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Make New Friends, but Keep the Old

ABSTRACT & COMMENTARY

Synopsis: *Thiazide diuretics should be the first-step antihypertensives because they are less expensive and more effective than calcium channel blockers or ace inhibitors.*

Source: ALLHAT Study. *JAMA.* 2002;288:2981-2997.

This report is part of the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT) comparing the cardiovascular effects of various first-step drugs for the treatment of hypertension. Participants were 33,357 individuals whose mean age was 67 years (minimum age, 55). Also, 47% were women, 35% were black, 19% were Hispanic, and 36% were diabetic. They were recruited from 623 centers in 4 countries. Successfully recruited subjects were divided into 3 groups that were well matched for important variables, including cigarette smoking, body mass index, aspirin use, education, blood pressure, diabetes, and most other known cardiovascular risks. To be included, a subject had to have stage 1 or 2 hypertension and at least 1 additional risk factor for coronary heart disease events, including myocardial infarction (MI) or stroke (CVA) within the previous 6 months, left ventricular hypertrophy (LVH), type 2 diabetes, current cigarette smoking, high-density lipoprotein (HDL) cholesterol of less than 35 mg/dL, or documentation of other atherosclerotic cardiovascular disease (CVD). Those with heart failure were excluded. Participants were randomly assigned to 1 of 3 arms: chlorthalidone (representing the thiazides), amlodipine (representing the calcium channel blockers), or lisinopril (representing the ACE inhibitors). They discontinued whatever antihypertensive they were on when the study drug was started.

Patients were followed at 1, 3, 6, 9 and 12 months and every 4 months thereafter. Length of follow-up ranged from 3.6 years to 8.1 years (average, 4.9). At each visit, blood pressure (BP) was measured, and drugs were titrated to achieve a blood pressure of less than 140/90. Clinicians in the trial could add other antihypertensives at their discretion. Nonpharmacologic approaches were also recommended to patients.

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INSIDE

The primary outcomes were fatal coronary heart disease or nonfatal MI. Secondary outcomes were all-cause mortality, stroke, combined coronary heart disease (including angina, revascularization, MI), and combined cardiovascular disease (including all coronary heart disease, stroke and heart failure).

In comparing outcomes between treatment groups, the following difference were noted:

1. Amlodipine vs chlorthalidone: The Amlodipine group had a 38% higher risk of heart failure;
2. Lisinopril vs chlorthalidone: The Lisinopril group had a 15% higher risk of stroke, a 19% higher risk of combined cardiovascular disease (including a 19% higher risk of heart failure), and a mean systolic BP at follow-up that was 2 mm Hg higher.

Angioedema occurred 4 times more commonly with lisinopril than with chlorthalidone, but cholesterol levels were higher and hypokalemia and new diabetes were more common with chlorthalidone than with either of the other drugs. All-cause mortality was the same between the groups.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

For those of us not classified by the pharmaceutical industry as "early adopters," these findings are vindicating. This report, which comes from the largest study of hypertension ever undertaken, clearly documents that old-fashioned diuretics are more effective and less costly than newer agents in lowering blood pressure and preventing cardiovascular complications. In their discussion, it is noted that the health care system would have saved $3.1 billion in estimated costs of antihypertensive drugs had the pattern of prescriptions for the treatment of hypertension remained at the 1982 level (when diuretic use comprised 56% of the antihypertensive market, compared with the current 27%). A companion article in the same issue of *JAMA* also notes that pravastatin did not reduce all-cause mortality or coronary heart disease significantly when compared with usual care in older patients.[1]

These and other findings have attracted the attention of the insurance industry and the media. My home-town newspaper[2] carried an editorial, reprinted from the *New York Times*, which said, in part: "The study . . . carries a compelling warning about the deficiencies of drug testing. The newer drugs had never been forced to prove they were better than diuretics, and their manufacturers had no incentive to risk conducting such tests . . . The government should either force manufacturers to compare their new drugs with existing remedies when seeking marketing approval or conduct such studies itself."

Two messages got through to me: Most all antihypertensive regimens should include a diuretic, and newer isn't necessarily better (though it's almost always more expensive). ■

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Caring for Late-Life Depression: Collaboration Is Best

ABSTRACT & COMMENTARY

Synopsis: *Depressed seniors fared better when treated by a team of primary care practitioners and psychiatrists.*

Source: Unützer J, et al. *JAMA*. 2002;288:2836-2845.

Building on their previous work that demonstrated that the combination of collaboration between primary care physicians (PCPs) and psychiatrists, patient education, and surveillance of antidepressant medication refills improved satisfaction with care and resulted in better depressive outcomes, Unützer and colleagues turned their attention to depressed elderly.[1,2]

The Improving Mood-Promoting Access to Collaborative Treatment (IMPACT) program enrolled patients from 18 primary care clinics in 5 states. The clinics were a mix of rural and urban; the PCPs were general internists, family physicians, nurse practitioners, and physician assistants. The patients could enter the study through 2 routes: referral from their PCP, other clinic staff, or themselves, or identification by a systematic depression screening of older adults who used the clinics. Accordingly, 2190 patients were referred to the study and 32,908 patients were approached for screening. These approximately 35,000 patients were pared to 1801 (average age, 71.2 years, 65% female, 23% ethnic minorities). Inclusion criteria were age 60 years or older, plans to use the clinic for usual care for the next year, and a current diagnosis of depression or dysthymia.

Patients were excluded if they refused to participate in the screening or eligibility interview, had an incomplete screen, or did not meet the criteria for depression or dysthymia (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition). Others were excluded if they had an active drinking problem, were bipolar, were currently under the care of a psychiatrist, were severely cognitively impaired, or were acutely suicidal. The 1801 remaining patients were randomly assigned to either "usual care" or the IMPACT intervention.

Briefly, IMPACT involved receiving an educational videotape and a booklet on late-life depression and encouragement to attend a visit with a depression care manager (a specially trained nurse or psychologist). After discussing the case with the supervising team psychiatrist, the care manager and the patient's PCP developed a treatment plan, following a treatment algorithm. The algorithm advised either a course of an antidepressant or a short course of structured psychotherapy. The care manager delivered the psychotherapy in the primary care office. Further treatment could include larger doses of the antidepressant, a different antidepressant, or adding the psychotherapy if the patient was not currently receiving it. Patients were followed for 12 months and evaluated at 0, 3, 6, and 12 months. All participants completed the study.

Analyses were by intention to treat. Not surprisingly, at 12 months IMPACT patients were more likely to use either antidepressants or psychotherapy than usual care patients (82% vs 61%). They were also more satisfied with the care of their depression (76% vs 47%), had lower depression severity (1.0 vs 1.4 on a 4-point scale), higher rates of treatment response (45% vs 19%), and higher rates of complete remission (25% vs 8%). The usual care patients had worse overall functional impairment (4.5 vs 3.6 on a 10-point scale) and worse quality of life (6.0 vs 6.7 on a 10-point scale) than the intervention patients. All of these results were statistically significant. Unützer et al estimated the cost of providing the IMPACT intervention for 12 months to be $533 per patient.

COMMENT BY ALLAN J. WILKE, MD

Studies of depression have been appearing with consistent regularity in the medical literature. A brief sampling includes managing depression as a chronic illness,[3] identifying patients with severe depressive symptoms,[4] and the US Preventive Services Task Force's recommendation for screening for depression in primary care settings.[5]

There was not much to quibble about in this study. The intervention lasted only 12 months; I would like to know what happens to these folks in the longer term. The measurements of health-related functional impairment and quality of life were self-reports. Given these limitations, is the juice worth the squeeze? At $533 per patient per year, I should think so!

Upward of 7% of people older than age 60 are depressed.[6] Depression in the elderly is attended by considerable morbidity and mortality. We have the tools to identify them,[7] the drugs to treat them (selective serotonin reuptake inhibitors are first line), and the colleagues (psychiatrists, psychologists) to refer them to for counseling if we are too busy to do it ourselves. Why aren't we doing this? ■

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Is the Frailty of Older Age Related to a Biological Inflammatory Response?

ABSTRACT & COMMENTARY

Synopsis: *There is a physiological basis to geriatric frailty characterized by inflammation and elevated markers of blood clotting.*

Source: Walston J, et al. *Arch Intern Med*. 2002;162: 2333-2341.

THE FINDINGS OF THIS STUDY SUPPORT THE CONCEPT that there is a physiological basis to geriatric frailty characterized by inflammation and elevated markers of blood clotting. The objectives of this study were to establish the biological correlates of frailty in the presence and absence of concurrent cardiovascular disease and diabetes mellitus.

The participants were 4735 community dwelling adults aged 65 years and older. Frail, intermediate, and nonfrail subjects were identified by a validated screening tool and exclusion criteria.

Of 4735 cardiovascular Health Study participants, 299 (6.3%) were identified as frail, 2147 (45.3%) as intermediate, and 2289 (48.3%) as not frail. Frail vs nonfrail participants had increased mean levels of C-reactive protein (CRP) (5.5 vs 2.7 mg/mg/L), factor VIII 13790 vs 11860 mg/dL and in a smaller subset of subjects, (400 subjects), (D dimer [647 vs 224 ng/mL]) (P = 0.001 for all $\times$ 2 test for trend). These differences persisted when individuals with cardiovascular disease and diabetes were excluded and after adjustment for age, sex, and race.

Walston and colleagues concluded that these findings support the hypothesis that there is a specific physiological basis to the geriatric syndrome of frailty that is characterized in part by increased inflammation and elevated markers of blood clotting. These physiological differences persist when those with cardiovascular disease or diabetes are excluded.

COMMENT BY RALPH R. HALL, MD, FACP

To arrive at a standardized screening tool for frailty, Walston et al previously synthesized the most commonly described attributes of frailty into a definable clinical criteria. These screening criteria consist of weight loss, muscle weakness, fatigue, declines in activity, and slow or unsteady gait. They have evaluated these criteria by showing ability to predict disability, hospitalization, and mortality.[1,2]

The frail subset had a higher Body Mass Index (BMI) than the intermediate and nonfrail groups despite the weight loss. Walston et al note that although they had no body composition data, the increased BMI and the trend toward glucose intolerance, which was also documented, and the lower walking speed and strength measures suggest a lower percentage of lean body mass.

The increase in D dimer, which has been shown to induce synthesis of biologically active interleukins and plasminogen activator inhibitor, supports the inflammation concept. Walston et al correctly point out, that although these associations are strong, they do not support a causal influence.

Where is this concept of inflammation going to take us? There remains much to explore in regards to the inflammation markers and their influence on atherosclerosis, frailty, and other degenerative diseases. What part do activity and diet play in this process? Studies show that in patients with congestive heart failure and type 2 diabetes, exercise decreases the levels of many, but no all, of the inflammatory and blood clotting markers.[3]

Two recent studies support the diet and exercise concept. Benjamin Wang working with James Fries at Stanford updated the studies on a group of 370 runners initially aged 50 years and older compared with a group of 249 sedentary control subjects.[4] This was a 13-year, prospective, cohort study. Control subjects were without disabilities at the onset of the study. Significantly lower disability levels in the runners vs controls were sustained for at least 13 years. Reaching the objective disability level that was significant was postponed by 8.7 years in the runners. The controls had a 3.3 times higher rate of death than the runners, with higher death rates in all diseases studied.

Stevens and associates at the University of North Carolina evaluated 2506 women and 2860 men between 1972 and 1976.[5] Vital statistics were collected through 1998. The mean age was 45.8 years at the start of the study.

They calculated mortality rates, BMI, and fitness levels. The subjects were classified as fit-not fat, fit-fat, unfit-fat, and unfit-not fat. Adjustments were made for age, education, smoking, alcohol intake, and Keys score

for dietary intake. For men whose level of fitness and BMI were both in the top quintile, the risk of all-cause mortality was 1.25 compared to those who were fit and not fat. The hazard ratio for the same group of women was 1.32. For women who were not obese but unfit, the hazard ratios for all-cause and cardiovascular disease were 1.30 and 1.53, respectively, and the ratios were 1.44 and 1.55 for men.

Until we have better solutions about how biological inflammation originates and can be controlled, it appears that we have a reasonable way to delay disability and death. Stay fit, non-fat, and eat a reasonable diet. Think of the billions in health care dollars that could be saved. ■

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Cardiopulmonary Resuscitation on the Wards: Who Survives?

ABSTRACT & COMMENTARY

Synopsis: *In this review of outcomes from cardiopulmonary resuscitation among non-ICU inpatients in 3 urban teaching hospitals, no patient who had an unwitnessed cardiac arrest survived to discharge. Forty-four percent of patients with witnessed respiratory arrest returned to their homes, as compared with 13% of patients with witnessed cardiac arrest (21% for pulseless ventricular tachycardia or fibrillation, and 7% for pulseless electrical activity or asystole).*

Source: Brindley PG, et al. Predictors of survival following in-hospital adult cardiopulmonary resuscitation. *CMAJ*. 2002;167(4):343-348.

Brindley and associates reviewed all cases of attempted resuscitation from cardiac and/or respiratory arrest that occurred during a 2-year period among hospitalized adult patients in all 3 teaching hospitals of the University of Alberta who were not in an ICU, the emergency department, or the operating room. Brindley et al sought to determine current overall survival rates, since existing data were mainly gathered decades ago, and both the hospital inpatient population and available therapies have changed. They also wished to determine associations among patient characteristics, the circumstances of the arrest, and other factors and survival.

There were 247 arrests during the study period, 58% of which were witnessed and 42% unwitnessed. Among patients with witnessed arrests, 48% were initially successfully resuscitated, 22% survived to hospital discharge, and 19% were able to return home. In contrast, only 21% of patients whose arrest was unwitnessed could be resuscitated, and only 1 patient (1%) survived to discharge and was able to return home. This latter patient had an isolated respiratory arrest; no patient who had an unwitnessed cardiac arrest survived to hospital discharge. The type of arrest strongly influenced outcome: Among the 143 patients with witnessed arrests, 44% with respiratory arrest returned home, as compared with 21% of those with pulseless ventricular tachycardia or ventricular fibrillation, and 7% of those with pulseless electrical activity (PEA) or asystole. The risk of not returning home after cardiac arrest was greater for patients whose events occurred on the night shift (11 PM-7 AM) as compared to the day shift (7 AM-3 PM), but age and sex were unrelated to survival.

COMMENT BY DAVID J. PIERSON, MD

This study updates survival statistics for in-hospital cardiopulmonary arrest in the context of present-day inpatient severity of illness assessment and resuscitation techniques. Despite these evolutionary factors in inpatient healthcare, outcomes do not appear to have changed much in the last 40 years. Patients who are found already in cardiac arrest do not survive, even if they are initially resuscitated. About 1 patient in 5 who experiences a witnessed cardiac arrest and whose initial rhythm is pulseless ventricular tachycardia or ventricular fibrillation has a good outcome (defined in this study as being able to return home). For patients found initially in PEA or asystole, the chance is much less—only about 7% in this series.

While outcomes from cardiac or respiratory arrest in the ICU were not examined in this study and would likely be different, the present findings underscore the fact that cardiopulmonary resuscitation in patients sick enough to be in the hospital has a generally poor overall result. This is often at variance with what patients and their families believe. Resuscitation works much more often in the movies and on television. A review of TV medical dramas published in 1996 found that the initial survival rate following cardiopulmonary resuscitation was 75%, with two-thirds of the patients who arrested in

the hospital surviving to discharge.[1] As discussed by Brindley et al, these outcomes are 2 to 6 times better than those in any reported study. The onus is thus on physicians and others in the health care system to discuss actual expected survival should cardiac arrest occur and to find out about the expectations of patients and families. ■

Dr. Pierson is Professor of Medicine, University of Washington Medical Director Respiratory Care Harborview Medical Center, Seattle, Wash.

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Pharmacology Update

Teriparatide Injection (Forteo—Lilly)

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

THE FDA HAS APPROVED TERIPARATIDE (rhPTH[1-34]) for the treatment of osteoporosis in men and women. The drug is a 34-amino-acid polypeptide that represents the biologically active portion of human parathyroid hormone. Teriparatide is produced by a recombinant DNA technique using *Escherichia coli* bacteria. The once-a-day injection will be marketed by Lilly under the trade name "Forteo."

Indications

Teriparatide is indicated for the treatment of postmenopausal women with osteoporosis at high risk of fracture. It is also indicated for the treatment of men with primary or hypogonadal osteoporosis at high risk of fracture.[1]

Dosage

The recommended dose is 20 µg daily given by subcutaneous injection into the thigh or abdominal wall. Patients and caregivers should be appropriately trained to administer the drug by a qualified health professional.[1]

Teriparatide is supplied as a 3-mL prefilled pen delivery device. The device delivers 20 µg per dose for 28 days. The device should be stored under refrigeration but not frozen.

Any unused solution should be discarded after 28 days.[1]

Potential Advantages

Teriparatide is a potent agent for bone formation (trabecular and cortical) by stimulating osteoblastic activity.[1] This differs from other drugs that modify bone resorption by affecting osteoclast activity. In postmenopausal women, 20 µg daily increased bone mineral density (BMD) of the spine by 10% and femoral neck by 3%, reduced the risk of new vertebral fractures by 65% (5% vs 14.3%) and risk of nonvertebral fractures by 35% (6.3% vs 9.7%) at a median follow-up of 21 months.[2] Increases in BMD are greater than that achieved with alendronate. In a comparative study, teriparatide, 40 µg daily, increased BMD of the lumbar spine by 12.5% at 3 months compared to 5.6% for alendronate 10 mg daily.[3] The FDA-approved dose of 20 µg was not compared in this study but increase in BMD is estimated to be 9-10% based on a comparison of the 2 doses, 13.7% and 9.7% for 40 µg and 20 µg respectively.[2]

Potential Disadvantages

Teriparatide requires daily subcutaneous injection and must be stored under refrigeration. It has been shown to increase the incidence of osteosarcoma in rats in a dose- and duration-related manner. Teriparatide is therefore not recommended for patients at risk for osteosarcoma. These include patients with Paget's disease, unexplained elevation of alkaline phosphatase, open epiphyses, or those who have had prior radiation of the skeleton.[1] Patients with metabolic bone disease or with active or a history of skeletal malignancies also should not be treated with teriparatide. Pain and induration at the injection have been reported and appears to be related to the vehicle, not teriparatide.[6] Side effects related to teriparatide included nausea (8.5% vs 6.7% for placebo), dizziness (8% vs 5.4%), and leg cramps (2.6% vs 1.3%). Mild hypercalcemia (>10.6 mg/dL on at least 1 occasion) has been reported in 11% of women on 20 µg/day compared to 2% in the placebo group.[2] Transient symptomatic orthostatic hypotension (beginning within 4 hours of administration) and elevation of serum uric acid have also been reported. In clinical studies, 7.1% of patients discontinued therapy due to side effects compared to 5.6% for placebo. The use of teriparatide for longer than 2 years is not recommended.[1]

Comments

Teriparatide is an N-amino-terminal fragment of the human parathyroid hormone produced by recombinant DNA technology. Clinical studies involving 1085 sub-

jects randomized to placebo or 20 µg showed that teriparatide increased BMD and reduced vertebral and nonvertebral fractures in postmenopausal women.[1,2] It has also been shown to be effective in increasing BMD in men with osteoporosis (n = 437).[4] After a median of 11 months on 20 µg daily, spine BMD increased by 5.9% above baseline, femoral neck by 1.5%, and whole-body mineral content by 0.6%. The effect of the drug on fracture risk in men has not been evaluated. Teriparatide does not increase BMD in the radius and actually decreased bone density at the one-third distal radius compared to alendronate.[3] In these trials, patients received 1000 mg of calcium and at least 400 IU of vitamin D per day. The effect of teriparatide does not appear to be affected by baseline BMD, age, gonadal status (men), or disease severity.[4,5] Teriparatide is generally well tolerated. Osteosarcoma has been reported in female rats, which prompted the early termination of the above trial. To date, no increase in risk of osteosarcoma in humans has been reported.

The wholesale cost of teriparatide is about $17 per day ($6200/yr).

Clinical Implications

Teriparatide is a potent agent effective in increasing BMD and reducing the risk of vertebral and nonvertebral fractures. This new drug may be suited for postmenopausal women or men with severe osteoporosis. Candidates may include those with a history of osteoporotic fracture, with multiple risk factors for fracture, or who have failed or are intolerant of other therapy.[1] Bisphosphonates, namely alendronate or risedronate, are currently regarded as first-line agents in preventing or treating osteoporosis.[6] ■

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4. Elderly depressed patients receiving collaborative care in the IMPACT study when compared to "usual" care patients:
   a. were less likely to be satisfied with their care.
   b. were more likely to rate their quality of life as good.
   c. were less likely to respond to treatment.
   d. were more likely to be functionally impaired.
   e. were less likely to achieve remission.

5. Which one of the following statements is *false*?
   a. The frail elderly have increased blood levels of C-reactive protein.
   b. Runners developed disabilities earlier than same-age controls who were sedentary.
   c. Being fit and fat is associated with greater morbidity and mortality than being fit and non fat.
   d. Exercise lowers the concentrations of some, but not all, of the inflammatory markers in patients with congestive heart failure and type 2 diabetes.

Answers: 4. (b); 5. (b)

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By Louis Kuritzky, MD

The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-Aged Men

THE METABOLIC SYNDROME (MBS) has 2 currently popular definitions. According to the National Cholesterol Education Program, MBS exists when a patient has at least 3 of the following characteristics: fasting glucose (FPG) > 110 mg/dL, abdominal obesity, triglycerides > 150, HDL < 40 mg/dL, and elevated blood pressure (> 130/85). The World Health Organization (WHO) definition stratifies things just a bit differently, defining MBS as either hyperinsulinemia (upper quartile of the adult, nondiabetic population) or FPG, and any 2 or more of abdominal obesity, dyslipidemia (triglycerides > 150 mg/dL or HDL < 35), and BP > 140/90. Despite these modest differences, the criteria basically define the same group of individuals. Lakka and associates prospectively studied for a mean of 11.6 years a random, age-stratified sample of men in Finland (n = 2682) aged 42 and older, to examine cardiovascular and overall mortality in relation to MBS.

MBS patients had reduced (79%) Kaplan-Meier estimates of overall survival when compared with patients without MBS. Similarly, CHD mortality was 2.4-3.4 times higher in persons with MBS. The prevalence of MBS at baseline was 9-14%. The public health impact of MBS is substantial. Whether specific treatment of MBS will reduce mortality has not been determined. ■

Lakka HM, et al. JAMA. 2002;288: 2709-2716.

Effects of Amlodipine Fosinopril Combination on Microalbuminuria in Hypertensive Type 2 Diabetic Patients

NUMEROUS STUDIES HAVE CONfirmed the role of ACE inhibitors in modulation of microalbuminuria. The data on effects of calcium channel blockers (CCB) have been conflicting, especially as concerns dihydropyridine CCB (eg, amlodipine, felodipine, nifedipine). Fogari and associates addressed the effects of fosinopril (FOS) and amlodipine (AML), alone or in combination (COM), in an open-labeled, randomized, prospective, parallel group study for 4 years (n = 309).

By 3 months' time, the FOS group had demonstrated a decline in urinary albumin excretion (UAE), which decreased slightly further in the first year, and then stabilized. The AML group also demonstrated a decline in UAE, but not until 18 months into the study, after which point the UAE stabilized. COM therapy produced an impact at 3 months, which increased at 12 months and again at 36 months, and was statistically significantly greater than either monotherapy.

The mechanism by which COM therapy is superior to either monotherapy is uncertain, but the greater reduction in BP achieved (approximately 12/5 greater reduction by the former) is thought to have figured prominently. ■

Fogari R, et al. Am J Hypertens. 2002;15:1042-1049.

Relation Between Alcohol Consumption and C-Reactive Protein Levels in the Adult United States Population

EPIDEMIOLOGIC DATA CONSISTENTly indicate that moderate intake of alcohol (ETOH) is associated with reductions in cardiovascular mortality. Though the mechanism by which this effect is achieved is uncertain, increases in HDL by alcohol may explain as much as 50% of the protective effect.

C-reactive protein (CRP) is increasingly recognized as an independent risk factor for cardiovascular endpoints, suggesting an important role of inflammation in promoting atherosclerotic events. To evaluate the relationship between CRP and ETOH, Mainous and associates analyzed data from the National Health and Nutrition Evaluation Survey (NHANES III), which included complete information on 11,572 US adults.

Almost half of the NHANES population were alcohol abstainers; CRP levels in abstainers were significantly greater than in those who drink alcohol, regardless of level of alcohol ingestion. The mechanism by which ETOH might reduce CRP (or inflammation) remains unknown. A small trial of ETOH in healthy volunteers has shown a reduction in CRP and is stimulus for follow-up evaluation in larger studies. ■

Stewart SH, et al. J Am Board Fam Pract. 2002;15:437-442.

In Future Issues: The Lung Health Study Results