

PSORIATIC ARTHRITIS NEWS AND VIEWS

VOLUME- 4 ISSUE- 14

October 15, 2004

PSORIATIC ARTHRITIS MEDICAL NEWS

\$30 BILLION VIOXX RECALL

Senior Journal - October 3, 2004

In a move that surprised and shook up many people - from patients to stock analysts -- Merck & Co. announced the withdrawal of the popular anti-inflammatory drug Vioxx from the market late last week due to a study that shows patients taking the drug face twice the risk of heart attack compared to those taking a placebo, especially those who had been taking the drug longer than 18 months.

Still, the Vioxx example raises concerns about FDA's review process along with how long it took Merck to remove the drug from the market. Vioxx is the first prescription drug to be pulled from pharmacy shelves in three years for safety concerns. A FDA spokeswoman says the agency has been pressured from all sides - medicine, industry and consumers - to approve new drugs more quickly or slowly depending on the demand or risk.

Another major concern: A Wake Forest professor who has researched clinical trials for three decades points out more than half of all drugs introduced in the market have a new side effect after their approval with the current system. In a related issue, medical experts are finding older, proven pharmaceuticals have become far more deadly when combined with newer drugs.

These issues point to a gap in FDA regulations to fail to assess the safety of pharmaceuticals after their approval. Although the federal agency received some 2,400 agreements these after-the-fact studies, less than 900 were actually conducted, according to a 2002 FDA report.

Some believe longer clinical trials could be the solution to the problem. For example, the increased risk of heart attacks and strokes among Vioxx users did not happen until they took the drug for 18 months. In fact, the Center for Drug Evaluations and Research says FDA will move in that direction for comparable drugs those that may be approved down the road.

The news also hit Merck hard on the Dow Jones Industrial Exchange. Shares of Merck & Co. lost more than a quarter of their value after the company pulled Vioxx from the market, plunging 26.8 percent to close at \$33.

In the meantime, a tidal wave of lawsuits has hit the courts in the United States, Canada and as far away as Israel. One lawsuit filed in Cook County Circuit Court alleges Merck knew about Vioxx's harmful side effects at least since the drug had been formally approved. Merck, argued one attorney, "intentionally tried to downplay the risks" until the evidence "was so overwhelming they had no choice."

The lawsuit could do serious harm to the company: Vioxx currently has 2 million users worldwide and some 84 million people have taken the drug since its approval by the FDA in 1999.

In reaction to the withdrawal of Vioxx, Pfizer Inc. has been informing wholesalers, pharmacy chains, pharmacy benefit managers and other managed care organizations that they will manufacture enough Celebrex, their Cox-2 inhibitor, to meet the patient demand. The company also cited three long-term studies of Celebrex that showed the drug does not have any significant safety issues.

October 3, 2004 The Senior Journal

Editors Note: These are some of my personal thoughts about the Vio xx recall. I have been on Vioxx for well over three years. Along with Psoriatic Arthritis, I also have Coronary Artery Disease and experienced one heart attack.

When I read the notice from Merck, I immediately stopped taking Vioxx and switched to generic ibuprofen until I could speak with my Rheumatologist. He has suggested that I switch to Bextra, not Celebrex. I am in the midst of doing extensive research on all Cox-2 inhibitors and NSAIDâ€™S before I decide what I am going to do. Then, I will have a discussion with my Doctor at my next appointment later this month.

Unfortunately, I have become quite skeptical of both the Pharmaceuticals and the FDA methodology for drug approval. I think it is mandatory for anyone on Vioxx to have a conversation with your main Caregiver. Please remember that you and only you are in charge of your health, which includes deciding what you are willing to take to gain relief. We know that all medications carry inherent risks and we alone are responsible for understanding and weighing those risk factors.

VIOXX WOES RAISE QUESTIONS ABOUT OTHER DRUGS
Are their problems with the FDAâ€™S review process?
The Associated Press - Oct. 4, 2004

WASHINGTON - Americans should feel reasonably safe taking government-approved prescription drugs â€™ with a few caveats â€™ even after a popular arthritis medication was pulled from the market, medical experts say.

Vioxx was the first prescription drug since 2001 to be taken off the market for safety reasons. Its maker, Merck & Co., cited an increased risk of heart attack and stroke in people who used the medication.

The withdrawal on Thursday came just weeks after the company defended the safety of the drug, which accounted for \$2.5 billion in worldwide sales in 2003,

and the Food and Drug Administration approved the use of Vioxx in children as young as 2 years old.

The problems with Vioxx raise questions about the agency's safety review process and the length of time it took Merck to pull the drug, observers say.

"No drug is fully safe," said Crystal Rice, an FDA spokeswoman. "Our job is to appropriately balance our decisions, based on the risk-benefit profile for a drug and the societal need and desire for new drugs," Rice said in an e-mail. "We believe that our actions regarding Vioxx were appropriate and consistent with our public health mission."

The FDA has come under intense pressure from the industry and elsewhere to approve drugs more quickly, despite clinical trials that some say enroll too few patients and for too short a time for worrisome side effects to surface.

Hidden problems

Research from Harvard, Vanderbilt University and Merck's own clinical trial long ago uncovered concerns about an increased risk of heart attacks and high blood pressure linked to Vioxx, said Dr. Jerry Avorn, who pointed to the issue in his book, "Powerful Medicines: The Benefits, Risks and Costs of Prescription Drugs."

"Why does it take this long for them to acknowledge the risk?" he asked.

"I

fear that FDA has gotten a little bit too cowed by industry demands to function as a good regulator," said Avorn, an associate professor of medicine at

Harvard Medical School who is affiliated with Brigham and Women's Hospital in

Boston.

An agency spokeswoman, Kathleen K. Quinn, said the FDA gets "pressure from all sides" — allegations that we're too fast, too slow. We make decisions based on the science. We weigh the benefits against the risks, ... and we make the tough calls."

Because of inherent limitations in clinical trials, problems can lie hidden until drugs go into wider use.

"More than half of all drugs introduced have a new side effect ... after approval with the current system. I find that disturbing," said Curt Furberg, a public health sciences professor at Wake Forest University School of Medicine. For three decades, Furberg has conducted research on how clinical trials are designed.

Dr. Wayne A. Ray, a Vanderbilt professor of preventive medicine, said the FDA has a reason to make judgment calls on less than perfect clinical trial data.

"The FDA is not going to hold up a medication for a generation to make sure it's safe. And similarly, they're not going to require you to study half a million people," Ray said.

Still, Ray acknowledged that after drugs are approved, data gaps loom larger.

Take a drug such as the widely used antibiotic erythromycin. When the antibiotic is used in concert with newer drugs, the risk of cardiac death is five times higher, according to a study that Ray conducted. The findings were published in early September in the New England Journal of Medicine.

An FDA spokesman said erythromycin labels already note that risk. Still, the agency is reviewing the study to see if additional label changes are warranted.

Ray said the single study points to a larger problem.

“There is no provision for systematically assessing and reviewing the safety of the many, many medications that are out there,” Ray said. “And the patients are the ones who are going to suffer.”

The vast majority of companies do not follow through on promises to conduct those reviews, the FDA says. The FDA received 2,400 agreements to conduct post-marketing studies on drugs. Only 882 such studies were completed, according to an FDA analysis from Feb. 8, 2002, the most recent data available.

The FDA could take a simple step that would improve clinical trial quality before it approved drugs, observers say. Drug companies with products comparable to Vioxx could be required to conduct longer clinical trials.

“If you’re the FDA, you’ll say ‘OK, all bets are off. We’re going to make you do studies lasting 18 months,’” said Dr. Sidney Wolfe, director of Public Citizen.

At the time of approval, the FDA had data from clinical trials on Vioxx that lasted for 12 months. The increased risk of heart attack and stroke that prompted Merck to pull Vioxx did not begin to appear until older patients had taken the drug for 18 months.

In a telephone briefing with reporters, Dr. Steven Galson, the agency’s acting director of the Center for Drug Evaluation and Research, said the FDA will move in that direction for comparable drugs on the market and for such drugs that might be approved in the future.

“It’s too early for me to say, right now, how we’re going to change our requirements,” Galson said. “But, obviously, we’re going to be more interested in long-term data.”

© 2004 The Associated Press. All rights reserved.

CENTOCOR WARNS OF REMICADE-LYMPHOMA RISK October 8, 2004

WASHINGTON (AP) -- Patients taking Remicade for rheumatoid arthritis suffered a type of cancer, lymphoma, at three times the rate of the general public,

manufacturer Centocor warned doctors on Thursday.

Centocor, a subsidiary of Johnson & Johnson, said the lymphoma incidence rate was six times higher among all patients who took the monoclonal antibody in completed clinical trials.

Experts said such toxic outcomes, however, are still rare, and that the new drugs, on balance, work markedly better than older medications, without such side effects as nausea and fatigue.

The Malvern, Pa.-based company, working with the federal drug regulatory agency, revised its label to reflect the lymphoma risk. According to NDCHealth,

Remicade was the 28th top selling drug in 2003, with \$1.5 billion in U.S. sales.

The label change is the drug's second in six weeks. In late August, Centocor warned that people taking Remicade for rheumatoid arthritis and Crohn's disease can sometimes experience fatal blood and central nervous system disorders. At least 12 people taking Remicade -- in combination with other drugs -- died worldwide.

The Food and Drug Administration said then that those deaths could not be linked definitively to Remicade use.

The company's new warning letter to doctors, released Thursday, said patients receiving Remicade suffered higher rates of lymphoma than seen in the general population. Lymphoma is cancer of the cells of the lymphatic system, tissues and organs involved in fighting infection.

Centocor said the label change is in line with warnings recently added to others drugs, such as Enbrel and Humira, in the new class that block overproduction of TNF, an inflammation-regulating protein thought to lie at the heart of rheumatoid arthritis and other autoimmune disorders.

Rheumatoid arthritis is a disease in which the body's immune system rebels, treating its own tissues as enemies to attack. Some 2.1 million Americans suffer from this illness, which ultimately deteriorates cartilage and destroys joints.

Centocor found that three people developed lymphoma among 2,410 patients taking Remicade to treat Crohn's disease or rheumatoid arthritis. That was six times higher than the lymphoma rate among healthy individuals.

But such autoimmune diseases up the odds of suffering lymphoma, making it difficult to determine whether to blame the drugs or the underlying disease.

"That's the issue here," said Dr. Tom Schaible, Centocor vice president of medical affairs. "There's not enough signal coming out of the population of patients receiving TNF blockers to distinguish it from what the underlying risk

is in those diseases."

By neutralizing the overproduced protein, the new class of biologically engineered drugs relieves painful symptoms.

But an FDA advisory panel last year debated whether Amgen and Wyeth's Enbrel, Abbott Laboratories' Humira and Centocor's Remicade were also linked to 170 cases of lymphoma reported among the drugs' recipients since 1998.

"The drugs that we use are powerful because they do affect the immune system. And that's how they work in arthritis," said Steven Abramson, who was acting chairman during that March 2003 advisory committee session that scrutinized the increase in adverse events, including lymphoma.

"The good news is that you don't feel rotten taking the drug every day," said Abramson, chairman of rheumatology at New York University Hospital for Joint Diseases.

Last week, the agency approved using a combination of Remicade and methotrexate as a first-line treatment for patients with rheumatoid arthritis.

Phase three clinical trials indicated one in three patients taking the drug showed marked improvement in their psoriatic arthritis. Later this year, the company will ask the FDA to expand the drug's usage. Copyright 2004 The Associated Press.

NEW ANTI-INFLAMMATORY DRUGS DAMAGE YOUR BONES

Some painkilling drugs may delay or even prevent the healing of fractures.

The main concern is the new generation of non-steroidal anti-inflammatory drugs (NSAIDs). Both drugs, Vioxx and Celebrex, are often used to ease the pain of broken bones.

But for over 20 years there have been occasional reports of impaired bone healing in patients taking NSAIDs. The issue may have escaped attention because

the older generation of NSAIDs, such as ibuprofen and indomethacin, only appear to delay healing by a few weeks instead of blocking it. Interestingly, aspirin is one of the few NSAIDs that appears to kill pain without this side effect.

Ibuprofen and indomethacin delay bone healing by about one to two weeks in rats, which is the equivalent to slowing it down by 25 to 50 per cent in humans. None of the rats treated with Vioxx managed to heal their bones. In those treated with Celebrex, none managed to completely heal their bones but about half had some form of bone regrowth.

Traditional NSAIDs inhibit the enzymes cox-1 and cox-2. Cox-2 catalyses the production of hormone-like chemicals known as prostaglandins involved in inflammation, while cox-1 has a variety of roles not specific to the inflammatory response. Since the new generation of NSAIDs such as Celebrex block cox-2

almost exclusively, it was hoped they would have fewer side effects.

But it now seems that cox-2 may be crucial in helping bone-forming stem cells and growth factors do their work.

Journal of Bone and Mineral Research June 2002 17:963

Comments from Dr. Mercola's website: You should always use drugs with caution as they frequently cause more harm than good. It appears that if you have a broken bone, you should avoid Celebrex and Vioxx if you want your bones to heal properly.

Although there are many reasons to avoid Celebrex and Vioxx, the primary reason is because they increase your risk of heart disease. Seeing that this is

the number one cause of death, it would seem prudent to avoid them. If you decide to treat pain with a drug, consider aspirin. Aspirin is not associated with causing heart disease, but has caused ulcers in some people. It is recommended to take aspirin with a large amount of food.

FOR ARTHRITIS ADVIL TOPS TYLENOL

Background: Perhaps the most common pain medications are ibuprofen and acetaminophen. Both are available OTC (over the counter) -- without a prescription. Ibuprofen is sold under the brand names Advil, Children's Advil/Motrin, Medipren, Motrin, Nuprin, Pediacare Fever etc. while acetaminophen is sold under the name of Tylenol.

Summary: Ibuprofen provides better relief of pain than acetaminophen in the most common type of arthritis (osteoarthritis), according to a direct comparison reported in the Annals of Rheumatic Diseases.

Comment: This information may be especially useful since one of the most popular prescription drugs for arthritis, Vioxx, has been pulled off the market.

Barbara K. Hecht, Ph.D.
Frederick Hecht, M.D.
Medical Editors, MedicineNet.com

IBUPROFEN TOPS ACETAMINOPHEN FOR ARTHRITIS - STUDY

NEW YORK (Reuters Health) - Ibuprofen provides better relief of osteoarthritis pain than does acetaminophen, according to results of a head-to-head comparison study.

Ibuprofen (the ingredient in Advil, Motrin and many other painkillers) and acetaminophen (also known as paracetamol, and the ingredient in Tylenol and numerous other brands) are both better than placebo for treating various types

of pain, researchers note in the Annals of the Rheumatic Diseases.

However, very few studies have directly compared the two drugs for treating pain due to osteoarthritis, the wear-and-tear form of joint degeneration.

Dr. Francois Boureau from Saint-Antoine Hospital, Paris, France and colleagues compared the pain-relieving effectiveness of single and multiple doses of ibuprofen and acetaminophen in 222 patients with knee or hip osteoarthritis.

Pain relief the first 6 hours after a single dose of ibuprofen (400 milligrams) was significantly greater than after a single dose of acetaminophen (1000 mg), the authors report.

After two weeks of thrice-daily treatment, participants taking ibuprofen had significantly less pain and significantly more improvement in stiffness and physical function than did the group given acetaminophen.

Sleep quality improved in both groups, the report indicates, with no meaningful difference between the treatments.

There were no significant differences in the number or severity of adverse events reported by the two groups.

SOURCE: Annals of the Rheumatic Diseases, September 2004. Copyright © 2004 Reuters Limited. All rights reserved.
© 1996-2004 MedicineNet, Inc. All rights reserved.

NEW ARTHRITIS DRUG SHOWS PROMISE

Experimental medication has few side effects, study finds

The Associated Press Nov. 12 - An experimental new drug designed to shut down the body's misguided assault on its own joints is showing promise against

rheumatoid arthritis, relieving its crippling effects with few if any side effects.

The drug, still in testing, neutralizes the immune system T cells that help direct the assault.

It could give doctors another weapon in their arsenal of drugs against rheumatoid arthritis, which afflicts 2.1 million Americans.

Other drugs target some of the processes that underlie rheumatoid arthritis, but this is the first to attack the disease in precisely this way.

In a study of 339 patients, CTLA4Ig was added to methotrexate - the standard drug - in arthritis sufferers who had not gotten enough relief from methotrexate and still had many swollen and painful joints.

After six months, 60 percent of these patients were feeling better - some of them dramatically so. Only 35 percent of the patients on methotrexate alone reported some relief.

â€œIâ€™m very excited about it. But thereâ€™s still a considerable amount of work to be done,â€ said Dr. Gary Firestein, chief of rheumatology, allergy and immunology at the University of California at San Diego and chairman of the Food and Drug Administrationâ€™s arthritis advisory committee.

Bristol-Myers Squibb Co. said it expects to apply to the FDA some time next year for approval to sell the drug.

More than 2,000 patients are taking part in the final round of tests needed to win FDA approval.

The findings were published in the New England Journal of Medicine. The study was led by Dr. Joel M. Kremer, director of research at the Center for Rheumatology in Albany, N.Y., and clinical professor of medicine at Albany Medical College.

The drug cannot be taken by mouth; it must be given by an intravenous infusion. In the study, it was given three times in one month, then once every month after that for five months. People who received it with methotrexate had no more side effects than those who got only methotrexate.

CTLA4Ig is one of many drugs on the market or in development that take advantage of scientistsâ€™ clearer understanding of the complicated processes of inflammation and autoimmune diseases. Different drugs take aim at different parts of the process.

TNF inhibitors, for example, target an inflammation-causing protein called tumor necrosis factor, or TNF.

Methotrexate, originally developed to fight cancer, replaced gold salts â€” which helped fewer than one-third of all patients â€” as the standard drug against rheumatoid arthritis in the late 1980s. But two-thirds of all patients still hurt. TNF inhibitors have helped some of them.

Firestein said there is a good chance that people who do not respond to TNF inhibitors will respond to the new drug.

â€œEach time, the slice of the pie of people who do not respond gets thinner and thinner,â€ he said.

Â© 2004 The Associated Press. All rights reserved.

FDA APPROVES CHOLESTEROL DRUG - VYTORIN

WASHINGTON (AP)-- The Food and Drug Administration has approved a new cholesterol-lowering drug called Vytorin, the agency said Friday.

The pill, manufactured and marketed by a joint venture between Merck & Co. Inc. and Schering-Plough Corp., is a combination of two other cholesterol drugs, Zetia and Zocor.

Vytorin has been shown in studies to lower cholesterol better than market leader Lipitor, which holds a 55 percent share of prescriptions and 49 percent of sales.

Zocor is from the class of drugs known as statins, and lowers cholesterol by cutting its production in the liver. Zetia, meanwhile, limits the absorption of cholesterol in the intestines.

Vytorin's approval coincides with the release last week of new guidelines that call for high-risk heart patients to lower their so-called bad cholesterol,

or LDL, to 70 instead of 100 as previously recommended. Copyright 2004 The Associated Press.

HIGH DOSES OF CHOLESTEROL DRUG RAISES QUESTIONS

ATLANTA (The Cox News Service) -- Like many people with heart disease, Eugene Guy was encouraged but a little confused. Guy, 79, read about a landmark

study last week that suggested that high doses of a cholesterol-lowering drug reduced the heart attack rate among patients with heart disease. Guy takes 5 milligrams daily of Lipitor, the drug used in the study.

He was curious: Because the patients were given 80 milligrams of Lipitor, should he take a higher dose to drive down his bad cholesterol levels? "I was wondering whether I should increase that thing (the Lipitor)," said Guy. "I just don't really know." Guy called his cardiologist to make an appointment to discuss his heart health, his cholesterol levels and the benefit of the cholesterol-lowering drugs, called statins.

Doctors and researchers said that's exactly what people with heart disease and others at risk for it should do. The findings showed that heart patients treated with a high dose of Lipitor, which has been called the gorilla drug of the statins, fared better than those treated with a lower dose of a less powerful drug, Pravachol. The study also suggested that bad cholesterol might need to be even lower than 100 for those at high risk for heart disease.

But the study, provocative and promising though it may be, left many patients with questions. If your bad cholesterol level is greater than 100 but you have no other known risk factor, do you need to take a statin to lower it? How do you determine your risk factors?

And, because the study also suggested that 25 million more people should take statins, in addition to the 12 million Americans who currently do, just who among us should be taking statins?

Dr. Mary Ellen Sweeney, an Emory University endocrinologist who is also a director of the Atlanta area American Heart Association, answered some general

questions about the study.

Q: If statins drive down bad cholesterol levels, does that mean everyone should take them?

A: No. There's always risk with medications, and taking statins is a lifelong treatment. Once you commit to it, you're on it. There's little data on the side effects of lifelong use of statins. This study was in a very specific population -- people at high risk, after they had suffered a heart attack or severe chest pains that required hospitalization. And, not everyone needs them.

Q: Who should take statins?

A: Those with high levels of bad, or LDL, cholesterol who are at high risk, and those at moderate risk level with high levels of bad cholesterol who are beyond a certain age -- 45 for men and 55 for women -- should talk to their doctors about statins.

Q: What is high risk?

A: Patients who have had a heart attack, those who have diabetes and those with a family history of heart attack, especially before age 40.

Q: If I'm not at high risk, am I off the hook?

A: No. All Americans are at some risk for heart disease; it is the nation's No. 1 killer.

Q: What is moderate risk, and what do I do if I'm at moderate risk?

A: If you have two or more risk factors -- male over age 45 or female over age 55, high blood pressure -- you are at moderate risk. Your treatment will depend on how high your cholesterol is. If your LDL level is up to 160, you need to change your diet and exercise as a first line of treatment. You may then need to add statins if diet and exercise do not work to lower your bad cholesterol.

Q: What is low risk, and do I need to do anything if I'm at low risk?

A: Low risk is generally only one risk factor, such as being a 40-year-old male. Talk to your doctor about lifestyle changes. All Americans -- even those at low risk -- need to eat five servings of fruits and vegetables, avoid smoking, exercise at least three times weekly and limit dietary fats.

Q: What are the drawbacks to statins?

A: In a small number of patients -- studies suggest between 1 (percent) and 3 percent -- the liver is harmed. They also are expensive, costing as much as \$100 a month.

Q: Are there options to statins?

A: Therapeutic lifestyle changes, or TLC, are options for many people to drive down their cholesterol. Losing weight, limiting dietary fat and exercise are all part of a heart-healthy lifestyle. But for millions of people, statins are the best line of treatment.

Q: What's the most important message from this landmark study?

A: The optimal LDL level for everyone is 100, but we don't necessarily need drugs to get there. More than anything, people need to know their risk factors, know their cholesterol numbers, and follow a heart-healthy lifestyle. Make

sure you ask your doctor to test for cholesterol. Women should ask their gynecologists about cholesterol testing, if their gynecologist is the only doctor they see once a year.

HIGH CHOLESTEROL RAISES RISK OF HEART DISEASE A total cholesterol of less than 200 is desirable. Even in the absence of other known risk factors, a cholesterol level of 240 or above doubles a person's risk for heart disease.

- Total cholesterol of less than 200: desirable
- Total cholesterol of 200-239: borderline high
- Total cholesterol of 240 or above: high

LEVELS OF BAD CHOLESTEROL OR LDL Cholesterol has many components, one of which is low-density lipoprotein, or LDL, the so-called bad cholesterol. The higher the LDL, the higher the risk of heart disease. A person with fewer than two risk factors should aim for an LDL of no higher than 160; more than two risk factors, no higher than 130; and those who already have heart disease should have LDL lower than 100.

- Less than 100: optimal
- 100-129: near or above optimal
- 130-159: borderline high
- 160-189: high
- 190 or above: very high

A STATIN A DAY TO KEEP HEART DISEASE AWAY?

Drugs called statins have been used successfully over the past 10 years to drive down cholesterol levels. They are so popular that they now are the most widely prescribed class of drugs in the country. But a healthy lifestyle -- eating a diet low in fat, losing weight, regular exercise -- also can lower cholesterol in many people.

A cardiologist can help assess your risk factors and whether you need a statin by looking at your medical and family history.

High risk:

- Previous heart attack
- Diabetes
- Family history of heart attack

Other risk factors for heart disease:

- Smoking
- Increased age (over 45 for men; 55 for women)
- Male gender
- Metabolic syndrome
- Low levels of high-density lipoproteins, or HDL
- High levels of triglycerides

Copyright 2004 The Cox News Service. All rights reserved.

POSSIBLE NEW CURE FOR PSORIASIS FOUND

(My thanks once again to our roving reporter from the United Kingdom - Michael Szczygiel.)

BONN, GERMANY: Cell biologists of the University of Bonn, in cooperation with the University of Leeds (U.K.) and industry may have discovered a new effective therapy for psoriasis -- a specific group of what are known as metalloproteinase inhibitors that can normalise the increased tendency of epidermis cells (keratinocytes) to divide, which is the cause of this unpleasant lepidosis.

The researchers were not able to detect any toxic side-effects, at least not in cell cultures. Their findings are being published in the Journal of Investigative Dermatology (Vol. 123, No. 3).

About 2 million Germans suffer from psoriasis (from the Greek psora meaning 'itching, scratching'). In this incurable disease the regeneration of the epidermis is speeded up enormously: whereas it normally renews itself in just under four weeks, this period is cut to four to seven days in psoriasis patients. The reason is the greatly increased rate of cell division of the keratinocytes. They form a layer that separates the epidermis from the dermis, which lies beneath it. The ageing cells pass from this germinal layer to the surface until they finally scale off.

The disease progresses in waves. Its typical features are clearly defined red areas covered with silvery white scales. In the Middle Ages they were thought to be the symptoms of leprosy; a large number of the 'lepers' who were persecuted and even burnt were probably suffering from psoriasis, which is not contagious. What is worse than the changes to the skin itself is the stigma attached to the disease.

"During one of the periods when the disease is more intense many patients think that it is unreasonable to expect people to put up with their presence," explains cytobiologist Professor Volker Herzog. "Some patients withdraw completely; depressions are not infrequent."

No toxic side effects

One of the substances that stimulate the division of the keratinocytes is the protein sAPPalpha. It is produced during the decomposition of a larger protein, APP. The keratinocytes produce an enzyme that cuts the APP down to size

as sAPPalpha: this is known as the alpha-secretase. Professor Herzog's research team has now blocked these "molecular scissors."

"We knew that certain metalloproteinase inhibitors impede the alpha-secretase. After adding these substances we observed that the discharge of sAPPalpha was almost completely arrested in the cells of psoriasis patients. As a result, after adding them the greatly increased division rate of the keratinocytes dropped back to normal values by 50 to 60%," explains Christina Siemes, a member of Professor Herzog's team. "We have been able to confirm this in skin specimens of five psoriasis patients," she says.

The inhibiting effect of the metalloproteinase inhibitors largely wore off within 72 hours. Moreover, even with fivefold concentration of the active ingredient the research team could not detect any toxic side-effects. For

example, among other aspects the number of skin cells, which entered into apoptosis, remained constant (apoptosis is the cells' "suicide" programme, which enables them to self-destruct when they are malfunctioning). The cellular protein synthesis was also unaffected.

"Treatment using the metalloproteinase inhibitors which we have been investigating seems to be a new and very promising therapeutic option for psoriasis," Professor Herzog therefore believes. "This won't be a magic solution to all our problems, of course -- after all, every skin reacts differently."

Furthermore, the substances only alleviate the symptoms. They do not remove the root of the evil, viz. the chronic inflammation of the skin caused by constant attacks by the body's own immune system, to which the keratinocytes react with feverish activity in the cell division field.

The researchers now intend to test their method on animals, using naked mice on which they have transplanted the skin tissue of psoriasis patients. They want to apply the active ingredients locally as an ointment. In addition, the first tests on human beings are planned for the immediate future. SOURCE: Institute of Cell Biology of the University of Bonn

Good Health to All,

Jack Nicholas
Newsletter Editor
Cornishpro@aol.com (mailto:Cornishpro@aol.com)

Issue 2004 10/15/04 -14