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New hope for those with rheumatoid arthritis

The world's most common autoimmune disease, rheumatoid arthritis strikes up to one in 100 people in the course of a lifetime. But new drugs and drug combinations are revolutionizing treatment

BY JANE E. BRODY
NY TIMES NEWS SERVICE, NEW YORK

Alan Moore was 52, teaching statistics at the University of Wyoming, playing the violin in the university's symphony and accompanying soloists on the piano when his health took a nosedive in April 2001.

"I felt like I had the flu," Moore recalled in an interview last month. "I was very weak and fatigued. I had extreme pain and swelling in a lot of my joints. I was in agony when I got up in the morning, so stiff I had to shuffle to the bathroom. I couldn't peel a banana, turn the key in the ignition or even pull the tab of a tea bag. My wife, Cindy, had to help me with the simplest of tasks. Needless to say, I couldn't play the violin or piano or use the computer."

Doctors diagnosed it as rheumatoid arthritis. "And I thought that my life as I knew it was over," said Moore, now 59, of Laramie, Wyoming.

But by enrolling in a clinical trial of one of the drugs and drug combinations that are revolutionizing the treatment of the disease, Moore got his life back.

Rheumatoid arthritis is the world's most common autoimmune disease, striking up to one in 100 in the course of a lifetime. It is most often diagnosed in people ages 30 to 60 but it can occur at any time, including childhood.

As with other autoimmune diseases, women are three to four times likelier than men to develop rheumatoid arthritis. About 80 percent of Caucasians with the disease have a genetic marker, a gene sequence in the HLA-D region of chromosome 6 that is found in only about 35 percent of the general population.

The disease causes chronic joint inflammation and progressive destruction of the cartilage at the ends of bones, which can result in an inability to use the affected joints. Other effects include fatigue, malaise, anemia and damage to organs throughout the body, including the cardiovascular system.

Untreated, 20 percent to 30 percent of people become permanently disabled within three to five years of diagnosis. Life expectancy may be reduced by as much as 15 years, with half of patients succumbing to cardiovascular disease.

Doctors traditionally treated the symptoms of rheumatoid arthritis, usually with anti-inflammatory and pain-relieving medications. But the underlying destruction of tissues continued, leading to chronic disability and premature death.

The goal today is suppression of the disease and prevention of progressive joint destruction by treating patients early with synthetic or biologic agents called disease-modifying antirheumatic drugs.

Though he did not know it at the time, Moore was randomly assigned to the study group that every two weeks self-injected a biologically derived drug called Humira, which acts to block a protein involved in the inflammation associated with rheumatoid arthritis. Humira is one of six biologic treatments for the disease approved by the US federal government. Three other biologic remedies are nearing approval by the Food and Drug Administration.

"Within days, my symptoms declined to nearly zero," Moore said, "and I've had no symptoms since." He has continued the injections of Humira and participates in a registry of patients to help assess the drug's long-term benefits and potential risks.

The costly biologic drugs are often used in combination with much cheaper synthetic disease-modifying drugs taken orally, like methotrexate. In

some cases, oral medications are all that patients need to keep symptoms and joint destruction under control.

But well-designed clinical trials have typically shown that in patients facing moderate to severe disease, combining the treatments often results in fewer symptoms and less destruction of joints, especially if therapy begins early.

In a study published on July 16 in *The Lancet*, researchers in Leeds, England, reported that among 542 patients randomly assigned to receive either methotrexate alone or in combination with Enbrel, another biologic agent, those receiving the combination were almost twice as likely to become symptom free and more likely to show no X-ray signs of progressive joint destruction a year later.

In a commentary with the *Lancet* report, Joel Kremer, a rheumatologist at Albany Medical College, in Albany, New York, said it was important to consider the long-term consequences and costs of the disease when deciding how much to spend on therapy.

"Most of the biologic agents cost in the range of US\$16,000 to US\$18,000 a year, whereas the oral medications cost only about a tenth that," Kremer said in an interview.

But, he added, inadequately treated rheumatoid arthritis typically leads to a need for multiple joint replacements, lost productivity, lost tax revenue and a greatly diminished quality of life, as well as an increased risk of life-threatening infections and cardiovascular disease.

"Most patients diagnosed at age 45 will be disabled in five or six years," Kremer said. "You have to consider what it costs to fix a bridge against what it will cost when the bridge collapses."

Before the use of disease-modifying drugs, direct medical costs from rheumatoid arthritis were estimated at US\$5.5 billion, and that did not include the indirect costs of lost wages and productivity, the need for custodial care and the emotional and social consequences of chronic disability.

While not everyone with rheumatoid arthritis responds to the new treatments as vividly as Moore did, many large studies have shown that there is no longer any reason for pessimism about the diagnosis. But it is vitally important to begin treatment early.

The recent therapeutic developments, Kremer said, mean that doctors in general practice need to remain alert to symptoms of the disease in its early stages and quickly refer patients to rheumatologists who can confirm the diagnosis and prescribe up-to-date treatment before irreparable damage to joints occurs. Treatment is most effective if begun within one year after symptoms appear.

There is no one treatment approach that works for everyone. Rather, studies have indicated that treatment should be tailored to individual patients: the nature and extent of their disease, their other health issues and how they respond to various therapies.

Kremer said that many patients could be started on a single, low-cost drug like methotrexate, as long as their condition was closely monitored and the treatment adjusted if there are signs of progressive disease.

Regular exercise and physical and occupational therapy, along with medication, can help patients maintain function. In addition to antirheumatic drugs to reduce inflammation, Kremer recommends fish oil at a daily dose of 2g of EPA and DHA — about six capsules as they are currently formulated.

How to troubleshoot and resolve Windows problems

With Microsoft software, what shouldn't happen often does. Here are some easy tips for nipping computer problems in the bud

BY JAY DOUGHERTY
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A Windows computer doesn't always do what you expect it to.

Sometimes the "shut down" command doesn't shut down the computer, for instance. Sometimes your mouse might not act the way it should and other times your PC slows down for no apparent reason.

How can you handle such glitches? Read on for some answers.

Q: My Windows XP PC refuses to shut down. It was shutting down fine a few days ago. Now when I click Shut Down, nothing happens. Why is this?

A: When something stops working that used to work fine, always look first at what has changed in the interim. Have you installed any new programs? Added any new hardware? Surfing any new Web sites? The solution can likely be found in the answers to those questions.

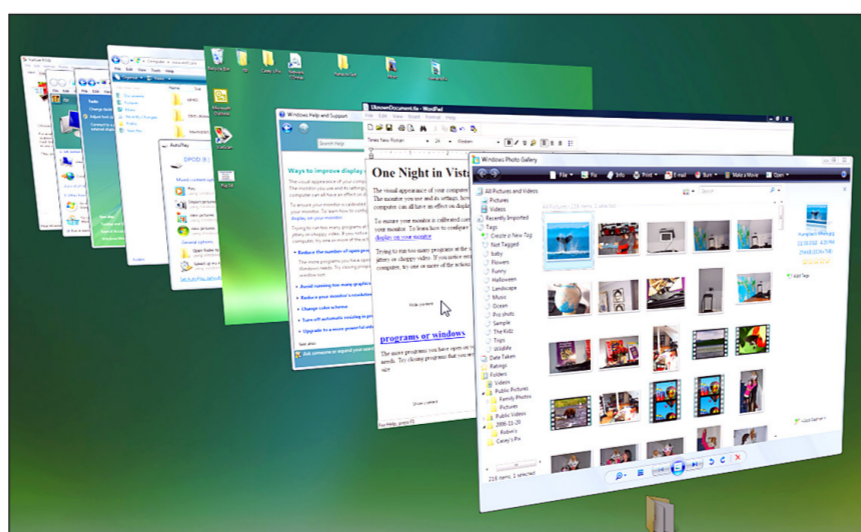
Lots of drivers and background programs have to be shut down before Windows itself will shut down. When one or more of these programs freezes or gets stuck, then Windows itself will

often seem not to respond to your shut down command. That shouldn't happen, but it does. If you've installed new software or hardware, you probably have new drivers or processes running that you didn't before. Undo your changes, one at a time, and see whether the problem goes away.

If you've visited any new Web sites or responded to unfamiliar e-mail recently, make sure that your computer is free of spyware or malware. Spyware often interferes with the normal operation of computers — especially shutdown. Download and run one of the free spyware removal programs — Windows Defender or Ad-Aware, for example.

Q: My mouse has started acting erratically. It moves on its own either to the lower left or the upper right of the screen. I can't control it. Do you have any suggestions?

A: There are a few things that can cause erratic mouse behavior. First, if you're using an optical mouse, swap the battery. A dead or dying battery could be the culprit. If you're using an older mouse with a roller ball on the



From refusing to shut down to annoying slowdowns, computers running Windows operating systems often do things users don't expect them to do.

PHOTO: NY TIMES NEWS SERVICE

underside, turn the mouse over, remove the ball, and clean any lint or dust from the mouse. Normally removing the ball is easy: Just twist the plastic cover that retains the ball, and it should drop right out.

Second, be sure that you do not have another input device attached to your computer that may be causing the problem. A drawing tablet with the pen left on the drawing surface, for instance, can cause the mouse cursor to move in

what appears to be a random fashion.

Finally, rely on the process of elimination: find yourself another mouse or input device, remove the existing one, and replace with the new to see if that one works as it should. If so, you may simply have a mouse that has gone bad.

Q: Lately, my Windows computer slows to a crawl. I'm not sure why. It's not exactly frozen, but everything takes a very long time. Switching from one window to another can take several minutes. How can I diagnose the problem?

A: First, make sure your PC has not become infected with spyware. Run Windows Defender and Ad-Aware to scan your system thoroughly.

If that doesn't work, find out what program or process is hogging your system resources. To do this, press Ctrl-Alt-Delete to bring up the Task Manager. From the Task Manager, Select the Process tab. There, you'll see a list of programs and processes that are currently running on your Windows computer.

The list of processes can be sorted by clicking on the column heading

according to which you would like to sort. For instance, to sort the list of active processes by CPU, click the CPU column heading. You want to do this in order to determine which process is consuming the most CPU cycles — and thus slowing down your computer.

Once you have sorted by CPU, you'll probably notice a process named System Idle Process at the top of the list. You can ignore this. Anything below that, however, that has a high number is probably responsible for the slowdown you experience.

Try to identify the program to which the process belongs simply by reading the name. If you can't figure it out, type the name into an Internet browser, and search for it on the Web. The application to which it belongs will probably be identified quickly. You can kill the process by right clicking its name in the Process tab, and selecting End Process from the resulting pop-up menu. Once you have identified the program that is consuming all of your CPU cycles, uninstall it. That should solve your problem.