the NSAIDs and COX-2 inhibitors with their physician, in relation to their particular case. That discussion needs to include how much pain the person has, which alternatives are available, what has worked for them in the past, their risk for ulcer and cardiovascular disease and their own personal preferences. Only by individualizing these factors can physicians discover the best course of action for each person.

Always consult your physician before taking any prescription medication.

Arthritis Education Program Grant Announcement

Greenberg Academy for Successful Aging, a Hospital for Special Surgery and New York-Presbyterian Hospital Wright Center on Aging collaborative project, has been awarded a grant to implement arthritis programs geared to older adults. Greenberg Academy for Successful Aging develops and implements education programs aimed at the interests and needs of people age 65 and over. The grant was awarded by the New York State Department of Health in March of 2005 and will support People with Arthritis Can Exercise (PACE®) and Spanish Arthritis Self-Help Course.

For more information, please contact the Education Division at 212.606.1057.

Sjogren’s Syndrome Support Group

Sjogren’s Syndrome is a chronic, autoimmune disorder affecting as many as four million Americans. In Sjogren’s Syndrome patients, the immune cells attack the glands that produce tears and saliva. The condition is also linked to rheumatic diseases like rheumatoid arthritis. Symptoms include dry mouth, eyes, skin and nose and may affect other organs such as the kidneys, blood vessels, lungs, liver, pancreas and brain. The New York City Sjogren’s Syndrome Foundation Support Group holds monthly meetings to provide a forum to share experiences and hear knowledgeable speakers address topics of relevance to Sjogren’s patients.

For more information, contact Susan Needles at 212.724.7110.

Healthy Food Facts Quiz Answers

1. True. A plain baked potato eaten with the skin not only contains zero grams of fat, but also provides nearly 50% of vitamins C and B6 as well as plenty of potassium and fiber.

2. False. Asparagus is an excellent source of folate acid, a B vitamin associated with a decreased risk of neural tube defects.

3. True. The strawberry is the fruit of a plant in the family Rosaceae.

4. False. Sweet potatoes are rich in vitamin A, while yams contain no vitamin A, are grown in the Caribbean and have rough, scaly skin.

5. True. Potatoes are in the same family as tomatoes and peppers.
In the workplace, it is easy to spend a long time in the same position, sitting behind a desk without moving the whole body. Even if you are sitting with good posture, it is helpful for the joints to move often. Movement keeps the joints fluid and flexible, and even the smallest movement can help balance the muscles around a joint and help with stability. The following exercises for the arms and upper body can be done sitting in a chair (without arms, if possible) and take only a few minutes.

First, breathe—feel your whole ribcage expand as you take a deep breath, and let it soften and release as you let the air go. Keep breathing as you do the movements, so that you are not holding your breath (if a movement is too hard, make it smaller and easier until you can breathe deeply). Lengthen your spine as much as you can, and try to have your feet flat on the floor.

- **Hand - “Starfish”**
  As you inhale, stretch your hand open. Exhale, and close your hand into a loose fist.

- **Wrist and Elbow Spiral**
  With your elbow bent at your side, hold your hand out in front of you. As you inhale, turn your palm down to face the floor. As you exhale, curl your fingers in, turn your palm to the ceiling and enclose your arm across to the left, forward and high (as if you were reaching for an apple on a tree).

- **Whole Arm**
  Inhale, and with your right hand open your fingers, turn your palm to the floor and spread your arm out to the right, down and back (as if you were pushing something away and behind you). As you exhale, curl your fingers in, turn your palm to the ceiling and enclose your arm across to the left, forward and high (as if you were reaching for an apple on a tree).

- **Head nodding**
  Beginning with the smallest possible movement, nod your head “Yes.” Let the movement very gradually get larger (but not so large you feel like you are straining your neck) and then make it very small again.

- **Head tilting**
  Now, tilt the head from side-to-side, in a “Maybe” movement. Start as small as possible; let the movement grow larger and then small again.

- **Arm Circle**
  Sit forward on the edge of your chair, with your feet about 18 inches apart. As you inhale, spread your right hand open and reach left, forward and high, and circle it up overhead to right, back and high. Then, as you exhale, continue the circle to the right, back and low and then left, forward and low. Watch your hand for as much of the circle as possible. Feel your legs supporting you, as your arms and spine spiral and gently rotate. Reverse the circle, then do both directions with the other hand and arm.

If any of these movements are painful, reduce the range of motion until it does not hurt. It is more important to do them with flow and ease than to make a big movement. Most importantly, enjoy the feeling of your body moving and your breath.

---

**From the Studio**

“This program helps me physically and socially. This class has made me feel sure of myself and has taught me how to relax and deep breathe.”

- Rosa Scott, Gentle Yoga for Wellness Program Participant
The Education Division’s Public and Patient Education Department provides information to the general public and patients through a variety of health education programs. Professionals provide practical information to help prevent or manage health problems related to different types of arthritis or orthopaedic problems. Programs are held at the hospital as well as in the community. The department is dedicated to providing education today, so that everyone can have a healthier tomorrow.

Laura Robbins, DSW
Vice President, Education and Academic Affairs

Chandler Wilson, MPA, CFMMS
Assistant Director
Publications and Communications Newsletter Editor

JBRH Advertising   David Rosenzweig
Layout Illustration

HealthConnection is published biannually by the Public and Patient Education Department at Hospital for Special Surgery as a service to the general public and patients. For further information regarding material contained in this newsletter or inquiries on how to obtain additional copies contact:

Public and Patient Education Department
tel: 212.606.1057  fax: 212.734.3833
e-mail: education@hss.edu

All rights reserved.
© 2005 Hospital for Special Surgery

Printed on recycled paper

Hospital for Special Surgery offers premier health care services in your community. Contact our affiliated physician offices for more information.

New York
• Burke Rehabilitation Office (White Plains) 914.948.0050 Ext. 2332
• Integrative Care Center 212.224.7900
• Uniondale (Long Island) 516.222.8881

New Jersey
• Princeton Office 609.683.5500

Connecticut
• Greenwich Office 203.698.8887

Health Connection is published biannually by the Public and Patient Education Department at Hospital for Special Surgery as a service to the general public and patients. For further information regarding material contained in this newsletter or inquiries on how to obtain additional copies contact:

Public and Patient Education Department
tel: 212.606.1057  fax: 212.734.3833
e-mail: education@hss.edu

All rights reserved.
© 2005 Hospital for Special Surgery

Printed on recycled paper