THE
Arthritis Research
NEWSLETTER

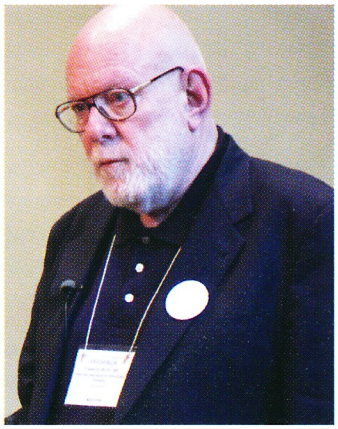
National Databank for Rheumatic Diseases January 2005

Research Notes from the Director:
What happened with Vioxx?

As almost everyone knows, Merck & Company withdrew Vioxx from the market October 2004 after two studies showed that it increased the risk of heart attacks. Vioxx first became available in 1999. So it took five years to determine that it was dangerous to some patients. Was this long delay due to negligence by Merck or malfeasance at the US Food and Drug Administration (FDA), or was it something else? There are lawsuits beginning and there will be congressional hearings. You'll hear a lot about this issue in the next several years. Here are some things to think about.

It is easy to detect a side effect if the side effect is common. Suppose a drug causes a side effect in one percent of people who take it, and that 1/10th of one percent of people who don't take the drug also get the "side effect," perhaps from another drug or maybe because the symptom is common in people generally. Believe it or not, it would take 3,200 people participating in a study to prove that the side effect was caused by the drug. That's a lot of people.

Could we have detected an increase in heart attack rates caused by Vioxx in the NDB with 15,000 people completing questionnaires? Well, first we need to know the normal rate of heart attacks. In the NDB, about one percent of people report that they had a heart attack during one of our 6-month surveys, and about two percent of people used Vioxx each 6 months. That's not a lot of heart attacks and not a lot of Vioxx use. When we analyzed NDB data, we found a tendency to an increase in heart attacks by Vioxx users. On average, we saw an increased risk of about 32 percent. But, because so few people were taking Vioxx in the NDB and the number of heart attacks was so small, we could not make a statistically valid conclusion. All we could have said is that the increase of risk could be as great as 223 percent but it also could be as low as –28 percent. That is, it was even possible that Vioxx might protect against heart attacks.



NDB Director Dr. Frederick Wolfe at the 2004 American College of Rheumatology meeting.

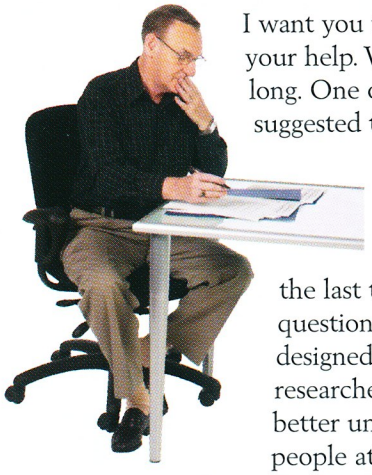
What it all comes down to is that when an event is rare, like heart attacks, and the drug only causes it in a few people, it is very hard to prove the cause and effect link. The end for Vioxx was the Kaiser-Permanente HMO study that found a 3-times increased risk for heart attacks among Vioxx users. The Kaiser study included 1.4 million people and 8,199 heart attacks. By contrast, among the 15,000 NDB participants there were only 560 heart attacks.

> ***"...we were able to detect that Vioxx caused hypertension and swelling (factors that might lead to heart attack) and we reported that in 2002."***

By the way, we were able to detect that Vioxx caused hypertension and swelling (factors that might lead to heart attack) and we reported that in 2002. The NDB research paper was published this year.

Although it seems clear now that Vioxx caused heart attacks, it wasn't clear when Vioxx was first released, although a few suspected a problem. It took many people taking the drug for a number of years before it became clear that the drug was at fault. In the flurry of lawsuits and investigations that will occur, remember that this knowledge came slowly. Was the drug company at fault, or maybe the FDA? Stay tuned, but remember that a problem like this is not always a sign of malfeasance. Perhaps researchers should change the way they identify serious side effects from clinical trials that have a small number of patients to large observational data banks, such as the NDB and Kaiser-Permanente.

Questionnaires

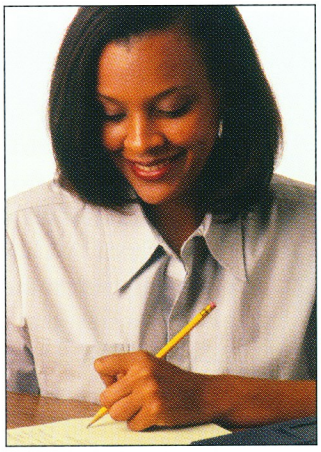


I want you to know how grateful we are for your help. We know the questionnaires are long. One of you wrote to us earlier and suggested that each year the questionnaire seems to get longer. This year it is slightly shorter, and it will lose several pages next year. The July questionnaire will be the last that includes the detailed work questions. These questions were designed by Boston University researcher Dr. Saralyn Allaire to try to better understand how arthritis affects people at work. The results will be important to the medical community and to lawmakers. Thank you all who have completed those questions.

If you haven't tried the web questionnaire, I'm asking you personally to consider doing so. It's a smart questionnaire that remembers some of your past answers and skips questions that are not needed. It is shorter and most people find it much easier.

I want to let you know that we read all of your comments and take them seriously. Some of you may have had responses from us concerning the comments. We learn from them. Keep them coming. We got a lot of flack from the question on the web survey that we called, "Do the most good." We asked you to choose how to spend money on health care as if you were a policy maker. In retrospect, we have to agree that the questions were a little silly. We won't do it again. Thanks for telling us.

One complaint that comes up over and over again is that questions seem repetitive. We plead guilty. We ask you about pain and function in many questions. The reason we do it this way is that these questions are a part of group questions that are scored together. If we eliminate apparent repetitive questions, we can't score the group questions.



Another complaint is that we repeat the same question over and over again every six months. For some questions in the web version, we don't, as the smart web questionnaire remembers things. But the paper questionnaire can't be individualized for each person. We want you to know that we try to limit this problem as much as possible.

Refer a Friend

Here's a really easy way to let a friend with arthritis know about the NDB. Just give us your friend's email address and we'll send out an email invitation to join the study. Go to http://www.arthritis-research.org/enrollfriend.htm.

FOR MORE INFORMATION OR TO PARTICIPATE

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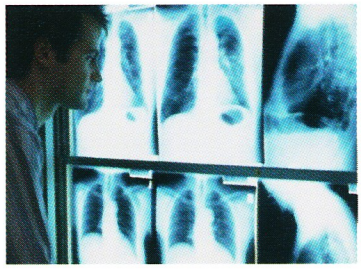
or email info@arthritis-research.org
or visit our website
www.arthritis-research.org

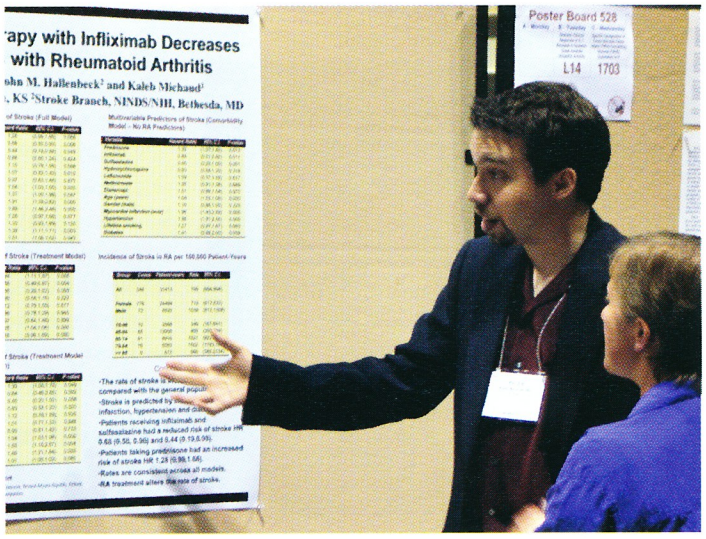
Research Results

Using your answers to our questionnaires, the NDB reported many important findings to American College of Rheumatology (ACR) annual scientific meeting in October 2004. The ACR meeting is the most important gathering for US Rheumatologists. You can find these reports as "posters" and PowerPoint presentations on our web site (look in the physician's section). The NDB presented more research than any other group in the world at this meeting. You can see it all on the web site. Here are some highlights.

Stroke reduced by Remicade. Working together with researchers in the stroke center at the National Institutes of Health (NIH), we found that people who took Remicade reduced the risk of stroke by 50 percent. This is an important finding, suggesting that control of inflammation by this treatment can alter the risk of cardiovascular problems. Zurab G. Nadareishvili and John Hallenbeck also authored this study.

Pneumonia, steroids, Remicade and Enbrel. We also reported that corticosteroids increased the risk of getting cataracts and pneumonia. They are also associated with increased risk of heart attack and stroke. Common names for corticosteroids are steroids, cortisone and prednisone. Like all drugs, there are benefits and risks that often balance each other. Corticosteroids help a great deal in reducing inflammation and may be responsible for other benefits. Things are not clearly black and white. In fact, we found an increased risk of pneumonia in people taking Remicade but not Enbrel. Dr. Liron Caplan was the primary author of this study.





Kaleb Michad of the NDB explains a poster. The NDB presented more research than any other group.

Statins reduce disability in RA. These drugs that reduce cholesterol also reduce inflammation. We found a modest beneficial effect among statin users. Dr. Eric J. Hochman and Dr. Hyon K. Choi contributed to this research.

RA does not increase the risk of sinus infections. However, among people taking Enbrel there was a suggestion of an increased risk of about 16 percent. This increase was not statistically significant, although users of Enbrel had higher rates of sinus infection than users of Remicade.

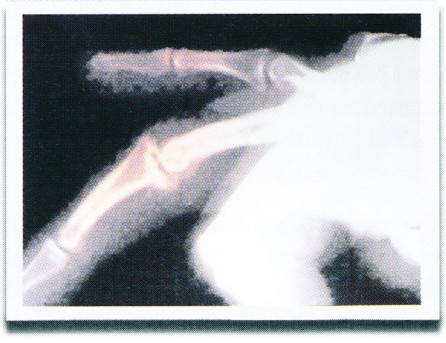
Joint Infection and Anti-TNF Therapy

Joint infection is a concern for RA patients who undergo total joint replacement surgery (TJR). Some recent research has shown that the risk of joint infection is much higher after TJR if the patient is taking anti-TNF therapy, such as Humira, Enbrel or Remicade.

We decided to look at the risk of joint infection in RA patients in the NDB. Joint infections are very rare. If we look at "patient years," or the number of years a person has RA, we found only 1.2 cases per 1,000 patient years among patients who've never had TJR. That means that on average, you would have to live 833 years with RA to get a joint infection.

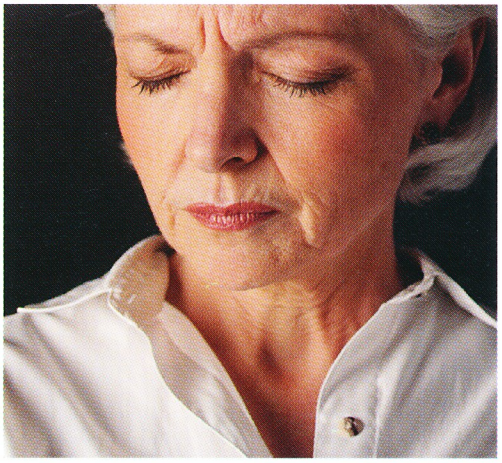
Patients who recently had TJR surgery have a greater risk, about 14 cases per 1,000 patient years. This makes sense, because any time the skin is broken, for surgery or just a scrape, the risk of infection goes up. Our skin is there to protect us, after all.

How did anti-TNF therapy affect the results? We found that the risk of infection doubled, but that if you haven't had recent TJR surgery your risk is still extremely small. You'd have to live about 500 years to have a joint infection. Thanks to your help and this research, doctors have better knowledge about infection risks with anti-TNF drugs, rather than having to guess about the risk. Other RA drugs did not increase the risk.



Research Results

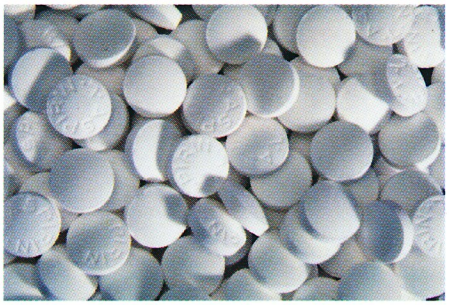
What does jaw pain mean?



Jaw pain can occur in Rheumatoid Arthritis (RA), Osteoarthritis (OA) and Fibromyalgia (FMS). We wanted to know what characteristics are common to people with jaw pain, and which form of arthritis they have. We found out that jaw pain is much more common in people with FMS, about 38 percent have it, whereas 18 percent of RA and OA patients have it. Does this mean that if you have jaw pain you probably have FMS? No. That determination can only be made by your doctor. It might indicate what we call a "general pain disorder" rather than a specific problem with your jaw joint. This means you, in general, might have more pain or decreased sensitivity to pain compared with people without jaw pain. Again, this information can be more useful to your doctor as he or she decides how to treat you.

For doctors, as they see patients with jaw pain, this research means that they may want to give more thought to whether a person has above-average pain that needs specific attention. Dr. Robert S. Katz was the primary author of this study.

Low-dose aspirin and stomach problems



Those of you taking Cox-2 drugs, such as Celebrex, may have heard that these cause fewer stomach problems than pain-killers like acetaminophen and ibuprofen. We wondered whether people with RA or OA still had fewer problems if they took Cox-2s along with low-dose aspirin, which is commonly used by people with heart problems. It turns out that people taking both do not have an increase in heartburn, ulcers or general stomach discomfort. However, we did find a small increase in the risk of nausea. Dr. Elizabeth Benito Garcia was the primary author of this study.

RA and non-melanoma skin cancer

Many studies have shown that RA patients have a higher risk of certain types of cancers. It is unknown whether this is because of the way RA affects the immune system, the way some RA drugs suppress the immune system, or both. In particular, European studies have shown that RA patients are at a higher risk of non-melanoma skin cancer (NMSC). Most NMSCs are found on parts of the body that get exposed to the sun, like the face and hands. They normally don't affect other body areas. NMSC is almost always cured if detected early.

We decided to calculate the risk of NMSC in RA patients by comparing them to OA patients. OA and OA drugs do not affect the immune system like RA. Indeed, there is a slightly increased risk for RA patients. Use of prednisone and use of combination TNF-inhibitor (etanercept, infliximab, adalimumab) and methotrexate were also associated with an increased risk for the development of NMSC.

What does this mean for NDB patients? Probably not too much, because everybody (especially those with light-colored skin or previous skin problems) should always be alert to changes in the skin. You should tell your doctor any time you notice

- Any change on the skin, especially in the size or color of a mole or other darkly pigmented growth or spot, or a new growth
- Scaliness, oozing, bleeding, or change in the appearance of a bump or nodule
- The spread of pigmentation beyond its border such as dark coloring that spreads past the edge of a mole or mark
- A change in sensation, itchiness, tenderness, or pain

Dr. Eliza F. Chakravarty was the primary author of this study.

All in all, the NDB had 26 presentations at the ACR meeting. Some of them are difficult to explain in a few short sentences, so be sure to look on the web site.

The Internet, the NDB, and You

We're happy to see more and more of you online all the time. If you haven't tried completing your NDB questionnaire online yet, well, there's no time like the present!

Getting more of you to do this online means a significant savings in printing and mailing costs. But the Internet also lets us do more with less. Please note that your email addresses and other information are always treated with the highest level of confidentiality.

Technical Support

If you are new online, you may have questions as you start working on the questionnaire or browse our website. We are here to answer your questions by email or phone, usually the same day. We want your online experience with the NDB to be free of frustration and hassle. Chances are, if you're stuck, we've heard your question before. The quickest way to get moving again is to get in touch with us.

"We want your online experience with the NDB to be free of frustration and hassle."

WebQuest

WebQuest is our online questionnaire. The questions are the same as what you get on the paper questionnaire, but computers make it all easier for you. WebQuest remembers who you are and doesn't ask you to complete questions for which we already have an answer. And it saves you time by remembering your medications and skipping questions that don't apply to you.

If you are not now using it, go to "Request NDB Questionnaire on the Web" (http://www.arthritis-research.org/webquest.htm) at our home page www.arthritis-research.org/patients.htm and make the request or send us an email at webquest@arthritis-research.org.

Email

For patients using WebQuest, email is our primary method of getting in touch with you. Even if you're not using WebQuest, we'd like to be able to send you important information by email. It's important that we have your current email address. To update your email address go to http://www.arthritis-research.org/UpdateEmail.htm.

Here's a VERY IMPORTANT step you can take to make sure our email gets to you: Add us to your email address book. Our address is webquest@arthritis-research.org. This will ensure that our mail makes it through the spam blockers.

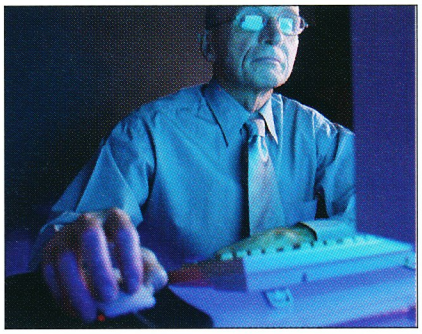
Website

The website continues to be the main Internet resource for NDB patients, researchers and physicians. Find it at www.arthritis-research.org. Please browse the site to learn what we do and how we do it. You'll meet the people who work here and see the important research that you make possible.

Forums

The Forum is an exciting feature available for NDB participants to post comments, ask questions, or find out new information. It will be mediated by an NDB Staff member, and allows all NDB participants a place to connect with others in the research project.

The three forums topics are: QUESTIONNAIRES: for questions and comments about our questionnaires. RESEARCH: This forum is a place you can ask about specific research we have done or suggest your own topics. ARTHRITIS-RHEUMATOLOGY: This forum is a great place to get information from others participating in the study. Popular questions here cover arthritis drugs and treatments.



You can find the NDB Forum at the following address http://www.arthritis-research.org/bbs.htm.

Blog

The NDB Connection is our new Blog (or Web log) where we'll let you know about important, interesting or fun news related to arthritis, research and/or the NDB. We update the blog every couple of days. It's a great way to check in with the NDB and the world of arthritis research. It's at ndb.blogspot.com

More Information

If you have any questions about the WebQuest or anything else related to the NDB, please let us know at webquest@arthritis-research.org or call us at 1-800-323-5871 x140.

Can you use our new pamphlet?

Now available for your support group or arthritis meetings....Our new pamphlets explain what we do and how you and can help. Each one has a postage-paid postcard to request more information or join the project. The pamphlets and a small table-top stand are available free from the NDB. Just contact us at info@arthritis-research.org or 800-323-5871 ext. 133 or 140. Thank you!

Meet the New Executive Director!

The NDB is pleased to introduce Rebecca Schumacher as our new Executive Director! Rebecca started with the NDB in 2001 as a verifier and coder processing incoming questionnaires. She then became the project manager of our Remicade safety study.

Rebecca Schumacher is the NDB's new Executive Director.

As Executive Director, Rebecca supervises NDB enrollment, the forms processing department, the management of data to prepare it for statistical analysis and directs the NDB staff. Her goals for the NDB are to continue to produce research that improves the quality of life for people who have rheumatic diseases. She also will be working on increasing enrollment in the NDB, and continuing our work on drug safety.

Rebecca lives in Wichita with her husband and 3-year-old daughter. She is originally from North Dakota, and is a big fan of playing golf and going to the movies.

Three $1,000 Awards to Arthritis Research Participants:

Return your research questionnaire within two weeks of receiving it and be eligible for one of three $1,000 awards. The research data bank can best contribute to research when the mailed questionnaires are completed and returned as soon as possible. Anyone who completes the questionnaire within two weeks of receiving it will be eligible for the award — given as a token of our gratitude in help with arthritis research.

The winners from the last questionnaire were:
Beverly Collins, College Grove, TN;
Mary Ann Eells, Whitesboro, NY;
Susan Drielts, Indian River, MI

Congratulations to all!!