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INSIDE

Got Stones? Get Milk

ABSTRACT & COMMENTARY

Synopsis: *Dietary calcium, phytate, and fluid intake are associated with a decreased risk of symptomatic nephrolithiasis in younger women.*

Source: Curhan GC, et al. *Arch Intern Med*. 2004;164:885-891.

The Nurses' Health Study II enrolled 116,671 female registered nurses in 1989 and continues to follow them. After completing an initial questionnaire, each participant receives follow-up mailings every 2 years. Curhan and colleagues began asking questions about diet in 1991. This prospective, longitudinal cohort study has already yielded intriguing information about the protective effect of vitamin D on multiple sclerosis[1] and the relationship between dietary animal fat and breast cancer.[2] Using data from the original Nurses' Health Study I, this same group of investigators demonstrated that a high intake of dietary calcium in older women appeared to decrease the risk of symptomatic kidney stones. On the other hand, supplemental calcium seemed to increase the risk.[3] The current study asked the question, "Is there a relationship between diet and kidney stones in younger women?"

A semiquanitative food inventory assessed average food and beverage intake. Information was obtained about supplemental calcium intake (separately and as part of a multivitamin). After excluding women with a history of kidney stones and those in whom the date of diagnosis could not be confirmed, 96,245 women remained. At the beginning of the study these women ranged in age from 25 to 42. If a subject reported a kidney stone in any of the biennial questionnaires, a follow-up questionnaire was mailed that gathered information about the date of occurrence, symptoms, relevant medical circumstances (for example, inflammatory bowel disease, hyperparathyroidism, hyperthyroidism, or urinary tract infection), and stone composition.

During 685,973 person-years of follow up, 1223 symptomatic kidney stones were reported. Only 5.1% of women reported a chronic illness that could conceivably be related to stone creation. However, 17.5% had a UTI. A family history of kidney stones was present in 36.4%, and gout in 21.1%. Stone composition was known in 439

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cases; 87.5% contained calcium, 10.0% were urate. In 95.2%, pain was the presenting symptom.

The subjects were divided into 5 groups based on dietary calcium intake. Dietary calcium intake was directly related to intake of animal protein, sodium, potassium, magnesium, phosphorus, vitamin B_6, vitamin C, vitamin D, and fluid. It was inversely related to the intake of sucrose and alcohol. The average consumption of calcium supplements and phytate did not vary across the 5 calcium groups. The age-adjusted relative risk (RR) of kidney stones fell dramatically as dietary calcium increased. The lowest quintile was the reference (RR = 1.00). At the upper quintile the RR = 0.54 (95% confidence interval [CI], 0.45-0.63). The RR rose to 0.73 (95% CI, 0.59-0.90) after adjusting for body mass index and multiple dietary constituents (including supplemental calcium and phytate). Supplemental calcium was not associated with risk of kidney stones.

Other dietary factors were studied, again by dividing the group into quintiles and using the lowest as the reference. In multivariate analysis, 2 were associated with a reduced RR of kidney stones: phytate (RR = 0.63; CI, 0.51-0.78) and fluid (RR = 0.68; CI, 0.56-0.83). Animal protein showed a trend toward protection (RR = 0.84; CI, 0.68-1.04). Sucrose intake was associated stone formation at the highest quintile (RR = 1.31; CI, 1.07-1.60).

COMMENT BY ALLAN J. WILKE, MD

In the United States, the annual incidence of kidney stones is 7 to 21 per 10,000 population.[4] What does this study add to our understanding of this disease (remembering that cohort studies such as this cannot prove causation, only show associations)?

1. That an increased intake of fluid reduces the risk of kidney stones makes sense intuitively and forms the basis of our advice to patients who have just completed their first episode of passing a stone: "I want you to drink water until your urine looks like it came fresh out of the faucet!" (This is such a teachable moment!) A previous study showed that coffee, tea, and wine, but not grapefruit juice,[5] reduced risk.
2. Current teaching is that we should instruct our patients to limit their intake of animal protein to reduce urate excretion,[6] although a randomized controlled study showed no more benefit to a low animal protein, high fiber, high fluid volume diet than just increased fluid alone.[7] The current study showed a trend favoring animal protein as a protective factor. This did not reach statistical significance.
3. Increased dietary calcium, but not calcium supplements, is associated with protection against stone formation. This is somewhat counterintuitive, since most stones contain calcium, but consistent with a previous study in men.[8] Why dietary calcium, but not calcium supplements? Curhan et al speculate that dietary calcium binds oxalate in the gut. (Calcium oxalate comprises 70% of kidney stones.) They previously reported that most people take calcium supplements without food or only with breakfast.[3] If so, there would be fewer opportunities for calcium to bind oxalate. Another theory is that dairy products contain some other constituent that mitigates the risk.
4. Sucrose intake is associated with a higher risk of kidney stones. At first I thought that is was the result of the subjects substituting soft drinks for milk, but sucrose intake remained a risk in multivariate analysis. Curhan et al note that sucrose promotes urinary calcium excretion.

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5. Phytate intake is associated with a reduced risk of stone formation. Phytate (a.k.a. phytic acid, inositol hexaphosphate) is a source of phosphorus from plants. It forms insoluble complexes with calcium in the gut. That would reduce urinary calcium excretion and, presumably, the formation of calcium containing stones. Another theoretical mechanism relies on phytate's ability to inhibit nucleation of calcium oxalate crystals. Phytate is an antioxidant and is present in high concentration in cereal grains, nuts, legumes, and seeds.

While remembering the caveats that this study's design can only show associations and that the study population was relatively young females, this study supports dietary recommendations that promote consumption of diary products, fluid in increased volume, cereal grains, nuts, legumes, and seeds, and limits consumption of sucrose. ■

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Can We Reassure Elderly Men with Normal PSA Levels?

ABSTRACT & COMMENTARY

Synopsis: *Of 2950 men aged 62 to 91 years with consistent PSA levels of 4.0 ng/mL or less over 7 years, prostate cancer was diagnosed by biopsy in 449 (15.2%). Sixty-seven of these cancers (14.9%) were high-grade tumors (Gleason score of 7 or higher). Normal PSA levels in elderly men should not be cause for reassurance that cancer does not exist. A rise in PSA level at any range should be a cause for concern about cancer.*

Source: Thompson IM, et al. *N Engl J Med*. 2004;350:2239-2246.

Over the past 2 decades, the serum PSA level has been increasingly used to screen for prostate cancer, considered an accompaniment to digital rectal exam. Despite the lack of solid evidence that PSA screening saves lives, its use has become widespread.[1] Once PSA screening became widespread in the United States, the rate of death from prostate cancer declined (50-70 percent decline between 1986 and 1999 among men 50 years and older).[2] Even though improvements in treatment may partially explain the decline, there is widespread acceptance of the test among primary care physicians and patients.

PSA levels rise with prostate disease, both benign and malignant. The cutoff for normal has been established at 4.0 ng/mL to detect the majority of cancers while avoiding the high cost of false-positive tests. Even levels above 4.0 ng/mL turn out to be benign disease (prostatic hypertrophy or chronic prostatitis) more often than cancer. Ninety percent of men aged 50 to 92 years have PSA levels of 4.0 ng/mL or less, so consideration for prostate biopsies would only come up in 10% of screened men.[3] Following a mildly elevated PSA level is done commonly to avoid the use of an invasive and uncomfortable biopsy.

How much can we reassure men with normal PSA levels (4.0 ng/mL or less)? The data from this large study show that such reassurance must be done with caution. The multicenter Prostate Cancer Prevention Trial gave Thompson and colleagues 2950 men with consistently normal PSA levels over seven years to undergo a prostate biopsy. This remarkable data set may never be repeated. Overall, in these men aged 62 to 91 years, 15.2% had prostate cancer on biopsy. There was no stratification with age, but there was by PSA level. When the PSA level was 0.5 ng/mL or less, the prevalence of prostate cancer was 6.6%. When the level was 0.6 to 1.0 ng/mL, the prevalence of cancer was 10.1%. When the level was 1.1-2.0 ng/mL, the prevalence of cancer was 17.0%. When the level was 2.1- 3.0 ng/mL, the prevalence was 23.9%. When the level was 3.1-4.0 ng/mL, the prevalence was 26.9%. The prevalence of high-grade tumors increased with PSA level, being 12.5% of the cancers with a PSA level of 0.5 ng/mL or less, and 25.0% of cancers with a PSA level of 3.1-4.0 ng/mL.

■ COMMENT BY JOSEPH E. SCHERGER, MD, MPH

This study caused me much alarm. I recall the reassurance that I have given hundreds of men with normal PSA levels. My words will now be one of reassurance mixed with caution. A look at this data made me think the normal cutoff for PSA should be lowered, at least to 3.0 ng/mL. The editorial in the same issue by Carter reversed my thinking, and I highly recommend reading it.[3] Carter was able to use previous data to show that

these results would be expected in a population of 90% of men in this age range. He argues effectively that the cutoff range for PSA should not be changed from the current level of 4.0 ng/mL. The new information for me to use in clinical practice is the tracking of "PSA velocity" in the normal age range. PSA velocity refers to the rate of rise of PSA levels, which has been shown to correlate directly with the risk of cancer.[4] Carter's work suggests that a rise of 0.75 ng/mL or more in a year would indicate a significant risk for cancer. This study was based on small number men (38).

So, what do we tell men about their PSA levels and when should screening be done? The answers to these questions are not definitive and may never be. Hopefully soon we will have better biomarkers for prostate cancer than the current PSA test. Meanwhile, I will provide cautious reassurance to men with normal levels, and will repeat them yearly to look for a significant change. ■

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A Little Tippling May Be Good for What Ales You

ABSTRACT & COMMENTARY

Synopsis: *Moderate alcohol consumption is associated with a decreased incidence of diabetes mellitus and a decrease in heart disease in persons with diabetes.*

Source: Howard AA, et al. *Ann Intern Med*. 2004;140: 211-219.

Alcohol consumption is prevalent in the United States: An estimated 109 million Americans 12 years of age or older drink alcohol.[1] Diabetes mellitus affects a large portion of the patients physicians care for. Howard and associates note that physicians are not well informed about how alcohol use affects the risk for or management of their patients with diabetes.

Howard et al conducted a systematic review assessing the effect of alcohol use on the incidence, management, and complications of diabetes mellitus in adults. They reviewed English-language studies in persons 19 years or older and that were identified by searching the MEDLINE database from 1966 to the third week in August 2003.

Two independent assessors reviewed 974 citations to identify all experimental, cohort, or case-controlled studies that assessed the effect of alcohol use on the risk, control, self-management, adverse drug effects or complications. The studies were evaluated on the basis of established criteria.

Thirty-two studies that met the inclusion criteria were reviewed. Compared with no alcohol use, moderate consumption (1-3 drinks/d) is associated with a 33% to 55% lower incidence of diabetes related coronary artery disease. Compared with moderate consumption, heavy consumption (> 3 drinks/d) may be associated with up to a 43% increased incidence of diabetes mellitus. Moderate consumption did not impair glycemic control in persons with diabetes.

Howard et al concluded that moderate alcohol consumption is associated with a decreased incidence of diabetes and heart disease in persons with diabetes.

■ COMMENT BY RALPH R. HALL, MD, FACP

It is noteworthy that the study used the criteria of the US Preventive Services Task Force for determining internal validity of the studies evaluated.[2]

Of the 32 included studies 27 were of type 2 diabetes only, 2 were of types 1 & 2. No study assessed the effects of alcohol consumption on self-care, or complications other than coronary heart disease and retinopathy.

Only 6 studies assessed the effect of alcohol on glycemic control. All of these studies were small and had only fair ratings on the evaluation scale. (I was unable to obtain these publications for review.) It would be helpful to know the number and age of patients in the study.

Two of the studies assessed the effect of alcohol consumption on medication-related complications. One rated "good" assessed troglitazone related complications and one rated "fair" studied sulfonylurea complications. There were no studies in patients taking other agents used in the treatment of diabetes.

Recently, Avgaro and colleagues studied subjects with intravenous glucose tests with and without administration of 40 g vodka given in sips over a one-hour period of time.[3] They measured insulin sensitivity and beta cell production of insulin. The study demonstrated a 17% and 55% improvement in insulin sensitivity in eight persons with and without type 2 diabetes. Circulating free fatty acids decreased in both sets of subjects but was statistically significant in only the diabetics. There was no measurable increase in beta cell production of insulin. This suggests that alcohol may mediate the improvement in insulin sensitivity and thus be relevant

to its cardio-protective effects. These are acute effects, however, and there are no long term studies to indicate what moderate alcohol consumption does to blood pressure or renal function.

There are other studies, recently reported, indicating the potential for prolonged benefit of moderate alcohol consumption. Thamer and associates reported that adiponectin levels, which increase insulin sensitivity, were significantly increased in those who consumed moderate amounts of alcohol.[4]

Since c-peptide has many favorable effects when administered to type 1 diabetics, the effects of alcohol on type 1 patients, who do not have adequate c-peptide levels may be quite different than in type 2 diabetics who do have c-peptide present.[5]

The Howard et al review is valuable in that it addresses moderate alcohol intake. Most textbook citations refer primarily to excessive alcohol intake and to hypoglycemia. As Howard et al indicate, there needs to be better studies regarding alcohol and compliance and self management. It seems obvious, however, that diabetics who can't control their alcohol intake are not likely to control other aspects of their lives. ■

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More Food for Thought?

ABSTRACTS & COMMENTARY

Synopsis: *The present results on the Cache County study provide some of the strongest evidence to date that intake of antioxidant vitamin supplements may be beneficial.*

Sources: Zandi PP, et al. *Arch Neurol*. 2004;61:82-88; Kalmijn S, et al. *Neurology*. 2004;62:275-280; Longstreth WT, et al. *Arch Neurol*. 2004;61:67-72.

There is increasing evidence that a number of dietary manipulations may significantly affect the risk of dementia and Alzheimer's disease (AD). Three studies in 2002 indicated that dietary intake of vitamins E and C lowered the risk of getting AD. However, there appeared to be no association with intake from dietary supplements. This is an important point since it is much easier to take dietary supplements than to increase one's dietary intake of antioxidant vitamins. The previous prospective study in the Chicago Health and Aging Project suggested that patients in the highest quintile of vitamin E intake from food were 70% less likely to develop AD. The present study, which is known as the Cache County Study, has further examined the risk of AD prospectively and in a cross-sectional study of dementia. Zandi and associates examined patients 65 or older who were initially assessed from 1995 to 1997 for prevalent dementia in AD and again in 1998 to 2000 for incident illness. Supplement use was ascertained on the first contact. In the initial cross-sectional analysis, 4740 respondents were assessed, and there were 200 prevalent cases of AD. In the patients studied prospectively, there were 3227 survivors at risk, and 104 instant AD cases were identified at follow-up. A diagnosis of AD was established by an examination including a medical history, a chronologic history of cognitive symptoms, and a structured neurologic examination. There was also a battery of neuropsychological tests administered by psychometric technicians. The diagnosis of AD was established using standard criteria. The findings were that the analyses of prevalent and incident AD yielded similar results. Use of vitamin E and C supplements in combination was associated with a reduced AD prevalence, with an adjusted odds ratio of 0.22. The incidence-adjusted hazard ratio was 0.36. A trend toward lowered AD risk was also evident in users of vitamin E and multivitamins containing vitamin C, but there was no protective effect for the use of vitamin E or C supplements alone or with multivitamins alone.

It has also been recently suggested that higher intake of fish and omega-3 fatty acids lowers the incidence of AD and dementia. Kalmijn and associates carried out a cross-sectional study on a population of 1613, ranging from 45 to 70 years old. The patients were administered an extensive cognitive battery, and compound scores were constructed for memory, psychomotor speed, cognitive flexibility, and overall cognition. Kalmijn et al administered a food-frequency questionnaire. Kalmijn et al found that the intake of marine omega-3 polyunsaturated fatty acids was inversely correlated to the risk of impaired overall cognitive function and speed. Results for fatty fish consumption were similarly inverse, while higher dietary intake of cholesterol was associated with an increased risk of impaired memory and flexibility.

Lastly, another study has examined the role of homocysteine levels using cranial magnetic resonance imaging in elderly persons. Longstreth and colleagues stud-

ied 622 elderly patients without a history of strokes or transient ischemic attacks. They had total homocysteine levels performed, as well as cranial MRIs. A number of other factors were controlled for. They examined white matter grade and infarcts, as well as ventricular grade and sulcal grade. In this study, there was no association of total homocysteine levels with individual MRI findings. There was a finding of a linear trend across quintiles of total homocysteine levels and a pattern of MRI findings combining infarcts and high white matter grade. This trend was significant.

COMMENT BY M. FLINT BEAL, MD

The present results on the Cache County study provide some of the strongest evidence to date that intake of antioxidant vitamin supplements may be beneficial. It is of interest that only a combination of vitamin E with C was effective. This is because the 2 vitamins may interact in their antioxidant functions. Vitamin C is typically active in the aqueous phase and in the cytoplasm, whereas vitamin E tends to have its antioxidant effects in lipid bilayer membranes. Vitamin C may therefore be able to reduce the oxidized alpha-tocopherol quinone radical. These studies are supportive of 3 other previous studies. The present study has the strength of being population-based, with a large sample and prospective design. The prevalence data, however, were cross sectional. The period of follow-up was also relatively short—an average of 3 years. The results may be confounded by a tendency toward a healthy lifestyle among supplement users. There, however, appear to be little evidence of such confounding when other nutritional supplements, such as multivitamins, calcium supplements, and B vitamin formulations, were considered.

The study on the intake of fish and omega-3 fatty acids also confirms other recent observations. This study was again cross sectional. It nevertheless provides further evidence that intake of fish, as well as omega-3 fatty acids, has protective effects against both vascular disease and impaired cognitive performance.

Lastly, the study of total homocysteine levels did show a linear trend toward an increased risk of stroke and white-matter damage. This also is consistent with some other recent findings suggesting that MRI imaging identifies more damage in patients with high homocysteine levels. The study, however, did not confirm the results of 2 other studies in which there was a much stronger association between total homocysteine levels and the degree of white matter damage assessed by MRI imaging. In addition, one of the previous studies had shown that there was a linear relationship between higher total plasma homocysteine levels and cortical atrophy, as well as hippocampal atrophy, which was not identified in the above-mentioned study.

Where does this leave us in the year 2004? I believe the evidence that dietary supplements of vitamin E and C may prevent dementia and AD is becoming increasingly strong. The data suggesting that intake of omega-3 fatty acids as well as fish are also quite strong. These findings, however, need to be confirmed in a prospective, primary prevention trial to determine whether intake of either antioxidant vitamins or omega-3 fatty acids will indeed prevent AD. Due to the increasing prevalence of AD in the population, this would be a valuable study to carry out.

Dr. Beal is Professor and Chairman, Department of Neurology, Cornell University Medical College, New York, NY.

Pharmacology Update

Apomorphine Injection (Apokyn™)

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

THE FDA HAS APPROVED AN INJECTABLE DRUG FOR treating Parkinson's patients during hypomobility periods known as off periods. In this state, patients become immobile or unable to perform normal daily activities. Apomorphine is the first drug to be approved for this use and is marketed by Mylan Bertek Pharmaceuticals as Apokyn. It has been used in Europe for more than a decade for intractable off periods in Parkinson's patients.[1]

Indications

Apomorphine is indicated for the acute, intermittent treatment of hypomotility, 'off' episodes (end-of-dose wearing off and unpredictable on/off episodes) associated with advanced Parkinson's disease.[2]

Dosage

The dose of apomorphine must be titrated on the basis of effectiveness and tolerance. The starting dose is 0.2 mL (2 mg) given subcutaneously and up to a maximum of 0.6 mL (6 mg). After the first (test) dose, both supine and standing blood pressure should be checked at 20, 40, and 60 minutes postdose. Patients with mild and moderate hepatic impairment should use a test dose of 0.1 mL (1 mg). If there is no clinically

significant orthostatic hypotension and the patient responds, this will be the starting dose. If needed, an increase of 0.1 mL every few days is reasonable. Patients with significant orthostatic hypotension are not candidates for apomorphine.[2]

Apomorphine is supplied as 2 mL glass ampule and 3 mL cartridge. The cartridge is intended for multiple uses with an injector pen. The concentration is 10 mg/mL.

Potential Advantages

Apomorphine has been shown to be effective in reversing off-state in patients with off-time despite aggressive oral therapy.[2,3] Effectiveness was assessed by change from baseline for Unified Parkinson Disease Rating Scale motor score (Part III).

Potential Disadvantages

Apomorphine causes severe nausea and vomiting and must be taken with an antiemetic such as trimethobenzamide. The use of 5HT3 antagonists is contraindicated due to reports of severe hypotension and loss of consciousness.[2] Common side effects associated with apomorphine include yawning (40%), dyskinesias (35%), drowsiness, or somnolence (35%), nausea and/or vomiting (30%), injection site reactions (26%), dizziness or postural hypotension (20%), rhinorrhea (20%), chest pain/pressure or angina (15%), hallucinations or confusion (10%), and edema (10%).[2] Caution should be exercise in patients at risk for QT prolongation as apomorphine may prolong QT interval. Other drugs that lower blood pressure may enhance the hypotensive effect of apomorphine.

Comments

Apomorphine is a dopamine receptor agonist. Due to significant first-pass metabolism, the drug the drug cannot be given orally. Given subcutaneously it has a rapid onset of action—generally within 10 minutes with benefit lasting up to 2 hours (usually 60-90 minutes).[1,4] While the drug has been used in Europe for decades, approval in the United States was based on 3 randomized, controlled trials involving 108 patients.[2] In one trial, patients were naïve to apomorphine while in the other two, patients used the drug for at least 3 months. Significant improvements were observed with apomorphine compared to placebo and the magnitude of effect appeared to be comparable to that of a usual dose of levodopa.[1,2,4] The persistence of benefit has been reported in other studies to be as long as 5 years although the frequency of injection increased.[1,5] Co-administration of apomorphine and levodopa results in increase duration of effect but not in the maximal response to levodopa.[2] The need for concomitant antiemetic prophylaxis may decrease over time.[1] Apomorphine is associated with a variety of side effects, potential drug interactions, and generally must be taken with an antiemetic.

The cost of apomorphine was not available at the time of this review. Apomorphine is expected to be available through a few selected specialty pharmacies to ensure proper patient/caregiver education and training.

Clinical Implications

Apomorphine offers an effective treatment in advanced Parkinson patients with recurring off periods. It is estimated that this affects about 10% of Parkinson patients who are unresponsive to standard therapy. ■

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CME Questions

30. What is the best message to a 65 year old man with a screening PSA level of 3.5 ng/mL and a normal digital rectal exam? His PSA level one year ago was 3.3 ng/mL.

a. His level is normal and he has virtually no risk of having prostate cancer today. Repeat the test in one year.
b. His level, while in the normal range, has jumped over the past year and a prostate biopsy should be done.
c. His level is in the normal range which makes his risk of having prostate cancer low. While the level has increased over last year, the increase is not significant. It is very important that he return annually for PSA testing since his risk of cancer is about 25 %.
d. He should have prostate biopsy new since his risk of having cancer is about 25% and his level has increased since last year.

31. In a study of nurses, consumption all of the following were associated with a decreased risk of kidney stones, except one. Choose the incorrect item.

a. dietary calcium
b. increased fluids
c. sucrose
d. dietary phytate

Answers: 30 (c); 31 (c)

By Louis Kuritzky, MD

Glucose Metabolism and Coronary Heart Disease in Patients with Normal Glucose Tolerance

THERE IS A CLEARLY ESTABLISHED relationship between frank diabetes (DM) and increased vascular risk, especially coronary heart disease. Whether more modest perturbations in glucose regulation might be reflected in coronary vascular pathology has not been satisfactorily elucidated. Results studying the association between cardiovascular risk and markers such as subsyndromal levels of hemoglobin A1c, fasting glucose, or postload glucose have not provided consistent results. The relationship between glucose metabolism amongst persons with coronary heart disease (CHD) but *without* frank evidence of glucose derangement (ie, diabetes, impaired fasting glucose, or postload glycemia) is unstudied.

Glucose metabolism was examined in patients admitted and underwent coronary angiography for suspected CHD (n = 234). Patients who met criteria for diabetes, impaired fasting glucose, or postload glycemia were excluded from evaluation.

The level of fasting glucose was similar amongst all subjects. The number of stenosed coronary vessels was associated in a linear fashion with the levels of post load glucose and hemoglobin A1c. Even amongst persons without demonstrable stigmata of deranged glucose metabolism, risk for CHD is associated with increasing A1c and postload glucose levels. These data suggest that the relationship between some markers of glucose metabolism and CHD may be linear and continuous, even below the currently recognized thresholds for intervention. ■

Sasso FC, et al. JAMA. 2004;291: 1857-1863.

Evidence of Airborne Transmission of the Severe Acute Respiratory Syndrome Virus

FOR THE MOMENT, THE IMMEDIATE threat of Severe Acute Respiratory Syndrome virus (SARS) appears to have passed in the United States. The serious morbidity and mortality of the virus mandate clarification of just how disease may be transmitted, which has been as yet incompletely understood.

A large outbreak of SARS cases (n = 187) in a single housing complex provided sufficient information to model potential transmission channels.

The place of residence of the SARS cases (Anoy Gardens, Honk Kong), was able to be stratified into distance between buildings in the complex, direction of prevailing winds, height of units from the ground (buildings were categorized into low, middle, and high distance off the ground), and presence or absence of a window admitting the prevailing wind. Computational fluid dynamics was utilized to model the airflow pattern in and around buildings in the complex.

Data analysis supports the hypothesis that there was a common source outbreak at this site, spread by virus-laden aerosol. Were SARS to recur, such knowledge may assist future disease prevention and containment. ■

Yu ITS, et al. N Engl J Med. 2004; 350:1731-1739.

Alcohol Intake and Risk of Incident Gout in Men: A Prospective Study

THE ASSOCIATION BETWEEN GOUT and alcohol consumption has been oft quoted, though never previously established by a prospective trial. It has been confirmed that alcohol loading acutely induces elevations in blood uric acid; case-control studies and cohort studies have found an association between gout and alcohol, but suffer from retrospectively reported alcohol consumption.

Subjects from the Health Professionals Follow-up Study (n = 51,529) comprise an all-male, predominantly white cross-section of clinicians including dentists, optometrists, physicians, and veterinarians. At enrollment, 5.6% of these men reported gout, and were excluded from this analysis. Subjects were periodically monitored for nutrient and alcohol intake from 1986-1998.

Alcohol intake and gout were found to be related in a linear fashion. Men consuming more than 50g/d alcohol (1 beer was designated as containing 12.8 g alcohol in this study) demonstrated a 3-fold increased likelihood of developing gout than non-drinkers. The strongest relationship between alcohol and gout was found for beer; a lesser relationship was seen with spirits. Wine intake was not associated with subsequent gout, regardless of type (white vs red) or level of intake. This prospective study is the first to confirm an association between alcohol intake and gout. ■

Choi HK, et al. Lancet. 2004;363: 1277-1281.

In Future Issues:

Human Bites: Fact and Fiction