



EFFECTS OF TIOTROPIUM WITH AND WITHOUT FORMOTEROL ON AIRFLOW OBSTRUCTION AND RESTING HYPERINFLATION IN PATIENTS WITH COPD

Background:

The combination of short-acting β_2 -agonists and anticholinergics in the treatment of COPD has been well documented, but data on combination of long-acting agents are lacking.

Methods:

A randomized, open-label, placebo-controlled, three-way crossover study was conducted comparing 2-week treatment periods of tiotropium alone to tiotropium plus formoterol once or twice daily following a 2-week pretreatment period with tiotropium. Lung function (FEV₁, FVC, and resting inspiratory capacity [IC]) serially over 24 h was measured in 95 patients with stable COPD at baseline and after 2 weeks of each treatment.

Results:

Mean baseline FEV₁ was 1.05 L (38% of predicted). There was a circadian variation in FEV₁, FVC, and IC at baseline that was maintained during all treatment periods. Average FEV₁ (0 to 24 h) improved by 0.08 L with tiotropium, by 0.16 L with tiotropium plus formoterol once daily, and by 0.20 L with tiotropium plus formoterol twice daily ($p < 0.01$ for all comparisons). Compared with tiotropium alone, add-on formoterol in the morning produced improvement in FEV₁, FVC, and IC for > 12 h. The second add-on dose of formoterol in the evening caused further improvement in FEV₁ for 12 h, but in FVC and IC for < 12 h. Peak increase in FEV₁ was 0.23 L (22% of baseline) with tiotropium and 0.39 L (37% of baseline) with tiotropium plus formoterol. Compared with tiotropium alone, add-on formoterol once and twice daily reduced the use of rescue salbutamol during the daytime and with add-on formoterol twice daily also during the nighttime. The combination of tiotropium and formoterol was well tolerated.

Conclusion:

In the treatment of COPD, there is benefit from adding formoterol once or twice daily to tiotropium once daily in terms of improvement in airflow obstruction, resting hyperinflation, and the use of rescue salbutamol.

.....Source: chestjournal.org



NUTRITIONAL STATUS, DIETARY ENERGY INTAKE AND THE RISK OF EXACERBATIONS IN PATIENTS WITH COPD

Summary

Loss of body weight, as a result of imbalance between increased energy demand and/or reduced dietary intake, is a common problem in patients with COPD. The aim of this investigation was to examine the relationship between nutritional intake, change in body weight and the risk of exacerbation in patients with COPD.

The study comprised 41 patients who were hospitalised because of an exacerbation of COPD. The follow-up period was 12 months. Weight, height and lung function were measured at baseline. At the 12-month follow-up, weight change and current weight were assessed by an interview and nutritional intake was recorded in a food diary for 7 days. An acute exacerbation was defined as having been admitted to hospital and/or making an emergency visit to hospital, due to COPD during the follow-up period.

At baseline, 24% of the patients were underweight (body mass index (BMI) < 20 kg/m²), 46% were of normal weight (BMI 20–25 kg/m²) and 29% were overweight (BMI > 25 kg/m²). Energy intake was lower than the calculated energy demand for all groups. During the follow-up period, 24 of the 41 patients had an exacerbation. A low BMI at inclusion and weight loss during the follow-up period were independent risk factors for having an exacerbation ($P=0.003$ and 0.006 , respectively).

We conclude that, in patients who are hospitalised because of COPD, underweight and weight loss during the follow-up period are related to a higher risk of having new exacerbations.

.....Source: *Respiratory Medicine* 100, 3



RESPONSE TO ASTHMA MEDICATIONS MAY BE AFFECTED BY OBESITY

As the nation's collective waistline has swelled in recent decades, rates of asthma diagnoses also have accelerated. Indeed, much research has affirmed a link between the two conditions. But doctors also recognize that asthma may not behave the same way among people who have different body types. With a variety of asthma medications on the market, what kinds work best for lean people and what kinds work best for obese people? The answer may be different for each group.

A new study suggests that people who are overweight or obese may have better results with the prescription pill sold as

Singular than with a type of inhaled steroid, while leaner people may have better luck with an inhaled steroid, called beclomethasone and sold as beclovent, vanciril and other brand names. The findings appear in the new issue of the European Respiratory Journal. "It is increasingly recognized that obese people are more prone to develop asthma, but there is no information about whether obesity influences people's responses to particular asthma medications," says lead author Marc Peters-Golden, M.D., professor of internal medicine and director of the Fellowship Program in Pulmonary and Critical Care Medicine at the University of Michigan Medical School. "Our findings are the first to suggest the possibility that obesity might be a factor that influences how well asthmatics respond to particular medications," Peters-Golden says.

Singular is the brand name of montelukast sodium and is sold by Merck & Co., which funded this study.

Researchers looked at data from four previous multi-center, randomized clinical trials from 3,073 patients with moderate asthma. The data included the patients' responses to Singular/montelukast, a beclomethasone inhaled steroid and a placebo, and the participants' body mass index numbers, which placed them in the categories of normal, overweight and obese.

In general, the severity of people's asthma was found to be greater among those in the overweight and obese groups, which supports findings from other studies. In addition, the inhaled steroid was found to be better than Singular at increasing the number of asthma control days (ACD) among people in the normal weight category. An ACD is defined as a day with no more than two puffs of an inhaler, no night-time awakenings and no asthma attacks. On the other hand, the inhaled steroid resulted in a reduced effect in the percentage of ACDs among obese people in the study -- that is, the benefit of the inhaled steroid declined with increasing body mass index.

In contrast, the positive impact of Singular did not decrease in obese and overweight people when compared to its impact on people of normal weight. The research also suggests that the higher a person's body mass index, the greater his or her response to Singular compared to a placebo, a pill with no medicinal benefit. This is an indication, Peters-Golden says, that obese and overweight people may in fact respond better to this medication. Still, he is not inclined to suggest that doctors change the way in which they prescribe medication -- not yet, anyway. "Our study looks back at material from previous trials. I'd like to see a prospective study in which lean patients and heavy patients are enrolled at the outset, and you compare both types of medications in both groups," Peters-Golden says. If verified by other studies, this insight may help physicians to better tailor medication regimens to meet individual patient needs. Peters-Golden also notes that much research about asthma and other conditions is exploring the possibility that genetic factors might explain individual variations in responses to medications. He says it is likely that a variety of factors, including genetic ones and acquired factors such as weight, combine in a complex and intertwined manner to influence a person's reaction to medications.

....Source: European Respiratory Journal, 27, 3.

USE OF MEDICATION AND QUALITY OF LIFE AMONG PATIENTS WITH COPD

Study objectives

To determine the medications prescribed to patients with chronic obstructive pulmonary disease (COPD) and their relationship to health-related quality of life (HRQL).

Methods

Cross-sectional study of 611 consecutive patients with stable, mild-to-severe COPD who attended at the respiratory service of a single hospital during a 1-year period. HRQL was evaluated using the St. George Respiratory Questionnaire (SGRQ) and the Short Form 36-item (SF-36) questionnaires. Linear regression analysis was used to determine the influence of the number or type of medication on the total SGRQ score, adjusting by disease severity and other relevant variables.

Results

Significant differences were observed among the number of drugs prescribed according to dyspnea levels, percentage of predicted FEV1 (FEV1%), SGRQ scores and some areas of SF-36. Fifty-nine percent of patients with an FEV1%>50% were prescribed inhaled corticosteroids (ICS). Those who took an ICS had a worse HRQL than patients with an FEV1%>50% who did not receive ICS.

Conclusions

A relationship exists between the number of medicines prescribed to patients with COPD and their HRQL, measured by the total SGRQ score, after adjustment by severity of the disease. Within the group of patients who should not have been prescribed ICS, there are subgroups that might benefit from this medication.Source: Respiratory Medicine 100, 3

THOUGHT..

COPD has only advantages for our soul; it makes us look around more and appreciate what we have. It makes us slow down and get out of the rat race - it is now more like turtle race (smile).

It makes us use our minds for figuring out how to do things easier so we have time and energy to do the things we love. It also makes us aware of a higher power and brings us closer to it.Francine, Texas

BRONCHOSCOPIC LUNG VOLUME REDUCTION FOR END-STAGE EMPHYSEMA* – REPORT ON THE FIRST 98 PATIENTS

Objectives:

To report the first multicenter experience on the treatment of end-stage emphysema using an endobronchial valve (EBV) [Emphasys EBV; Emphasys Medical; Redwood City, CA].

Design:

Retrospective analysis from prospective multicenter registry.

Patients and interventions:

This is a study of the use of EBVs in the treatment of end-stage emphysema at nine centers in seven countries. Ninety-eight patients with mean FEV1 of 0.9 ± 0.3 L and residual volume (RV) of 5.1 ± 1.3 L were treated over a period of 20 months. Spirometry, plethysmography, and diffusing capacity of the lung for carbon monoxide (DLCO) and exercise tolerance testing were performed at 30 days and 90 days after the procedure.

Results:

RV decreased by $4.9 \pm 17.4\%$, FEV1 increased by $10.7 \pm 26.2\%$, FVC increased by $9.0 \pm 23.9\%$, and 6-min walk distance increased by $23.0 + 55.3\%$. There was a trend toward improvement in DLCO, but this did not reach statistical significance. Patients treated unilaterally showed a trend toward greater improvement than those treated bilaterally. A similar trend toward improvement was observed in patients who had one entire lobe treated compared to those with just one or two bronchopulmonary segments treated. Eight patients (8.2%) had serious complications in the first 90 days, including one death (1.0%).

Conclusion:

This multicenter analysis confirms that improvement in pulmonary function and exercise tolerance can be achieved in emphysematous patients using EBVs. Future efforts should be directed to determining how to select those patients who would benefit most from this procedure and the best endobronchial treatment strategy.

.....Source: chestjournal.org



DO HEAVIER ASTHMA PATIENTS NEED DIFFERENT MEDS?

As obesity rates rise across the nation, so too the number of people with asthma, but successfully treating asthma in an overweight individual may require different medication than treating asthma in a person of average weight.

People who are overweight and have asthma may respond better to leukotriene-inhibitor pills than inhaled steroid medications, according to a preliminary study sponsored by the maker of the pills. Moreover, these inhaled steroids seem to have less of an effect the more a patient weighs. The results of the study, which were published in the European Respiratory Journal, are the first to suggest that weight plays in role in a person's response to asthma medications. "It is increasingly recognized that obese people are more prone to develop asthma," said study author, Dr. Marc Peters-Golden, professor of internal medicine at the University of Michigan Medical School. "But there is no information about whether obesity influences people's responses to particular asthma medications."

Peters-Golden and colleagues reviewed four asthma studies which included over 3,000 patients with moderate asthma. All of the studies had documented the patients' body mass index (BMI), a measurement that uses both height and weight to determine obesity, and how the patients' asthma responded to the two main types of asthma medications: a leukotriene-inhibitor (Singulair) and an inhaled steroid.

Looking at BMI, the review found that inhaled steroids worked best in patients who were considered to be of normal weight. These patients woke up less often at night because of breathing difficulties and needed fewer puffs of an inhaler to stop asthma attacks than patients' of a similar weight taking the leukotriene-inhibitor. However, inhaled steroids showed less of an effect as a person's weight increased. In other words, the higher a person's BMI, the more asthma-related problems he had while on the inhaled steroid.

In contrast, while overweight patients tended to have more severe asthma-related problems, the leukotriene-inhibitor was able to consistently control asthma attacks better than an inhaled steroid in those with a BMI above 25, a number that is considered to be the threshold between being normal weight and overweight. Peters-Golden suggests that weight itself may cause this difference in response to medications. He theorizes that the inflammation of the lungs that causes asthma may be fundamentally different in overweight or obese people than in patients of a normal weight. Since leukotriene-inhibitors and inhaled steroids work differently to control this inflammation, one may be better suited to controlling asthma in obese people.

However, Peters-Golden doesn't recommend that anyone switch their medications on account of this early review. "This is an exploratory study," he said and emphasizes the need for more research on the topic as many factors other than weight may influence response to asthma medications.

....Source: Healthology, Inc.



AIR POLLUTION UPS HOSPITALIZATIONS IN SENIORS

More seniors end up in the hospital due to cardiovascular and respiratory diseases on days when air pollution levels rise. That's the conclusion of a large-scale study in the March 8 issue of the Journal of the American Medical Association that compared air pollution levels to the number and types of hospitalizations occurring at the same time. "This study provides strong evidence that daily hospital admission rates for cardiovascular diseases and respiratory diseases are higher when the fine particulate matter levels are increased from one day to the next," said study author Francesca Dominici, an associate professor of biostatistics at Johns Hopkins University's Bloomberg School of Public Health. Dominici said just a small rise -- each 10 micron per cubed meter increment increased -- in the air pollution level results in about 11,000 extra hospitalizations for cardiovascular and respiratory disease. She said the reason is clear: Small particles of air pollution can travel deep into the lungs.

To get an idea of how small these air pollution particles are, George Thurston, an associate professor of environmental medicine at New York University School of Medicine, said to imagine the width of a human hair. That's about 100 microns. The particulate matter measured in this study was 2.5 microns.

In the late 1990s, the National Ambient Air Quality Standard required a nationwide monitoring system to measure the amount of fine particulate air pollution -- that's air pollution

equal to or less than 2.5 microns in size (PM 2.5) -- present on any given day in 204 urban counties.

For the new study, Dominici and her colleagues used information from this monitoring system and compared it to daily rates of hospitalizations for a number of different conditions, including injuries, cardiovascular diseases and respiratory diseases. The hospitalization information came from records of more than 11.5 million Medicare enrollees, who were 65 years and older. The researchers found that for every 10 micron per cubed meter increment rise in PM 2.5, hospitalizations for heart failure rose by 3,156 per day, respiratory tract infections by 2,085, ischemic heart disease by 1,523, stroke by 1,836 and for chronic obstructive pulmonary diseases such as emphysema by nearly 1,000 per day. The total increase in hospitalizations for each 10 micron per cubed meter rise in fine particulate matter was 11,000 daily. "I think this is powerful new evidence that fine particulate matter air pollution is indeed a major public health threat," Thurston said. He pointed out that the researchers didn't find an increase in injuries associated with the days that air pollution was increased, proving the findings of increased cardiovascular and respiratory diseases weren't a chance or random occurrence. Dominici said the other important finding was that "risks were higher in the Eastern part of the United States."

Both Dominici and Thurston said this was likely because there are more power plants operating in the Eastern portion of the United States than in the West, and power plants are a large source of PM 2.5. Dominici also emphasized that these results are likely an underestimation of the extent of the problem because they only included people over 65 and monitoring stations are only set up in urban areas. So, while this study was probably the largest done to date on fine particulate matter air pollution, many parts of the country weren't represented. "This is more evidence that we should do as much as possible to protect the public from this health threat, and the clean air standards are under federal review right now," said Thurston. "From a policy perspective, this gives more impetus than ever for supporting more stringent clean air standards," he said.

On an individual level, both Dominici and Thurston said there's not much you can do to protect yourself from this type of pollution because it's so small it easily travels indoors. However, Thurston said it probably makes sense to exercise in the morning if you're heading outdoors because this type of pollution is highest in the afternoon. Additionally, they both said that conserving energy, particularly electricity, helps to keep the air pollution levels lower.Source: HealthDay.



VITAMIN E'S CONFLICTING MESSAGES EXPLAINED

The way two forms of vitamin E affect the body may explain the conflicting messages about the antioxidant.

Recent studies tout the benefits of consuming vitamin E while others show it may increase the risk of conditions including heart disease and cancer. New research shows the risks and benefits may depend on the type of vitamin E.

The study from The Ohio State University in Columbus

compared the two most common forms of the antioxidant. One is mainly in plants like corn and soybeans, while the other is in olive oil, almonds, sunflower seeds, and mustard greens. The main difference is a slight variation in their chemical structures. Researchers conducted laboratory experiments on cells taken from the brains of mice. They found the type of vitamin E in corn and soybean oil -- gamma-tocopherol -- destroyed animal cells. The other form -- alpha-tocopherol -- did not. "In the United States we tend to eat a diet rich in corn and soybean oil, so we consume much greater amounts of gamma-tocopherol than alpha-tocopherol," says David Cornwell, an emeritus professor of molecular and cellular biochemistry at The Ohio State University. "But most of the vitamin E coursing throughout veins is alpha-tocopherol -- the body selects for this version. We want to know why that is, and whether the selection of the alpha-tocopherol confers an evolutionary benefit in animal cells."

The study does not analyze the possible health effects. Researchers say there is still a lot that isn't known about how antioxidants act in the body. To find out, they say scientists must study how they interact with cells on their most fundamental levels.Source: www.ivanoe.com



JOSLIN DIABETES CENTER STUDY PROVIDES FIRST PHYSIOLOGICAL EVIDENCE THAT INSULIN IS CRITICAL FOR BLOOD VESSEL FORMATION STUDY ONE DAY MAY LEAD TO WAYS TO REDUCE HEART ATTACKS IN DIABETES PATIENTS

For people with type 2 diabetes, the death rate from a first heart attack is two to three times the death rate of patients without the disease. Similarly, patients with diabetes and ischemic (reduced blood flow) heart disease have a much higher mortality rate than the general population.

Now, a team of researchers at Joslin Diabetes Center led by George L. King, M.D., Director of Research and Head of Vascular Cell Biology, and Zhiheng He, M.D., Ph.D., a Juvenile Diabetes Research Foundation International Research Fellow and former Iacocca Fellow, has shown a potential physiological mechanism behind this difference. The discovery could one day lead to new treatments to improve the ability of patients with diabetes to survive heart attacks and live with coronary artery disease. The report was published in the Feb. 9 online edition of the American Heart Association journal, *Arteriosclerosis, Thrombosis, and Vascular Biology*, and is scheduled to appear in the April print edition.

Normally, when a coronary artery becomes blocked, the body responds by forming new blood vessels around the blockage to maintain blood and oxygen flow and limit heart damage. Heart cells produce the vessels by making VEGF, a growth factor that causes new blood vessel formation. "We have long recognized that in patients with diabetes, this blood vessel formation is not as robust as in people without diabetes," says Dr. King, Professor of Medicine at Harvard Medical School. "Now we have a potential explanation."

The researchers showed that insulin is the source of the

signal the heart cells need to increase VEGF production. "We found that when insulin in the bloodstream binds with the insulin receptors on the outer membranes of heart cells, it activates the PI3K/AKT pathway, which is the pathway that produces VEGF," says Dr. King. "We also found that this response is blunted in patients with insulin resistance, a major cause of type 2 diabetes that makes it harder for cells to use insulin. The heart produces less VEGF and forms fewer new blood vessels."

The researchers made their findings by working with two types of rodents: Zucker rats, which are genetically obese and, like humans, develop type 2 diabetes through insulin resistance; and MIKRO (muscle-specific insulin receptor knockout) mice, a mouse model whose insulin receptor has been removed from the heart cells so they can no longer respond to the hormone.

"We found that when we stimulated the heart cells of Zucker rats with insulin and compared them with cells of normal rats, the insulin action in the Zucker rats was abnormal and that may be responsible for the reduced VEGF and blood vessel formation in the heart," Dr. King explains. "Using a variety of interventional approaches, we then showed that the blood vessel formation was reduced because this one pathway was inhibited. The mice with the insulin receptor removed also exhibited less VEGF production and fewer new blood vessels, proving that the insulin receptor is critical to this process."

"The study suggests that if we improve VEGF and insulin action in the heart, then the heart will be able to produce more new blood vessels," says Dr. King. "Scientists have already established several ways of improving insulin actions in general, so once we figure out which is best for the heart muscle, we should be able to decrease the mortality rate."

.....Source: Joslin Diabetes Center



EAT SMART

Foods may affect the brain as well as the body

At family dinner tables around the globe, prodding mothers have dished out the same refrain for decades: "Eat your fish," they say. "It's brain food!" For children picking at crusty fish sticks or blobs of pink poached salmon, the statement raises suspicions. But the message is turning out to be more than just an attempt to get children to clean their plates. Recent research is suggesting that what you eat can influence the function of your brain.

Scientists are providing hints that what you choose to consume or avoid in your daily diet can have consequences on the brain's resiliency in the face of injury or disease. Studies suggest that foods such as fish and a curry spice called curcumin, for example, can give the brain an added edge to stay healthy. On the other hand, a steady diet of high-fat and starchy foods, such as that double cheeseburger from a favorite fast-food joint, may eventually do the brain a serious disservice. On the extreme end of dieting, some research indicates that paring food intake to the bare minimum may

protect the brain from a lifetime of everyday insults. Taken together, these results point in a direction that any kid could have seen coming: Once again, Mom was right.

Fish curry

Besides a mother's goading, there are plenty of reasons to eat a succulent fillet of fish. The strongest incentive, neuroscientists say, may lie in the growing number of benefits attributed to nutrients known as omega-3 fatty acids, found in small amounts in some plants and in abundance in oily, cold-water fish such as salmon. Neurosurgery professor Fernando Gómez-Pinilla operates a traumatic brain-injury center at the University of California, Los Angeles (UCLA). Because his past studies suggested that exercise affects how well brains function, he wondered whether diet might also change how his patients coped with brain injuries. Working with rats, Gómez-Pinilla and his colleagues compared the effects of two diets. Both included healthy, low-fat chow. However, one diet contained 8 percent fish oil—the amount people would receive by eating fish about twice a week. After 4 weeks, Gómez-Pinilla's team subjected some of the rats to a mild percussion injury—a knock on the head in a machine specially designed to standardize the force of its blows. The researchers tested all the animals a week later in a water maze to see how quickly the rats could learn the location of a platform hidden beneath the water's milky surface. They found that brain-injured rats fed the fish oil-supplemented diet found the platform's location in about two-thirds of the time it took the injured rats that ate the standard rat chow to do so. Surprisingly, Gómez-Pinilla says, the injured rats fed the fish oil mastered the maze almost as quickly as rats that weren't injured did. He and his colleagues found that rats that had eaten unsupplemented chow had lower brain concentrations of a protein called brain-derived neurotrophic factor (BDNF). This compound encourages nerve cells to grow and make new connections. BDNF concentrations are typically low after the type of injury that the rats had experienced. In contrast, BDNF concentrations in rats fed fish oil were much like those in rodents that hadn't received brain injuries. Gómez-Pinilla and other scientists have shown in previous studies that nerve cells produce BDNF when animals exercise. This protein may be a prime player in the neurological benefits that animals get from exercise.

Researchers aren't yet sure how the components of fish oil change BDNF amounts in the brain. However, Gómez-Pinilla says, "eating a diet rich in omega-3 fatty acids could have some of the same [neurological] effects as exercise." Neuroscientist Greg M. Cole, working in another laboratory at UCLA and also at the Veterans Administration Medical Center in Sepulveda, Calif. is finding that supplementing food with just the omega-3 fatty acid DHA—rather than the complex blend of fish-oil ingredients—can dramatically slow neurodegenerative symptoms in mice bred to develop an Alzheimer's-like disease. In a study published in the March 23, 2005 *Journal of Neuroscience*, Cole's team peered into the brains of Alzheimer's-susceptible mice that had been fed diets either high or low in DHA for about 3 months. They found that mice on the high-DHA diet had only about 30 percent as many deposits of a waxy protein called beta-amyloid—a hallmark of Alzheimer's

disease—compared with mice that ate little or no DHA.

Curcumin, a yellow polyphenol that's a component of the curry spice turmeric, has similar effects in reducing the amount of beta-amyloid in Alzheimer's-susceptible mice. Cole's team fed mice a daily dose of curcumin that was similar, in proportion to food intake, to the amount that a person in India typically eats each day. Those mice had about half as many beta-amyloid deposits as did mice that weren't given the spice. In a study published in the Feb. 18, 2005 *Journal of Biological Chemistry*, Cole and his colleagues reported that curcumin binds to bits of amyloid-beta protein, discouraging them from aggregating into the waxy clumps associated with Alzheimer's symptoms. He says that both fish oil and curcumin may eventually become widely used in preventing neurodegenerative diseases, while causing few side effects. On the other hand, recently created drugs for treating neurodegenerative diseases are expensive and often have troubling side effects. Cole notes that people have been eating fish and curries safely for centuries. "We're interested in these approaches that have cost-effectiveness and safety built into them," he says.

Fat attack

Just as fish oil and curcumin seem to aid the brain, other foods—such as those in the typical high-fat, sugary U.S. diet—could take brain health down a notch. Four years ago, Gómez-Pinilla and his colleagues tested how the typical diet of people in industrialized Western countries affected brain function in rats. The researchers fed half of a group of rats a regular lab diet composed of about 13 percent fat and 59 percent complex carbohydrates, among other nutrients. The other animals received a high-fat and high-sugar (HFS) diet made with 39 percent fat, primarily from lard and corn oil, and 40 percent refined white sugar. After just 2 months, Gómez-Pinilla's team found that animals on the standard diet learned the water-maze task faster than did rats on the HFS diet. When the scientists dissected the animals' brains after a year on the special diets, they found that rats on the HFS diet had less than half as much BDNF as mice on the healthy diet did. The HFS rats also had reduced amounts of several other proteins associated with learning and memory.

In another experiment published 2 years later, Gómez-Pinilla tested how rats on the two diets fared after a mild brain injury such as the one that the rats on the fish oil diets had been subjected to. Animals ate their assigned diet for 4 weeks then received a mild brain injury. In the water maze, both sets of animals had performed equally well before being injured. However, rats fed the HFS diet showed greater deficits in learning the maze a week after their percussion injuries than did rats fed the regular diet. When the scientists examined the animals' brains, they found that rats on the HFS diet had lower

amounts of BDNF than those on the healthy diet did. A shortage of BDNF could underlie the animals' inability to recover from their neurological injuries as well as the other rats did, says Gómez-Pinilla. "A lot of the problems of consuming this diet become more obvious when animals are exposed to some insult, like a traumatic brain injury," he adds. Gómez-Pinilla suggests another possible reason for the HFS rats' poor performance: damage in the brain caused by a chemical process called oxidation. Diets high in fat and sugar are also usually high in calories. The more calories an animal eats, the more its body generates free radicals: negatively charged molecular particles that cause oxidation damage in cells, particularly those in the nervous system.

The HFS rats may also have had less brain power because a steady fare of fat and sugar can change how the body responds to insulin, says Carol E. Greenwood, who studies nutrition and aging at the University of Toronto. Animals eating such food can become less sensitive to insulin, the compound that signals cells to take up glucose from the blood for processing into

energy. Low insulin sensitivity effectively starves these animals' cells, including brain cells. Numerous studies by Greenwood's lab and others indicate that a steady diet of such food can decrease an animal's ability to learn and remember. Furthermore, Greenwood and her colleague Gordon Winocur report in a supplement to the December 2005 *Neurobiology of Aging* that the already poor learning and memory abilities of insulin-resistant people get even worse after they consume



"It's the hottest new diet! You attach this special modem to your stomach and upload your fat to a skinny person on the Internet!"

a sugary snack, which raises glucose concentrations. The researchers aren't sure why high glucose concentrations have such a detrimental effect on brain function. "Our instinct at this point is that when glucose gets too high in the blood, it launches a cascade of oxidative reactions. Various components of that cascade may contribute to cognitive deficits," says Greenwood.

Ascetic eater

Since taking in calories generates damaging free radicals, some researchers have hypothesized that simply eating less may protect the brain from harm. Recent studies support this hypothesis. For example, teams led by neuroscientist Mark Mattson of the National Institute on Aging in Baltimore have shown that cutting back calories in lab animals can reduce the symptoms seen in Huntington's- and Parkinson's-like diseases. In one experiment, Mattson and his colleagues worked with mice that carried a mutant form of the human huntingtin gene. People who have this mutation show a variety of emotional and physical symptoms, such as mood swings and loss of muscle control, generally starting in adulthood. They eventually die of the disease. Mattson's team gave the Huntington's mice a normal diet for 8 weeks. Then, the researchers began to feed

some of the animals only every other day to cut by about 20 percent the number of calories consumed. Other mice were permitted to eat as much as they wanted. Those eating fewer calories showed their first symptoms of the Huntington's-like disease an average of 12 days later than the other group did. Mice eating restricted diets also lived longer. At 21 weeks, all the free-eating mice had died from the disease. However, 60 percent of those on the restricted diets were still alive. When researchers dissected the animals' brains, they found that the animals on the every-other-day diets had less atrophy and fewer clumps of the mutant huntingtin protein than the free-eaters did.

Mattson has had similar success by decreasing the calorie intake of monkeys with a Parkinson's-like disease. After feeding some of the monkeys 30 percent less food over 6 months, Mattson's team found that those animals had fewer symptoms of the disease, such as muscle tremors and rigidity, compared with monkeys that ate as much as they wanted. Examination of the animals' brains showed that those that ate fewer calories had higher concentrations of dopamine, even though the majority of their dopamine-producing neurons had died.

Use your brain

Mattson says that the reason calorie restriction seems to save neurons probably extends beyond simply protecting them from free radicals. Eating less cuts energy to all the body's cells, including those in the brain. This mild stress makes brain cells more active and triggers production of protective proteins, such as BDNF and heat-shock protein. Mattson suggests that the lightly stressed neurons tend to cope better with more-severe stress—such as that imposed by neurological disease—than cells of animals on a steady diet do. "When you put animals on dietary restriction, some studies suggest that their brains are more active because they're apparently looking for food," says Mattson. While caloric restriction seems to protect animals from neurological diseases, Mattson notes that people rarely want to cut back so stringently. So, should they just eat fish curries every night while conscientiously avoiding fast-food fare? "That's the kind of talk that raises the hair on the backs of nutritionists," says Greenwood. Different foods have different benefits, and studies show that patterns of food consumption influence health. "Everything we see out there suggests that variety is what we need in our diets," she concludes. She argues that in laboratory studies, it's difficult to separate effects of different diets on the brain from the diets' effects on the rest of the body. Nevertheless, a healthy diet seems to be good all around. "The idea is that by taking care of your body, your brain also benefits," she says.

Now, that's an idea that any mom would approve.

....Source: Science News, 169, 9.

MEDITERRANEAN DIET HAS ANTI-INFLAMMATORY EFFECTS

Sticking to a Mediterranean diet, high in fruits and vegetables and low in saturated fats, lowers levels of inflammation in the elderly, as reflected by lower levels of

C-reactive protein (CRP), research shows. This effect should, in turn, lead to a lower risk of cardiovascular disease that has been associated with this type of diet. CRP is a marker of inflammation that has been tied to the risk of heart disease, heart attack, and stroke. Researchers from the Stanford School of Medicine in California studied the effect of diet on CRP levels in blood in 911 healthy individuals -- 326 women and 585 men -- whose average age was 66 years. Subjects were followed from January 2002 through December 2003.

Researchers assessed adherence to a Mediterranean diet with a food frequency questionnaire, from which they formulated the Mediterranean Diet Score, based on intake of fruits, vegetables, legumes, nuts, seeds and grains, meat and meat products, dairy products, fish, alcohol and the mono-unsaturated-to-saturated fat ratio. Total scores ranged from 0 to 9 for adherence to the diet. Plasma CRP levels were measured periodically.

At the American Heart Association's 46th Annual Conference on Cardiovascular Disease Epidemiology, held this past weekend in Phoenix, Dr. Joan M. Fair reported that Mediterranean Diet Score correlated negatively with CRP level. Each one-point increase in Mediterranean Diet Score was associated with a decrease in CRP of 0.14 mg/L in women and a decrease in CRP of 0.10 mg/L in men. "The (positive) effects of the Mediterranean diet might be the anti-oxidant components of fruits and vegetables," Fair said, "and the anti-inflammatory effects of the diet may be one explanation for its protective effect against cardiovascular disease. "There are other markers of inflammation that we haven't assessed yet in terms of diet, such as high coronary artery content, which we found in 200 patients. We have the blood available, we just haven't run the tests yet."

....Source: MDlinx

EXPERTS REVEAL THE SECRET POWERS OF GRAPEFRUIT JUICE

In 1989, a group of Canadian researchers studying a blood pressure drug were astonished to discover that drinking a glass of grapefruit juice dangerously increased the drug's potency. They were testing the effects of drinking alcohol on a medicine called Plendil. The scientists needed something that would hide the taste of alcohol so that subjects would know only that they were taking the drug and not know whether they were drinking alcohol with it. "One Saturday night, my wife and I tested everything in the refrigerator," said David G. Bailey, a research scientist at the London Health Sciences Center in London, Ontario, and the lead author on the study. "The only thing that covered the taste was grapefruit juice."

So they used it in their experiment, expecting the grapefruit juice to be irrelevant to their results. But blood levels of the drug went up significantly in the control group that drank just grapefruit juice, without alcohol. "People didn't believe us," Dr. Bailey said. "They thought it was a joke. We had trouble getting it published in a major medical journal." Eventually the paper

was accepted and published by Lancet, in February 1991. Finding why juice had that effect was the next question.

The answer, it turned out, lay in a family of enzymes called the cytochrome P-450 system, in particular one known as CYP 3A4. This enzyme metabolizes many drugs, and toxins as well, into substances that are less potent or more easily excreted or both.

Grapefruit juice interferes with the ability of CYP 3A4 to do that, increasing the potency of a drug by letting more of it enter the bloodstream, in effect producing an excessive dose. Grapefruit interacts with this enzyme only in the intestines, not in the liver or other places where it is found. As a result, the effect is seen only with medicines taken orally, not with injected drugs.

Numerous studies now show the interaction of grapefruit juice with many widely used medicines. Most interactions have no serious consequences, but a few do. For example, drugs used to lower cholesterol, like Lipitor, Mevacor and Zocor, have increased potency when taken with grapefruit juice. Excessive levels of those drugs can lead to a serious and sometimes fatal muscle disorder called rhabdomyolysis.

Does this mean a person could reduce the amount of medicine required simply by drinking grapefruit juice? No, according to Dr. Bailey. "The problem is the unpredictability of the effect," he said. "You can't just lower your dose of Lipitor and increase your consumption of grapefruit juice. There's no uniformity from one individual to another or from one bottle of grapefruit juice to the next. "There's huge variation in the amount of enzyme people have in their guts. Fooling around with grapefruit juice is not a good idea."

Grapefruit juice can also interfere with the metabolism of selective serotonin reuptake inhibitors, or S.S.R.I.'s, like Prozac, which are used to treat depression. Dr. Marshall Forstein, an associate professor of psychiatry at Harvard, said he told patients to switch from grapefruit juice to something else because most oranges and other citrus fruits do not have the same effect. "If they insist," Dr. Forstein said, "I try to prescribe the S.S.R.I. or other medication to be taken at a time when the grapefruit juice would have mostly been metabolized." Among fruit juices, grapefruit has the strongest effect, but lime juice and orange juice made from Seville oranges similarly inhibit the CYP 3A4 enzyme. With some drugs, apple juice may interact in the same way.

While Dr. Bailey suggests avoiding grapefruit juice entirely when taking medicine, some experts say the effect of the juice should not be exaggerated. "The circumstances under which an interaction will occur are relatively unusual," said Dr. David J. Greenblatt, a professor of pharmacology at Tufts. First, he said, the drug has to be metabolized significantly by intestinal CYP 3A4, and relatively few are. "When you look at the actual data for each drug, the scientific conclusions are that the interactions are unusual, sometimes quite small and not of clinical importance. But there are some cases in which it's significant."

Dr. Greenblatt and his co-investigators at Tufts have conducted research sponsored by the National Institutes of

Health in this field for years, and he has been a paid consultant to the Florida Citrus Commission. Dr. Richard B. Kim, a professor of medicine and pharmacology at Vanderbilt University, agreed that the interaction was a serious health concern in some patients. Grapefruit consumption is a clinically relevant issue, especially for the elderly, who are most likely to be taking the drugs affected by it," Dr. Kim said. "If you're taking multiple medications, or have recently switched to a different type of medication, you should be particularly careful. The easiest thing to do under those circumstances is to take the medicine with water and avoid the juice completely."

.....Source: The New York Times Company



100-CALORIE SNACKS

Between-meal treats that won't blow your diet

It can happen when you least expect it ... or show up at about the same time every day. It's a "snack attack" -- that moment when the munchie monster grabs your appetite and won't let go! Many people blame these between-meal urges for making it difficult to control their weight. But experts say it's not snacking in itself, but the size of the snacks, that can really do a dieter in. We are supersizing everything, but particularly snack foods. So even if you eat just one portion, it can really be like three portions, and that can definitely derail your diet.

One way around the problem: Have your snacks, but keep them to 100 calories or fewer. If you focus on the calorie count, it can make it much easier to choose a snack and much easier to stick to your diet, and you can't stray too far if you only allow yourself that 100-calorie limit. To keep your appetite in check, make sure those 100 calories contains a bit of protein, fiber, and fat, along with some carbohydrate. While junk food may satisfy your brain, it does little to satiate your hunger. These kinds of balanced snacks -- like some peanut butter on a whole-wheat cracker, for example, or a light cheese with a pear -- will satisfy your appetite as well as help reduce the amount of food you'll eat at the meal that follows. When snacking becomes bad for a dieter is when you choose empty-calorie foods. If you're trying to keep your calorie count down, you want to make sure that you spend every calorie you have wisely, in terms of both satisfying your hunger and your nutritional needs. And keep in mind that fat grams do matter. In general, the snack should be less than 30% fat -- and, when possible, should not be laden with sugar. And if you're craving something sweet? People hate to hear it, but a piece of fruit is really the perfect snack -- it's usually less than 100 calories and it can satisfy your sweet craving without adding too much sugar to your diet.

What to Do When Only a Cookie Will Do

Fruit is great, but let's face it: There are times when it simply won't tame the raging munchie monster. The good news is that experts say it's OK to indulge in a few cookies or chips as long as you eat reasonable portions. Of course, that's not so easy to do when faced with a big box or bag of your favorite indulgence. So one major food manufacturer is now offering pre-measured, 100-calorie packages of its favorite treats.

Kraft/Nabisco is marketing "100-Calorie Packs" of things like Oreos, Chips Ahoy, Wheat Thins and Cheese Bits. Each grab-and-go package of 15-20 "bites" has 7-9 grams of sugar (except the Cheese Nips, which have 0), less than 3 grams of fat, and no trans fat. Some say that having such pre-portioned foods at hand could help dieters get over the rough spots.

"Having these 100-calorie snacks can really help some people get through a bad time and still not totally derail, calorie-wise," says Wilson.

At the same time, Gerbstadt points out that these snacks aren't a particularly nutritious choice. "Two to 2 1/2 teaspoons of sugar in each cookie pack is a lot," says Gerbstadt. "Would you eat that from a spoon, or put it in your coffee? Once in a while it's not going to harm you, but eating these cookies every day or several times a day -- well, the unhealthy effects are going to add up." New York nutritionist Samantha Heller, MS, RD, says she is concerned because some of these treats contain high-fructose corn syrup. A few studies have indicated a possible link between high-fructose corn syrup and obesity that goes beyond calorie counts. "More and more studies are starting to look at what high-fructose corn syrup does. It seems to metabolize a little differently than glucose ... so it may have greater consequences than regular table sugar. We just don't know yet," says Heller, a nutritionist at NYU Medical Center. If price is a concern, these pre-packaged treats might disappoint you. They can be more costly per ounce than a regular box of cookies, which you could divide up into single-serving packets on your own (if you can resist the urge to sneak a few). Plus, the treats in the snack packs don't always taste exactly like their regular counterparts. The Oreos, for example, don't have the white filling, just the crunchy chocolate wafer.

That said, Nabisco's 100-Calorie Packs do contain less fat and sugar than regular cookies and crackers, and their taste will certainly satisfy your salt or sweet tooth -- and probably your craving.

Snacks That Measure Up

Of course, you can easily prepare your own 100-calorie snacks, built around foods you like to eat. The key to controlling calories is to work with a reliable calorie-counting guide, then weigh and measure every ingredient -- at least at first. "If you are not measuring, you will underestimate the portion; that's almost a guarantee," says Heller. She also recommends you study how the snack looks on the plate before you take the first bite, to get an idea of what a portion should look like. When you're buying a snack on the run at a restaurant, deli, or street vendor, use your hands and fingers to estimate how much you're eating. "The palm of the hand is usually a 3-ounce serving; a tablespoon is about the size of the last digit on your thumb; and if it's a long item, like string cheese, an ounce is about the length of your forefinger," says Wilson. "Most restaurant portions are two to three times what a true single-serving portion is, particularly if you are buying a sweet treat, so keep that in mind when ordering," Wilson tells WebMD. One temptation it's usually best to avoid, she says, is buying snacks from a vending machine. "Unless that machine

is stocking fruit, I can guarantee it's almost always going to be over 100 calories -- and probably not very healthy," says Wilson.

100 Calorie Snacks:

Need some ideas? To get you started on the road to calorie-controlled snacking, our experts offer some suggestions for healthy 100-calorie munchies:

1. Half an apple with 2 teaspoons of peanut butter
 2. An orange and a few dry-roasted nuts
 3. 10 cashew nuts
 4. 10 almonds
 5. 2 ounces of lean roast beef
 6. Half a small avocado
 7. 3 ounces cooked whole-grain noodles with 1 fresh tomato and 1/2 ounce hard cheese
 8. 1 seven-grain Belgian waffle
 9. 4 mini rice cakes with 2 tablespoons low-fat cottage cheese
 10. 3 ounces low-fat cottage cheese and 3 whole-wheat crackers
 11. 1/4 cup fat-free ranch dressing with mixed raw veggies
 12. 6 Wheat Thins crackers with two teaspoons of peanut butter (or any nut butter)
 13. 1 small baked potato with 1/2 cup salsa and 2 tablespoons of fat-free sour cream
 14. 1/3 cup of unsweetened applesauce with 1 slice of whole-wheat toast, cut into 4 strips for dunking
 15. 1/2 cup frozen orange juice, eaten as sorbet
 16. 2 large graham cracker squares with 1 teaspoon peanut butter
 17. 3 handfuls of unbuttered popcorn, seasoned with herbs
 18. 4-6 ounces of no-fat or low-fat yogurt
 19. A 5-ounce tossed salad with lettuce, tomato, cucumber and 1/4 cup fat-free dressing
-Source: WebMD



BUTTERNUT SQUASH AND APPLE CASSEROLE

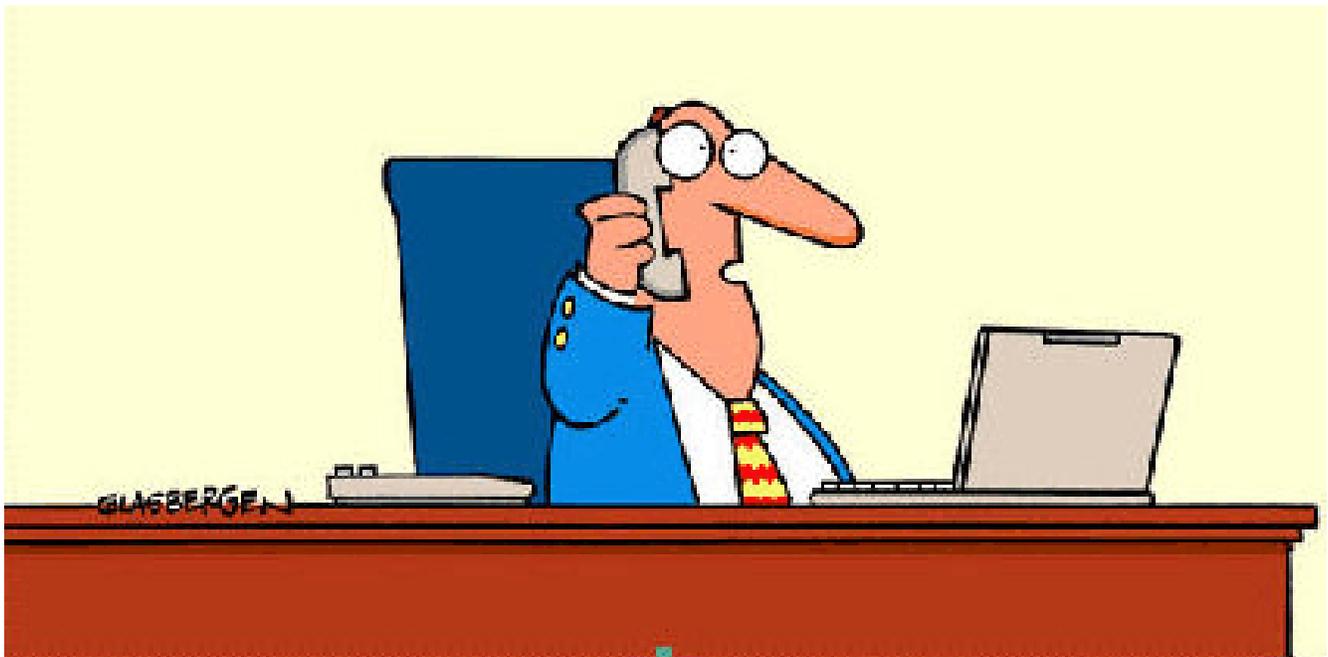
- a.. 1 small butternut squash, about 2 pounds
- b.. 2 apples, cored, peeled, sliced
- c.. 1/2 cup brown sugar, firmly packed
- d.. 1/4 cup cold butter
- e.. 1 tablespoon flour
- f.. 1 teaspoon salt
- g.. 1/4 teaspoon ground cinnamon
- h.. 1/4 teaspoon ground nutmeg

Peel squash, scoop out seeds, and cut in small pieces. Place squash and apple slices in oblong baking dish (7x11-inch). Blend remaining ingredients with fork or pastry cutter until crumbly. Distribute over squash and apple.

Cover and bake butternut squash casserole at 350° for about 45 to 50 minutes.

Butternut squash recipe serves 6 to 8.





Could you ask people to call me The Big Cheese instead of
The Janitor? I'm on Atkins!

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