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Fat City

ABSTRACT & COMMENTARY

Synopsis: *The metabolic syndrome affects more than 1 in 5 Americans and is increased substantially in Mexican Americans and by several modifiable lifestyle factors.*

Source: Park YW, et al. *Arch Intern Med*. 2003;163:427-436.

THIS REPORT EMANATES FROM THE THIRD NATIONAL HEALTH AND Nutrition Examination Survey (NHANES III), a face-to-face survey of individuals selected to represent the entire US population. Data collected included educational level, economic status, smoking status, alcohol consumption, physical activity, carbohydrate intake, and menopausal status.

In addition to questionnaire data, standardized medical examinations that included blood pressure, plasma lipid and blood glucose levels, and waist circumference took place at mobile medical centers. After exclusion of those who consumed anything besides water 6 hours prior to venipuncture, those who had missing data, and pregnant women, a total of 12,861 individuals were sampled in 89 locations between 1988 and 1994.

The definition of the metabolic syndrome used in this report comes from the Third Report of the National Cholesterol Education Program Adult Treatment Panel (ATP III)[1] and includes 3 or more of the following:

1. abdominal obesity (waist circumference > 102 cm in men, > 88 cm in women);
2. high triglyceride level (> 150 mg/dL);
3. low HDL cholesterol level (< 40 mg/dL for men, < 50 mg/dL for women);
4. high blood pressure (systolic > 130 mm Hg or diastolic > 85 mm Hg) or taking antihypertensives; and
5. high fasting glucose (> 110 mg/dL) or taking hypoglycemics.

Prevalence rates of the metabolic syndrome were calculated, and multiple logistical regression analysis was used to estimate odds ratios (ORs) by age, ethnicity, and other variables collected.

The overall prevalence of the metabolic syndrome was 22.8% for

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men and 22.6% for women. Among men, the overall prevalence rates were 13.9%, 20.8%, and 24.3% for blacks, hispanics, and whites; all differences were significant except that between hispanic and white men (P = 0.06). Among women, the prevalence of metabolic syndrome was 20.9%, 22.9%, and 27% for black, white, and hipanics. The prevalence was statistically significantly higher among Mexican American women. The prevalence of metabolic syndrome rose steeply for both genders older than 30, but appeared to peak between 50 and 70 years in men and between 60 and 80 years in women.

Body mass index was the strongest correlate of the risk of metabolic syndrome, but current cigarette smoking also greatly increased the risk. There were some gender differences between lifestyle factors and the ORs of metabolic syndrome. For men, high carbohydrate intake and low physical activity increased the odds. For women, previous smoking, nondrinking, low household income, and postmenopausal state increased the odds of metabolic syndrome.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

One in 5 of us had the metabolic syndrome almost 10 years ago (data collection for this study ended in 1994). Our trajectory toward national obesity has accelerated since that time, and I would guess that the rate of the metabolic syndrome is now 1 in 4. While we have been focusing on high technology and new pharmacologic agents, suicide by lifestyle has continued unabated.

There are a variety of definitions of the metabolic syndrome, but all include some measure of obesity, hypertension, hyperlipidemia, and insulin resistance. The criteria outlined above and promulgated by the ATP III Expert Panel are likely to be the ones we live with for awhile. The applicability of these criteria to different age, gender, and ethnic groups is a little suspect, though, since blacks had the lowest prevalence of the metabolic syndrome, but are more insulin resistant than are whites for any degree of obesity[2] and have the highest overall coronary heart disease mortality of any US ethnic group.[3]

About once a week, one of my patients asks me about the Atkins diet. I suggest you check out what's out there at http://atkinscenter.com. I no longer passionately discourage my patients (many of whom are morbidly obese, since I practice sleep medicine in Kentucky) from attempting this diet. The infamous Atkins diet, which focuses on reducing carbohydrates and increasing fat and protein, has some things going for it. At a time when many of our patients are "rediscovering" the Atkins diet, it is worth mentioning that the current study demonstrates that high carbohydrate intake is a risk factor for metabolic syndrome in men. In fact, there is plenty of evidence that increased carbohydrate intake may predispose to lipid abnormalities, insulin resistance, pancreatic cancer, and reduced bone density.[4-11] I have lost my confidence in the low-fat diet, and do not think that it is a coincidence that the prevalence of obesity and the metabolic syndrome have skyrocketed while we were urging our patients to avoid fat and eat carbohydrates.

And, once again, as always: ***Exercise is good for you!!*** (and your patients). ■

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Outcomes with Angiotensin-Converting Enzyme Inhibitors and Diuretics for Hypertension in the Elderly

ABSTRACT & COMMENTARY

Synopsis: *Initiation of antihypertensive treatment involving ACE inhibitors in older subjects, particularly men, appears to lead to better outcomes than treatment with diuretic agents, despite similar reductions of blood pressure.*

Source: Wing LMH, et al. *N Engl J Med*. 2003;348:538-592.

This is a prospective, randomized, open-labeled study that compared enalapril (ENAL) to hydrochlorothiazide (HCTZ) in the treatment of hypertension (HTN). Analysis was by intention to treat. The study was conducted in family practice offices in Australia with randomization beginning in 1995. Eligibility criteria were: aged 65-84 years; average systolic blood pressure (SBP) = 160 or average SBP = 140 and average diastolic blood pressure (DBP) = 90; and no cardiovascular events in the last 6 months. Subjects were excluded if they suffered from a life-threatening disease; had a contraindication to either of the study drugs; had a plasma creatinine = 2.5 mg/dL; had malignant HTN; or were demented.

Treatment goals were a reduction in SBP = 20 to < 160 and DBP = 10 to < 90. If patients could tolerate it, further reduction of SBP to < 140 and DBP to < 80 was encouraged. The physicians could use other antihypertensives (beta-blockers, calcium-channel blockers, and alpha-blockers) to achieve goal. The primary study end point was all cardiovascular events or death from any cause. Cardiovascular events included: myocardial infarction, sudden or rapid cardiac death, therapeutic coronary artery procedures, heart failure, acute occlusion of any major artery (except coronary or cerebral), dissecting or ruptured aortic aneurysm, stroke, and transient ischemic attacks. From a pool of 54,288 patients screened for eligibility, 6083 underwent randomization.

A total of 3044 were assigned to the ENAL group and 3039 to the HCTZ group. The 2 groups were well matched at baseline in regard to gender (50% vs 48% male), age (average, 72.0 vs 71.9 years old), blood pressure (average, SBP 167 vs 168 and average DBP 91 in both groups), previous antihypertensive therapy (62% in both groups), body mass index (average 27 in both groups, tobacco use (7% current smokers in both groups), alcohol use (74% vs 72%), physical activity (78% vs 76%), coronary heart disease (8% in both groups), cerebrovascular disease (5% vs 4%), diabetes mellitus (8% vs 7%), hypercholesterolemia (38% vs 36%), and treatment with lipid-lowering drugs (13% in both groups). Fully 95% of the participants were white. The patients' physicians had the option of not starting therapy immediately; 83% of patients in both groups started with the drug to which they had been assigned.

At study's end, 58% of the ENAL group was still taking ENAL vs 62% of the HCTZ group. ENAL was the only antihypertensive used by 65% in that group; HCTZ was monotherapy in 67% in its group. The percentage receiving 3 or more antihypertensives was 6% vs 5%, respectively. At the end of the first year, both drugs had achieved nearly identical reductions in BP (20/9 vs 22/9) and this reduction persisted until the study's end after 5 years (26/12 in both groups). However, the ENAL group had 695 primary end point events compared to the HCTZ group, which had 736. This represents a hazard ratio (HR) of 0.89 (95% confidence interval [CI], 0.79-1.00) favoring ENAL when the survival curves were compared. The HR for fatal stroke was 1.91 (CI, 1.04-3.50) favoring HCTZ. The HR for nonfatal myocardial infarction was 0.68 (CI, 0.47-0.99). When men and women were analyzed separately, the HR for all primary end point events was 0.83 (CI, 0.71-0.97) for men favoring ENAL and 1.00 (CI, 0.83-1.21) for women. The result for women is not statistically significant.

■ **COMMENT BY ALLAN J. WILKE, MD**

You are probably scratching your head right now, thinking, "Didn't I just read that the ALLHAT study showed that a diuretic beat out an ACE-inhibitor and a calcium-channel blocker for the treatment of hypertension?" Yes, you did. So what gives? The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) results were published late last year[1] and reviewed recently in this publication.[2] It compared chlorthalidone, lisinopril, and amlodipine, and indeed, chlorthalidone was better than amlodipine in preventing heart failure and better than lisinopril in preventing stroke, angina, heart failure, myocardial infarction, and revascularization procedures. The apparent contradictory results can probably be explained by carefully comparing the 2 studies, especially the study populations. The current study enrolled 6083 overwhelmingly white Australians. ALLHAT enrolled 33,357 North Americans; more than than one third were black. At the start of the study, the "average" ALLHAT participant was younger (66.9 years vs 71.9), more overweight (BMI 29.7 vs 27.0), less hypertensive (146/84 vs 167/91), more likely diabetic (36% vs 8%), more likely smoking (21.9% vs 7%), and more likely to have preexisting coronary heart disease (25% vs 8%). On the face of it, the Australian group was more active and much healthier. In his editorial in the same issue, Frohlich also reminds us that while the drugs are from the same classes, diuretics and ACE-inhibitors, they are not equivalent. Perhaps the drugs have different effects beyond their ability to lower blood pressure.

In the end, what are we to do? I think that the current study demonstrates a slightly better outcome for older, hypertensive males who are treated with enalapril. I do not see my approach to drug therapy for hypertension radically changing, however. I will continue to tailor treatment to the patient in front of me who may be diabetic (think ACE-inhibitor), in heart failure (think diuretic and/or ACE-inhibitor), or a survivor of a heart attack (think beta-blocker or ACE-inhibitor), and so forth. More importantly, with an estimated one-quarter of Americans with high blood pressure and one-third of them unaware they have it, I will continue to work to identify patients with the disease. ■

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To Drink or Not to Drink? That is the Question!

ABSTRACT & COMMENTARY

Synopsis: *A randomized, diet-controlled interventional study demonstrates that moderate alcohol consumption reduces plasma C-reactive protein and fibrinogen levels.*

Source: Sierksma A, et al. *Eur J Clin Nutr*. 2002;56: 1130-1136

C-REACTIVE PROTEIN (CRP) IS A MARKER FOR SYSTEMIC inflammation and predicts cardiovascular events among apparently healthy men and women.[1] This study was done to evaluate the effect of moderate alcohol consumption on CRP and fibrinogen.

It was a randomized, diet-controlled, crossover study.

Ten middle-aged men and 10 postmenopausal women, all apparently healthy, nonsmoking, and moderate alcohol drinkers, were included. One women dropped out because of a treatment-unrelated cause. The remaining 19 subjects completed the experiment successfully.

Men consumed 4 glasses and women 3 glasses of beer or nonalcoholic beer (control) with evening dinner during 2 consecutive periods of 3 weeks. The total diet was supplied to the subjects and had essentially the same composition during these 6 weeks.

Before each treatment period there was a 1-week washout period to compensate for possible carry-over effects.

Plasma CRP and fibrinogen levels were decreased by 35% ($P = 0.02$) and 12.4% ($P = 0.001$), respectively, after 3 weeks consumption of beer, as compared to nonalcoholic beer consumption.

Moderate alcohol consumption significantly reduced CRP and fibrinogen levels. An anti-inflammatory action of alcohol may explain the link between moderate alcohol consumption and cardiovascular death.

■ **COMMENT BY RALPH R. HALL, MD, FACP**

There are many facets to this study. First of all, this is a very small but well-designed experiment. As studies have shown, it is not only red wine that has protective effects on cardiovascular disease but rather alcohol in general. Many will be delighted to note that the alcohol in beer has these beneficial effects.

Preliminary guidelines have been established regarding the use of the CRP and the management of patients with elevated levels.

Table

Risk Levels Interpretation[2]

< 1microgram = low risk

1-3 micrograms = intermediate risk

3-10 micrograms = high risk

> 10 micrograms = repeat test in 1 month, exclude other processes

Kereiakes in a mini-review,[2] notes that high-sensitivity CRP testing is available in clinical settings throughout the world. Since only about half the patients with coronary heart disease have hypercholesterolemia, perhaps the addition of measuring and lowering the CRP will significantly lower the morbidity and mortality from this disease. It is of note that statins lower CRP levels 25-50 %.

Who should have a CRP test? Individuals who are at high risk for cardiovascular disease should be treated aggressively regardless of the CRP level (*see Table*). The test is therefore superfluous in high-risk patients. In patients who are at intermediate risk, using American Heart Association criteria, a positive test result may add incentive to adhere to therapy. Many physicians believe the test is not useful in low-risk patients. However, a positive test in a low-risk patient may be an indication for a more aggressive approach. We have much to learn about the usefulness of the CRP test.

A recent editorial by Goldberg, regarding the studies on the effectiveness of alcohol in the prevention of coronary heart disease, discusses the impossibility of eliminating confounding differences between groups such as exercise and smoking.[3] As he points out, however, the reproducibility of the association between alcohol and heart disease is compelling.

Do these studies mean that we should recommend alcohol for our patients? I think not! Abuse of alcohol comes at a devastatingly high price.[4] We should be recommending the reduction of intake in those patients who are consuming more than 2 drinks per day. We can reassure those who have moderate alcohol intake their habits are not harmful, but there is a need to guard against higher rates of consumption later in life.

For a more detailed discussion on the management of elevated CRP, the review by Kereikes[2] is recommended. ■

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Vitamin A and Fracture Risk

ABSTRACT & COMMENTARY

Synopsis: *The findings of this study, which are consistent with the results of studies in animals, as well as in vitro and epidemiologic dietary studies, suggest that current levels of vitamin A supplementation and food fortification in many Western countries may need to be reassessed.*

Source: Michaelsson K, et al. Serum retinol levels and the risk of fracture. *N Engl J Med*. 2003;348:287-294.

Although studies in animals and epidemiologic studies have indicated that a high vitamin A intake is associated with increased bone fragility, no biologic marker of vitamin A status has thus far been used to assess the risk of fractures in humans.

A total of 2322 men, 49-51 years of age, were enrolled in a population-based, longitudinal cohort study. Serum retinol and beta-carotene were analyzed in samples obtained at enrollment. Fractures were documented in 266 men during 30 years of follow-up. Cox regression analysis was used to determine the risk of fracture according to the serum retinol level.

The risk of fracture was highest among men with the highest levels of serum retinol. Multivariate analysis of the risk of fracture in the highest quintile for serum retinol (> 75.62 micrograms/dL [2.64 micromoles/L]) as compared with the middle quintile (62.16-67.60 micrograms per deciliter [2.17-2.36 micromoles/L]) showed that the rate ratio was 1.64 (95% confidence interval, 1.12-2.41) for any fracture and 2.47 (95% confidence interval, 1.15-5.28) for hip fracture. The risk of fracture was further increased within the highest quintile for serum retinol. Men with retinol levels in the 99th percentile (> 103.12 micrograms per deciliter [3.60 micromoles per liter]) had an overall risk of fracture that exceeded the risk among men with lower levels by a factor of seven ($P < 0.001$). The level of serum beta-carotene was not associated with the risk of fracture.

These findings, which are consistent with the results of studies in animals, as well as in vitro and epidemiologic dietary studies, suggest that current levels of vitamin A supplementation and food fortification in many Western countries may need to be reassessed.

■ COMMENT BY JOHN La PUMA, MD, FACP

In Sweden, hip fracture is more than twice as common among men than women. Michaelsson and colleagues

postulate that serum retinol is a biological marker for fracture. Consuming more than 1.5 mg (4500 IU) of vitamin A (retinyl palmitate) daily increased fracture risk.

What does vitamin A do? In premature and malnourished children it prevents some diseases of the eye, but in Western countries it appears to accelerate osteoporosis and promote bone fracture. The Harvard-based Nurses Health Study, of more than 70,000 nurses, found a similar association: Postmenopausal women whose daily intake of vitamin A exceeded 3000 micrograms (about 10,000 IU) were 40% more likely to fracture a hip, compared with women whose daily intake was less than 1250 micrograms (3750 IU).

The therapeutic window of vitamin A is narrow and its serum levels increase with age. Editorialist Paul Lips writes, "One may conclude from such data that supplements containing vitamin A should not be routinely used by men or women and that fortification of cereals with vitamin A should be questioned."

Vitamin A is found in fatty fish, liver, kidney, and dairy products, and many are fortified with vitamin A, including milk and yogurt. Many processed cereals are augmented too. Beta-carotene and other carotenoids also are converted into vitamin A in the body, but these amounts are small relative to the direct intake and absorption of vitamin A.

How does fracture occur? Dietary vitamin A is converted to retinoic acid, which binds to specific receptors. In vitro, these receptors then curb osteoblast activity and encourage osteoclast formation. Osteoclasts take up old bone, and while this makes way for new bone, it also may cause susceptibility to fracture.

The Recommended Daily Intake for vitamin A is just 0.7 mg of vitamin A for women and 0.9 mg for men. Most multivitamins easily supply this—even twice this—on top of what people get from food.

What are the study's limitations? It followed 2322 middle-aged men older than 30 years, but blood levels of vitamin A were taken once, at the beginning of the trial. Vitamin A is stored in fat cells, like the other fat-soluble vitamins (D, E, and K), but one time measurements are just that. A study of this duration and power is unlikely to be repeated prospectively.

Vitamin A toxicity has been well known for decades: Administration as a dietary supplement to adults should be avoided. For this vitamin, what patients get from food is enough. Advise your patients to take a multivitamin that derives all of its vitamin A from beta-carotene; patients also should avoid eating liver and reconsider fish oil supplements. ■

Dr. La Puma is Director, Santa Barbara Institute for Medical Nutrition & Healthy Weight, Santa Barbara, Calif.

Pharmacology Update

Eletriptan Hydrochloride (Relpax—Pfizer)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

ELETRIPTAN IS THE NEWEST "TRIPTAN" TO BE approved for the treatment of migraine headaches. It marks the seventh entry into this crowded market. Eletriptan, a selective 5-hydroxytryptamine (serotonin) 1B/1D receptor (5-HT1B, 5-HT1D) agonist will be marketed by Pfizer as "Relpax."

Indications

Eletriptan is indicated for the acute treatment of migraine with or without aura in adults.[1]

Dosage

The initial dose of eletriptan is 20 mg or 40 mg. Results from clinical studies indicated a higher response rate with the 40-mg dose but individual response may vary.[1] If the headache improves with the initial dose but returns, a second dose may be taken. The second dose should be taken at least 2 hours after the initial dose. If the initial dose is not effective, a second is not likely to be beneficial.[1]

Eletriptan is available as 20 mg and 40 mg tablets.

Potential Advantages

Eletriptan has high lipid solubility, favorable elimination half-life (4-6 hours), and good bioavailability (50%).[1,2] In addition, it has slow dissociation from 5-HT1D receptors and very low affinity for 5-HT2 receptors in coronary arteries.[2,3] In a comparative study, eletriptan was reported to be superior to sumatriptan in response at 2 hours.[5] Headache responses ranged from 64-67% for eletriptan (40 mg-80 mg) vs 50-53% for sumatriptan (50 mg-100 mg). Pain-free response was 31-37% and 19-18%, respectively.

Potential Disadvantages

Eletriptan is metabolized by cytochrome P450 isoenzyme 3A4 (CYP3A4) and should not be used within at least 72 hours of any potent CYP3A4 inhibitors.[1] These include ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, and nelfinavir.

Comments

Eletriptan is the seventh "triptan" to be approved for the treatment of acute migraine headaches. It does not offer any single unique advantage but does possess favorable pharmacokinetic and pharmacodynamic properties including good lipid solubility, long elimination half-life (except for naratriptan and frovatriptan), good bioavailability, low affinity for 5-HT2 receptors of the coronary arteries, and slow dissociation from 5-HT1D receptors. In a phase III clinical trial (n = 1153), eletriptan 40 mg produced headache relief at 2 hours in 62% of patients, 65% for 80 mg, and 19% for placebo.[4] Corresponding results for complete pain relief were 32%, 34%, and 3%, respectively. A lower recurrence rate, compared to placebo, was found with the 80-mg dose only. In 5 of 6 studies, the response (mild or no headache) rate ranged from 64.6% to 77.1% for the 80-mg dose, and 53.9% to 65% for the 40-mg dose.[1] In the sixth study, the response rate was 61.4% for 40 mg and 58.6% for 80 mg. In a study of adolescents (n = 274), there were no statistical differences among treatment groups and placebo.[1] Common side effects include asthenia, nausea, dizziness, paresthesia, and somnolence.[1] These were higher for the 80 mg dose compared to the 40-mg dose (5-12% vs 3-7%).[4] The approval of eletriptan was delayed as Pfizer had to address the FDA's concerns about the cardiovascular safety of the higher dose.[6] The 80-mg dose was ultimately not approved, and the recommended dose is now 20-40 mg. Side effects reported more frequently in patients receiving the 80-mg dose were asthenia and dizziness.[7] The number needed to treat (NNT) were 9.9, 4.0, and 3.7 for 20 mg, 40 mg, and 80 mg, respectively. The corresponding number needed to harm (NNH) were 11, 7.0, and 3.7 for minor adverse effects.[7] The wholesale cost for eletriptan (both strengths) is $12.64 per tablet and is comparable to other "triptans" such as sumatriptan 100 mg and rizatriptan 5 mg and 10 mg.

Clinical Implications

Eletriptan enters a crowded "triptan" market. It does not appear to provide any clinical advantage over currently available "triptans," particularly since the higher and more effective dose of eletriptan was not approved due to concern for adverse effects. ■

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CME Questions

14. Which of the following are risks for the metabolic syndrome?

a. Obesity, cigarette smoking, alcohol consumption, and black ethnicity
b. Obesity, cigarette smoking, alcohol nonconsumption, and hispanic ethnicity
c. Premenopausal state, cigarette smoking, alcohol consumption, and black ethnicity
d. Postmenopausal state, cigarette smoking, alchohol nonconsumption, and hispanic ethnicity
e. Premenopausal state, cigarette smoking, alcohol consumption, and white ethnicity

15. Which statement is *false*? In the Australian study of hydrochlorothiazide and enalapril:

a. patients taking enalapril had fewer fatal strokes.
b. patients taking enalapril had fewer nonfatal myocardial infarctions.
c. neither drug outperformed the other in women.
d. both drugs achieved similar reductions in blood pressure.

16. Which one of the following statements is *false*?

a. Beer significantly lowers CRP and fibrinogen levels.
b. Drinks containing alcohol lower the CRP levels to a greater extent than statin drugs.
c. The use of CRP testing is not indicated in patients who are at high risk for cardiovascular disease.
d. There may not be a clear indication for CRP determination in patients at low risk for cardiovascular disease.

Answers: 14 (d); 15 (a); 16 (b)

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In Future Issues:

NSAIDs and Diarrhea

By Louis Kuritzky, MD

Use of Hip Protectors in Nursing Homes: Cluster Randomized Controlled Trial

DESPITE THE FACT THAT USE OF HIP protectors (HIP) has demonstrated excellent outcomes reduction when used among elderly persons ie, as much as a 50% reduced incidence of hip fractures, actual use among at-risk populations is markedly suboptimal. For clinicians who have not seen hip protectors before, they are disk-shaped cushions that can be worn under clothing to act as a mechanical defense if a patient falls.

One of the reasons for tepid responsiveness of senior citizens to use of HIP may be inadequate education of healthcare providers and nursing home staff. To that end, Meyer and associates studied a 2-part intervention in 86 German nursing homes. The initial intervention included a 60-90 minute education session for nursing home staff about risk factors for hip fracture, consequences of hip fracture, and effectiveness of hip protectors. Staff was also instructed in steps to address potential obstacles to successful HIP implementation. HIP-educated staff members were assigned to provide a similar information base to resident patients in their nursing homes. Nursing staff also used a documentation sheet on resident falls and their outcomes. HIP were provided for residents free of charge in the intervention group. The control group ("usual care") received a brief informative demonstration of HIP, and 2 HIP for demonstration purposes. The primary end point of the trial was hip fracture. The secondary end point was frequency of HIP use.

The relative risk of hip fracture was 0.57 in HIP users (NNT = 29). Frequency of HIP use was significantly higher in the intervention group (68% vs 15%). Use of HIP, especially when accompanied by an intensive staff education, can reduce hip fractures by more than 40%. ■

Meyer G, et al. BMJ. 2003;326:76-78.

Disclosing Unanticipated Outcomes and Medical Errors

ACCORDING TO THE 1999 INSTITUTE of Medicine report, medical errors are an important cause of loss of life, resulting in as many as 98,000 deaths annually in the United States. The Lexington, Kentucky VA has followed a policy of full disclosure about medical errors for more than 15 years. They rank in the lowest quartile of VA centers for liability costs, which appears to have resulted not from a reduction in the frequency of malpractice claims—indeed, the absolute number of claims actually has increased—but rather from willingness of injured persons and their families to negotiate fair settlements, after complete and open disclosure.

Steps in adequate disclosure after unanticipated adverse outcome *without* medical error should include: 1) Without defensiveness, be aware of and respond to the needs of the patient and their family; 2) Keep family members apprised of continued clinical care progress; 3) Clarify how the unanticipated outcome may have occurred; 4) Communicate your understanding, empathically, of the concerns of the family; 5) Acknowledge the areas of uncertainty, with an offer to clarify these areas as soon as possible.

When medical error *has* led to injury, additional steps should include 1) apology and acceptance of responsibility—reluctance to provide a full accountability may actually drive patients to seek legal counsel; 2) determine who best should be included in future disclosure conversations and identify an individual to respond to the family's nonclinical (eg, financial compensation) inquiries; and 3) be proactive in addressing the patient's financial needs, such as costs of family members needing to stay in hotels for a prolonged hospital stay. ■

O'Connell D, et al. J Clin Outcomes Man. 2003;10(1):25-29.

Noninvasive Positive Pressure Ventilation to Treat Respiratory Failure Resulting from Exacerbations of COPD

WHEN THE TRADITIONAL INTERventions (eg, bronchodilators, steroids, antibiotics, oxygen) for COPD exacerbation are insufficient to reverse clinical deterioration, clinicians typically rely upon invasive ventilation, with its attendant morbidity, and occasional difficulty in weaning. Noninvasive positive pressure ventilation (NPPV) provides an air/oxygen mixture from a flow generator through a full facial or nasal mask. The subsequent unloading of flagging respiratory musculature enhances respiratory efficiency. Failure rates of this technique have been reported between 9-50%. Lightowler and colleagues performed a Cochrane review and meta-analysis to ascertain effectiveness of NPPV in patients with respiratory failure secondary to COPD exacerbations.

NPPV, when coupled with usual medical care of COPD exacerbations, was shown to significantly reduce mortality (59%), need for intubation (58%), treatment failure (49%), complications (68%), and length of hospital stay. These data should encourage clinicians to use NPPV earlier in the therapeutic course, before serious acidosis ensues. ■

Lightowler JV, et al. BMJ. 2003;326: 185-187.