



## MERCK, NYCOMED TO JOINTLY MARKET COPD TREATMENT

Merck & Co. and Nycomed agreed to jointly market Daxas, a once-daily tablet under assessment to treat patients with chronic obstructive pulmonary disease. In a Monday statement, the companies said they would co-promote the drug, generically known as roflumilast, in Canada and certain European countries. And they signed an agreement under which Merck will distribute the drug in the U.K. as well. Under the terms, Nycomed will receive an up-front payment from the Whitehouse Station, N.J., health-care giant (MRK 35.48, +0.23, +0.65%), and is eligible for milestone payments. Terms weren't disclosed. In 2009, closely held Nycomed filed a new drug application for Daxas with the U.S. Food and Drug Administration. On April 23, 2010, Nycomed, Zurich, said that a panel within the European Medicines Agency had urged the agency to approve the drug for marketing in the E.U. <http://tinyurl.com/2axtyk2lung> disease, but a new Dutch study suggests the tradition is wrong.

A study of more than 2,200 people with chronic obstructive pulmonary disease (COPD), a diagnosis that includes emphysema and chronic bronchitis, found better survival among those given beta blockers than those who did not get the drugs, claims a report in the May 24 issue of the Archives of Internal Medicine by physicians at University Medical Center Utrecht.

"To our knowledge, this is the first observational study that shows that long-term treatment with beta blockers may improve survival and reduce the risk of exacerbation of COPD in the broad spectrum of patients with a diagnosis of COPD," the researchers wrote.

"This is strikingly different from what our medical students are taught today," said Dr. Don D. Sin, a professor of medicine at the University of British Columbia in Vancouver, Canada, and co-author of an accompanying editorial. "Our traditional teachings are wrong."

The rap against beta blockers has been that while they improve heart function, they can cause airways to contract, a problem for people with COPD, Sin explained. "They demonstrate in this article that even people with COPD who use beta blockers did very well, better than people who didn't use beta blockers," he said.

Fears about beta blockers and COPD date back to the 1980s, when there were reports of "some nasty effects in patients with asthma, especially with high doses," said study author Dr. Frans

H. Rutten, an assistant professor of medicine at Utrecht. The study demonstrates that the drugs can be handled safely for people with COPD, he noted.

"I know of no real problems now, especially when you start with a low dose so that the bronchial airways can adjust to the drug," Rutten said.

COPD was diagnosed in 560 patients at the start of the study in 1996, and 1,670 developed the condition by the end, in 2006. Of these, 665 were prescribed beta blockers for heart conditions, while 1,565 were not.

During an average follow-up time of 7.2 years, 27.2 percent of the people who took beta blockers died, compared to 32.3 percent of those not given the drug. The incidence of exacerbation -- severe flare-up -- of COPD was 42.7 percent among beta blocker users and 49.3 percent among nonusers.

The study isn't the final word on beta blockers and COPD, Sin said. That would have to come from a randomized, controlled study, which almost certainly will never be done, he said.

"If I had a heart attack, I wouldn't want to be in a clinical trial where there was a 50 percent chance I would get a sugar pill," Sin said. "So, this study may be the best evidence we get."

And the incentive of profit from increased use of beta blockers isn't there to have a drug company fund such a trial, since beta blockers are widely available in inexpensive, generic form, he added.

Sin acknowledged that he has an "outlier" on the issue, already prescribing beta blockers for people with

COPD. "But with this paper, I am much more confident that COPD patients can tolerate beta blockers," he said.

There are some exceptions, Sin noted. "For people with very bad asthma who have very reactive airways, I am much more cautious," he said. "I would start with the lowest dose possible, and then titrate upwards." <http://tinyurl.com/38gmpux> asthma symptoms by relaxing airways, making breathing easier."

Professor Bradding added: "Despite their usefulness in rapidly relieving asthma, relievers may cause asthma to worsen when used too frequently. Moreover, they are not always as effective as predicted. We investigated mechanisms behind this by studying interactions between reliever medicines and the immune system.



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"Our immune system uses antibodies (a type of protein found in blood and other body fluids) to identify foreign bacteria and viruses and neutralise their effects. Asthma is commonly associated with allergies, which are caused by antibodies called IgE which react with allergens such as house dust mite and grass.. IgE binds to mast cells in lungs of asthma sufferers. This, in turn, causes mast cells to release chemicals such as histamine, which cause narrowing of lung airways and thus, lead to an asthma attack."

Mast cells need a chemical known as stem cell factor to survive and function and this chemical is present in asthmatic lungs. Professor Bradding's research shows that when lung mast cells are exposed to reliever drugs, in the presence of both IgE and stem cell factor, relievers lose their ability to prevent chemical release from mast cells. Interestingly, under these circumstances, relievers may actually cause mast cells to release more chemicals, causing asthma to worsen.

Professor Bradding says, "This research might explain why reliever drugs are not always as effective as predicted, why they might worsen and destabilise asthma." This research has important consequences for individuals with poorly controlled asthma and for those who rely too heavily on relievers, whilst not using their preventer medication regularly. Professor Bradding adds, "If we can inhibit the function of stem cell factor in the lungs of asthmatic patients, reliever drugs such as salbutamol, might be more effective."

If future research reinforces these findings, then this work could lead to the development of new treatment strategies that could benefit thousands of people. The research is funded by Asthma UK.

Dr Elaine Vickers, Research Relations Manager at Asthma UK says: "Millions of people around the world use reliever inhalers that contain medicines such as salbutamol and these devices play a crucial role in relieving asthma symptoms. Professor Bradding aims to understand why it is that people who use their reliever inhalers too often, without using a preventer inhaler, are putting themselves at risk of worse asthma symptoms.

"We hope that the results of Professor Bradding's work will lead to the development of drugs that overcome the problems associated with over-use of reliever inhalers but in the meantime we would urge anyone who needs to use their reliever inhaler three or more times a week to visit their doctor or asthma nurse to have their symptoms reviewed. We would also urge people with asthma to use their preventer inhalers as prescribed. This should not only control symptoms, but also guard against any harmful effects of frequent reliever use."

<http://tinyurl.com/yc2mnjv>



### **HEART ATTACK RISK DOUBLES AFTER COPD EXACERBATION, STUDY FINDS**

Patients with chronic obstructive pulmonary disease (COPD) who experience an exacerbation have an increased risk for both myocardial infarctions (MI) and ischemic stroke.

Researchers from the United Kingdom analyzed the risk of MI or stroke after exacerbation of COPD in 25,857 patients with

the disease. Among the patients, 524 MI were identified in 426 patients and 633 ischemic strokes in 482 patients.

Results showed that exacerbation rates were significantly higher in patients with COPD experiencing MI or stroke compared with those who did not suffer from these conditions. In addition, there was a 2.27-fold increased risk of MI 1 to 5 days after a COPD exacerbation and a 1.26-fold increase of stroke 1 to 49 days after a COPD exacerbation.

Researchers suggest the findings provide good rationale for treating patients with COPD in both the stable and exacerbation states to reduce cardiovascular events.

This study is published in the May issue of CHEST, the peer-reviewed journal of the American College of Chest Physicians

<http://tinyurl.com/24kqbgj>



### **COPD FLARE-UP MAY RAISE RISK OF HEART ATTACK, STROKE**

*Findings show need for treatment even when pulmonary disease looks stable, researchers say*

Worsening of chronic obstructive pulmonary disease (COPD) leads to increased risk for heart attack and ischemic stroke, a new study finds.

British researchers looked at 25,857 COPD patients and identified 524 heart attacks in 426 patients and 633 ischemic strokes (blockage of blood flow to brain) in 482 patients. The patients who suffered heart attack or stroke had significantly higher rates of worsening (exacerbation) of COPD.

The study also found a 2.27-fold increased risk of heart attack one to five days after COPD exacerbation and a 1.26-fold increased risk of stroke one to 49 days after COPD exacerbation.

The findings suggest that patients with COPD in both the stable and exacerbation states require treatment to reduce the risk of heart attack and stroke, the researchers concluded.

The study is published in the May issue of the journal Chest.

<http://tinyurl.com/2334nhk>



### **EARLY ANTIBIOTIC TREATMENT FOR SEVERE COPD SYMPTOMS LINKED WITH IMPROVED OUTCOMES**

Among patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease (COPD), those who received antibiotics in the first 2 hospital days had improved outcomes, such as a lower likelihood of mechanical ventilation and fewer readmissions, compared to patients who received antibiotics later or not at all, according to a study in the May 26 issue of JAMA.

The fourth leading cause of death in the United States is COPD, which affects at least 12 million U.S. residents. "Acute exacerbations of COPD are responsible for more than 600,000 hospitalizations annually, resulting in direct costs of more than \$20 billion," the authors write. "Guidelines recommend antibiotic therapy for acute exacerbations of COPD, but the evidence is based on small, heterogeneous trials, few of which include hospitalized patients."

Michael B. Rothberg, M.D., M.P.H., of Baystate Medical Center, Springfield, Mass., and colleagues examined the association between use of antibiotics and outcomes among patients (40 years of age or older) hospitalized for acute exacerbations of COPD at 413 acute care facilities throughout the United States, between January 2006 and December 2007. The primary outcomes analyzed included a composite measure of treatment failure, defined as the initiation of mechanical ventilation after the second hospital day, inpatient mortality, or readmission for acute exacerbations of COPD within 30 days of discharge; length of stay, and hospital costs.

Of 84,621 patients, 79 percent received at least 2 consecutive days of antibiotic treatment. The researchers found that compared with patients not receiving antibiotics in the first 2 days, antibiotic-treated patients were less likely to receive mechanical ventilation after the second hospital day (1.07 percent vs. 1.80 percent), had lower inpatient mortality (1.04 percent vs. 1.59 percent), a lower incidence of treatment failure (9.77 percent vs. 11.75 percent), and lower rates of readmission for acute exacerbations of COPD (7.91 percent vs. 8.79 percent). Patients treated with and without antibiotics had similar lengths of stay, but patients treated with antibiotics had lower costs.

Patients treated with antibiotic agents had a higher rate of readmissions for the bacterial infection *Clostridium difficile* than those who were not treated. After further analysis, the risk of treatment failure was lower in antibiotic-treated patients. "Analysis stratified by risk of treatment failure found similar magnitudes of benefit across all subgroups," the authors write.

The researchers add that two findings, that all patient groups seemed to benefit from therapy and that harms were minimal, support the notion that all patients hospitalized with acute exacerbations of COPD should be prescribed antibiotics. "This recommendation, however, is not consistent with the fact that roughly 50 percent of COPD patients do not have a bacterial etiology for their exacerbation. Identifying these patients remains a challenge, because sputum cultures do not distinguish between active infection and colonization. New bacterial infections may cause exacerbations and are associated with increases in inflammatory markers, ... whereas colonization is not."

"... until more data are available, routine use of antibiotics for acute exacerbations of COPD may be appropriate," the authors conclude.

<http://tinyurl.com/3515xx6>



## VITAMIN E MAY PROTECT LUNGS

Experts believe vitamins A, C, and E combat oxidative stress in the lungs that can lead to COPD. COPD includes emphysema and chronic bronchitis; often, but not always, caused by smoking.

People who take vitamin E supplements regularly for years -- whether they are smokers or nonsmokers -- may lower their risk of chronic obstructive pulmonary disease, the lung condition that is the fourth leading cause of death in the United States. COPD includes emphysema and chronic bronchitis and is often, but not always, caused by smoking.

While the risk reduction is relatively small, 10 percent, COPD is a common and life-threatening condition in which a

decline in lung function can be slowed down but not reversed. COPD symptoms include shortness of breath, coughing, and fatigue.

"The effect appears to be modest. But for something for which there isn't really any effective therapy and tends to be a degenerative condition, anything that would reduce the risk even somewhat is not an insubstantial benefit," says Jeffrey B. Blumberg, Ph.D., a professor of nutrition at Tufts University in Boston who was not involved in the study.

The research, from the government-funded Women's Health Study, included 39,876 women 45 years and older who were free of COPD before they were randomly assigned to take a placebo, vitamin E supplements (600 IU every other day) or aspirin (100 mg per day), either alone or in combination. At the end of 10 years, 760 of the 19,937 women who took vitamin E alone or with aspirin developed COPD compared with 846 of the 19,939 who took a placebo or aspirin alone -- a 10 percent risk reduction. Vitamin E did not lower the risk of asthma, a condition associated with a higher risk of COPD.

The researchers took into account factors such as cigarette smoking and age, which can affect COPD risk. The study, conducted by Cornell University and Brigham and Women's Hospital researchers, is to be presented this week at the annual American Thoracic Society meeting in New Orleans.

The idea that vitamin E can reduce the risk of developing COPD is "biologically plausible," says Yvonne Kelly, Ph.D., an associate professor in the department of epidemiology and public health at University College London. Experts believe vitamins A, C, and E -- the so-called ACE antioxidants -- combat oxidative stress in the lungs that can lead to COPD.

Several studies have shown that these vitamins, as well as vitamin D, may help improve lung health. In a 2003 study, Kelly and her collaborators found that men and women with diets high in vitamins C and E had greater lung capacity and produced less phlegm, respectively. Phlegm production and wheezing are also COPD symptoms.

One limitation of the study is that the researchers relied on the women to report whether or not they had a diagnosis of COPD, says Michael Sims, M.D., an assistant professor in the pulmonary critical care division at the University of Pennsylvania Medical Center. He points out that people with asthma may think they have COPD, or vice versa, since the symptoms are similar. In addition, early diagnoses can be inconclusive or due to lung problems that don't turn out to be COPD.

In future studies, Sims says that the researchers should diagnose COPD using a breathing test called spirometry. "If you showed in a similar study with a gold standard outcome [like spirometry], among smokers and nonsmokers, that you could affect the incidence of COPD, I would imagine the committees that meet on this would take a serious look at increasing daily recommended intake [of vitamin E] for the general population," he says.

Currently, no vitamin supplements are recommended to prevent or treat COPD. The best way to prevent the disease is to quit smoking, says Dr. Sims. About 24 million people in the

U.S. have COPD -- 12 million who've been diagnosed with the disease and another 12 million who have COPD but don't know they have it. In the study, women who smoked were four times more likely than nonsmokers to develop COPD.

The daily recommended intake of vitamin E is about 22 international units for those 14 and older, and is relatively easy to obtain from oils such as sunflower, almonds, peanut butter, and spinach.

The vitamin E intake in the study was far higher, at 300 IU per day. However, Blumberg says this is within the range of most over-the-counter vitamin supplements, which deliver 100 or 400 IU daily. "This study is still five times below the highest dose at which no adverse effect has been found," he says.

Vitamin E intake is generally a concern only at very high doses, above 1500 IU per day. Several studies have suggested that these levels promote hemorrhaging and interfere with normal blood clotting. For this reason, high doses of vitamin E are not recommended for people taking blood-thinners such as warfarin (Coumadin) and aspirin.

For people concerned about their lung health, taking vitamin E and C is not a bad idea, says Blumberg. "If I were talking to somebody who was a former smoker and who was concerned about minimizing their risk of not only lung disease but also heart disease and cancer, then taking a supplement of C and E would be a reasonable thing to do," he says. In fact, anyone who thought he or she was at increased risk of COPD could potentially benefit from these supplements, he adds.

Supplements of beta-carotene, which is a precursor of the antioxidant vitamin A, should be used with caution, however. While a 2006 French study found that people with diets high in beta-carotene had a slower decline in lung function over an eight-year period, heavy smokers and drinkers may not benefit. Two studies found that beta-carotene supplements increased the risk of lung cancer in people who smoked more than one pack a day and drank heavily.

According to Sims, the new study offers an incentive to look closer at the potential to use vitamin E or other antioxidants to help prevent COPD. "If it could be done with something like vitamin E, that's a relatively low-risk intervention, that would be the Holy Grail." <http://tinyurl.com/2udaj7n>

**Note that the findings came from a retrospective review of a large database, not a prospective clinical study.**

**Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.**



### **HIGH-FAT MEALS A NO-NO FOR ASTHMA PATIENTS**

People with asthma may be well-advised to avoid heavy, high-fat meals, according to new research. Individuals with asthma who consumed a high-fat meal showed increased airway inflammation just hours after the binge, according to Australian researchers who conducted the study. The high fat meal also

appeared to inhibit the response to the asthma reliever medication Ventolin (albuterol).

"Subjects who had consumed the high-fat meal had an increase in airway neutrophils and TLR4 mRNA gene expression from sputum cells, that didn't occur following the low fat meal," said Dr. Lisa Wood, Ph.D., research fellow of the University of Newcastle. "The high fat meal impaired the asthmatic response to albuterol. In subjects who had consumed a high fat meal, the post-albuterol improvement in lung function at three and four hours was suppressed."

The research was presented at the ATS 2010 International Conference in New Orleans.

Asthma prevalence has increased dramatically in westernized countries in recent decades, suggesting that environmental factors such as dietary intake may play a role in the onset and development of the disease. Westernized diets are known to be relatively higher in fat than more traditional diets.

High dietary fat intake has previously been shown to activate the immune response, leading to an increase in blood markers of inflammation. However, the effect of a high fat meal on airway inflammation, which contributes to asthma, had not been investigated.

Researchers recruited 40 asthmatic subjects who were randomized to receive either a high-fat, high-calorie "food challenge", consisting of fast food burgers and hash browns containing about 1,000 calories, 52 percent of which were from fat; or a low-fat, low-calorie meal consisting of reduced fat yogurt, containing about 200 calories, and 13 percent fat.

Sputum samples were collected before the meal and four hours afterward, and analyzed for inflammatory markers.

Subjects who had consumed the high-fat meal had a marked increase in airway neutrophils and TLR4 mRNA gene expression. TLR4 is a cell surface receptor that is activated by nutritional fatty acids: TLR4 'senses' the presence of saturated fatty acids, and prompts the cell to respond to the fatty acids as if they were an invading pathogen, releasing inflammatory mediators. While the study didn't definitively distinguish between high fat and high energy, this increase in TLR4 activity suggests that dietary fat is important to the effects.

Subjects who had consumed the high fat meal also had reduced bronchodilator response as measured by FEV1% predicted and FEV1/FVC%, when compared to those had consumed the low-fat meal.

"This is the first study to show that a high fat meal increases airway inflammation, so this is a very important finding," said Dr. Wood. "The observation that a high fat meal changes the asthmatic response to albuterol was unexpected as we hadn't considered the possibility that this would occur."

The mechanism by which a high fat meal could change the bronchodilator response requires further investigation.

"We are designing more studies to investigate this effect. We are also investigating whether drugs that modify fat metabolism could suppress the negative effects of a high fat meal in the airways," said Dr. Wood. "If these results can be confirmed by further research, this suggests that strategies

aimed at reducing dietary fat intake may be useful in managing asthma." <http://tinyurl.com/2ewxzrb>



## FOUNTAIN OF YOUTH FOR YOUR BRAIN

You walk into a room and can't remember why. Sound familiar? Research shows that once we turn 25, our brains slow production of chemicals linked to memory. Now, a new supplement can help keep your memory sharp!

Lisa Lichon Pietenpol's friends used to call her scatterbrained. She'd start things and not finish them. "Hitting your 40th birthday, that memory somehow goes out the door," Lichon-Pietenpol told Ivanhoe.

She's right. Deborah Yurgelun-Todd, Ph.D., a psychiatrist at the University of Utah's Brain Institute in Salt Lake City, says after age 25 our brains start to shrink, losing chemicals called neurotransmitters that help with memory. She did a study where people took 500 to 2,000 milligrams of cognizin citicoline for six weeks. All of them showed significant increases in memory with no side effects.

"What we did, which was not done before, was to look at actual metabolic changes in the brain after supplementation, and therefore could show this is not just 'a feeling I have,' but a feeling linked to a physiological change," Dr. Yurgelun-Todd explained.

Lisa already notices a difference. "One of the greatest things I've been given back is the ability to remember to go back and finish what I started, and I'm getting a better reputation now because I can actually finish what I start," Lichon Pietenpol said. No one calls her scatterbrained any more.

Cognizin citicoline is the purest form of citicoline. You can buy it over-the-counter in pharmacies and health food stores. The lowest doses will cost a dollar a day. Dr. Yurgelun-Todd says it's safe to take for the rest of your life.



## FOUNTAIN OF YOUTH FOR YOUR BRAIN - SCIENCE INSIDER

### *How Citicholine Improves the Brain:*

When people ingest citicoline, it breaks down into two components. In the brain, these components recombine, where they are used as a raw material to stabilize neurons in the brain. This leads to increased production of neurotransmitters, and research indicates it improves the function of the brain, assisting with cognitive function and memory.

### *What Are Neurotransmitters:*

Whenever a cell receives a signal from another cell, an electrochemical impulse passes between them. The second cell passes the signal on by releasing a chemical known as a neurotransmitter that stimulates the nearest neighboring cell to release its own chemical messenger, and so on. This is how the brain communicates with the rest of the body and controls the various functions. There are many different kinds of neurotransmitters: molecules whose primary function is to deliver packets of information from one neuron to another.

<http://tinyurl.com/2ehguqv>



## CITICOLINE (COGNIZIN) IN THE TREATMENT OF COGNITIVE IMPAIRMENT.

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### Abstract

Pharmacological treatment of cerebrovascular disorders was introduced at the beginning of the 20th Century. Since then, a multitude of studies have focused on the development of a consensus for a well defined taxonomy of these disorders and on the identification of specific patterns of cognitive deficits associated with them, but with no clear consensus. Nevertheless, citicoline has proved to be a valid treatment in patients with a cerebrovascular pathogenesis for memory disorders. A metanalysis performed on the entire database available from the clinical studies performed with this compound confirms the experimental evidence from the animal studies which have repeatedly described the multiple biological actions of citicoline in restoring both the cell lipid structures and some neurotransmitter functions.

<http://www.ncbi.nlm.nih.gov/pubmed/18046877>



## MORE 'GOOD' CHOLESTEROL IS NOT ALWAYS GOOD FOR YOUR HEALTH

### *HDL cholesterol can transform from good to bad actor in heart-disease process*

We've all heard about the importance of raising HDL, or the so-called "good" cholesterol, and lowering LDL, or "bad" cholesterol, to improve heart health. While we've come to assume HDL cholesterol is an inherently good thing, a new study shows that for a certain group of patients, this is not always the case. The study is the first to find that a high level of the supposedly good cholesterol places a subgroup of patients at high risk for recurrent coronary events, such as chest pain, heart attack, and death.

The findings, published in *Arteriosclerosis, Thrombosis, and Vascular Biology*, a journal of the American Heart Association, could help explain disappointing results from a high-profile Pfizer clinical trial testing torcetrapib, an experimental drug designed to increase levels of HDL cholesterol, that some predicted would become a blockbuster medicine. The trial was halted in 2006 due to a surprisingly excessive number of cardiovascular events and death. As in the current study, cardiovascular events in the torcetrapib trial were associated with higher levels of "good" HDL cholesterol, though the reasons were unclear.

"It seems counterintuitive that increasing good cholesterol, which we've always thought of as protective, leads to negative consequences in some people," said James Corsetti, M.D., Ph.D., professor of Pathology and Laboratory Medicine at the University of Rochester Medical Center and lead author of the study. "We've confirmed that high HDL cholesterol is in fact associated with risk in a certain group of patients."

Using a novel graphical data mapping tool – outcome event mapping – Corsetti and his team identified a group of patients in which elevated levels of HDL cholesterol place them in a high-risk category for coronary events.

"The ability to identify patients who will not benefit from efforts to increase HDL cholesterol is important because they can be excluded from trials testing medications that aim to raise HDL cholesterol," said Charles Sparks, M.D., professor of Pathology and Laboratory Medicine and co-author of the study. "With these patients excluded, researchers may find that raising HDL cholesterol in the remaining population is effective in reducing cardiovascular disease risk."

Despite the outcome of the Pfizer torcetrapib trial and findings in the existing literature, including the current study, that suggest high HDL cholesterol can be a bad thing, drug companies remain invested in identifying drugs to increase HDL cholesterol. Merck recently announced plans to launch a major clinical trial in 2011 to test whether anacetrapib – a molecular cousin to torcetrapib designed to raise good cholesterol – reduces the risk of heart attack and death.

Patients in the high-risk subgroup were characterized as having high levels of C-reactive protein (CRP), a well-known marker of inflammation, in addition to high HDL cholesterol. Study authors believe genetics and environmental factors, particularly inflammation, influence whether high levels of HDL cholesterol are protective or if they increase cardiovascular risk in individual patients. Given an inflammatory environment, an individual's unique set of genes helps determine whether HDL cholesterol transforms from a good actor to a bad actor in the heart disease process.

In the high-risk subgroup of patients with elevated HDL cholesterol and CRP, researchers also identified two genetic factors associated with recurrent coronary events. The activity of cholesterol ester transfer protein (CETP), which moves cholesterol away from the vascular system and is associated with HDL cholesterol, and p22phox, which influences inflammation-related processes and is associated with CRP, are both risk predictors in this subgroup of patients.

"Our research is oriented around the ability to better identify patients at high risk," said Corsetti. "Identifying these patients and determining what puts them at high risk may be useful in choosing treatments tailored to the specific needs of particular patient subgroups. This gets us another step closer to achieving the goal of personalized medicine."

Corsetti's team identified individuals at high risk for recurrent coronary events among 767 non-diabetic patients who experienced at least one prior heart attack. Outcome event maps plot risk over an area defined by high and low levels of two biomarkers, in this case HDL cholesterol and CRP. Peaks and valleys in the maps correspond to high- and low-risk patient subgroups. Patients were followed for recurrent events for approximately two years and were part of the Thrombogenic Factors and Recurrent Coronary Events (THROMBO) study led by cardiologist Arthur Moss, M.D., professor of Medicine at the University of Rochester Medical Center and study co-author.

The current results parallel findings from a study of a healthy population. The Prevention of Renal and Vascular End-Stage Disease (PREVEND) study also identified a high-risk subgroup of patients with elevated HDL cholesterol and CRP levels among individuals who had no prior coronary events.

<http://tinyurl.com/26vj5x9>

## **HIGH CHOLESTEROL RISKS: TOP 2 DANGERS**

***There are usually no symptoms of high-risk cholesterol, yet the dangers are very real -- even fatal.***

A lot of people don't take the risks of high cholesterol very seriously. After all, one out of five people have high cholesterol. A staggering 50% of Americans have levels above the suggested limit. Could something so common really be a serious health risk?

Unfortunately, yes. Cholesterol is a direct contributor to cardiovascular disease, which can lead to strokes and heart attacks.

"Despite all of the amazing medicines and treatments we have, cardiovascular disease is still the number one cause of death and illness in our society," says Laurence S. Sperling, MD, director of preventive cardiology at the Emory University School of Medicine, Atlanta, Ga.

The World Health Organization estimates that almost 20% of all strokes and over 50% of all heart attacks can be linked to high cholesterol.

But if you've been diagnosed with high cholesterol, don't despair. The good news is that high cholesterol is one risk factor for strokes and heart attacks that you can change. You just need to take action now, before your high cholesterol results in more serious disease.

### **All About High-Risk Cholesterol Numbers**

When it comes to high cholesterol risks, it's tough to keep the details straight. We might have a vague idea of whether our cholesterol is "good" or "bad," but we forget the actual numbers by the time we get to the parking lot outside our doctor's office. So it may be worth reviewing the basics.

Cholesterol is a fat-like substance circulating in your blood. Some of your cholesterol comes from the foods you eat. But the bulk of it is actually made in your own body, specifically in the liver. Cholesterol does have some good uses. It is needed to make some hormones and it is important for the function of our cells. But an excess of it in the bloodstream can lead to trouble.

Cholesterol comes in several different forms, but doctors focus mostly on two: LDL cholesterol and HDL cholesterol.

LDL is also called "bad cholesterol" -- Sperling suggests that you think of the "L" as standing for lousy. LDL cholesterol can clog your arteries, increasing the risk of heart attack and stroke. Most people should aim for a level of less than 100 mg/dL. However, people who already have heart disease may need to aim for under 70 mg/dL.

HDL is "good cholesterol." Imagine the "H" stands for healthy, Sperling suggests. This type of cholesterol attaches to bad cholesterol and brings it to the liver, where it's filtered out of the body. So HDL cholesterol reduces the amount of bad cholesterol in your system. You should aim for 60 mg/dL or higher.

Triglycerides are not cholesterol but another type of fat floating in your blood. Just as with bad cholesterol, having a high level of triglycerides increases your risk of cardiovascular problems. Aim for a level of less than 150 mg/dL.

So although we all talk about high cholesterol risks, the term is a little misleading. What we really mean is high levels of bad LDL cholesterol and triglycerides and a low level of good HDL cholesterol.

What about total cholesterol, which is the sum of your LDL and HDL? While anything under 200 mg/dL is still considered the target, most experts don't focus on the number. It doesn't mean all that much. "Someone can have a total cholesterol of under 200 -- which is lower than average for Americans -- but still have unhealthy levels of HDL or LDL," says Sperling.

### **Realizing the Risks: How Harmful Is High Cholesterol?**

Everyone has cholesterol in their blood. But if your levels of LDL are too high, the excess can accumulate on the walls of your arteries. This build-up of cholesterol and other substances -- called plaque -- can narrow the artery like a clogged drain. It can also lead to arteriosclerosis, or hardening of the arteries, which turns the normally flexible tissue into more brittle.

Plaques can form anywhere. If they form in the carotid artery in the neck, it's carotid artery disease. When they form in the coronary arteries -- which supply the heart muscle with blood -- it's called coronary artery disease. Like any organ, the heart needs a good supply of blood to work. If it doesn't get that blood, you could get angina, which causes a squeezing pain in the chest and other symptoms.

There are other high cholesterol risks. If these plaques break open, they can form a clot. If a clot lodges in an artery and completely chokes off the blood supply, the cells don't get the nutrients and oxygen they need and die.

If a clot gets to the brain and blocks blood flow, it can cause a stroke. If a clot lodges in the coronary arteries, it can cause a heart attack.

### **Do We Underestimate High Cholesterol Risks?**

The risks of high cholesterol are quite clear. "If you look at populations of people," says Sperling, "the higher the cholesterol, the higher the level of heart and blood vessel disease." It's that simple.

But experts say that people don't take high cholesterol risks seriously enough. According to the CDC, in 2005 almost a quarter of American adults said they hadn't had their cholesterol checked in the last five years.

One problem is that high cholesterol doesn't cause symptoms that make people pay attention.

"People naturally respond more to medical conditions that cause symptoms," says Nathan D. Wong, PhD, fellow of the American College of Cardiology and director of the Heart Disease Prevention Program at the University of California, Irvine. Since you won't feel your rising cholesterol levels, you won't go to the doctor about it.

By the same token, people may be less likely to stick to treatment for high cholesterol than they would be for a painful condition.

"People on cholesterol-lowering medicine don't feel any better," says Sperling. "It's not like taking a painkiller for an aching knee, where you know it's working." As a result, people may be less likely to follow their treatment plan over the long-term, Sperling says.

Also, high cholesterol risks are usually not immediate. The damage accumulates over years and decades -- high cholesterol in your 20s and 30s can take its toll in your 50s and 60s. Because the effects take time, many people don't feel real urgency in treating it. They feel they can just deal with it later.

"Unfortunately, I think that many people are too casual about their high cholesterol," says Adolph Hutter, MD, a cardiologist at Massachusetts General Hospital and a professor of medicine at Harvard Medical School. "They ignore it for years and it only gets their attention when they actually develop vascular disease."

### **Taking Action to Lower High Cholesterol Risks**

There are many good treatments for heart disease, arteriosclerosis, and other serious conditions caused by high cholesterol. But it's a terrible shame to let things get that far when making changes now could prevent these life-threatening illnesses. Reducing your high cholesterol risks is a crucial step.

So what should you do? First, go to the doctor. "It's very important for all adults to get their cholesterol tested," says Wong. Every adult over 20 should have a cholesterol test at least once every five years.

Also, keep track of your cholesterol levels yourself. Write down your current numbers and, if they're high, what numbers you should be striving for.

If you do have high cholesterol, get serious. Talk with your doctor about what your goals should be and how you should achieve them. Make sure you understand what lifestyle changes you need to make. If you already have heart disease or other risk factors like diabetes, you need to be even more careful.

Whatever you do, don't ignore your high cholesterol risks. Don't put off treatment for another year.

"Having high cholesterol may not hurt you today or tomorrow," says Sperling. "But if you don't do something about it, it can have a terrible cost down the road."

<http://tinyurl.com/2akjvlp>



## **UPDATE 2: EU AGENCY BACKS NYCOMED'S DAXAS AFTER U.S. REBUFF**

Privately owned Swiss drugmaker Nycomed [NYCMD.UL], which is aiming for an initial public offering (IPO) at some stage, won a consolation prize on Friday as European regulators backed a key lung drug after a recent rebuff in the United States.

The European Medicines Agency said it was recommending approval of Daxas as a maintenance treatment for severe chronic obstructive pulmonary disease (COPD) in conjunction with a bronchodilator. Nycomed said the once-a-day tablet medicine was expected to be launched in the first European countries later this year, once it was formally given marketing authorisation by the European Commission.

Earlier this month, a U.S. Food and Drug Administration panel voted 10-5 not to recommend Daxas, dealing a blow to Nycomed and its partner Forest Laboratories <FRX.N>, which has U.S. marketing rights to the drug.

The fate of Daxas is key to its developer Nycomed, which has said in the past it wants to launch an IPO but has never given an exact timetable for listing its shares in Switzerland. Daxas is also pivotal for Forest, which is trying to build its portfolio ahead of the 2012 patent expiration for its huge-selling antidepressant Lexapro.

Industry analysts have estimated peak annual sales could hit \$500 million or more -- but the drug's setback in the U.S. has placed its commercial prospects under a cloud.

Daxas, known generically as roflumilast, works by inhibiting an enzyme called PDE4 that is linked to inflammation. Nausea, diarrhoea and weight loss are known side effects of the PDE4 inhibitors.

It could win a niche in the multibillion-dollar worldwide COPD market, alongside rivals such as GlaxoSmithKline's <GSK.L> Advair and Spiriva, marketed by Pfizer <PFE.N> and Boehringer Ingelheim, analysts believe.

-<http://tinyurl.com/37kgssq>



## **PNEUMOCOCCAL VACCINE DOES NOT INCREASE HEART ATTACK RISK**

Many studies have shown that the influenza vaccine can reduce the risk of recurrent heart attack, sudden cardiac death, heart-related hospital admissions, and stroke. The effect of the pneumococcal vaccine on vascular events is more controversial. In the May 5, 2010 issue of the Journal of the American Medical Association, receipt of the pneumococcal vaccine was not associated with a subsequent decrease in the risk of acute heart attack or stroke among men aged 45 or older.

Researchers from Kaiser Permanente in California studied 84,170 men aged 45 to 69 who participated in the California Men's Health Study in order to examine the association between pneumococcal vaccine administration and the risk of acute heart attack and stroke. During follow-up, there were actually more first heart attacks and strokes in men who received the pneumococcal vaccine

Although a previous study supported the protective role of the pneumococcal vaccine against acute heart attack and stroke, this latest study took into account dietary factors, disease history, and lifestyle factors and also included an ethnically and socioeconomically diverse population. Current guidelines recommend that the pneumococcal vaccine be given to adults aged 65 or older, and to people who have underlying medical conditions that may increase the risk for pneumococcal infection.

Based on the findings of this study, the pneumococcal vaccine helps to prevent bacterial infections, but does not protect against acute heart attack or stroke.

<http://tinyurl.com/2awprnh>



## **PULMONARY SPECIALISTS CONFIRM EVIDENCE THAT COPD IS AN AUTOIMMUNE DISEASE IN MANY PATIENTS**

Pulmonary specialists at the University of Pittsburgh School of Medicine are reporting solid evidence that chronic obstructive pulmonary disease (COPD) is an autoimmune disease in many patients. Previous speculation that COPD may have an

autoimmune component has remained unproven until now. The finding, reported recently in the American Journal of Respiratory and Critical Care Medicine, holds particular relevance regarding possible future treatments, including a clinical trial of inhaled cyclosporine now enrolling patients at the University of Pittsburgh. This approach also is scheduled for discussion on Friday, Feb. 29, at the Pittsburgh International Lung Conference being held at the Omni William Penn Hotel Downtown.

The fourth-leading cause of death and second-leading cause of disability in the United States, COPD is a lung disease commonly related to smoking that diminishes breathing capacity over time and includes conditions such as chronic bronchitis and emphysema. The National Institutes of Health estimates that 12 million adults have a current diagnosis of COPD, with an additional 12 million unaware that they have the disorder.

"COPD damages the lung tissue, expanding and breaking down the walls of air sacs, which hinders air flow out of the lungs and the transfer of oxygen into the blood," said Steven R. Duncan, M.D., a senior author of the study and professor of medicine at the University of Pittsburgh School of Medicine. "This new work shows that in some patients with COPD, immune system antibodies attack the cells that line the airways and air sacs of the lungs called epithelial cells."

The Pitt researchers tracked immune system antibodies in 55 smokers or former smokers (47 with COPD) compared to 21 healthy people who had never smoked. Abnormal antibodies were found in 68 percent of smokers and former smokers with COPD but in only 13 percent of former smokers without COPD and 10 percent of those who had never smoked.

"COPD is responsible for 120,000 deaths a year," said Frank C. Sciurba, M.D., a study senior co-author, associate professor of medicine and director of Pitt's Emphysema Research Center. "Available treatments, including inhaled bronchodilators, have little effect on disease progression. New information learned may help us to develop better treatments and perhaps even halt disease progression."

Investigators at the Emphysema Research Center are conducting a clinical trial of an inhaled form of cyclosporine, long used to suppress the immune system in transplant patients. "We are working every day to increase awareness of the disease and find new ways to help our patients," added Dr. Sciurba.

Symptoms of COPD include a recurring cough, sometimes underestimated as "smoker's cough," wheezing, shortness of breath, overproduction of sputum and inability to breathe deeply. The most important step patients can take to reduce the risk of developing COPD or slow progression of the disease is to quit smoking.

"We expect to see increasing numbers of patients with COPD in the Pittsburgh area since our smoking rates -- some 25 percent -- are higher than elsewhere in the United States," said Dr. Sciurba.

Patients with more severe COPD interested in additional information on these research findings and the inhaled cyclosporine trial may call the Emphysema Research Center at

412-692-4800. For a copy of the paper, call Michele Baum at 412-647-3555.

<http://copdnewsoftheday.com/?p=85>



## VITAMIN D (CALCITRIOL)

Bioactive vitamin D or calcitriol is a steroid hormone that has long been known for its important role in regulating body levels of calcium and phosphorus, and in mineralization of bone. More recently, it has become clear that receptors for vitamin D are present in a wide variety of cells, and that this hormone has biologic effects which extend far beyond control of mineral metabolism.

### Structure and Synthesis

The term vitamin D is, unfortunately, an imprecise term referring to one or more members of a group of steroid molecules. Vitamin D<sub>3</sub>, also known as cholecalciferol is generated in the skin of animals when light energy is absorbed by a precursor molecule 7-dehydrocholesterol. Vitamin D is thus not a true vitamin, because individuals with adequate exposure to sunlight do not require dietary supplementation. There are also dietary sources of vitamin D, including egg yolk, fish oil and a number of plants. The plant form of vitamin D is called vitamin D<sub>2</sub> or ergosterol. However, natural diets typically do not contain adequate quantities of vitamin D, and exposure to sunlight or consumption of foodstuffs purposefully supplemented with vitamin D are necessary to prevent deficiencies.

Vitamin D, as either D<sub>3</sub> or D<sub>2</sub>, does not have significant biological activity. Rather, it must be metabolized within the body to the hormonally-active form known as 1,25-dihydroxycholecalciferol. This transformation occurs in two steps.

Within the liver, cholecalciferol is hydroxylated to 25-hydroxycholecalciferol by the enzyme 25-hydroxylase.

Within the kidney, 25-hydroxycholecalciferol serves as a substrate for 1-alpha-hydroxylase, yielding 1,25-dihydroxycholecalciferol, the biologically active form.

Each of the forms of vitamin D is hydrophobic, and is transported in blood bound to carrier proteins. The major carrier is called, appropriately, vitamin D-binding protein. The half-life of 25-hydroxycholecalciferol is several weeks, while that of 1,25-dihydroxycholecalciferol is only a few hours.

### Control of Vitamin D Synthesis

Hepatic synthesis of 25-hydroxycholecalciferol is only loosely regulated, and blood levels of this molecule largely reflect the amount of amount of vitamin D produced in the skin or ingested. In contrast, the activity of 1-alpha-hydroxylase in the kidney is tightly regulated and serves as the major control point in production of the active hormone. The major inducer of 1-alpha-hydroxylase is parathyroid hormone; it is also induced by low blood levels of phosphate.

### The Vitamin D Receptor and Mechanism of Action

The active form of vitamin D binds to intracellular receptors that then function as transcription factors to modulate gene expression. Like the receptors for other steroid hormones and thyroid hormones, the vitamin D receptor has hormone-binding and DNA-binding domains. The vitamin D receptor forms a complex with another intracellular receptor, the retinoid-X receptor, and that heterodimer is what binds to DNA. In most

cases studied, the effect is to activate transcription, but situations are also known in which vitamin D suppresses transcription.

The vitamin D receptor binds several forms of cholecalciferol. Its affinity for 1,25-dihydroxycholecalciferol is roughly 1000 times that for 25-hydroxycholecalciferol, which explains their relative biological potencies.

### Physiological Effects of Vitamin D

Vitamin D is well known as a hormone involved in mineral metabolism and bone growth. Its most dramatic effect is to facilitate intestinal absorption of calcium, although it also stimulates absorption of phosphate and magnesium ions. In the absence of vitamin D, dietary calcium is not absorbed at all efficiently. Vitamin D stimulates the expression of a number of proteins involved in transporting calcium from the lumen of the intestine, across the epithelial cells and into blood. The best-studied of these calcium transporters is calbindin, an intracellular protein that ferries calcium across the intestinal epithelial cell.

Numerous effects of vitamin D on bone have been demonstrated. As a transcriptional regulator of bone matrix proteins, it induces the expression of osteocalcin and suppresses synthesis of type I collagen. In cell cultures, vitamin D stimulates differentiation of osteoclasts. However, studies of humans and animals with vitamin D deficiency or mutations in the vitamin D receptor suggest that these effects are perhaps not of major physiologic importance, and that the crucial effect of vitamin D on bone is to provide the proper balance of calcium and phosphorus to support mineralization.

It turns out that vitamin D receptors are present in most if not all cells in the body. Additionally, experiments using cultured cells have demonstrated that vitamin D has potent effects on the growth and differentiation of many types of cells. These findings suggest that vitamin D has physiologic effects much broader than a role in mineral homeostasis and bone function. This is an active area of research and a much better understanding of this area will likely be available in the near future.

<http://tinyurl.com/ygrsdb>



### VITAMIN D BEST TAKEN WITH LARGEST MEAL OF DAY, STUDY FINDS

***Blood levels increased more than 50% after timing change, researchers say***

Your body may make better use of a vitamin D supplement if you take it with your largest meal, new research suggests.

Researchers at the Cleveland Clinic examined 17 patients with vitamin D deficiency who weren't getting better under treatment. Over a period of two to three months, the patients were told to take vitamin D supplements with the biggest meal they ate each day.

This boosted the level of vitamin D in their blood by an average of 56 percent, the researchers said.

"This is an important finding for patients being treated for vitamin D deficiency," study senior author Dr. Angelo Licata said in a news release from the Cleveland Clinic. "By doing something as simple as changing when you take your vitamin

D supplement, you can improve the level in your blood by over 50 percent."

The study was recently published in the Journal of Bone and Mineral Research. <http://tinyurl.com/22s7ctx>



### **DIFFERENCES BETWEEN BETA-BLOCKERS IN PATIENTS WITH CHRONIC HEART FAILURE AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A RANDOMIZED CROSSOVER TRIAL** **Clinical Trial:** yes

**Study Question:** What are the respiratory, hemodynamic, and clinical effects of switching between  $\beta$ 1-selective and nonselective beta-blockers in patients with chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD)?

**Methods:** A randomized, open-label, triple-crossover trial involving 51 subjects receiving optimal therapy for CHF was conducted in two Australian teaching hospitals. Subjects were a mean age of 66 years (standard deviation [SD] 12 years) and had New York Heart Association (NYHA) functional class I (n = 6), II (n = 29), or III (n = 16); and left ventricular ejection fraction (mean of 37%, SD 10%); 35 had coexistent COPD. Subjects received each beta-blocker, dose-matched, for 6 weeks before resuming their original beta-blocker. Echocardiography, N-terminal prohormone brain natriuretic peptide (NT-BNP), central augmented pressure from pulse waveform analysis, respiratory function testing, 6-minute walk distance, and NYHA functional class were assessed at each visit.

**Results:** The investigators found that NT-BNP was significantly lower with carvedilol than with metoprolol or bisoprolol (mean: carvedilol 1001 [95% confidence interval (CI), 633-1367] ng/L; metoprolol 1371 [95% CI, 778-1964] ng/L; bisoprolol 1349 [95% CI, 782-1916] ng/L;  $p < 0.01$ ), and returned to baseline level on recommencement of the initial beta-blocker. Central augmented pressure (a measure of pulsatile afterload) was lowest with carvedilol (carvedilol 9.9 [95% CI, 7.7-12.2] mm Hg; metoprolol 11.5 [95% CI, 9.3-13.8] mm Hg; bisoprolol 12.2 [95% CI, 9.6-14.7] mm Hg;  $p < 0.05$ ). In subjects with COPD, forced expiratory volume in 1 second was lowest with carvedilol and highest with bisoprolol (carvedilol 1.85 [95% CI, 1.67-2.03] L/s; metoprolol 1.94 [95% CI, 1.73-2.14] L/s; bisoprolol 2.0 [1.79-2.22] L/s;  $p < 0.001$ ). The NYHA functional class, 6-minute walk distance, and left ventricular ejection fraction did not change. The beta-blocker switches were well tolerated.

**Conclusions:** The authors concluded that switching between  $\beta$ 1-selective beta-blockers and the nonselective beta-blocker carvedilol is well tolerated, but results in demonstrable changes in airway function, most marked in patients with COPD. Switching from  $\beta$ 1-selective beta-blockers to carvedilol causes short-term reduction of central augmented pressure and NT-BNP.

**Perspective:** Managing two conditions simultaneously involves trade-offs. Typically, HF specialists have chosen bisoprolol first-line in patients with clinically significant reactive airways disease such as asthma. In this study, carvedilol was associated with a 'better' hemodynamic response, as evidenced by lower NT-BNP and central aortic pressure, but associated with poorer forced expiratory volume in 1 second (FEV1)

responses. However, the poorer FEV1 responses were not associated with worsening NYHA functional class or 6-minute walk test. Larger blinded randomized studies are needed to determine which beta-blocker has the best clinical outcome in CHF patients with COPD. <http://tinyurl.com/y2w59gu>



### **PSORIASIS LINKED TO HEART DISEASE, CANCER** *Studies Also Show Link to Increased Risk of Diabetes and Depression*

Psoriasis is more than skin deep. The 7.5 million Americans who suffer from the thick, red, scaly, itchy plaques of psoriasis are at increased risk of a number of other serious medical conditions.

One new study, presented this week at the annual meeting of the American College of Cardiology in Atlanta, suggests people with psoriasis are more likely to have heart attacks and strokes than people who don't have the skin disorder.

Researchers from Copenhagen University Hospital in Denmark tracked rates of psoriasis, heart disease, stroke, and death in the entire adolescent and adult population of Denmark between 1997 and 2006. They found that people with severe psoriasis were 54% more likely to suffer a stroke, 21% more likely to have a heart attack, and 53% more likely to die over a 10-year period than people without the skin disorder. They were also more likely to need a procedure such as angioplasty to open up clogged heart arteries. Patients with mild psoriasis were at increased risk of stroke and artery-opening procedures. "People with severe disease at a younger age were at highest risk for cardiovascular problems," says study researcher Ole Ahlehoff, MD.

The analysis took into account other risk factors for heart disease, including age, sex, medication, and other health conditions. "People with psoriasis should not only seek care for the symptoms of that disorder, but should also be screened for heart disease risk factors and make lifestyle changes to minimize their risk of future cardiovascular problems, such as maintaining a healthy weight," Ahlehoff tells WebMD.

#### **Psoriasis and Cancer**

Another study, presented last week at the annual meeting of the American Academy of Dermatology in Miami Beach, Fla., shows psoriasis is associated with an increased risk of cancer, including skin cancer, prostate cancer, and lymphoma. Researchers from Health Economics and Outcomes Research at Abbott Laboratories combed through their insurance claims database that has information on about 93 million Americans. They identified 37,159 people with psoriasis and compared their rates of cancer to 111,473 people without the condition; their ages were similar. People with psoriasis were more likely to have high cholesterol, high blood pressure, and heart disease and to be obese.

Over an average period of about two-and-one-half years, 34.8% of people with psoriasis were diagnosed with cancer. In contrast, only 23.2% of those without the skin condition developed cancer. That translated to a 56% higher risk of cancer for people with psoriasis, the researchers report.

As for types of cancer, people with psoriasis had a 75% higher risk for skin cancer, 87% higher risk for lymphoma, and 22% higher risk for prostate cancer, the study showed.

Some of the treatments used for psoriasis may have increased their risk of skin cancer, says Alan Menter, MD, chair of the psoriasis research unit at Baylor Research Institute in Dallas. But the link to the other cancers can't be explained by therapy, he says.

### **Psoriasis Linked to Obesity, Depression**

The list of medical conditions associated with psoriasis doesn't end there, Menter says. Among others, he tells WebMD, are obesity, Crohn's disease, diabetes, depression, sexual dysfunction, arthritis, and chronic obstructive pulmonary disease (COPD).

In addition, studies have shown that people with psoriasis tend to drink and smoke a lot, Menter says. Detrimental behaviors can aggravate some conditions associated with psoriasis, such as heart disease and COPD, he says.

According to Ahlehoff, the underlying inflammation that drives the development of psoriasis appears to predispose people to cardiovascular disease, which also is thought to be fueled by inflammation.

But in the case of the other medical conditions, "we are unsure whether psoriasis causes other diseases or that these other diseases cause psoriasis," Menter says. The important thing is that people with psoriasis undergo a thorough health evaluation, he says.

<http://tinyurl.com/ybf2klh>



### **PROCESSED MEATS MAY BE THE CULPRIT IN HEART DISEASE**

Previous research has linked heavy consumption of red meat with a shorter lifespan and a higher risk of diabetes, colon cancer, and cardiovascular disease. U.S. dietary guidelines recommend limiting consumption of red and processed meats, and now it seems that the type of meat you eat may make a difference in your health risk. According to a new analysis published online in the journal *Circulation*, eating processed meats such as bacon, sausage, and deli ham increases the risk of heart disease and diabetes. This is the first study of its kind to differentiate between the potential health effects of unprocessed red meat and processed meats.

Researchers from the Harvard School of Public Health and their colleagues reviewed almost 1,600 studies and found that eating 1.8 ounces of processed meats per day, or the equivalent of a single hot dog, increased the risk of heart disease by 42 percent. The same daily consumption of processed meats increased the risk of diabetes by 19 percent. On the other hand, eating the same amount of unprocessed meats, such as beef or pork, seemed to have no effect on heart disease or diabetes risk.

It seems that the difference may be in the sodium content of processed meats. While both unprocessed and processed meats have approximately the same amounts of saturated fat and cholesterol, processed meats have about four times more sodium. Based on the findings of this new analysis, consumption of unprocessed red meat is not associated with an increased risk of heart disease or diabetes. However, it is not associated with a reduced risk, either, so increasing consumption of that have been

shown to have a protective effect, such as fruits, vegetables, fish, nuts, and whole grains, is still important.

<http://tinyurl.com/2v6dom6>



### **WHAT IS THE RELATIONSHIP BETWEEN FEAR OF FALLING AND GAIT IN WELL-FUNCTIONING OLDER PERSONS AGED 65 TO 70 YEARS?**

#### **Objective**

To investigate the association between fear of falling and gait performance in well-functioning older persons.

**Design** Survey.

**Setting** Community.

#### **Participants**

Subjects (N=860, aged 65–70y) were a subsample of participants enrolled in a cohort study who underwent gait measurements.

#### **Main Outcome Measures**

Fear of falling and its severity were assessed by 2 questions about fear and related activity restriction. Gait performance, including gait variability, was measured using body-fixed sensors.

#### **Results**

Overall, 29.6% (210/860) of the participants reported fear of falling, with 5.2% (45/860) reporting activity restriction. Fear of falling was associated with reduced gait performance, including increased gait variability. A gradient in gait performance was observed from participants without fear to those reporting fear without activity restriction and those reporting both fear and activity restriction. For instance, stride velocity decreased from  $1.15 \pm .15$  to  $1.11 \pm .17$  to  $1.00 \pm .19$  m/s ( $P < .001$ ) in participants without fear, with fear but no activity restriction and with fear and activity restriction, respectively. In multivariate analysis, fear of falling with activity restriction remained associated with reduced gait performance, independent of sex, comorbidity, functional status, falls history, and depressive symptoms.

#### **Conclusions**

In these well-functioning older people, those reporting fear of falling with activity restriction had reduced gait performance and increased gait variability, independent of health and functional status. These relationships suggest that early interventions targeting fear of falling might potentially help to prevent its adverse consequences on mobility and function in similar populations.

<http://tinyurl.com/28vubrb>



### **NEW ATHEROSCLEROSIS VACCINE GIVES PROMISING RESULTS**

A new study by researchers at the Swedish medical university Karolinska Institutet shows that the immune defence's T cells can attack the "bad" LDL cholesterol and thereby cause an inflammation that leads to atherosclerosis. By producing a vaccine against the T cell receptors, the researchers have managed to inhibit the development of atherosclerosis in animals.

The study is presented online in the distinguished periodical *Journal of Experimental Medicine* and is expected

to be of considerable significance to the future treatment of atherosclerosis, heart attack and stroke.

Cholesterol is transported in the blood in LDL particles, which are a kind of fat drops that can accumulate in the walls of blood vessels. LDL activates the immune defence and triggers an inflammation in the blood vessels that leads to atherosclerosis (also known as arteriosclerosis). When the atherosclerotic plaque finally ruptures, a blood clot is formed that in turn can cause a heart attack or stroke.

It was previously thought that the inflammation in the blood vessels arises when the T cells react to oxidised LDL particles located in the atherosclerotic plaque. Now, however, the team at Karolinska Institutet has found that the opposite is true, namely that the T cells react to components in the normal LDL particles, and that they no longer recognise LDL once it has been oxidised.

"Since reactions to LDL can be dangerous, T cells are normally held in check by inhibitory signals," says Professor Göran K Hansson, who led the study. "The body's own control works well as long as the LDL keeps to the blood, liver and lymph glands. But when it accumulates in the artery wall, this inhibition is no longer enough, the T cells are activated and an inflammation arises."

Together with his research group at Karolinska Institutet he now presents a new principle for inhibiting atherosclerosis. Vaccination against the receptor that the T cells use to recognise LDL can block the immune reaction and reduce the disease by between 60 and 70 per cent. The vaccine has been successfully tested on animals and the researchers are now hoping to see if it can be developed into a treatment for patients with a high risk of myocardial infarction and stroke.

The researchers also now believe that their results explain why antioxidants are ineffective against cardiovascular disease when they have been tested in large clinical studies.

"If one takes antioxidants, one simply prevents the oxidation of LDL," says Professor Hansson. "It retains its ability to activate the T cells, and so the inflammation in the blood vessels can increase. This could give the opposite results to what one was hoping for."

<http://tinyurl.com/2flhthb>



## **ESTROGEN MAY REDUCE AIRWAY CONSTRICTION IN WOMEN PATIENTS WITH ASTHMA**

***Female sex hormones may work with beta-agonists in reducing airway constriction, according to new bench research from the Mayo Clinic.***

The findings are being presented at the ATS 2010 International Conference in New Orleans.

After puberty, women tend to have worse asthma symptoms and exacerbations than men. Women also experience changes in airway reactivity throughout their menstrual cycle, with pregnancy, and at the onset of menopause.

"Given these clinical observations, it is of interest to determine whether sex steroids (estrogen, progesterone) play a role in modulating airway tone," said lead student researcher, Elizabeth A. Townsend, of the Mayo Clinic Department of Physiology and Biomedical Engineering, where she is completing her Ph.D. "What is less clear is whether sex steroids,

especially estrogens, are detrimental or beneficial to airway function."

"Increased bronchoconstriction, as in asthma, is directly influenced by the amount of intracellular calcium in airway smooth muscle. Therefore, we set out to explore the effect of estrogens on calcium regulation in airway smooth muscle. Calcium regulation is a key factor in determining bronchoconstriction" said Ms. Townsend. "Since asthma symptoms have been documented to be worst when estrogen levels are lowest in the late luteal phase, we hypothesized that estrogens facilitate bronchodilation, rather than constriction."

To test this hypothesis, Ms. Townsend and colleagues exposed human airway smooth muscle tissue and cells isolated from surgical lung samples to small doses of estradiol comparable to physiologic levels found in women. They found that acute (15 minute) exposure to estradiol at concentrations comparable to those experienced during a woman's menstrual cycle decreased intracellular calcium in airway smooth muscle cells. Furthermore, small amounts of estradiol significantly decreased force production by human airways that had been stimulated with bronchoconstrictors, indicating increased bronchodilation.

Townsend and colleagues then asked whether estrogens could produce bronchodilation, and might the combination of commonly used bronchodilators (beta-2 agonists) and estrogens be used to produce even greater bronchodilation? In laboratory studies using human airway smooth muscle cells, they found that combined treatment with estradiol and the beta-agonist, isoproterenol (which non-selectively activates both beta-1 and beta-2 adrenergic receptors), had a synergistic effect on decreasing intracellular calcium and force more than either estradiol or isoproterenol alone. They also found that these effects may involve a common signaling pathway.

"These novel data suggest that estradiol has bronchodilatory properties, and may potentiate beta-2-agonist effects," said Ms. Townsend. "The finding that estrogens interact synergistically with beta-adrenoceptor signaling (perhaps using common pathways) to facilitate bronchodilation was exciting, and lends itself to further studies on interactions between sex steroids and beta-2-agonists." But she and her team also cautioned that there is still considerable research necessary to fully understand the association between sex steroids and factors that contribute to asthma, before the information can be used clinically in patients to relieve asthma symptoms.

"Our work has only focused on the acute exposure of estrogens and the observed dilatory effects," said Ms. Townsend. "In other organ systems and disease states, estrogens can have complex effects on inflammation, cell signaling and other factors also important in asthma and airway inflammation. Given our findings, we can ask a number of questions to guide future research: what is the effect of chronic exposure to estrogens on airway smooth muscle tone? Are there interactions between estrogen and progesterone in the airway? Are men and women different in their response to sex steroids in terms of airway tone? Can an inhaled combination of beta-2-agonist and estrogen be more effective

at controlling asthma exacerbations, and potentially have a beta-2-agonist sparing effect?" <http://tinyurl.com/24h53va>



## EFFECTIVENESS OF PULMONARY REHABILITATION IN REDUCING HEALTH RESOURCES USE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

### ABSTRACT

*Effectiveness of pulmonary rehabilitation in reducing health resources use in chronic obstructive pulmonary disease.*

#### Objective

To determine the effectiveness of a multidisciplinary, outpatient pulmonary rehabilitation (PR) program in patients with severe and very severe chronic obstructive pulmonary disease (COPD). PR is recommended in advanced COPD, but there is limited evidence on the effectiveness of PR in reducing health care resources when applied in outpatients.

#### Design

Before and after intervention, a prospective research trial of patients enrolled in a PR program.

#### Setting

Outpatient respiratory department in a specialized hospital.

#### Participants

We considered prospectively 82 consecutive patients with advanced COPD and finally studied 72 patients who completed the PR intensive phase.

#### Intervention

PR program.

#### Main Outcome Measures

The effectiveness of this PR program was assessed by comparing health resources use from the year before and the year after PR. Clinical variables including dyspnea; the body mass index, obstruction, dyspnea, exercise capacity (BODE) index; and the Chronic Respiratory Questionnaire and health resources use including the number of exacerbations, the number of hospitalizations, and days of hospitalization.

#### Results

Patients had a forced expiratory volume in the first second percentage predicted (mean  $\pm$  SD) of  $33.0 \pm 9.8$  and a BODE index of  $5.0 \pm 2.0$ . Significant improvements after PR were found in dyspnea, exercise capacity, and quality of life and on the BODE index ( $P < .05$ ). Compared with the 12 months before PR, there were also significant reductions during the year after PR on exacerbations ( $3.4 \pm 3.5$  vs  $1.9 \pm 2.0$ ,  $P = .002$ ), hospitalizations ( $2.4 \pm 2.0$  vs  $0.9 \pm 1.2$ ,  $P < .001$ ), and days of hospitalization ( $36.1 \pm 32.7$  vs  $16.1 \pm 31.3$ ,  $P < .001$ ) (ie, a reduction of 44%, 63%, and 55%, respectively; all  $P < .05$ ).

#### Conclusions

We conclude that a multidisciplinary, outpatient PR program substantially reduces health resources use in patients with severe and very severe COPD.



## NEW RESEARCH REVEALS GENETIC OVERLAP BETWEEN COPD AND LUNG CANCER SUSCEPTIBILITY

New research shows genes that make smokers more likely to develop chronic obstructive pulmonary disease (COPD), or emphysema, are also closely linked to an increased likelihood of developing lung cancer, according to studies presented today at the American Thoracic Society's annual meeting. Research on seven genes critical to determining the lung's response to cigarette smoke in both COPD and lung cancer confirm a strong genetic overlap for susceptibility to both diseases, Dr Robert Young, Associate Professor of Medicine and Molecular Genetics at the University of Auckland, told the meeting. The genes, implicated in inflammation and repair pathways, were studied in current and former smokers.

Together, COPD and lung cancer account for close to half of all smoking-related deaths each year. Past research has suggested that susceptibility to lung cancer is closely tied to COPD, but until now specific genes linking the two diseases have not been well understood, and the clinical utility of this information has been overlooked, Dr Young said.

"Gaining a better understanding of which patients are at greatest risk of premature death or disability, based on their smoking habit and genetic make-up, can help us identify those in urgent need of help while there is still time to prevent lung cancer or diagnose it earlier," said Dr Young.

Lung cancer diagnosis and treatment often comes too late for the approximately 1 in 10 smokers who develop it. By the time symptoms are evident, cancer has often progressed to a point where it becomes very difficult to treat successfully. Survival rates are poor: 80% of those diagnosed with lung cancer die within two years of diagnosis and half are dead within a year. Lung cancer remains the leading cancer killer in the United States and most other developed countries.

Dr Young's research has led to the development of a genetic test for lung cancer risk assessment in current and former smokers called Respiragene™, which is based on a cheek swab. Respiragene combines a test for 20 specific genetic variants called SNPs (or single nucleotide polymorphisms) linked with lung cancer risk and an assessment of patient clinical factors including age, family history and prior lung disease to derive a score that places current or former smokers into Moderate, High and Very High risk categories.

The utility of the Respiragene score (to be presented on Wednesday in the ATS Seminar "Beyond Pack Years: Who's really at risk of developing lung cancer") has been validated in four separate studies among lung cancer patients in three different countries.

"By including the genetic factors in the lung cancer risk assessment, we are now able to personalize the risk for people who smoke with much more precision than ever before," said Dr Young. "Astonishingly, many smokers still believe that their risk of lung cancer is no greater than that of non-smokers."

Preliminary data from a study of smokers in New Zealand randomly selected to take the Respiragene test suggests it encourages people to stop smoking. The quit rate among participants six months after testing was over 30%. This

compares with the 4-5% of smokers overall who manage to give up smoking each year.

“In our clinical trials we have learned two things about Respiragene,” said Dr Young. “First of all, it is a popular test – people want to find out their individual risk of lung cancer. It is also proving to be highly motivating in getting people to quit smoking, which is, of course, among the best things anyone can do for their health.”

Genetic-based improvements to risk prediction should also prompt closer monitoring of higher risk individuals by their doctors and prioritization for potential screening and earlier lung cancer detection efforts. Such an approach to preventing coronary heart disease has been used by doctors for over 20 years to identify people most at risk and help promote healthier lifestyle choices and target drug therapies, said Dr Young.

“Currently, there are over 400 people a day dying of lung cancer in the US and over 1000 a day in Europe. Nearly 90% of them are current or former smokers,” said Dr Young. “Lung cancer is preventable and accounts for 1 in 3 cancer deaths. COPD is soon to be the 3rd leading cause of death in developed countries and worsening – but we can identify the people most at risk from these diseases now.” <http://tinyurl.com/248ckce>



## **PULMONARY HYPERTENSION CAN BE EASED BY VIAGRA**

Paul Coates, a rugby player, says his life was normalized by Viagra. No, it is not his sexual life, but something very different. Paul has idiopathic pulmonary hypertension.

This is a condition that restricts blood flow in the lungs raising the pressure in that area. One of the first symptoms of Idiopathic Pulmonary Hypertension is blue lips caused by lack of oxygen in the blood.

Viagra has always been touted to help ease the condition. Just as it increases blood flow to the erectile tissue in the penis, Viagra also increases blood flow in the arteries of the lung.

The drug has helped Mr Coates carry on with his life. Paul got married recently and paid tribute to his condition by painting his lips blue. <http://tinyurl.com/y6u48a4>



## **RETRAIN YOUR BRAIN TO LOVE EXERCISE!**

The best diet for weight loss may still be under debate, but there's no doubt that the dynamic duo of diet and exercise continues to be the gold standard for weight loss and, more importantly, maintaining a weight loss. In spite of the much-publicized benefits of exercise, too many people fail to stick with an exercise program. Here are three ways to think about exercise and its benefits that will help you love it — especially if your goal is to lose weight.

**Tip #1** – Without the appropriate fuel, exercise can feel more like punishment than pleasure.

For those seeking a quick fix, a very low-carbohydrate diet can seem like the magic bullet. But a balanced diet with adequate carbohydrates is necessary to optimize energy for exercise.

Any diet, especially a weight-loss diet, that is too low in carbohydrates — 125 grams or fewer a day — is a recipe for disaster when it comes to exercise. The primary fuel for muscles

is glucose (from carbohydrates) and its storage form, glycogen. Without them, you're likely to feel tired or have sore muscles early in your workout.

Planning an exercise routine includes timing meals and snacks to prevent exercising on empty. If you feel sluggish while walking at 5 p.m. because you haven't eaten since lunchtime, try having a pre-workout snack. The same walk just an hour or so after dinner will probably be adequately fueled from that meal.

To boost your stamina, eat a 150- to 200- calorie snack that contains one to two servings of carbohydrates about 30 minutes to 1 hour before exercise. Here are some examples:

An apple with 1 tablespoon of peanut butter or mixed nuts  
One ounce of string cheese and 6 crackers  
A granola or protein bar with about 150 calories and five to seven grams of protein

**Tip #2** – Think of exercise as a savings account.

With a savings account, you make deposits, watch your money grow with interest and then reap the rewards. You don't deposit money so you can immediately withdraw it. Exercise is similar. It also gathers interest: As you get more fit, your body rewards your hard work by using more calories during and after your workouts.

Here are some other ways that exercise contributes to long-term weight loss and weight maintenance.

- Muscle burns calories while fat does not. A pound of muscle also takes up less room than a pound of fat.
- Exercise builds muscle, which increases your body's resting metabolic rate, so you expend more calories even when you're not exercising. Exercise also helps maintain muscle. Because muscle burns calories, exercise can also help you maintain the weight you lose, which is often harder than losing weight.
- Some studies show that vigorous exercise can help reduce appetite, therefore exercisers take in fewer calories during the day without even thinking about it.
- Researchers estimate that your body continues to burn calories at a higher rate for between 2 and 24 hours after you finish exercising.

If you have not exercised in a while or plan to do more than walking, check with your physician prior to starting to exercise.

**Tip #3** – The benefits of exercise aren't measured just by a scale, but by a better working body.

Instead of focusing on the minutes that tick by, the calories racked up on the treadmill, or the number on the scale, focus on how exercise changes your body from the inside out.

- It reduces depression and can be especially effective for women who have postpartum depression.
- It can increase insulin sensitivity if you have diabetes; if you're at risk for diabetes, exercise can help prevent it.
- It can help reverse sarcopenia, a condition associated with inactivity and aging in which fat replaces muscle. According to one study, postmenopausal women were able to reverse muscle-mass loss after two months of small increases in physical activity and strength

training. This was linked to better overall health, better balance and fewer falls.

Many people are discouraged by the slow weight loss associated with moderate calorie restriction (250-500 fewer calories per day) plus exercise (mobilizing another 250 calories a day) especially in light of the old adage that muscle weighs more than fat. It can be disheartening not to see your hard work reflected in a lower number on the scale. Some changes can't be measured on the scale. Rather they create a better functioning body. Success isn't about any one workout, but if you challenge yourself for the long-haul and continue to exercise even if your weight isn't changing, you can affect more lasting improvements in your body.

<http://tinyurl.com/yc37g5b>



## 2 EFFECTIVE CORE EXERCISES FOR ADULTS

Before you teach Baby Boomers and older adults a core conditioning routine, remember that in order to maintain stability and support, the core is activated milliseconds before any movement occurs in the body, so don't limit your thinking of core exercises to the abdominals or lower back.

Even small movements in the periphery of the body are sufficient to recruit and condition the core musculature.

Many older people just want to be able to do the things that make them happy--spend time in the garden, travel the world, play with grandkids--and all that these activities require is the ability to move safely and confidently. Here are two exercises that will help them do this—and start sculpting that core as well!

**Ankle Rotations** - Poor ankle mobility affects the ability to walk with a safe and confident gait. It also reduces sensory input to the brain and disrupts balance, potentially causing falls. Building better flexibility in the ankle is simple--just move it! Ankle rotations in each direction are a great way to go, because they result in triplanar motion and increased neural drive to this important joint. And if you think ankle rotation does not recruit the core, just try doing this movement yourself while palpating your lower abdominals!

If seated in chair, sit as tall as possible with back in least supported position in order to best recruit core musculature. Lift right foot off floor approximately 8 inches, and perform 10 slow clockwise rotations of foot. Repeat with 10 slow counterclockwise rotations. Look at foot while moving it. Drawing attention and concentration to the movement will increase range of motion. If capable, perform this movement standing up with only one hand (or even just one finger!) on stable item for balance assistance.

**Side Steps** - Most older clients walk in one direction only--straight forward. At some point during life, we tend to "forget" how to move in different directions, even though a bump from a person walking past in a crowded mall may lead to a nasty sideways spill. Practicing side steps helps develop comfort with a movement strategy that may come in handy in a situation such as this. Additionally, alternating between the narrow and wide foot positions requires recruitment of the core musculature for these large lower-body movements.

Stand behind chair or other stable object (a ballet bar is great for this exercise). Place fingertips of one or both hands on stabilizing object for balance control. Do not lean excessively

into hands. Start with feet together, or as close together as is safe. Then, lift right foot up, as if stepping over low curb, and take full step directly right. This will result in wide stance. Next, lift left foot at same height and bring it back to being directly next to right foot. Return to original position by stepping left foot left, followed by right foot. Build up to several steps in each direction, and try varying hand positions.

<http://tinyurl.com/35277qu>



## ADD THESE TO YOUR SANDWICH TO STOP STROKES

Whether you're noshing on a lean turkey with tomato or a veggie delight, add these to your sandwich to reduce your risk of stroke: onions.

Onions are brimming with flavonols, and new research suggests that these nutritional goodies could downsize the risk of stroke by as much as 20 percent.

### Fabulous, Flavorful Flavonols

The key flavonol compounds for stroke prevention appear to be myricetin, apigenin, luteolin, kaempferol, and quercetin. But don't worry about pronouncing them. Just know that they have inflammation-cooling effects -- especially the quercetin -- and that translates into a lower risk of stroke-inducing blood clots. Flavonols also appear to relax and dilate blood vessels, another buffer against strokes. (Top your grilled veggies, fish, and sandwiches with this easy-to-make Red and White Onion Relish.)

<http://tinyurl.com/2fjg8ok>



### Red and White Onion Relish

From Country Living

Red and white onions simmer with vinegar, sugar, and aromatic cumin seeds to create a tangy-sweet alternative to traditional pickle relishes. Since it needs to marinate for several days, this relish should be prepared at least a week before you want to serve it.

Yields: About 2 1/2 cups

Cook Time: 15 min

Ingredients

1½ cup(s) chopped red onion  
1½ cup(s) chopped white onion  
1 cup(s) distilled white vinegar  
½ cup(s) sugar  
½ teaspoon(s) tricolored peppercorns, crushed  
½ teaspoon(s) cumin seeds

Directions

Combine all ingredients in a small saucepan over medium heat and bring to a boil. Reduce heat to medium low and cook the onions for 15 minutes. Cool completely. Place the relish in a covered container and let marinate, in the refrigerator, for 1 week. Store refrigerated in a covered container for up to 3 weeks.



Information in this newsletter is for educational purposes only. Always consult with your doctor first about your specific condition, treatment options and other health concerns you may have.



**"Thanks for changing the tire, Mr. Cromwell.  
Bob and I both have back problems."**

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