

EFFORTS

Emphysema Foundation For Our Right To Survive



Emphysema Takes Your Breath Away

December 2005

DOCTORS SEEKING VOLUNTEERS FOR GROUNDBREAKING STUDY

New South Wales doctors are calling for volunteers aged between 45 and 80 with Chronic Obstructive Pulmonary Disease (COPD) for a new study involving a groundbreaking test designed to improve treatment of this debilitating illness. The innovative AridoITM Challenge test could potentially change the way that doctors treat COPD — the name given to the family of lung diseases that includes chronic bronchitis and emphysema. There is currently no reliable test available to help determine response to corticosteroid treatment.

Doctors are seeking 140 volunteers who meet the following criteria for the 13 week-long study:

- Aged 45 to 80 years old
- Have mild-to-moderate COPD
- Are a current or ex-smoker
- Have a bad cough or are often short of breath

According to Associate Professor Alvin Ing, Senior Thoracic Physician at Bankstown-Lidcombe Hospital, Sydney the study is open to adults of both sexes with symptoms of COPD. "This could include those people who have recently been diagnosed with mild-to-moderate COPD, or those who have been experiencing symptoms for some time and have been using medications, such as inhaled corticosteroids, as part of their treatment," said Dr Ing.

Dr Ing is urging people who wish to volunteer for the AridoITM Challenge COPD study to call the Australian Lung Foundation COPD hotline on (free call) 1800 818 545 or visit www.lungnet.com.au to register their interest by December 19, 2005. Volunteers are required to attend treatment centres in New South Wales, Victoria, Queensland, South Australia or Western Australia. The New South Wales treatment centres include the Bankstown-Lidcombe Hospital, Sydney and the Peninsula Medical Centre, Umina.

The AridoITM Challenge test is a simple bronchial provocation test (up to 25 minutes long) that requires the patient to inhale small doses of mannitol — a naturally-occurring sugar that has been specially formulated for inhalation. The way in which the patient's airways react to the test may indicate whether or not they will respond to specific treatments, such as inhaled corticosteroids. Doctors can then use the results of this test to measure the patient's disease severity and therefore determine which medications and what dosage are needed to treat it.

According to principal coordinating Investigator and Head of Respiratory Services at Flinders Medical Centre, Adelaide,

Professor Peter Frith, participation in this groundbreaking study will help Australian doctors diagnose the severity of a patient's COPD, assess their need for medication both simply and accurately and monitor how effectively their medication is working. This will permit treatment of a person's COPD using the most appropriate medication.

COPD is the most burdensome respiratory disease in Australia and the fourth most common cause of death. The disease affects one in 10 Australians (approximately one million) over the age of 45. Of these people, only around one in four have been diagnosed. At least half-a-million Australians with COPD remain undiagnosed. The disease is particularly increasing among women.

"The standard approach to treating COPD has been to trial inhaled corticosteroids. Even when response has been poor, patients are often continued on this course of treatment, resulting in less than optimal treatment and possibly unnecessary side-effects," said Professor Frith. "We need a tool that helps identify accurately who will respond to treatment, because not everyone will respond to the same approaches, no matter what the symptoms may tell us. With the right treatment, a patient's quality of life can improve significantly."

Once eligibility is confirmed, the patients will need to visit their closest treatment centre on four occasions over a period of 13 weeks. They will be asked to complete questionnaires, undertake the AridoITM Challenge test, perform lung function tests, take an inhaler for 12 weeks, and to keep a diary of their symptoms. All patients enrolled in the study will receive quality medical care plus their transport expenses to and from appointments.

About COPD

It is a disease in which the airways and air sacs inside the lungs are partially obstructed or destroyed, making it hard to breathe. People with COPD suffer from constant coughing, excessive production of phlegm and increasing shortness of breath that restricts their physical capacity.

"COPD is characterised by restricted airflow to and from the lungs, causing breathlessness, cough and phlegm production," said Dr Bob Edwards, respiratory physician, Chairman of The Australian Lung Foundation and study co-investigator. "It is a major cause of sickness and disability, particularly in smokers or reformed smokers over 40 years of age. "When it is not effectively diagnosed and treated, COPD can lead to a decrease in quality of life and poor participation in exercise activities, hospitalisation, and in some cases, death," said Dr Edwards. It is anticipated that the AridoITM Challenge test will streamline this process and help doctors to more

accurately gauge the severity of the disease and prescribe the right amount of medication.

About the ALF

The Australian Lung Foundation (ALF) is a national, not-for-profit, non-government organisation whose mission is to reduce the burden of lung disease in Australia and promote lung health, through research, education, advocacy and patient support. Established in 1990 and linked to the Thoracic Society of Australia and New Zealand (TSANZ), the ALF national secretariat is located in Brisbane and the organisation has medical and patient representation nation-wide, with more than 100 patient self-help support groups comprising approximately 12,000 members. ...*Source: National Nine News*



INCREASING DIAGNOSES OF COPD UNDERScore NEED FOR EDUCATION

American Lung Association Offers Free Online Resource to Support Millions Affected by COPD

Sharon O'Hara, 66, was humbled by her loss of physical strength. She realized she had reached a low point when she had to crawl on the kitchen floor to feed her dogs. O'Hara, a former smoker, had ignored her diagnosis of Chronic Obstructive Pulmonary Disease (COPD) for two years and now found herself unable to stand. She knew she had no choice but to turn her life around.

O'Hara is not alone. The American Lung Association estimates 10.7 million adults in the United States have been diagnosed with COPD and an estimated 120,000 people will die as a result this year - making COPD America's fourth leading cause of death. According to a recent report in the Journal of the American Medical Association(1), the death rate from COPD has doubled in the last 30 years and is estimated to be the third largest cause of death worldwide by 2020.

To raise public awareness about COPD and provide support to those coping with the disease, the Lung Association and ALTANA Pharma US have partnered for their third annual educational awareness campaign: "Hungry For Air: Breathing Better Together." Beginning November 1, individuals can visit www.lungusa.org to download the free Discover How We Are Breathing Better Together booklet. The booklet features inspirational stories, like O'Hara's, along with advice and support from other COPD patients and caregivers, the latest facts about COPD, questions to ask if you think you have COPD, and additional resources. The booklet will be updated three times throughout November and December to encourage an ongoing dialogue among the new online community.

"Being diagnosed with COPD is difficult news for patients to hear. The incurable disease presents patients with a need to relate with people experiencing the same symptoms, emotions and challenges," said Dr. Norman Edelman, chief medical officer for the American Lung Association and vice president for Health Sciences and professor of medicine at SUNY Stony Brook University. "Many times emotional support is as therapeutic as the medical treatment. It provides motivation for patients to make a significant change for the better."

The Facts About COPD

COPD refers to a large group of lung diseases characterized by obstruction to airflow that interferes with normal breathing. Emphysema and chronic bronchitis are the most important conditions that compose COPD and they may co-exist, hence physicians prefer the term COPD. Primary symptoms of COPD include chronic cough, shortness of breath, a greater effort to breathe, increased mucus production, and frequent clearing of the throat. Long-term smoking is responsible for 80-90 percent of all COPD cases and is the most common cause of COPD, which claims the lives of more than 120,000 Americans annually. A smoker is 10 times more likely than a non-smoker to die of COPD. Other risk factors include occupational hazards, air pollution, heredity, second-hand smoke and a history of childhood respiratory infections.

"Since it seems many smokers or ex-smokers are often unaware of the disease and may harbor feelings of guilt, shame or fear, the signs of COPD may be ignored or misinterpreted," Dr. Edelman said. "While more than 10 million Americans have COPD, it is estimated that 24 million adults have impaired lung function, which indicates that COPD is undiagnosed in more than nearly half the people who may have it." Data continues to indicate that the number of deaths due to COPD is higher among women than men. In 2002, 61,000 females died compared to 59,000 males. "This maybe due to the increasing smoking rate among females compared with the steady smoking rate of men throughout the last half of the century," Dr. Edelman said.

Emerging evidence indicates that COPD also is a disease of systemic inflammation dominated by the production of neutrophils, which may cause epithelial and endothelial damage and lung remodeling. According to estimates by the National Heart, Lung and Blood Institute, chronic bronchitis and emphysema take a heavy toll on our economy. In 2004, the annual cost to the nation for COPD was \$37.2 billion. This included \$20.9 billion in direct health care expenditures, \$7.4 billion in indirect morbidity costs and \$8.9 billion in indirect mortality costs.

Treatable and Preventable Despite Statistics

Despite the statistics, COPD is preventable and treatable. According to the Lung Association, with proper treatment, patients can improve lung function, reduce the number of necessary hospital visits, prevent acute episodes, minimize disability and delay early death. For this reason, a spirometry (lung function) test is strongly recommended at the first sign of symptoms, before the condition has a chance to worsen.

"This disease affects every area of an individual's life, limiting what they can do," Dr. Edelman said. "While we cannot cure COPD, early diagnosis can open the door to treatment options that can dramatically improve the quality of life."

According to O'Hara, the process of regaining an improved quality of life was slow, but she acknowledges an upbeat attitude, optimistic mindset, exercise regimen and support network were influential. "You have to go beyond your shortness of breath and take what you have and turn it around to something positive - this is an opportunity," said O'Hara. "Exercise, have goals, and remember, we don't 'suffer' from

anything. We are not victims." Exercising made such an impact that O'Hara, who once was not able to pick up her granddaughter, will participate in the Lung Association's 3,330-mile bike ride, the Big Ride Across America in June 2006. Sharon is a member of EFFORTS.

.....Source: American Lung Association



EFFORTS MEMBER'S EFFORTS PAY OFF!



Joining Sharon O'Hara-WA ALA trike rider; Lyn Cole-CO Wonder Woman High Altitude competitor; Robert Diday-FL, Ironman; among other EFFORTS members who compete in state, national and international competitions, EFFORTS member Bob Phillips from Ohio, competed and completed the



NYC Marathon this November, as a highlight for World COPD Month. Congratulations to all our EFFORTS athletes, including those who try daily to increase their exercise and endurance levels!



NON-INVASIVE VENTILATION: NEW TOOL FOR THE TREATMENT OF ADVANCED COPD

Treatment of patients with advanced chronic obstructive pulmonary disease (COPD) frequently includes several non pharmacological approaches, such as pulmonary rehabilitation, lung volume reduction surgery and lung transplantation. One additional method is the so-called non-invasive ventilation (NIV), based on a mechanical device which rhythmically blows air through a mask attached over the nose and mouth into the lungs of the patients.

For many years NIV has rendered conflicting results regarding its effectiveness, and adherence to the treatment has been rather poor. This was bad news for a treatment which is costly and time consuming. In a recent study, Orlando Diaz (Catholic University, Santiago, Chile) and his Canadian and Chilean colleagues have challenged this notion. The authors used a schedule which is different from current practices, to apply NIV. Instead of applying unsupervised NIV overnight at home, they used it during daytime, for only 3 hours a day, in ambulatory patients, under close supervision at the hospital.

Patients not only tolerated the procedure better than in previous studies, but also achieved clinically significant improvements in breathlessness during daily activities. These effects were clearly evident after only three weeks of treatment. Another interesting finding was that the benefits obtained still persisted two weeks after suspension of NIV.

These new data suggest that NIV can be used intermittently for short periods, thus improving compliance and quality of life of patients with advanced disease that remain symptomatic despite full standard pharmacological therapy.

.....Source: ERJ, Vol. 26, No 6



SELF-MANAGEMENT EDUCATION IN COPD - KEY TO LOWER HOSPITAL ADMISSIONS

A self-management programme specifically developed for COPD patients, "Living Well with COPD ©", involving communication with a trained health professional over a year, has been shown to reduce hospital admissions and emergency room visits.

Although the original study has important connotations, the present follow-up examination was welcome. It was undertaken by the same team, at the Respiratory Epidemiology and Clinical Research Unit (Montreal Chest Institute, McGill University Health Center, Québec, Canada), under the leadership of Jean Bourbeau.

In this study, patients were kept under observation for two years. Most of them were elderly, not highly educated, and had advanced COPD. The self-management programme included a patient workbook, a written action plan with a customised prescription of antibiotic and prednisone to be used when the patient had exacerbations, and non supervised exercise teaching at home.

Results suggest that the benefit of a reduction on all-cause hospital admissions and emergency room visits is sustained in the long-term. It is the first study that shows beneficial effects of self-management in COPD patients after two-years of follow-up.

These sustained benefits to the health care system could potentially add to patients' quality of life by reducing institutionalisation. It is well known that COPD exacerbation and hospitalisation are determinants of poor quality of life, and important cost drivers.

.....Source: European Respiratory Journal (ERJ), Vol. 26, No 5



PATIENT EDUCATION ALONE NOT ENOUGH TO IMPROVE COPD

Among patients with chronic obstructive pulmonary disease (COPD), increased education, improved self-management skills and enhanced follow-up components of pulmonary rehabilitation do not seem to lead to better health-related quality of life in compared with usual care without such extras, new research shows. Instead, other aspects of pulmonary rehabilitation, such as peer interactions and exercise, may be more essential to improving health, the study authors speculate.

"In contrast to other chronic diseases such as asthma, enhanced patient education and follow-up by a nurse among patients with COPD does not lead to clinically relevant improvements in health outcomes compared to the ongoing care that they are getting from their regular physicians," study author Dr. David Coultas, of the University of Texas Health Center at Tyler told Reuters Health. Coultas conducted the research while

he was at the University of Florida Health Science Center in Jacksonville.

Most commonly caused by cigarette smoking, COPD includes the lung disease emphysema and chronic bronchitis, and is marked by progressively worsening shortness of breath and coughing. COPD is currently the fourth leading cause of death in the United States and worldwide.

To reduce the worldwide economic burden associated with the condition, various teams have published international guidelines on the best way to manage COPD patients. Those guidelines state that optimal management includes pulmonary rehabilitation, which consists of patient education, self-management training, psychosocial interventions and several other components. Many affected individuals do not have access to such rehabilitation services, however, as such care is usually provided at specialized centers.

Coultas and his team speculated that one way to improve patients' access is to offer the most integral components of pulmonary rehabilitation at other off-site locations. Since little is known about which components are most essential, they focused on providing study participants with nurse-assisted home care consisting of patient education, efforts to improve patient self-management skills and enhanced follow-up.

Their study group consisted of 151 adults ages 45 years or older, who were current or former smokers, had previously been diagnosed with COPD, had experienced cough, shortness of breath, or some other respiratory symptom during the previous year and had evidence of airflow obstruction. The study participants were randomly divided into a group that received usual care, a group that received nurse-assisted medical management, which was particularly focused on patient education, or a group that received nurse-assisted collaborative management, which was an even more enhanced type of care. The usual care group received two COPD-related educational booklets from the American Lung Association and was advised to follow their physician's recommendations.

At the end of the six-month study period, the researchers found that neither of the two nurse-assisted groups exhibited a marked improvement in their health-related quality of life compared with the usual care group. Although visits to the emergency department and hospitalizations were infrequent, the intervention groups exhibited no decreases in emergency department visits or hospitalizations as a result of the pulmonary rehabilitation services, the researchers note.

In light of the current findings, "disease management programs that only address patient education and follow-up by a nurse should not be implemented," Coultas told Reuters Health. "To improve health outcomes, patients with COPD need access to the other components of pulmonary rehabilitation, particularly regular physical activity/exercise. In addition, there is a high level of distress (i.e., depressive and anxiety symptoms) that is not being adequately addressed" in COPD patients, Coultas added.

A grant from the Robert Wood Johnson Foundation funded this study.SOURCE: Chest, October 2005.



SEPSIS RISK HIGHER FOR PATIENTS WITH COPD

With data from 15,586 patients included in the Atherosclerosis Risk in Communities (ARIC), as well as up to 11 years of follow-up data, researchers identified patients with COPD, pneumonia, and sepsis. The analysis shows that patients with COPD are more likely to get sepsis, but the risk was dramatically reduced after controlling for pneumonia. Researchers from the University of Kentucky conclude that pneumonia is a very strong predictor of sepsis in patients with COPD.

.....Source: CHEST 2005



WALKING AND SPORTS LINKED WITH HEART HEALTH BENEFITS IN JAPAN, TOO

First study of its kind extends linkage beyond North America and Europe

Even in an Asian nation where people generally have higher levels of physical activity on the job than is typical in North America or Europe, those who walk more or engage in regular sports activity tend to have lower levels of ischemic stroke and coronary heart disease, according to a new study in the Nov. 1, 2005, issue of the Journal of the American College of Cardiology. "The strength of the present study is a statistical power sufficient to detect the effects of physical activity on mortality from cardiovascular disease. We found a significant inverse association between time spent walking and the risk of ischemic stroke in addition to an inverse relationship between sports participation and risk of coronary heart disease in Asian countries, where job-related physical activity is generally higher than in Western countries," wrote the authors, including Hiroyuki Noda, M.D. and Hiroyasu Iso, M.D., from the University of Tsukuba in Ibaraki and the Graduate School of Medicine at Osaka University in Osaka, Japan.

The researchers used data collected as part of a large population study of cancer risk in Japan. Between 1988 and 1990, 31,023 men and 42,242 women aged 40 to 79 years in 45 communities across Japan were given a questionnaire about their lifestyles and medical histories. The participants had no history of stroke, coronary heart disease or cancer. Through 1999, almost 2,000 participants died of cardiovascular disease. For this analysis, the researchers separated the participants into four categories according to the amount of daily walking or weekly sports activity they reported.

Consistent with results of studies done in North America and Europe, those who walked a least an hour a day or engaged in sports at least five hours per week had age-adjusted death rates from cardiovascular disease that were 20 to 60 percent lower than those in the second-lowest category of reported physical activity. Specifically, physical activity was associated with reduced risk of ischemic stroke (stroke caused by a blood clot or other blood flow blockage), coronary heart disease and total cardiovascular disease. There was no statistically significant relationship between physical activity and the risk of a stroke caused by bleeding (either intraparenchymal hemorrhage or subarachnid hemorrhage). "Limitations of the present study included the fact that we did not have systematic information on pre-clinical disorders that prevented the

participants from walking or participating in sports. This might have led to a bias of cause-effect reversal, even though most of the subjects were apparently healthy," the authors wrote.

In order to try to avoid such bias, the researchers used the group with the second-lowest activity level as the reference group, rather than compare those with high levels of physical activity to those with the lowest levels. Thus they hoped to prevent a possibly misleading comparison with people who didn't exercise because they were already ill. The researchers also analyzed the data after excluding anyone who died within two years of the beginning of the study, in order to allow a reasonable amount of lead time for physical activity to potentially have an effect on the health of study participants. Interestingly, the analysis suggested that walking and sports may have different effects. "Our data suggest a potential differential effect of walking versus sports participation on ischemic stroke and coronary heart disease risk. We found that participation in sports was associated with a reduced mortality due to coronary heart disease, but this association did not exist with walking time. Walking time, however, was associated with a reduced risk for mortality from ischemic stroke, but sports participation was not," they wrote.

By demonstrating an association between walking or sports and reduced cardiovascular disease deaths in this Asian population, similar to the results of studies in Western nations, despite differences in average levels of job-related physical activity, the researchers conclude that "the present study provides epidemiological evidence that engaging in physical activity through walking and sports participation might reduce risk of mortality from ischemic stroke and coronary heart disease among Japanese men and women."

Russell V. Luepker, M.D., F.A.C.C., at the University of Minnesota in Minneapolis, who was not connected with this study, noted the strengths of the study design and the valuable health message in the results. "Important strengths of this study include the large number of participants, the inclusion of both leisure and work activity and the extended follow-up period. The use of prevalent cases, short-term mortality and the use of the second lowest exercise category as referent minimizes the effects of those who do not exercise because they are already ill. The graded reduction of coronary heart disease and stroke mortality associated with increasing levels of walking and sports sends a strong message supporting regular physical activity recommendations. The adjustment for other cardiovascular risk factors strengthens the relationship's validity," Dr. Luepker said.

The American College of Cardiology, a 33,000-member nonprofit professional medical society and teaching institution, is dedicated to fostering optimal cardiovascular care and disease prevention through professional education, promotion of research, leadership in the development of standards and guidelines, and the formulation of health care policy.

.....Source: The American College of Cardiology (ACC)



WALKING SPEED PREDICTS HEALTH STATUS AND HOSPITAL COSTS FOR FRAIL ELDERLY PATIENTS

Walking speed screening during hospital admission could help clinicians identify patients who will need the most care in the first year post-hospitalization.

Baseline walking speed and change in speed over one year were used to predict health status, health service use, and costs during the same time period in 1,388 hospitalized elders identified as frail and at risk for functional decline.

A reduction in baseline gait speed was associated with poorer health status and physical functioning; more disabilities, rehabilitation and medical-surgical visits, hospital days; and higher costs. Improved gait speed resulted in higher health status, improved physical function, fewer disabilities, less hospitalization, and a one-year cost reduction of \$1,188.

.....Source: Journal of Rehabilitation R&D



FARM EXPOSURES FREQUENTLY CAUSE COPD

Although smoking is the main cause of COPD, new research shows that patients with COPD frequently have a history of agricultural exposures. Researchers at the Omaha Veteran's Administration Hospital, Omaha, NE, administered a telephone survey to 150 veterans with COPD and found that 68 percent had a history of agricultural exposure. Of these, histories of agricultural exposures included dairy farms (30 percent), hog confinement barns (21 percent), and poultry farms (12 percent). The researchers from the University of Nebraska Medical Center and the Department of Veterans Affairs Medical Center, in Nebraska, suggest that agricultural exposures be included in the health-care analysis of patients living with COPD living in rural areas.

.....Source: CHEST 2005 Abstract Highlights



MINIMALLY INVASIVE SURGERY MAY INCREASE OPTIONS FOR OCTOGENARIANS WITH SOME LUNG CANCERS

Like their younger counterparts, some elderly patients who have early stage non-small cell lung cancer can benefit from a minimally invasive surgical procedure to remove part or all of a lung, according to a study conducted by thoracic surgeons at Cedars-Sinai Medical Center and described in the current issue of *The American Surgeon*, the journal of the Southeastern Surgical Congress and the Southern California Chapter of the American College of Surgeons.

When non-small cell lung cancers (NSCLC) are detected at an early, localized stage, surgical removal of the affected area often can prevent metastasis to other tissues and organs. But while some patients, including the elderly, might not be good candidates for the physical demands of open chest surgery, this study of 159 patients between ages 80 and 94 suggests that video-assisted thoracoscopic surgery should be considered a viable option.

"Some patients and their doctors wonder why a person that age should bother to go through any major pulmonary surgery. The reason is that whether the patient is 80 or 95, if they are in reasonably good physical condition without any other major

medical problems that are imminently life threatening, the odds are that the cancer is going to progress and the patient will live long enough to go through several unpleasant months with widespread cancer," said Robert McKenna Jr., M.D., thoracic surgeon, surgical director of the Center for Chest Diseases and chief of Thoracic Surgery and Trauma at Cedars-Sinai.

"Our study shows that we can do a standard, complete lung cancer surgery in people over 80 with very low risk and good success so that older patients with lung cancer do not have to suffer the consequences of widespread cancer," said McKenna, senior author of the journal article.

According to previous studies, the average 80-year-old can expect to live another 8.6 years, but the average life expectancy of a patient with untreated or palliated early-stage NSCLC is only 1.5 years.

"If you knew that you could get several additional years to live by having a procedure with low risk and good success in preventing widespread cancer, you might want the option of putting up with the short-term inconvenience of having that operation," McKenna said.

In the study, there were no surgery-related deaths and relatively few complications. "Compared to the percentage of people who experience any type of complication after a major pulmonary resection, our numbers were low, and especially low for patients in this age range," said McKenna. Open surgery – accomplished through an eight- to 10-inch incision – continues to be used in about 95 percent of lobectomies nationally. McKenna and his colleagues at Cedars-Sinai, however, use the minimally invasive approach in 89 percent of their cases. VATS requires only several small incisions through which instruments and a thoracoscope are inserted. A camera lens at the tip of the scope feeds high-resolution images to a video monitor, giving the surgeon a detailed, magnified view.

"We have been doing minimally invasive lung cancer surgery for a long time and have the largest experience in the world," said McKenna, a pioneer in the development and use of the technology who has performed VATS procedures since 1989. "We follow our patients carefully and have shown that this is the standard cancer operation with the same survival rates as with invasive surgery, but it has tremendous advantages for patients. The stay in the hospital is less and the complication rate is less. It is not pain-free, but patients are able to recover more quickly and get back to their regular activities much more quickly with this operation."

The term non-small cell lung cancer includes several types of lung cancer that when detected at an early and localized stage may be cured with surgical resection. NSCLC accounts for about 75 percent of all lung cancers.

.....Source: Cedars-Sinai Medical Center



BIG DRUG MAKERS SEE SALES DECLINE WITH THEIR IMAGE

The drug industry's image problems are beginning to hurt pharmaceutical companies where it matters most - at the

bottom line. A year after Merck's withdrawal of its arthritis medicine Vioxx led to an industrywide credibility crisis, the Food and Drug Administration is blocking new medicines that might previously have passed muster. Doctors are writing fewer prescriptions for antidepressants and other drugs whose safety has been challenged, like hormone replacement therapies for women in menopause. Meanwhile, insurers and some states are taking advantage of the backlash against the industry to try shifting patients to older, generic drugs, arguing that they work as well as newer and more expensive branded medicines. Overall, prescriptions continue to rise slightly, but an increasing share of prescriptions are going to generic drugs. Also, consumers seem to be less responsive to aggressive drug marketing.

"A lot of the demand that the industry has created over the years has been through promotion, and for that promotion to be effective, there has to be trust," said Richard Evans, an analyst covering drug stocks at Sanford C. Bernstein and Company. "That trust has been lost." In the background, new competitors are forcing the old-line drug giants to struggle to keep pace. Biotechnology companies like Genentech are taking the lead in finding new treatments for cancer, a promising and lucrative field. Executives of the major drug companies say they expect public scrutiny in the wake of problems with Vioxx and other drugs. But they say they are concerned that consumer mistrust has led to unrealistic expectations about drug safety and risks, stunting the development of new medicines. "I think there is an overall unreasonable expectation right now that there is such a thing as a risk-free drug," said Sidney Taurel, chief executive of Eli Lilly & Company.

The major drug makers remain highly profitable. But at some, including Pfizer and Merck, the largest and third-largest American companies in terms of revenue, sales are stagnant and profits are falling, leading to layoffs and - for the first time in years - cuts in research budgets. In the third quarter, United States sales of prescription drugs fell 3 percent at Bristol-Myers Squibb, 4.5 percent at Johnson & Johnson, and 15 percent at Pfizer. Merck said its overall revenues fell 2 percent despite favorable foreign exchange trends.

The companies are reticent concerning details of layoffs, but both Pfizer and Merck have said they are cutting workers. Even Eli Lilly, where United States sales rose about 5 percent in the third quarter, said it has cut about 1,600 employees - almost 4 percent of its work force - so far this year. No one expects a quick end to the crunch, because several top-selling drugs will lose American patent protection by early 2007. They include Norvasc, a blood pressure medicine from Pfizer, and Zocor and Pravachol, cholesterol drugs from Merck and Bristol-Myers Squibb. Together, those three drugs have almost \$10 billion in annual United States sales.

The drug industry, which is dominated by companies based in this country, is hardly in a full-blown crisis, and layoffs are occurring mainly on the margins of its work force. Pfizer alone will make about \$8 billion in profit this year, on sales of about \$51 billion, and invest more than \$7 billion in research and development - although the company's research spending fell 6 percent in the third quarter of 2005 compared with the same

period in 2004, and Pfizer expects it to stay flat or decline in the coming years. Overall, the industry spends more than \$30 billion annually on research and development.

But for the companies, and for patients who are counting on industry research to produce new treatments for diseases like rheumatoid arthritis and diabetes, these are trying times. Wall Street has also taken notice of the industry's woes. Shares of Pfizer are near their lowest levels since 1997, closing Friday at \$22.43, and a broad index of drug stocks has fallen 25 percent in five years. In contrast, shares of biotechnology companies are soaring. Without new drugs to promote as patents expire, and with the bar set so high by the blockbusters of the last decade, the old-line companies have depended on stopgap measures to protect sales, like reformulating existing drugs so they can be taken once a week instead of once daily. At the same time, they have used consumer advertising to drive patient demand. But those strategies appear to be losing their effectiveness, as consumers become more skeptical and insurers rebel against high prices for drugs that are not therapeutic breakthroughs. For example, in June Pfizer began selling Zmax, an antibiotic that contains the same active medicine as Zithromax, which was introduced in 1992 and lost its patent protection last week. Pfizer calls Zmax a major advance because it is designed to be taken in a single dose, while Zithromax must be taken for up to five days. Both drugs cost about \$52 for a course of treatment, according to Pfizer. However, clinical trials show that the convenience of Zmax comes with a side effect: it causes diarrhea in 12 percent of patients, compared with 5 percent for Zithromax.

"Is the public more cynical? Yes," said Dr. John LaMattina, Pfizer's president of global research. "There's a perception that we don't bring much to the party." Consumers have been irritated for years by drug prices in the United States, which are higher than in other industrialized countries. But anger at the industry reached a new pitch in the summer of 2004, with the disclosure that several companies had suppressed the results of clinical trials that showed an increased risk of suicidal thoughts by people taking antidepressants.

Then Merck stopped selling Vioxx after a clinical trial showed that the painkiller increased the risk of heart attacks and strokes. Internal Merck documents showed that company executives and scientists were concerned about Vioxx as early as 1997 but rejected plans to conduct a study of the heart risks. Merck has said it acted properly in its handling of Vioxx studies. A poll last month showed that only 9 percent of Americans believed drug companies were generally honest, down from 14 percent in 2004. In contrast, 34 percent of people said they trusted banks, and 39 percent trusted supermarkets. "The incessant direct-to-consumer advertising on television I think has boomeranged," said Dr. Marcia Angell, a former editor-in-chief of *The New England Journal of Medicine* and a frequent industry critic. Dr. LaMattina and other executives say that perception unfairly disregards the billions of dollars that drug companies spend on research each year and the hundreds of important medicines they have

discovered since World War II. Even the industry's staunchest defenders agree that it needs to explain risks better.

"We've created an impression with the American public that when a drug is approved, it's perfectly safe," said Billy Tauzin, president of the Pharmaceutical Research and Manufacturers of America, a lobbying organization for brand-name drug companies. "We have not done a good job about educating the patients of America that all drugs come with significant side effects." Mr. Tauzin said the industry was "beginning to make progress and turn things around." He said it was addressing its image crisis by being more careful with its advertising, by pledging more disclosure of clinical trial results and by working to make low-priced drugs available to poor and uninsured Americans.

The industry is counting on research into genetics and the basic mechanisms of cellular behavior to produce genuine breakthroughs in treatment for diseases like diabetes. But executives and outside analysts warn that such a revival will probably not happen before the end of this decade at the earliest. "Early stage pipelines are very, very full in a lot of companies," said Mr. Taurel of Lilly, which is the sixth-largest American drug company, and one of the few that is substantially increasing research spending. "But it will take some time for all of these products to reach the marketplace." Further, the companies are victims of their own success in some important drug categories, such as diabetes, where existing treatments work well enough to discourage the F.D.A. from approving new drugs if they have significant side effects. Last month, Bristol-Myers Squibb said it might stop research on Pargluva, a new diabetes drug, because the F.D.A. had said it would not approve it without additional clinical trials that might take up to five years. Pargluva is not the only drug the federal regulatory agency has blocked recently. In September, the agency turned down two drugs from Pfizer, a painkiller and an osteoporosis medicine. Last month, it rejected Johnson & Johnson's bid to market a drug to treat premature ejaculation. Before the Vioxx withdrawal, the F.D.A. would probably have approved Pargluva, and the other drugs would have had a better chance, said Les Funtleyder, an analyst with Miller Tabak. Now the agency is taking longer to review drugs and weighing side effects more seriously, "The F.D.A. has changed," Mr. Funtleyder said. "Nobody wants to be on '60 Minutes' " being asked about why a dangerous drug was approved. *New York Times*



GROUP PROVES IT'S POSSIBLE TO GROW NEW LUNG ALVEOLI BY GROWING NEW BLOOD VESSELS
University of Alberta researchers pioneer gene therapy to restore alveoli and lung capillaries in damaged rat lungs; first step in one day helping premature babies

The good news is that medical advances in perinatal care have allowed us to save many more premature babies. The bad news is they're often at risk of developing bronchopulmonary dysplasia--a chronic lung disease caused by having to place the tiny infants on ventilators and oxygen-rich therapy for acute respiratory failure. It's really a win-lose situation: the babies are

saved but they pay the price with dramatically underdeveloped lungs--forcing them to spend their early days outside the womb fighting for every breath. And now, with many of these premature babies reaching their adolescent years, clinicians and researchers are also waiting to see whether longer term health problems are going to begin occurring. "Right now we simply don't have any treatments," says Bernard Th  baud, a clinician-scientist and neonatologist in the Department of Pediatrics. "So, if we can't prevent it, we've started to think about how we might repair it."

Using animal models, Dr. Th  baud and a team of University of Alberta researchers have taken what they say is the first important step towards a treatment--in effect, growing new blood vessels and alveoli--the tiny air sacs where gas exchange occurs between the lungs and blood vessels--in tiny rat lungs.

The results have caused a stir in the scientific community: In an accompanying editorial in the October 18 issue of the journal, Kurt Stenmark, a University of Colorado Divisions of Critical Care and Pulmonary Medicine researcher, said the studies "...raise new possibilities for the treatment of infants with severe chronic lung disease. It seems possible that by augmenting or restoring vascular growth, overall lung growth and ultimately lung function can be restored." Doing that involved a new gene therapy technique, explains Dr. Th  baud. Knowing that a particular protein, VEGF, a vascular endothelial growth factor, is crucial for the normal development of the lung, and that angiopoietin-1, another angiogenic growth factor is crucial for blood vessel maturation, the team attached the proteins to an adenovirus and administered it through an aerosol directly into the lungs. In effect, the virus carried the protein to the heart of millions of lung cells. Once inside the cells, the growth factor proteins went to work doing the job they were programmed to do.

The results were striking: In microscopic images, the scientists have charted the growth of alveoli and lung capillaries. In a typically healthy lung, a complex network of capillaries encircles the alveoli. Oxygen flows from the lungs through ultra-fine epithelial and endothelial tissues into the blood; carbon dioxide diffuses from the blood into the alveoli. In an infant's underdeveloped lungs, the alveoli are larger and fewer and there are fewer developed capillaries. It's a condition that leaves them gasping--and one that is shared by people who have emphysema. "At this stage it's simply proof of principle," says Dr. Th  baud, also a pediatrician at the Stollery Children's Hospital's Neonatal Intensive Care Unit. The next step is to prove it's possible to replicate safely in larger mammals. Once that's done, it's possible the concept--growing blood vessels to cure a disease that is traditionally thought of as an airway disease--could be tested clinically in people.

.....Source: University of Alberta



EMBRYONIC STEM CELLS

New experiments that prevented rat sperm stem cells from changing permanently into sperm have brought researchers one step closer to coaxing such cells to behave like embryonic stem cells, capable of growing into many other types of cells in the body. Researchers at the Cecil H. and Ida Green Center for Reproductive Biology Sciences at UT Southwestern Medical Center devised methods to keep male rat germ-line stem cells - sperm precursor cells - from differentiating, or changing, into sperm proper. The researchers also froze the sperm stem cells, thawed them, and transplanted them back into rat testes, where they developed into normal sperm.

Dr. David Garbers, professor of pharmacology, director of the Green Center and senior author of a study appearing in an upcoming issue of the Proceedings of the National Academy of Sciences, said the new work has many potential applications, including a possible alternative to embryonic stem cells, the development of new male contraceptives and new animal models to test stem cell-based therapies. Germ-line cells are those such as egg and sperm and their precursors whose genetic material can be passed to offspring. "The ability to manipulate male germ-line stem cells and get them to grow and self-renew is a major step," said Dr. Garbers, a Howard Hughes Medical Institute investigator at UT Southwestern. "We're only one step removed from another major step, the Holy Grail for us certainly, which is pushing these cells back a level to a state that is pluripotent-like, similar to embryonic stem cells. That's what we're focused on now."

Pluripotent cells have the potential to change into many other types of cells in the body, such as liver cells and brain cells. Their potential use in humans to treat diseases like diabetes and Parkinson's is controversial because currently the only source of such cells for research is human embryos or mouse cells. Recently another research team published results showing that mouse male germ stem cells could be made to exhibit pluripotent characteristics, but those findings have yet to be repeated.

Ordinarily, when germ stem cells divide into two cells, one "daughter" cell differentiates to become a sperm while the other remains a stem cell. Until recently, researchers had been unable to keep such germ-line stem cells from differentiating for extended periods of time. In contrast, embryonic stem cells from mice and humans have been kept from differentiating indefinitely. A research team in Pennsylvania recently reported similar results with rat sperm to those of the UT Southwestern work; however the UT Southwestern team used substantially different techniques for sorting, growing and maintaining their stem cells in culture. Armed with a long-lived, renewable source of rat sperm stem cells, researchers at UT Southwestern are now working to genetically manipulate those cells. For example, the scientists want to delete specific genes from the sperm stem cells and transplant the cells back into male rats, with the goal of producing "knockout," or genetically altered, animals to study health and behavioral effects related to those missing genes. Knockout mice are often used in research, but

SPERM STEM CELLS CLOSER TO BEING LIKE

they are produced using a different method than the new sperm-cell approach.

"It will be quite valuable to bring this to the rat because it would enable us to generate knockout rats to do genetic studies," said Dr. Kent Hamra, assistant professor of pharmacology at UT Southwestern and lead author of the PNAS study. "It is a larger animal, it's often better for toxicology and physiology studies, and its behavior is more in tune with that of humans in many cases. It's also important to be able to produce pluripotent rat cells, because we would then have another animal model to test stem cell-based therapies, such as correcting diabetes." One of the next steps is to determine whether human male germ-line stem cells can also be immortalized in culture. Although genetic modification of human sperm is not one of their goals, the researchers say it may be possible someday to correct genetic defects in humans - cystic fibrosis, for example - by identifying and eliminating in culture a man's sperm stem cells that carry the gene.

Dr. Garbers said that a renewable source of cultured sperm stem cells, rat or human, also could be used to test for male-directed contraceptives, and a company is already interested in this possibility. One of the breakthroughs in this study was developing a new type of medium to grow the cells in, and another was the use of a genetically manipulated "tag" that specifically labeled germ cells with a green fluorescent protein, making the germ cells easier to identify when mixed with other cell types. "The rat testes contain other cells types in addition to stem cells," Dr. Hamra said. "If these other cells are included in the culture, they produce chemicals that block the ability of the stem cells to remain stem cells. We're still trying to figure out why. But the key is to start with a sample that is 100 percent pure germ cells, which we achieved using the fluorescent marker and other purification methods that are different from those used by other research groups."

.....Source: medicalnewstoday.com



STAR RISES IN FIGHT AGAINST BIRD FLU

Demand for a Chinese Fruit Skyrockets

For the past three decades, Qin Chenghao has lived the life of an ordinary farmer. He has tended to the trees covering the mountains that rise from the musty soil of southern China, harvesting the star-shaped fruit on their branches. Year after year, the same few traders arrive to buy his crop to sell as seasoning and traditional medicine. This year, however, Qin's world changed. The star anise dangling from his trees emerged as a source for the key ingredient in Tamiflu, a pharmaceutical known to lessen the severity of avian flu. The output from his 1,300-acre Darong Mountain Star Anise Plantation in Guangxi province is now more than a simple means of spicing up stewed pork -- it is a crucial weapon in a global campaign against a pandemic that health experts say could kill tens of millions of people.

With its semi-tropical climate and crowded cities and villages chockablock with pork and poultry farms, southern China is believed to be the source of the H5N1 avian

influenza, which has been blamed for the deaths of at least 64 people in Asia since 2003. Now the very same area may hold the antidote as well. It literally grows on trees.

Dried star anise -- or *bajiao*, as it is called in Mandarin Chinese -- is a spice found in many Chinese kitchens, imparting a licorice-like taste to stewed meats. For as long as anyone can remember, Chinese doctors have prescribed *bajiao* to treat colic in babies, as well as headaches, abdominal pain and intestinal distress in adults. More recently, farmers in northeastern China have mixed *bajiao* into animal feed because it keeps livestock warm through near-arctic winter months. Although most star anise is consumed domestically, a small export market also exists. The French, for example, are increasingly using star anise as flavoring for Pernod and other anisette liqueurs. And in the United States, star anise is found in five-spice powders available in grocery stores.

When Tamiflu was invented nearly a decade ago by researchers at Gilead Sciences Inc. in California, they used a different substance, quinic acid from the tropical cinchona tree. But when Roche Holding AG, the Swiss pharmaceutical giant, bought a license to make the drug, it substituted a form of star anise found in southwestern China. This year, with bird flu hopperscotching from Southeast Asia to Turkey to Britain, Roche has embarked on an expansion campaign aimed at increasing the production of Tamiflu tenfold over 2003 levels by the end of next year. Guangxi province -- home to 90 percent of China's star anise, which is itself the source of 90 percent of the global supply -- has become the heart of a crucial industry.

Health authorities do not recommend using star anise to try to ward off the flu. While production of Tamiflu starts with the acid contained in star anise, it involves multiple chemical steps, some using dangerous explosives, and the resulting drug does not remotely resemble the original material. Moreover, the U.S. Food and Drug Administration warned in 2003 that some star anise teas sold in health-food stores were making people dangerously ill. These were thought to be made from Japanese star anise, which contains a dangerous compound not present in the Chinese spice. The FDA warned that "Japanese star anise in its dried or processed form cannot be distinguished from Chinese star anise through visual examination."

In a written statement, Roche said it relies on Chinese star anise for about two-thirds of its needed shikimic acid. The company said it is expanding efforts to increase production of the compound through a fermentation process that does not require star anise.

.....Source: The Washington Post



SOAP DOPE

Claim: A bar of soap between the bedsheets will prevent leg cramps.

Status: Undetermined.

Origins: Many people are plagued by nocturnal leg cramps, those involuntary and agonizing muscle contractions that strike in the depths of the night, waking sleepers with jolts of pain that leave them

awash in waves of suffering until the kinks finally relax.

While many possible causes have been posited for these contractions, those afflicted by them are far more concerned with getting rid of these debilitating cramps than they are with understanding their origin. Over the years, many preventions have been suggested, including:

- Stretching one's calf muscles prior to going to bed.
- Swearing off caffeine in the evening.
- Increasing one's intake of potassium, magnesium, calcium or Vitamin E.
- Sleeping on one's back with toes pointed towards the ceiling.
- Taking quinine (now available only by prescription) or drinking tonic water (which contains small amounts of quinine).
- Increasing one's intake of water during the day.

While all of the above have been said to avert the problem in at least some cases, one further suppression trick appears to work, at least according to anecdotal information, for almost everyone so bedeviled: sleeping with a bar of soap in the bed. No one has yet produced a plausible explanation as to why snoozing with one's Ivory might stave off those devastating nocturnal leg cramps, yet the reports of its doing so are numerous.

Slipping a bar of soap into the bed as a leg cramp prevention has been advanced by a number of authorities, both medical and otherwise. Ann Landers has mentioned the soap cure in her column on a number of occasions, with each airing prompting a load of letters from readers thanking her for this information because it worked wonders for them. "They were thrilled and grateful to be liberated from those leg cramps," said Ms. Landers.

As to how this works — or even if it does — we're still in the dark. Perhaps soap releases something into the air that is beneficial to those predisposed to this condition, with the bedsheets working to contain the helpful emissions to the area where they are needed. Or perhaps this is a case of believing making it so — the soap itself has no effect, but the sufferer's faith in the procedure serves to effect the miracle.

Yet skepticism aside, for those subject to nocturnal leg cramps, this bit of folk wisdom is clearly worth a try, in that the only potential downside is their having to share their beds with slivers of soap. (Well, that and having their spouses think them a bit loony.) As to what sort of product and where to place it in the bed, although some who pass along this bit of housewifely lore indicate specifics such as the soap's having to be unwrapped or not be a specific brand (Dial and Dove are often mentioned as bars to eschew), those who swear by the procedure have had success whether they used large bars or the small ones commonly found in hotel rooms, whether the cakes of soap were wrapped or unwrapped, and whether the afflicted leg was rested on top of the soap or not. As for which brand is best, cautions against Dove and Dial to the contrary, they all seem to work about the same.

As to what to do about an existing leg cramp, folk wisdom

once again offers a variety of potential answers:

- Ingest a teaspoon of yellow mustard.
- Drink a glass of water that has a quarter of a teaspoon of baking soda mixed into it.
- Pour salt into your hand and lick it.
- Pinch the skin between the nose and the upper lip.

.....Source: snopes.com



THE TASTY SPICE WITH NUMEROUS INCREDIBLE HEALTH BENEFITS

For years, cooks have used turmeric in their kitchens to impart a unique flavor. In fact, turmeric is what gives yellow mustard its distinct color. It's also found in Worcestershire sauce, another favorite staple. You might even find it among the spices being added to your holiday turkey.

The truly amazing parts about turmeric are the powerful effects outside the kitchen, particularly regarding the brain, joints and immune system. In an article just published (October 2005) in the Journal of Neuroscience Research, investigators from the University of Missouri studied the effects of curcumin (the active component of turmeric) against brain injury. Gerbils were exposed to global cerebral ischemia (basically cutting off the blood supply to the brain). When their brains were studied, it was noted that there was a large amount of reactive cells leading to what is known as lipid peroxidation and eventual cell death through apoptosis—this is where the cell literally kills itself. The animals were then pretreated with curcumin, either orally or through injection. Blood supply to the brain was again cut off. What the researchers found in the gerbils pretreated with curcumin is that there was a decrease in the lipid peroxidation along with a decrease in cell death. It was felt that the neuroprotective effects of curcumin were attributed to its antioxidant capacity in reducing oxidative stress. It is well proven that the actual stroke a person may be afflicted with does not immediately cause the most severe brain death. It is actually flood of free radicals that occur hours and days after the stroke occurs.

In another study published in Neurobiology of Aging last month, researchers out of UCLA attempted to identify potential preventive strategies for Alzheimer's disease. One of the ways that researchers would follow the damage of Alzheimer's disease was through the accumulation of a protein called amyloid within the brain. It was found that curcumin, along with DHA (an omega-3 essential fatty acid from fish oil) limited amyloid deposits, oxidative damage and cognitive deficits in mouse models. The researchers indicated that both DHA and curcumin have favorable safety profiles, epidemiology and efficacy, and may exert general anti-aging benefits. There have been multiple other laboratory studies published likewise confirming this.

Earlier this year (April 2005) in the journal Current Alzheimer Research, researchers again out of UCLA, indicated that there was substantial in-vitro data indicating that curcumin had anti-inflammatory and anti-amyloid activity, and that it may be a promising agent for patients with Alzheimer's disease.

Work is now underway to initiate a study of curcumin in patients with Alzheimer's disease.

Curcumin also appears to be a potentially-powerful nutrient against cancer cells, although the mechanism is unclear. It may be related to its anti-inflammatory/antioxidant effects. Curcumin may also inhibit cancer development by inhibiting a certain enzyme system known as cytochrome P-450. There is other research indicating that curcumin may arrest the proliferation of cancer cells in various phases of the cell cycle. There is even data to indicate that curcumin can have what is known as an anti-angiogenic quality; in other words, it can help stop the spread of tumors. This is very important, because most people die from cancer because of this spreading (metastasis) to other healthy organs in the body. A study from the October 2005 Clinical Cancer Research found that curcumin suppressed the growth of tumors in mice afflicted with head and neck cancer¹. For tumors to grow, they require a constant supply of oxygen and nutrients. As they continue to grow, they develop new blood supplies to help maintain this flow of nutrients. By inhibiting the growth of new blood vessels, you can basically starve cancer to death. Curcumin is currently being actively studied in many prestigious medical centers, not only in this country, but throughout the world. Currently there is an open-label human trial with curcumin at the M.D. Anderson Cancer Center in Texas in patients with multiple myeloma. It is important to point out the dosages being used in this study are in the many thousands of milligrams per day; you cannot obtain this level from diet alone.

In a study with NSAIDs, including COX-2 inhibitors and ibuprofen (JAMA, August 2001), the study indicated people who had heart attacks and took these drugs increased their risk of death by up to 500%! There are safer and natural ways to reduce pain, inflammation and improve joint function. In a study published in The Veterinary Record from April 2003, sixty-one client-owned dogs with osteoarthritis were recruited for a double-blinded, placebo-controlled study. Approximately half the dogs were treated with a curcumin and essential oil formula, with the other half being treated with placebo. At the end of the eight-week trial, the investigators' overall assessment showed a statistically-significant beneficial effect in favor of the curcumin formula, but the owners' assessments just failed to reach statistical significance. This study was interesting because there is no placebo effect in animals.

While glucosamine and chondroitin are probably the most known and researched of the natural joint pain remedies, they are certainly not the only ones of which you should be aware. Turmeric, or the curcuma longa plant, is one of the key ingredients in many curries, and has been used for thousands of years by practitioners of traditional Indian (ayurveda) medicine as an effective anti-inflammatory agent. Remember, it is inflammation in your joints that causes the vast majority of pain. The active agent in turmeric, known as curcumin, has been shown to reduce inflammation by lowering histamine levels and possibly by increasing production of natural cortisone by the adrenal glands. In a study published last

August in the journal Life Sciences, researchers in Thailand showed that the active ingredients in turmeric suppressed the overproduction of nitric oxide, which can cause inflammation. These results suggested that the active ingredients in turmeric possess strong anti-inflammatory activity and have a potential to be developed as a therapeutic compound for diverse neurological disorders associated with inflammation.

Several other important clinical studies have also shown turmeric's power as an anti-inflammatory. In a study published in the Indian Journal of Medicine the anti-inflammatory action of curcumin in patients with rheumatoid arthritis was researched. The study demonstrated a significant improvement in the duration of morning stiffness; walking time and joint swelling with curcumin. Another study published in the International Journal of Clinical Pharmacology Therapy evaluated the anti-inflammatory property of curcumin in patients with post-operative inflammation. The researchers tested the effects of the NSAID drug phenylbutazone and curcumin vs. placebo. They both had better anti-inflammatory responses in patients, compared to the placebo. The anti-inflammatory properties of this ancient herb may provide many with joint-pain relief.Source: Dr. Allen Josephs



EMERGING TREATMENT FOR DIABETES, OBESITY, AND SMOKING

A new drug, rimonabant, may soon be available to treat obesity, diabetes, and metabolic syndrome. In addition, it promises to aid smoking cessation. Rimonabant is the first of a new class of pharmaceuticals: selective CB1 blockers. To date, results of phase III studies indicate that rimonabant helps overweight/obese patients lose weight while improving their metabolic profiles. Data also show that patients with diabetes were able to lower their HbA1c in one year of therapy and that smokers had a higher quitting success rate in 10 weeks without the usual postcessation weight gain.

Obesity, diabetes, and tobacco dependence seem to be related to an overstimulated endocannabinoid (EC) system. This system is believed to be important in regulating energy homeostasis and is thought to have a role in nicotine dependence. In overweight or obese people, overeating and fat accumulation is associated with overactivation of the EC system. The system also becomes imbalanced with chronic tobacco use.¹ In the brain, antagonizing the CB1 receptors in the EC system tends to reduce hunger and helps people stop smoking. In adipose tissue, antagonism of the CB1 receptors increases the levels of adiponectin--a cytokine secreted by fat tissue. Obese individuals have reduced plasma adiponectin levels, a reduction that is associated with increased insulin resistance and a higher risk of developing diabetes.

Obesity

Obesity is a complex disease that arises from the accumulation of excess fat in the body from overconsumption of fatty foods and carbohydrates. An estimated 97 million people in the United States are overweight or obese, and obesity is the second-leading cause of preventable death in the U.S. It

substantially raises the risk of morbidity from a variety of conditions, including hypertension, dyslipidemia, and diabetes. The relative risk of developing diabetes increases by 9% for every kilogram of body weight above the recommended range. In the last decade, the percentage of obese/overweight people living in the U.S. has risen to 54.9% of adults 20 years or older. It is now known that intra-abdominal adiposity is a strong predictor of myocardial infarction. Abdominal fat content is positively correlated with waist circumference. Nearly half of adult Americans have a waist circumference that exceeds the at-risk level, which is defined as 40 inches for men and 35 inches for women. Abdominal obesity is also associated with dyslipidemia and insulin resistance that may lead to type 2 diabetes and cardiovascular disease.

Diabetes

During the 1990s, the worldwide incidence of diabetes increased by one third. The number of people in the world diagnosed with diabetes may rise from the current 194 million to 333 million by the year 2025 if nothing can be done to slow this epidemic. Conclusive evidence indicates that good control of blood glucose can substantially reduce the risk of complications and slow disease progression in all types of diabetes. Both management of high blood pressure and lipid control are equally important. Weight loss lowers blood glucose levels in overweight and obese people with or without diabetes. It decreases the chance of developing diabetes, and in some patients diagnosed with diabetes, it can reduce HbA1c and blood glucose levels.²

Metabolic Syndrome

Metabolic syndrome is a constellation of risk factors that collectively increase the risk of cardiovascular disease. Some risk factors for metabolic syndrome include abdominal obesity, elevated fasting blood glucose, lipid disorders, and elevated blood pressure. Metabolic syndrome is a precursor to diabetes, and it is becoming increasingly common as a result of an increased prevalence of obesity. More than 22% of Americans meet the criteria for this syndrome. The goal of treatment is to reduce the likelihood of the development of diabetes and to decrease cardiac risk factors. Diet and exercise target the underlying causes of metabolic syndrome and are the cornerstone of any treatment plan. Statins and gemfibrozil are used successfully to normalize lipid profiles, thereby lowering the risk of cardiovascular events. Optimal goals for hypertensive therapy are needed, and emerging evidence suggests that angiotensin-converting enzyme inhibitors may have a role in reducing the incidence of new-onset diabetes.

The RIO Program

Over 6,600 patients have participated in the four studies in the Rimonabant in Obesity (RIO) Program. These studies have shown rimonabant's efficacy in treating obesity, diabetes, and metabolic disorders. RIO-Lipids: This study enrolled 1,036 overweight or obese patients with untreated dyslipidemia. During the trial, subjects were put on a reduced calorie diet for one year and were randomized to take 5 or 20 mg of rimonabant daily or placebo.

The complete set of results for this trial has not yet been

published. Thus far, reported data indicate that subjects who completed the study and were taking 20 mg of rimonabant lost more weight than those taking either 5 mg daily or placebo, and their lipid profiles improved significantly. Researchers also found a 41% increase in adiponectin versus a 13.6% increase in placebo. The increase in adiponectin may explain the beneficial effects of the drug on some metabolic risk factors. Additionally, C-reactive protein was decreased by 27% in subjects taking 20 mg of rimonabant daily, and insulin sensitivity.

Smoking

Smoking is the leading cause of preventable death in the U.S. and can negatively impact people at all stages of life. Nearly one fourth of adults in the U.S. smoke cigarettes. Almost half a million of U.S. deaths are attributable to smoking each year. Once nicotine addiction has occurred, it is very difficult to quit smoking. Patients who attempt to quit should be encouraged to use effective pharmacotherapies for smoking cessation, except in the case of special circumstances. There is a vital need to increase smoking cessation counseling for patients with diabetes, considering the strong, consistent data on smoking prevalence and the combined risks of smoking and diabetes for morbidity and mortality.

The Stratus Program

Rimonabant may be effective in helping patients quit smoking. The Studies with Rimonabant and Tobacco Use (Stratus) Program consists of three phase III trials designed to explore the role of rimonabant in smoking cessation and long-term abstinence. In addition, the aim of the program is to examine the prevention of weight gain in association with smoking cessation. Over 6,500 patients have been enrolled in the trials worldwide. Stratus-U.S. and Stratus-EU are both 10-week trials, with 42-week follow-up treatment. Stratus-WW is a one-year study, with one year of follow-up treatment. Stratus-U.S. Trial: This trial was one of the largest smoking cessation trials ever conducted in the U.S. Investigators enrolled 787 smokers who were motivated to quit but had failed in previous attempts. Subjects were an average age of 42, smoked 23 cigarettes per day, had smoked for 11 to 24 years, and were classified as moderately to heavily dependent on nicotine, based on the Fagerstrom Scale. For 10 weeks, patients received a daily dose of 5 or 20 mg of rimonabant or placebo. Results of Stratus-U.S. show that of those who completed the trial, 36.2% of subjects taking 20 mg of rimonabant remained tobacco-free, compared to 20.2% of subjects taking 5 mg of rimonabant and 20.6% of the placebo group. The rate of side effects in the rimonabant groups was slightly higher than that in the placebo group. Side effects were mostly mild and transient. No cardiovascular safety concerns were identified with rimonabant.

Conclusion

Currently, rimonabant is unavailable in all countries. Some potential indications of rimonabant are smoking cessation, obesity, insulin resistance, hyperlipidemia, and prediabetes. Several CB1 antagonists have been synthesized. Rimonabant is currently the only endocannabinoid receptor antagonist in clinical development. With its unique method of action,

successful clinical trial results, and mild side-effect profile, rimonabant exhibits promise in becoming an important therapeutic tool to treat diabetes, metabolic syndrome, smoking, and obesity. Sanofi-Aventis, the drug's maker, filed a new drug application with the FDA and hopes to bring rimonabant to the U.S. market in 2006.

.....Source: U.S. Pharmacist



ROLE OF VITAMIN D IN BONE HEALTH IN AMERICANS OVER 50

Leading Osteoporosis Experts Reach Consensus

The American Medical Women's Association (AMWA) today issued physician recommendations to generate greater understanding of the role of vitamin D in bone health in women and men over 50, calling for an increase in currently recommended vitamin D intake and encouraging individualized treatment in patients. According to an analysis published in 2004 and based on the Third National Health and Nutrition Examination Survey (NHANES III), over 70 percent of women ages 51-70 and nearly 90 percent of women over 70 are not getting the recommended adequate intake of vitamin D. For this reason, AMWA recently convened a panel of experts to discuss the importance of vitamin D for overall bone health, the challenges of ensuring adequate vitamin D intake and how to best communicate this information to primary care physicians, specialists and patients.

Vitamin D, an essential component in bone health, helps ensure that the body absorbs and retains calcium, which is critical for building strong, healthy bones. Vitamin D deficiency has often been linked to osteoporosis, a condition that affects more than 10 million Americans and threatens 34 million others. "We agreed that there is a need for increased awareness of the role of vitamin D in osteoporosis treatment," said Felicia Cosman, MD, clinical director of the National Osteoporosis Foundation and associate professor of clinical medicine at Columbia University School of Medicine, and chair of the expert panel. "These recommendations will serve to call attention to the high prevalence of vitamin D deficiency and help ensure that patients, particularly women and men over 50, receive optimal care for bone health."

The panel outlined the following action points regarding vitamin D and its role in bone health for physicians treating women and men over 50, including:

- Optimum treatment for bone health should be individualized and may include a combination of exercise, healthy diet, vitamin D and calcium supplements, and potentially, prescription medications.
- Women and men over 50 receiving treatment for osteoporosis need to receive adequate vitamin D. Supplements are recommended as one of the best sources of vitamin D.

- Current daily vitamin D intake requirements for women and men over 50 should be increased to 800-1,000 International Units (IU).

An Increase in Current Vitamin D Intake

Current recommendations from the Institute of Medicine (IOM) for vitamin D intake are 400 IU for women and men ages 51-70 and 600 IU for women and men over 70. The roundtable panelists expressed concern that current recommendations do not provide for optimal bone health and recommended that intake levels be increased to 800-1,000 IU per day for patients over age 50. In addition to the government data that found 70-90 percent of postmenopausal women are not taking the recommended adequate intake of vitamin D, an additional study found that over half of postmenopausal women already being treated for osteoporosis have inadequate levels of vitamin D, underscoring the need for more aggressive treatment guidelines and greater overall awareness of the role of vitamin D in bone health.



Fortified milk is a primary source of vitamin D for many people in the United States. In Iceland, many people instead turn to cod-liver oil—a far richer their intake source—to boost e of this vitamin.

"The recommendations we provided are designed as a guide for primary care physicians and specialists and are sufficient for most patients. However, some patients may need to obtain serum levels of vitamin D, as determined by their physician, to ascertain vitamin D adequacy. Vitamin D deficiency should ultimately be treated on a patient-by-patient basis" said Kimberly Templeton, MD, AMWA representative and associate professor of orthopedic surgery at the Kansas University Medical Center and fellow of the American Academy of Orthopaedic Surgeons (AAOS). "I

encourage people to speak to their physicians about whether vitamin D supplementation may be appropriate. In addition, patients can access an online brochure on the AMWA web site to learn more about the role of vitamin D in overall bone health."

Obtaining Adequate Levels of Vitamin D

Vitamin D is produced in the body after exposure to UVB rays. Indeed, individuals can obtain over 90 percent of vitamin D through sun exposure, but the panel agreed that this is becoming increasingly difficult as a result of the wide use of sunscreen and protective clothing, due to concerns about skin cancer and other skin diseases, aging and geographic limitations. Vitamin D is also found naturally in a limited number of foods, such as fatty fish, and in certain fortified foods such as milk, orange juice and ready-to-eat cereal. However, many of these foods are not part of most people's diets or must be consumed in large volumes to meet the requirement. Therefore, supplements were recommended as one of the best sources of vitamin D for many older Americans.

In using supplements, the panel advised that physicians should help their patients choose the supplement that is right for them by explaining the medical terms associated with the different forms of vitamin D. Although bone health was the primary focus of the recommendations, the panelists also

reviewed other research studies published in the recent months that reflect on vitamin D's ability to potentially protect against lymphoma and cancers of the prostate, breast, colon, ovary and other cancers, and noted that a variety of research is currently underway to examine the effects of vitamin D on other health conditions.

The Fundamentals of Vitamin D in Bone Health

Vitamin D plays an important role in building and maintaining healthy bones by promoting calcium absorption. Suboptimal levels of vitamin D are associated with reduced calcium absorption, bone loss and an increased risk for osteoporosis - a condition characterized by low bone mass, bone fragility and susceptibility to fractures, especially of the hip and spine. In fact, the first-ever Bone Health and Osteoporosis: A Report of the Surgeon General (2004) listed vitamin D, along with calcium and physical activity, as the three key elements to maintaining optimal bone health. Based on relevant clinical practice experience and involvement in various research that highlights the role of vitamin D in bone health, the panel concluded that it is of paramount importance that vitamin D be considered in patients being treated for osteoporosis and other bone diseases.

.....Source: American Medical Women's Association



VITAMIN D BOOSTS CALCIUM POTENCY

Many older adults, especially women, face a constant battle to preserve their bones' density. They pop dietary supplements and try to stick to menus with foods rich in calcium. Nevertheless, they can still develop osteoporosis, a condition characterized by brittle bones and a high risk of fractures. A new study shows that how much calcium a woman needs to keep bones strong depends largely on an individual's daily intake of vitamin D, the sunshine vitamin that's also in many fortified foods. Indeed, the new study finds that in a country where vitamin D intakes are high, women can reduce their daily calcium intake to about one-third of the officially recommended daily amount without compromising their bones' health, says Gunnar Sigurdsson, an endocrinologist at University Hospital in Reykjavik, Iceland, and a study coauthor.

The rub: Few women in North America come close to getting the 400 to 600 international units (IU) of vitamin D per day needed to achieve this calcium-sparing effect (see Understanding Vitamin D Deficiency). Many women in Iceland do, Sigurdsson's team found, but largely because these people tend to subscribe to the age-old local practice of fortifying their diets with a daily dose of cod-liver oil. This oil is a rarity: a food naturally rich in vitamin D. The new study supports a trend seen in earlier studies: that as people consume more vitamin D, the efficiency with which their bodies absorb calcium from food improves, notes Boston University endocrinologist Michael F. Holick. However, he's skeptical about the applicability of numerical data from the new study to populations outside Iceland.

So is Robert P. Heaney, a Crieghton University

endocrinologist who studies bone formation and loss. He says that the new Icelandic numbers for the minimum vitamin D and calcium concentrations needed to protect our bones are low—in vitamin D's case, by 50 percent—compared with findings from studies conducted in North America and Europe. Noting that Iceland's population exhibits little ethnic diversity, Heaney questions whether "it might well be different, genetically, in terms of this population's absolute requirements [for these nutrients]." In fact, he points out that few recruits in the new study had vitamin D intake that put them in the range considered optimal by his and several other recent studies. Therefore, Heaney told Science News Online, Sigurdsson's team couldn't tell whether the bone health of women in the new study would have benefited more by consuming additional vitamin D.

One point on which all of these researchers agree: Bone health depends at least as much on vitamin D as on calcium. And for most people living in northern-temperate latitudes, sunshine and diet alone won't provide sufficient vitamin D throughout much of the year. This is one instance in which almost everyone should take a vitamin supplement—especially the elderly and people of color—say the researchers. Elderly people's skin needs more because it manufactures the vitamin less efficiently, and the pigments in dark skin screen out much of the sunlight needed to produce vitamin D.

In Iceland

Sigurdsson's group recruited some 2,300 women between the ages of 30 and 85 who lived in or around Reykjavik, Iceland's capital. In addition to filling out a survey on their food consumption and use of dietary supplements, the participants had blood drawn for measurements of parathyroid hormone (PTH) and 25-hydroxy vitamin D (25-D). PTH is a marker of bone health, and 25-D is the precursor of vitamin D's activated form. PTH concentrations typically climb as a person's calcium intake falls. When that happens, the hormone triggers a host of changes that keep enough calcium in the blood for use in a host of essential biological processes. The process breaks down bone to liberate its calcium and converts 25-D into the active, hormonal form of vitamin D.

Although the skin can manufacture vitamin D, it needs a threshold amount of ultraviolet (UV) light to do so. The farther one gets from equatorial regions, the lower the sun's UV intensity. In northern latitudes, the UV intensity for 2 to 5 months a year can be so low that it would be virtually impossible to generate as much vitamin D as the body apparently needs. Hence, the growing appreciation among nutrition scientists for the need to supplement the diet with fortified foods and vitamin pills. Sigurdsson's team recruited the participants for its study monthly, so that the blood values of PTH and 25-D would capture not only summer highs for the vitamin but also winter lows.

To tease out where vitamin D and calcium intakes appeared sufficient in the Reykjavik women, Sigurdsson and his colleagues compared PTH values in relation to vitamin D and calcium consumption. In the Nov. 9 Journal of the American Medical Association, they report that in women getting no more

than 200 international units (IU) of vitamin D, the need for calcium was high—at least 1,200 milligrams per day. That's the amount of calcium that has been recommended by the Institute of Medicine, which sets dietary requirements in the United States. However, in Icelandic women getting roughly 500 IU of vitamin D per day, the need for calcium, as evidenced by their PTH values, was only about 800 mg per day.

Interpreting calcium sufficiency

What Sigurdsson's group did was graph how 25-D values in blood correlate inversely with PTH values: Women with high 25-D concentrations had low PTH concentrations. The PTH reading appeared to have bottomed out and stayed there in some women. This value marked a point where bones had enough calcium to prevent a fall in density, the endocrinologist says. And in his population, it occurred where 25-D values were about 18 nanograms per milliliter (ng/ml) of blood. However, in the October *Journal of Steroid Biochemistry & Molecular Biology*, Heaney reviewed previously published research linking the bone's absorption of calcium and vitamin D intake. The data showed that bones don't get all the calcium they need to retain their density until vitamin D values in blood climb to at least 32 ng/ml. That figure was derived in people with calcium intakes of roughly 1,200 milligrams per day.

Heaney's own data have demonstrated how the gut's absorption of calcium from foods climbs with vitamin D intake. In one study, reported 2 years ago, his team brought in the same group of postmenopausal Nebraska women for testing on a spring morning in two successive years. They chose spring, Heaney explains, "because that's when their background vitamin D level would be an at annual low—just coming out of winter, when they hadn't made the vitamin in their skin for several months."

Each time, the women were fed a breakfast containing 500 mg of calcium. At the first visit, the women hadn't been taking vitamin D supplements and their blood values of 25-D were around 20 ng/ml—or roughly comparable to high values in the new Icelandic study. On average, the Nebraska women absorbed only about 22 percent of the calcium from their food, Heaney and his colleagues reported in the April, 2003 *Journal of the American College of Nutrition*. The next year, these women received 25-D supplements for more than a month prior to the testing, an amount calculated to be equivalent to some 1,200 to 1,500 IU of vitamin D per day. This led to 25-D blood values of about 35 ng/ml and a mean absorption of 37 percent of the calcium in food.

Such data drive home how important sufficient vitamin D intake is to calcium, Holick says. First, it can boost by almost 70 percent how much calcium can be absorbed from foods or supplements. Moreover, by getting enough calcium, the body doesn't have to waste some of its valuable vitamin D to suppress PTH values. And that's important, Holick notes, since vitamin D offers a host of therapeutic benefits beyond bone strengthening. It boosts immunity and muscle strength and shows some evidence of fighting diabetes and gum disease

(SN: 10/09/04, p. 232).

So, how much vitamin D do studies suggest most U.S. residents need? Probably at least 1,000 IU per day, Holick and Heaney agree. Indeed, Heaney concludes in his October paper, if one accepts the 32 ng/ml value of 25-D as the necessary minimum for preventing bone loss in the United States, a minimum daily intake of some 2,600 IU of vitamin D per day would be needed to meet the needs of 97 percent of U.S. residents. That's well above the existing 400 to 600 IU intake recommended 8 years ago by the Institute of Medicine. That's why there's a move afoot to change vitamin D's recommended intake, says Heaney. Indeed, he notes that last year, the Institute of Medicine convened a conference on how to go about updating its recommended-intake values. At that meeting, he says, vitamin D emerged as "the poster child" for the vitamin most critically in need of a boost in its recommended-daily intake.

.....Source: Science News, 168, 20



DO YOU GET ENOUGH VITAMIN B-12?

Adults over 50 may have problems absorbing it, new research shows

Most Americans don't worry about vitamin B-12. Health experts once thought that only strict vegetarians were likely to have a shortage. As long as basic blood counts didn't show any anemia, even these people were considered safe. Now research shows that vitamin B-12 may be a concern for many more people. Vitamin B-12 is the shorthand term for a group of substances called cobalamins. Cyanocobalamin is the major form in supplements. We need this vitamin for healthy nerve and blood cells and the production of DNA. Researchers are also studying its role in brain function. It is possible that it could help prevent Alzheimer's disease and other forms of dementia.

Strict vegetarians - those who avoid meat, poultry, fish and dairy products - are among those most likely to lack vitamin B-12, because animal foods are the primary sources. Plant foods like cereal, soy products, nutritional yeast and meat substitutes (for example, veggie burgers) only provide the vitamin if they are fortified with it. According to surveys, most Americans do meet the recommended dietary allowance (RDA) of 2.4 micrograms (mcg) of vitamin B-12 per day. The average consumption ranges from 2.9 to 5.1 mcg. However, if people cut back on animal foods, as they should, to eat a mostly plant-based diet that will lower their cancer risk, careless choices could leave them short.

Two modest servings of poultry, lean meat, or seafood plus two cups of lowfat, skim, or nonfat milk or yogurt allow a person to meet this RDA. But if you skip dairy products and have only a moderate serving of meat at one meal, you could fall short without including fortified cereal or soy products in your daily choices. Falling below the RDA occasionally isn't a problem for most adults, because the body can store enough to cover days with a low intake for several years. Children need less vitamin B-12, too, but their ability to store less means that they can develop health problems more quickly with an

inadequate diet.

Supplements encouraged

Now, a new concern about vitamin B-12 has arisen. It seems that adults over the age of 50 may have a reduced ability to absorb it. Eating sufficient amounts of animal foods daily won't help these people. Since acids in our stomachs' digestive juices release the bonds that bind vitamin B-12 to protein in food, we need enough of these acids for proper absorption. As we get older, however, we secrete less digestive acids. Studies suggest that 10 to 43 percent of people over the age of 50 may lack the acids to release vitamin B-12 from protein so it can be absorbed. To meet the RDA of 2.4 mcg, people over 50 are encouraged to take a multivitamin supplement, or eat fortified foods, where vitamin B-12 is not bound to protein. Others who may have trouble absorbing this vitamin are people with digestive disorders such as Crohn's and celiac disease, those who have had substantial portions of their stomach or lower intestine removed, and those who take certain medications for gastroesophageal reflux (GERD), ulcers, or diabetes. Individuals who have had gastric surgery for weight control may also be at risk.

Although it was thought that a simple test for anemia would show a lack of vitamin B-12 before any other damage could occur, health experts no longer agree. A high intake of folate from fortified grains can hide the changes in red blood cells that show a lack of vitamin B-12. Studies also indicate that nerve and brain changes can occur without blood cell variations. If you are at risk of not getting enough vitamin B-12 - either because of your food choices or your inability to absorb it - you should discuss the matter with your doctor. To be on the safe side, you could undergo tests that measure the function of vitamin B-12 through blood levels of homocysteine or methylmalonic acid (MMA). Or you could have a test that measures blood levels of vitamin B-12 using updated standards.

.....Source: MSNBC.com



GOT POTASSIUM? CHECK THE LABEL

If you're a close reader of nutrition labels, you may have noticed that a small but growing number of foods now list how much potassium they contain. The Food and Drug Administration doesn't require food producers to reveal this information, but "there's both consumer and industry interest to provide potassium information on a voluntary basis," notes Robert Earl, senior director of nutrition policy at the Food Products Association, which represents food processors. That's because in recent years several well-regarded groups -- the U.S. Dietary Guidelines Advisory Committee, the National Academy of Sciences' Food and Nutrition Board and the National Heart, Lung, and Blood Institute (NHLBI) -- have underscored the health benefits of potassium and the risks of not getting enough of this nutrient. Besides, the food industry has been criticized for adding too much salt to many products. High blood pressure is a problem that afflicts nearly one in three adults in the United States, according to the American Heart Association. Studies show that a potassium-rich diet can

help counter the hypertensive effects of eating too much sodium.

How much potassium do you need daily? The National Academy of Sciences says 4,700 milligrams daily is adequate for adults. But men routinely consume only about two-thirds of that, and women get about half, according to a 2004 study cited in a report from the dietary guidelines committee. "Our diet is remarkably different from what we evolved on," says Lawrence Appel, professor of medicine at Johns Hopkins Medical Institutions in Baltimore who has examined potassium's importance in the human diet. "We evolved on a low-sodium, high-potassium diet. Now we eat a high-sodium, low-potassium diet. This flip may be in part responsible for many of the [health] problems that are commonplace today."

Besides high blood pressure, count among those possible problems stroke, kidney stones and osteoporosis -- one of the major causes of broken bones in the elderly and a frequent reason for admission to nursing homes. Potassium protects health by blunting salt sensitivity, regulating blood pressure, keeping the heart at a steady beat and muting calcium loss from bones.

While you can eat food fortified with potassium, sprinkle potassium chloride in place of table salt or take dietary supplements with potassium, "you can get all the potassium you need through foods," Appel says. Most adults can meet their needs by consuming two cups of fruit, 2½ cups of vegetables and three glasses of milk, preferably low-fat or nonfat daily. In fact, studies show that the Dietary Approach to Stopping Hypertension (DASH) eating plan developed by NHLBI supplies all the potassium needed daily.

Naturally occurring potassium seems to cover the health bases better than potassium chloride fortification alone, which only appears to offer protection against salt sensitivity and high blood pressure, not against kidney stones or bone loss. There's another drawback to taking potassium supplements or sprinkling potassium chloride on your food: These steps could be harmful for those who have kidney damage or who take blood-pressure-lowering drugs known as angiotensin converting enzyme (ACE) inhibitors. "If you have problems with kidney function or are taking medication to lower blood pressure, check with your doctor before increasing your potassium intake," Appel says.

National nutritional surveys conducted by the federal government show that milk, white potatoes, coffee, beef, tomatoes, orange juice and grapefruit juice are among the leading sources of potassium in the American diet. But the more varied the diet -- and the less processed food eaten -- the higher the potassium intake. Here are a few other potassium-rich options:

Have a sweet potato . One baked sweet potato contains nearly 700 milligrams of potassium, twice that found in six ounces of orange juice.

Dig into some cooked greens. A cup of cooked beet greens provides about a quarter of a day's worth of potassium and clocks in at just 40 calories -- less than the calories found in half a cup of grapefruit juice. A cup of cooked spinach provides

nearly as much -- about 20 percent of the daily intake.

Toss some white beans on your salad. And while you're at it, add edamame, green soybeans and some tuna. About half a cup of soybeans, half a cup of white beans and three ounces of tuna together provide about a third of the daily adequate intake for potassium.

Snack on yogurt . An eight-ounce container of plain low-fat yogurt has more than 500 milligrams of potassium. Add a banana (422 milligrams) and you'll get nearly 20 percent of the daily intake. Other good high-potassium snack options are apricots, peaches, prunes, cantaloupes and honeydew melons.

Dine on fish. Cod, halibut, clams, rockfish and rainbow trout are also packed with potassium, providing about 10 percent of the daily intake per three-ounce serving.

Sip tomato juice . Or add some tomato-based spaghetti sauce regularly to your fare. Tomato products are rich sources of potassium. Just be sure to choose canned low-sodium tomato products since the standard tomato products in cans and jars are generally high in sodium and could undermine your efforts.

.....Source: The Washington Post



LEADEN CHOCOLATES

Here's something that might give you pause after Halloween: Chocolates are among the more lead-contaminated foods. A new study has probed the source of chocolate's lead and concludes it's not the cocoa bean. Its concentrations of the toxic metal were among the lowest recorded for any foodstuff.

The issue of lead-tainted chocolates is hardly new. Indeed, it was the basis of a 2002 lawsuit brought in California. That suit against chocolate makers was withdrawn, however. The new study, which appears in the October Environmental Health Perspectives, was triggered by that litigation. The litigants that commissioned the testing had hoped the researchers would identify the source of the candy's lead. Even after completion of the study, however, the major source remains unidentified, notes study leader Charley W. Rankin of the University of California, Santa Cruz. That's too bad, the environmental chemist says, because since it's nevertheless obvious that most of chocolate's lead isn't from cocoa beans when they're picked, the contaminant should be easy to eliminate—once scientists pin down at what stage of chocolate production it originates.

How serious is the lead problem? "I'm not going to suggest that you curb your chocolate consumption," says Rankin. For most people, he says, the amount of lead in even the more-tainted chocolates isn't high enough to cause health problems. However, he worries, for young children or elderly individuals living with lead-tainted pipes or paint, eating lots of chocolate could aggravate health risks by offering an unnecessary additional source of the metal. Most other people, he says, can take heart in the many research studies suggesting that the constituents of chocolate offer a host of health benefits. Indeed, Rankin concludes, unless taken in excess, "chocolate may actually be pretty good for you".

Spongy husks

The shell of cocoa beans is a remarkably efficient sponge for lead. It can tightly bind the metal, preventing it from reaching the interior bean. That explains, Rankin says, why samples of shells from Nigeria, where beans were sampled, contained so much lead—between 60 and 417 nanograms per gram. That's at least 300 times as much lead as was in the beans inside, Rankin says. Researchers at the University of Quebec have published findings over the past few years confirming the particularly efficient uptake and storage of lead by cocoa shells, or husks. The husks are so effective that researchers have begun exploring them as the basis of a new industrial system for removing metals from industrial wastes. Because Nigeria is among countries that still use octane-boosting lead additives in gasoline, it's possible that airborne lead from fuel might have settled onto shelled cocoa beans that were left outside to dry and then sampled in the recent study.

However, Rankin points out, the overall lead increase in beans was small while they were drying, so most lead enters the chocolate-making process further downstream. The finding that cocoa beans leave the farms with low lead concentrations is also consistent, he says, with his team's finding that "there's not that much lead contamination of the soils" in Nigeria's cocoa-growing regions, which should also reflect impacts of leaded-fuel use in the area. In fact, U.S. soils along roadways are much more tainted by decades of cars' use of leaded gasoline, he notes. As environmental toxicologists, Rankin says, his team had expected that leaded gasoline would prove a major contributor to chocolate's lead contamination—and that such a finding might offer strong economic ammunition for phasing out the heavy metal's addition to fuel in cocoa-growing countries. However, he says, his team's data just don't support that scenario.

Bittersweet findings

The new study shows that dark chocolates, including bittersweet and semisweet candies, had the highest lead concentrations—roughly 30 to 70 nanograms of the heavy metal per gram versus just 11 to 35 ng/g in milk chocolate. Dark chocolates are the types frequently used in gourmet confections and in most chocolate chip cookies. They also contain the highest concentrations of heart-friendly chemicals. The reason for the dark-chocolate-lead correlation is simple, Rankin says. These chocolates have more cocoa per gram of finished product than do milk chocolates. This fact also explains why unsweetened baking chocolates and cocoa powder, which have the highest concentration of cocoa per manufactured product, topped the lead list. Cocoa powders tested by the team had 150 to 190 ng/g of lead; baking chocolates tended to average roughly 250 ng/g. However, Rankin notes, candies aren't the only items affected. Studies have shown that even chocolate pudding will have more lead than a vanilla pudding does.

It's legal

In May 2002, the American Environmental Safety Institute (AESI)—a California-based nonprofit group—filed a lawsuit against chocolate companies charging "various breaches of

duties associated with their exposure of hundreds of thousands of California citizens to toxic lead and cadmium contained in various chocolate products manufactured and sold by [those companies]." AESI argued that the companies were violating consumer health-protection provisions of a California law known as Proposition 65. The suit claimed that these companies "know, while the general public does not, that a number of their products contain lead and cadmium, which are poisonous metals While the quantities of these poisons in Defendants' products are small in an absolute sense, they are significant in relation to the total intake that children under six get from all food sources They are also significant in relation to the warning-requiring levels set under the Safe Drinking Water and Toxic Enforcement Act of 1986 . . . (popularly known as Proposition 65)." AESI also charged that the candy companies "have not done all they could to minimize the amounts of lead and cadmium in their products . . . [by bringing] about changes in growing, cultivation, storage, processing and quality control concerning chocolate products"

In a separate action, AESI petitioned the State of California to find such companies in violation of Proposition 65—a move that the government ultimately rejected. In a letter to attorneys in the suit, the state argued that the law "does not apply to low levels of chemicals in foods that are deemed 'naturally occurring,'" which Attorney General Bill Lockyer's office said clearly appeared to be the case with chocolate. As part of its lawsuit against the candy manufacturers, AESI hired the University of California, Santa Cruz team to do lead analyses of chocolate products and constituents. However, Rankin recalls, his group warned AESI that "we're not going to guarantee our data will say what you want it to. We'll just get objective data." As the researchers began planning their studies, they decided to expand their inquiries into a broader project looking at lead in chocolate—largely removed from the objectives of the litigation. In the end, he says, most of the money to fund this work came from unrestricted grants to the university from sources other than AESI.

Ultimately, AESI's lawsuit never went to trial, says Michèle B. Corash, a San Francisco-based attorney representing the candy companies. "On the eve of trial, the plaintiffs [AESI] threw in the towel," says Corash. Representatives of AESI didn't respond to a request for comments for this article.

The bottom line for consumers in California and elsewhere is that current concentrations of lead typical of U.S. chocolate products, while high compared with those in other foods, remain quite legal.

Lead—all natural?

Lead usually occurs as a mix of different isotopes, each of which has slightly different constituents in its atomic nuclei and therefore slightly different weights. Depending on where any given sample of lead comes from, it can contain a different—and potentially unique—ratio of lead isotopes. The Santa Cruz team tried to probe whether the lead-isotope ratios in cocoa beans, their husks, cocoa-farm soil, and chocolate

candy were all the same. If not, this would suggest the lead from each entity came from various sources—perhaps leaded gasoline, a metal smelter, or even contaminants in fertilizers and other agricultural amendments. The new paper reports that overall, the picture was muddy, indicating no one major common source of lead. However, significant overlaps did exist between samples, suggesting that some share of the lead in each might trace to a common factor. In essence, the new study couldn't prove that the lead in chocolate isn't naturally occurring, Corash says. This finding meant AESI had few grounds for arguing under Proposition 65 that chocolate manufacturers had adulterated or otherwise created unsafe products. Indeed, Corash contends, any lead in chocolate most likely comes from its contamination with some of the lead-laden husk.

Rankin doesn't challenge that traces of husk can end up in the finished cocoa. Indeed, the U.S. Food and Drug Administration allows husk material to constitute up to 3 percent of the finished chocolate. However, he adds, lead-laden husks can't explain all of the lead that his team found in finished chocolate. Why? Because "if you take the [lead] concentration typical of cocoa-bean shells and tried to apply it to what you find in the finished product, your product would have to consist of 104 percent cocoa-bean shell"—a physical impossibility.

To the Santa Cruz scientists, the interesting question has become: At which point does most of the lead enter constituents of chocolate—in the field, after harvest, during shipping, during some other stage? At present, they have no answers. Nevertheless, Rankin says that their chocolate investigations amounted to some fun and toxicologically-relevant food chemistry.

.....Source: Science News, 168, 19



LIGHT BULBS AND LOW CARB DIETS

Researchers from the University of Connecticut and SUNY Downstate recently had one of those rare moments of scientific discovery -- while reviewing the medical literature about low-carb diets, something suddenly became very clear, the list of things carbohydrate restriction improves happens to be the same list of features a patient presents with in the diagnosis of Metabolic Syndrome. It was a classic light bulb moment -- one that is destined to radically alter the clinical management of Metabolic Syndrome, a cluster of metabolic markers that increase the risk of diabetes, stroke and heart disease: obesity, high triglycerides, low HDL ("good" cholesterol), high blood sugar, high blood pressure and insulin resistance.

For decades, the medical community has been searching for a non-drug therapy to treat those diagnosed with metabolic syndrome. In the article published today in the journal, *Nutrition & Metabolism*, researchers point to the data already in the literature that clearly shows that the features of Metabolic Syndrome are precisely those improved with dietary carbohydrate restriction. "It's been staring us in the face for years," said Dr. Richard Feinman, PhD, of SUNY Downstate. "Now we've connected the dots."

Dr. Jeff Volek, the lead researcher of the article added,

"Make a list of the features of metabolic syndrome, then, make a list of the things that carbohydrate restriction is good at fixing. They're the same list. Somehow, we never really noticed that. We know the cause of metabolic syndrome is often linked to disruption of insulin. Thus, the key to treating metabolic syndrome is to control insulin, and carbohydrates are the major stimulus for insulin."

The article also highlights major research studies where study subjects followed low-fat diets to drive home their findings. The review of research showed that in studies where the dietary intervention was to restrict fat intake, study subjects actually had the features of their metabolic syndrome worsen following a low-fat diet. "The most obvious factor in the obesity epidemic is the drastic increase in carbohydrate consumption in recent years and the decrease in fat consumption," Feinman points out, "so the story is consistent. I think people have learned the value of reducing carbohydrates during the media popularization of low-carb diets, but they are still making it hard for themselves by also trying to reduce fat, when fat seems to be much less important a factor than carbohydrates."

This new study brings into focus a very clear target for future discussions about evidence-based dietary recommendations. Dr. Feinman believes there are positive signs that various major medical organizations are already backing away from many of the decades-old dietary recommendations, "I think official agencies are trying to back off from recommending high carbs and low fat across the board," Feinman added, "so I think there are real signs of progress. The bottom line is that if you reduce carbohydrates, you can be less concerned about your fat intake, and that often makes it much easier to stick to a beneficial new diet or lifestyle change."

With a very specific focus -- metabolic syndrome -- it is hard to disagree with Dr. Feinman's assessment of the future of the dietary approach. The findings are not controversial when viewed as a way to approach treatment of metabolic syndrome. These new findings also have the potential to firmly establish a set of criteria for the diagnosis of metabolic syndrome - a diagnosis which has recently been the subject of question in a recent position statement from the American Diabetes Association, countered by a position statement from the American Heart Association. With an estimated 25% of adult Americans already presenting to their doctors with features classic to metabolic syndrome, practitioners will find this additional piece of the puzzle a welcome addition of not only an intervention that the research clearly shows works for improving metabolic syndrome, but also can be the foundation upon which diagnosis criteria is firmly established in the future.

.....Source: medicalnewstoday.com



WAY TO BEAT DIETERS' HUNGER PANGS

Scientists believe they are closer to understanding how to control appetite.

Two studies in Science magazine look at brain cells, and their signals, that appear to drive weight loss and suppress hunger. Killing off particular neurons or boosting a protein that keeps neurons alive makes mice lose weight by eating less. The US teams from Boston and Seattle say the similar appetite pathways are present in humans.

Appetite control

Scientists have already been trying to develop weight-loss drugs that act on these brain pathways. The first study in Science looked at a compound called ciliary neurotrophic factor (CNTF). This protein has been shown to cause weight loss in both humans and mice. It is thought to work by blocking the hunger signals that stimulate appetite, but its exact action is not clear.

Dr Maia Kokoeva and colleagues at Harvard Medical School looked what happened when they gave CNTF to mice. CNTF prompted the growth of new neurons in an area of the brain called the hypothalamus, which plays a crucial role in controlling appetite and energy balance. They believe that CNTF has a dual action. During treatment it activates a pathway in the hypothalamus that makes the brain more responsive to the hormone leptin, which is made by fat cells and tells the body how well fed it is. By triggering the growth of more leptin-responsive neurons, it also makes the body more sensitive to leptin even after the treatment is stopped, they told Science.

No hunger

The second study, by a team at the University of Washington, looked at the neurons involved in appetite - POMC and NPY/AgRP. POMC neurons are known to send signals to the brain to reduce appetite and mice with defects in these neurons eat excessively and become obese. In comparison, when the researchers eliminated NPY/AgRP neurons in adult mice the animals began to eat less and less, suggesting these neurons act in opposition to POMC. However, when they killed off the NPY/AgRP neurons in baby mice these animals continued to eat normally and maintained a normal body weight. The findings suggest that if NPY/AgRP neurons are eliminated before they become fully functional, then animals somehow compensate.

Lead researcher Dr Richard Palmiter said: "Everybody in the field believes that NPY/AgRP neurons and POMC neurons are undoubtedly doing the same in humans as they do in rodents. So I would predict that if you could do the experiment in humans, the results would be the same." He believes that mutations in human genes that affect the survival of these neurons or their ability to respond to hormonal signals could explain why some people are naturally very thin and others are overweight.

Dr Gavin Bewick, Dr James Gardiner and Professor Steven Bloom at Imperial College London, UK, have been looking at NPY/AgRP and were the first to demonstrate that loss of these neurons leads to reduced appetite and weight. They said: "We are at last beginning to understand how the brain works. Together these papers suggest that switching NPY neurons off could cure obesity."

.....Source: BBC NEWS



EFFORTS
Suite D239 NE US HWY 69
Claycomo, Mo. 64119