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Antibiotic Resistance in Uncomplicated UTIs

ABSTRACT & COMMENTARY

Synopsis: *The days may be numbered when trimethoprim/sulfamethoxazole should be used for empiric therapy for uncomplicated UTI.*

Source: Gupta K, et al. *JAMA* 1999;281:736-738.

Prevalence and trends in antimicrobial resistance among the narrow spectrum of organisms responsible for acute uncomplicated cystitis were examined in this study from Washington state. Included were those patients with a positive urine culture (≥ 103 CFUs/mL) from a population of women, ages 18-50, in a health maintenance organization, who sought treatment at an outpatient clinic or ED. The study spanned five years, controlled for seasonal variation, and included 4342 urine isolates. Selected chart review confirmed that more than 95% of the study population included visits for uncomplicated cystitis.

The distribution of causative uropathogens was not surprising: *Escherichia coli*, 86%; *Staphylococcus saprophyticus*, 4%; Proteus species, 3%; Klebsiella species, 3%; Enterobacter species, 1.4%; Citrobacter species, 0.8%; Enterococcus species, 0.5%; and others, 1.3%. More than 20% of *E. coli* isolates were resistant to ampicillin, cephalothin, and sulfamethoxazole.

Alarmingly, resistance among *E. coli* to trimethoprim/sulfamethoxazole doubled over the course of the study, rising from 9% to 18%. A significant increasing linear trend in resistance was found for all isolates to ampicillin, cephalothin, trimethoprim, and trimethoprim/sulfamethoxazole. Ciprofloxacin, nitrofurantoin, and gentamicin fared the best with regard to limited resistance.

Recognizing that in vitro resistance may not directly translate to altered patient outcome, Gupta and colleagues conclude that the days may be numbered when trimethoprim/sulfamethoxazole should be used for empiric therapy for uncomplicated UTI.

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INSIDE

COMMENT BY RICHARD A. HARRIGAN, MD

And so, more evidence of emerging antimicrobial resistance is published; important news, but is it time to stop using trimethoprim/sulfamethoxazole as the first-line antibiotic for uncomplicated UTI? Not yet. As Gupta et al caution, this is not a clinical outcomes study, but rather a report of a microbiological trend. Moreover, trimethoprim/sulfamethoxazole is concentrated in the urine, achieving higher concentrations than in the blood;[1] thus, the pathogen might still be eradicated. Finally, a treatment failure in cases of uncomplicated UTI generally does not result in life-threatening illness, but, rather, persistence of symptoms. Thus, treatment failures should make us think not only of an alternative diagnosis, but also of the antimicrobial resistance issue. (*Dr. Harrigan is Associate Professor of Medicine, Temple University School of Medicine, Associate Research Director, Division of Emergency Medicine, Temple University Hospital, Philadelphia, Pa.*) ❖

Reference

1. *Physicians' Desk Reference*, 53rd ed. Montvale NJ: Medical Economics Company; 1999:2655.

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Isoflavones from Red Clover Improve Systemic Arterial Compliance but not Plasma Lipids in Menopausal Women

ABSTRACT & COMMENTARY

Synopsis: *Arterial compliance was improved in menopausal women who ingested isoflavones derived from red clover. The effect size was comparable to that seen in hormone replacement therapy.*

Source: Nestel PJ, et al. *J Clin Endocrinol Metab* 1999; 84:895-898.

Isoflavones (phytoestrogens) are found in many legumes, including soy. They have been credited with conferring cardioprotection. For example, epidemiological studies suggested the reason Japanese women living in Japan had less cardiovascular disease than Japanese women living in the United States was due to consumption of a diet high in legumes and, therefore, isoflavones. Nestel and associates have performed several studies looking at modification of arterial compliance in postmenopausal women by weight loss, diet, hormone replacement therapy, and soy-derived isoflavones. The present study extended their previous work by examining isoflavones derived from red clover. Specifically, red clover contains genistein, diadzein, and their methylated precursors biochanin A and formononetin. (Soy contains genistein and diadzein.) Twenty-six women began the trial and 13 completed all aspects of the active intervention. Most of the drop-outs were menopausal women who quit their hormone replacement regimen to enroll and then could not tolerate the ensuing hot flashes. Subjects were postmenopausal women younger than 70 years of age who were not currently taking hormones or who had discontinued hormones at least four weeks before the study began. The study involved a three-week observation and dietary training interval followed serially by five weeks of placebo, five weeks of 80 mg of red clover-derived isoflavones, and five weeks of a 160 mg daily dose of isoflavones. Arterial compliance was measured by ultrasound at the end of each treatment window. Decreased arterial compliance is an important risk factor for cardiovascular disease because it leads to systolic hypertension and increased left ventricular work. Compliance was unchanged after placebo and increased after

five weeks of either dose of isoflavones. Blood pressure and lipids did not change throughout the study.

COMMENT BY SARAH L. BERGA, MD

This study is a good example of what needs to be done to determine the effects of various food supplements now being "hawked" to the American public. In this study, isoflavones derived from red clover had a similar effect upon arterial compliance as did isoflavones derived from soy or flax. Notably, estrogen replacement therapy also had a similar effect upon arterial compliance as did isoflavones. Nestel et al interpret the relatively short response time as evidence for endothelial-related arterial relaxation.

A logical question that one might ask after reading this report is whether isoflavones might be recommended as a substitute for hormone replacement therapy. One needs to keep in mind that the present study only looked at a few cardiovascular end points, so it would not allow one to adequately determine if isoflavones were a substitute for hormones for cardioprotection. Further, based on this report, nothing can be said about the effects of isoflavones upon other tissues and age-related disorders. Thus, it is premature to recommend isoflavones as substitutes for hormones.

This brings me to the next point. Nestel et al should study the effects of isoflavones and estrogens together to see if there is synergism. The rationale for such a study includes the observation that many women were unable to complete the study because of vasomotor symptoms. Clearly, isoflavones will not be a panacea for the spectrum of symptoms linked temporally to menopause. Although isoflavones are referred to as phytoestrogens, they are primarily antioxidants and they do not have the same range of effects upon the brain as do estrogens, which are also antioxidants. The two together might be far better than either one alone. Synergism of this type is the rule rather than the exception. I raise this point because the choice facing patients regarding the use of dietary supplements is often framed as an either/or scenario. The either/or approach is likely to be short-sighted and I recommend abandoning such a simplistic line of reasoning. It reminds me of the old question about whether calcium and exercise could substitute for estrogen use for protection against osteoporosis. We now know that there is synergism between exercise, calcium and vitamin D intake, and estrogen use in bone maintenance. Performing all of these interventions is far better than any one of them alone. I predict we will find similar synergism between estrogens and isoflavones in cardiovascular protection and possibly in protection from dementia. (*Dr. Berga is Associate Professor, Departments of Obstetrics, Gynecology, Reproductive Sciences, and Psychiatry, University of Pittsburgh, Pa.*) ❖

More on ECG Diagnosis of Acute MI with Concurrent LBBB

ABSTRACT & COMMENTARY

Synopsis: *Electrocardiographic criteria are poor indicators of AMI in LBBB situations; they further suggested that all patients suspected of AMI with LBBB should be considered for thrombolysis.*

Source: Shlipak MG, et al. *JAMA* 1999;281:714-719.

Shlipak and colleagues performed a retrospective, cohort study to investigate the impact of the ECG on diagnosis and treatment of patients with LBBB pattern and suspected acute myocardial infarction (AMI). The study population was composed of patients with LBBB and possible AMI on ED presentation; 30% of the study group was ultimately found to have AMI by CPK-MB elevations. In the first portion of this study, a single physician who was blinded to the clinical information interpreted the ECGs in retrospective fashion, using pre-existing criteria for AMI diagnosis developed by previous investigators. The ECGs were interpreted as either diagnostic or not diagnostic for AMI; the electrocardiographic diagnosis was then compared to the clinical diagnosis.

In the second phase of the study, Shlipak et al investigated the impact of the ECG on specific management—the administration of a thrombolytic agent. This question was explored by means of a decision tree that compared three treatment pathways: thrombolysis for all patients, thrombolysis for only those patients with an ECG diagnostic for AMI, or no thrombolysis regardless of the ECG interpretation; the treatment algorithm was also evaluated from the perspective of stroke occurrence. Outcomes were then assessed and compared among the three management strategies.

One hundred three patient encounters made up the study population. Of the electrocardiographic features assessed, none effectively distinguished the patients who had AMI from those patients with noncoronary diagnoses. The various electrocardiographic criteria indicated AMI in only 3% of cases, with a sensitivity for the diagnosis of only 10% (95% confidence intervals, 2-26%). Using the management strategy of thrombolysis for all patients with suspected AMI and LBBB, out of 1000 patient presentations, 929 patients would survive

without stroke if all patients were treated, compared to 918 patients if the electrocardiographic criteria were used as the only indication for thrombolysis.

Shlipak et al concluded that electrocardiographic criteria are poor indicators of AMI in LBBB situations; they further suggested that all patients suspected of AMI with LBBB should be considered for thrombolysis.

COMMENT BY WILLIAM J. BRADY, MD

Common medical opinion holds that the electrocardiographic diagnosis of AMI is impossible in the presence of LBBB. Such a statement, however, is too encompassing; alternatively, the electrocardiographic diagnosis of ischemic heart disease—both its acute and chronic manifestations—is made more difficult in the setting of LBBB. Shlipack et al provide support for this statement; further, they have begun to explore the manifestations of this thought process on management and outcome issues.

Previously, authors developed criteria that assist the physician in a complicated scenario—the electrocardiographic diagnosis of AMI in the setting of LBBB.[1] More recent work has tested these criteria in ED patients, suggesting that the recommendations of the original investigation are much less helpful than was previously thought.[2] This study by Shlipak et al reinforces the opinion that the Sgarbossa criteria must be used with caution. AMI is still a possibility, given the appropriate clinical scenario, even if an ECG with LBBB is not diagnostic of AMI using the Sgarbossa criteria. (*Dr. Brady is Assistant Professor of Emergency Medicine and Internal Medicine, Medical Director, Chest Pain Center, University of Virginia, Charlottesville.*) ❖

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Spinal Surgical Alternative: Exercise?

ABSTRACT & COMMENTARY

Synopsis: *Provided there is no physical deterioration, emphasizing activity tolerance as a means to symptom relief is sensible, empowering, and precise.*

Source: Nelson BW, et al. *Arch Phys Med Rehabil* 1999;80:20-25.

To determine if patients recommended for spinal surgery can avoid it through an aggressive strengthening program, a privately owned medical clinic treated consecutive referred patients. Study entry criteria included a physician's recommendation for lumbar or cervical surgery, no medical condition preventing exercise, and willingness to participate in an outpatient 10-week program.

Intensive, progressive resistance exercise of the isolated lumbar or cervical spine was practiced and continued to failure, and patients were encouraged to work through their pain. Forty-six of 60 participants completed the program; 38 were available for follow-up (average 16 months, range 12-30 months after discharge); three required surgery after completing the program.

COMMENT BY JOHN La PUMA, MD, FACP

Back pain hurts. It is the leading cause of disability in the United States, and a pile of frustration among practitioners and patients alike. It is also expensive—early 1990s data from the Worker's Compensation Back Pain Claim Study show that "the average cost per industrial back injury in the U.S. is now more than $24,000." Here, Nelson and colleagues present surgical cost data of $60,000 for a cervical laminectomy and more than $168,000 for a lumbar fusion.

Of 651 patients referred for rehab, 62 with chronic pain (mean 28 months) met the inclusion criteria. Sixty began the outpatient program; 14 dropped out. Twenty-eight men and 18 women, mean age 42, completed the 10 weeks in an average of 21 visits, most to physical therapists. Nearly all patients—90%—had already tried and failed some type of exercise program.

The program emphasized progressive resistance, and used lumbar and cervical extension devices to isolate and strengthen lumbar extensors, cervical extensors and rotators, and thoracic rotators. A self-monitored maintenance program was also taught to maintain strength, vigor, self-care, and newly improved body mechanics.

Statistically significant gains in strength for lumbar and cervical extensor and rotator muscles in men and women were reported, and only three patients underwent surgery.

Nelson et al acknowledge their methodologic limitations—unblinded, no control group, no randomization, selection bias, variable follow-up, only regrets offered for the nearly one-quarter drop-out. Yet they observe that even patients recommended for spinal surgery can tolerate intensive, specific exercise. By specific they mean isolated musculature; by intensive they mean muscular exercise against dynamic resistance to volitional failure, through a full range of motion.

These bold investigators take a hands-on approach to patients famed for fragility, who "develop a keen sense of fear when it comes to spinal motion ... few under-

stood that literally millions of people develop the same radiologic diagnoses with few or no symptoms." Provided there is no physical deterioration, emphasizing activity tolerance as a means to symptom relief is sensible, empowering, and precise.

Committed, motivated patients who wish to avoid back or neck surgery may be able to do just that. This innovative program deserves better evaluation. (*Dr. La Puma is Adjunct Professor of Nutrition, Kendall College, Director, C.H.E.F. Clinic, C.H.E.F. Skills Research, Alexian Brothers Medical Center, Elk Grove Village, Ill.*) ❖

Encouraging Needlestick Reporting

ABSTRACT & COMMENTARY

Editor's Note: *Please see the Rapid Reference Card, "Determining the Need for HIV Postexposure Prophylaxis (PEP) After an Occupational Exposure," enclosed with this issue of Internal Medicine Alert.*

Synopsis: *While educational interventions regarding actual risk may enhance reporting behaviors, establishing user-friendly mechanisms by which needlestick injuries can be dealt with quickly and appropriately, as well as adequate follow-up, is essential.*

Source: Haiduven DJ, et al. *Hosp Infect* 1999;41:151-154.

Failure to report needlestick injuries is remarkably common, especially among physicians and medical students (Osborn EH, et al. *Ann Intern Med* 1999;130:45-51). Haiduven and colleagues distributed confidential surveys to healthcare personnel at a public teaching hospital in San Jose between 1992 and 1995. A total of 549 individuals responded to the survey, 83% of whom were nurses and 7% of whom were physicians. The remaining subjects included operating room technicians, dentists, and other hospital personnel.

COMMENT BY CAROL A. KEMPER, MD

About one-half of the nurses and physicians and 84% of the remaining personnel reported at least one percutaneous needlestick injury within the previous five years. However, 46% failed to report all of their injuries, including 80% of the physicians and 45% of registered nurses. Reasons for nonreporting included the perception that the stick was sterile or clean (39%), or represented no risk (26%), too busy (9%), and dissatisfaction with follow-up (8%).

While educational interventions regarding actual risk may enhance reporting behaviors, establishing user-friendly mechanisms by which needlestick injuries can be dealt with quickly and appropriately, as well as adequate follow-up, are essential. The use of the ER for after-hours injuries is, in my experience, inadequate in that patients are often required to wait longer than that recommended for the administration of post-exposure prophylaxis (< 1 hour), and the management is often inconsistent and occasionally incorrect. This is despite the availability of approved hospital protocols. A designated 24-hour hotline, such as the one established at the San Francisco General Hospital (which, after-hours, usually rings a knowledgeable fellow or faculty member), appears to more consistently meet the needs of hospital personnel. The hotline number is prominently posted in blazing colors throughout the hospital to encourage reporting. (*Dr. Kemper is Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases; Santa Clara Valley Medical Center.*) ❖

Sleep Disorders and Anxiolytics Increase the Risk of Traffic Accidents

ABSTRACT & COMMENTARY

Synopsis: *Physicians who participate in providing polysomnographic sleep studies or even hear complaints of hypersomnia must warn their patients against driving when feeling drowsy. The dangers of alcohol and anxiolytics must be emphasized.*

Source: Teran-Santos J, et al. *N Engl J Med* 1999;340: 847-851.

Based on simulated driving tests, obstructive sleep apnea has been thought to increase automobile accidents by as much as two- to three-fold when compared with healthy persons.[1] Teran-Santos and colleagues approach the problem directly, selecting all interurban highway drivers involved in traffic accidents and brought to a regional Spanish hospital for immediate treatment. Patients without known chronic illnesses or traffic accidents during the past two months were selected as controls for each above patient involved in a traffic accident. Subjects were questioned for personal habits, diseases, medication, past accidents, and possible causes of drowsiness. Histories of sleep apnea were scaled and tested technically

and by low-level nocturnal polygraph. More detailed maneuvers were applied when considered desirable.

Outcomes of 102 case patients and 152 matched controls were compared. Persons who had a clinically abnormal apnea-hypopnea ratio more than 10 had a traffic accident odds rate 4.1 greater than normals. Those who additionally had consumed alcohol on the accident day increased the rate to 11.2.

Psychoactive drugs have often been blamed as contributing to at least 10% of all fatalities in road traffic accidents.[2] Alcohol carries the greatest dangers, but other psychoactive drugs also may contribute. Barbone and colleagues report from an area in Scotland that 1731 out of 19,386 drivers involved in accidents between August 1, 1992, and June 30, 1995, at least sometimes used a psychoactive drug.[3]

To be specific: on any given accident day, an average of 189 of the users were taking tricyclic antidepressants, 84 serotonin-reuptake inhibitors, 235 benzodiazepines, and 47 other psychoactive drugs. Only benzodiazepines increased the risk ratio compared to nondrugged drivers' rate. Overall, odds ratio was 1.62, but the rate was measurably higher in persons younger than 40 years (3.42). Add a positive alcohol test and the odds ratios climbed to 9.55 (n = 4). Barbone et al refer to two reports providing similar results.[4,5]

COMMENT BY FRED PLUM, MD

Most studies that identify a relationship between sleep apnea syndromes and traffic accidents reflect the airway-pulmonary obstructive type rather than a faulty central regulation of breathing during sleep. Nevertheless, many physicians who participate in providing polysomnographic sleep studies or even hear complaints of hypersomnia must warn their patients against driving when feeling drowsy. The dangers of alcohol and anxiolytics must be emphasized. As the data show, these same attitudes must hold for young persons, especially those who combine benzodiazepines with alcohol and sleep deprivation. Therapy that can help outpatients prevent brain trauma is far greater than trying to restore them from traumatic brain injury. (*Dr. Plum is University Professor, Weill Medical College; Attending Neurologist, New York Presbyterian Hospital.*) ❖

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Pharmacology Update

Lansoprazole, Amoxicillin, and Clarithromycin (Prevpac—TAP)

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

Helicobacter pylori infection is associated with 90% of non-NSAID-related peptic ulcers. The bacterium, which commonly infects the upper GI tract, has also been implicated as a risk factor for gastric adenocarcinoma and low-grade gastric lymphoma of mucosa-associated lymphoid tissue.[1] In January, the FDA approved TAP's Prevpac, an administration pack containing one of the highly effective regimens for the eradication of *H. pylori*—the antibiotics clarithromycin and amoxicillin and a proton pump inhibitor, lansoprazole.

Indications

Prevpac is indicated for the treatment of patients with *H. pylori* infection and duodenal ulcer disease.

Dosage

Prevpac provides a daily dose of lansoprazole 30 mg (1 capsule), amoxicillin 1000 mg (2 capsules), and clarithromycin 500 mg (1 tablets) taken twice daily before meals (morning and evening) for 10 or 14 days.

Prevpac is supplied as a daily administration pack containing a sufficient number of capsules and tablets of the three-drug regimen.

Potential Advantages

Prevpac provides a highly effective and convenient regimen for the eradication of *H. pylori*. It is the only highly effective regimen in which all the components are available as a dispensing unit. This regimen also minimizes the risk of bacterial resistance since the rate of *H. pylori* resistance to either clarithromycin or amoxicillin is low, especially compared to metronidazole. A proton pump inhibitor-based triple-therapy regimen may be better tolerated with amoxicillin than with metronidazole.[1] Dosing of this combination is convenient (twice daily) compared to the four times daily dose for bismuth subsalicylate, metronidazole, and tetracycline (e.g., Helidac). Compliance and side effects have been reported to be problematic with bismuth regimens.[3]

Potential Disadvantages

Prevpac should not be used in patients with penicillin allergy, these who are pregnant, or those who are receiving concomitant therapy with cisapride, astemizole, or pimozide.[2] Potential drug interactions may occur between clarithromycin and ergotamine, triazolam, HMG-CoA reductase inhibitors, carbamazepine, cyclosporine, tacrolimus, phenytoin, disopyramide, alfentanil, bromocriptine, valproate, rifabutin, digoxin, protease inhibitors (e.g., ritonavir, indinavir), and warfarin.[2] Lansoprazole may affect the absorption of ketoconazole, iron, and digoxin by reducing gastric acidity.[2] Most common side effects reported with Prevpac are diarrhea (7%), headache (6%), and taste perversion (5%).[2]

Comments

Patients with peptic ulcers who have evidence of *H. pylori* infection benefit from eradication of the organism. Effective treatment promotes ulcer healing and reduces the rate of ulcer recurrence. Efficacious treatment regimens should have a cure rate of 90% and greater on per-protocol analysis and 80% or greater on intent-to-treat analysis.[1] Prevpac has reported eradication rates of 81-86% on intent-to-treat analysis and 84-92% on per-protocol analysis.[2] The intent-to-treat analysis is considered more reflective of clinical practice as this analysis includes patients who did not complete the treatment regimen for various reasons.[7] A 10-day regimen appears to be as efficacious as a 14-day regimen.[4] Lansoprazole also appears to be as efficacious as omeprazole.[5]

The cost of a 14-day treatment regimen with Prevpac is about $200. A combination of bismuth, metronidazole, and tetracycline (Helidac) with a proton pump inhibitor is about $170.

Clinical Implications

H. pylori infection is a common infection; however, most infected individuals are asymptomatic. Treatment is beneficial to those who have peptic ulcer disease or gastric mucosa-associated lymphoid tissue lymphoma.[1] *H. pylori* eradication with one of the appropriate regimens should be first-line therapy for infected patients with peptic ulcer. *The Guidelines for the Management of Helicobacter pylori Infection* by the Ad Hoc Committee on Practice Parameters of the American College of Gastroenterology stated that the highest eradication rates are achieved with a proton pump inhibitor, clarithromycin, and amoxicillin or metronidazole for two weeks, ranitidine bismuth citrate, clarithromycin, and ether amoxicillin, metronidazole, or tetracycline for two weeks, or a proton pump inhibitor, bismuth, metronidazole, and tetracycline for 1-2 weeks.[1] Diagnostic testing for *H. pylori* should only be performed if treatment is intended. There is no clear evidence that eradication of *H. pylori* will relieve symptoms of nonulcer dyspepsia.[1] While *H. pylori* eradication significantly reduces ulcer recurrence, a recent meta-analysis indicated that 20% of patients had ulcer recurrence within six months. Laine and colleagues suggest that non-*H. pylori* or non-NSAID ulcers may be more common than previously believed.[6] Prevpac is a regimen that is highly efficacious, convenient, and also minimizes the risk of developing bacterial resistance. ❖

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CME Questions

33. With regard to *Escherichia coli* as a uropathogen, which of the following antibiotics has been linked to increasing resistance in uncomplicated UTI?

a. Trimethoprim/sulfamethoxazole
b. Ciprofloxacin
c. Nitrofurantoin
d. Gentamicin

34. Which of the following statements is *false*?

a. Phytoestrogens derived from soy, flax, and red clover have comparable effects upon arterial compliance when administered to menopausal women.
b. The degree to which phytoestrogen use benefits a given menopausal woman can be monitored by longitudinally following lipoprotein profiles.
c. Phytoestrogen use has not been shown to be a substitute for hormone replacement therapy in menopausal women.
d. Two common phytoestrogens are genistein and diadzein.
e. The phytoestrogens that are isoflavones are best thought of as antioxidants.

35. Patients suspected of acute MI (AMI) who have LBBB pattern on the ECG should be considered for thrombolysis if:

a. the physical examination strongly suggests AMI.
b. the history supports AMI.
c. the ECG does not suggest AMI but a strong clinical suspicion is present for AMI.
d. the pain is similar to the patient's past angina.

By Louis Kuritzky, MD

Oral Cefpodoxime and Parenteral Ceftriaxone in Hospitalized Adults with CAP

Hospitalized patients with community-acquired pneumonia (CAP) are most often treated with parenteral antibiotics, usually with a switch to oral formulations when the clinical course is stabilized. This double-blind study compared oral cefpodoxime proxetil (Vantin) with ceftriaxone (Rocephin) in adult patients admitted for CAP (n = 88).

CAP was defined by the following criteria: 1) lung infiltrate on CXR; 2) purulent sputum with more than 25 WBCs/hpf. The study group was highly selected in that they must not have leukopenia, neutropenia, renal impairment, hepatic dysfunction, ARDS, CHF, pulmonary infarction, HIV, neoplasia requiring treatment, respiratory failure, or concomitant systemic antimicrobial therapy. Pregnant women, nursing women, and women without adequate contraception were excluded from the trial. End-of-treatment bacteriologic and clinical response were the efficacy variables.

In the cefpodoxime group, 60.6% of patients were cured (vs 57.7% ceftriaxone); 24.2% were improved (vs 23.1% ceftriaxone), and 15.2% were failures (vs 19.2% ceftriaxone). The only adverse effect difference between the therapies was that six ceftriaxone recipients developed drug-related diarrhea; none of the cefpodoxime group sustained this adversity. Bittner and associates conclude that oral cefpodoxime is equally efficacious as ceftriaxone in the treatment of CAP. ❖

Bittner MJ, et al. JCOM 1999;6(3): 38-45.

The Association of Chronic Cough with the Risk of MI

Some recent studies have noted an association between nontraditional cardiac risk factors and cardiovascular disease. Included among these are chronic bronchitis, bacterial, and viral infections (e.g., Chlamydia, Helicobacter, cytomegalovirus). The relationship between cough and cardiovascular disease has been incompletely evaluated. Studies that associate chronic bronchitis and cardiovascular disease have omitted important potential confounders such as hampered lung function.

The Framingham heart study began in 1948 with a cohort of 5209 men and women between the ages of 28-62 who agreed to have follow-up visits every two years. A questionnaire was included, which asked about chronic cough (lasting at least 3 months of the previous year), and if chronic cough was present, was it productive or not productive.

As anticipated, chronic cough was more prevalent in smokers and men. Persons with chronic cough, whether productive or nonproductive, had a 1.9-2.1 odds ratio for MI. Since cough could represent a symptom induced by heart failure, multivariate analysis adjusted for this, without change in odds ratio. For risk of MI, in the fully adjusted multivariate analysis, persons with either productive or nonproductive chronic cough had odds ratios 1.6-1.8. Fibrinogen levels were higher in persons with chronic productive cough; it is known that persistent infection, inflammation, and cigarette smoking are all associated with increased levels of fibrinogen. It remains undetermined whether the association between cough and coronary disease is causal. ❖

Haider AW, et al. Am J Med 1999; 106:279-284.

Isolated Clinic Hypertension is not an Innocent Phenomenon: Effect on the Carotid Artery Structure

Isolated clinic hypertension (ICH), alternatively called by such names as "white coat hypertension," presents a clinical dilemma to clinicians, since no large-scale, long-term, randomized controlled trials have examined this specific subset of patients. Zakopoulos and colleagues defined ICH as a combination of clinic blood pressure of more than 160/90 accompanied by a normal blood pressure by 24-hour ambulatory monitoring. In their group of 63 patients, they compared patients with sustained hypertension (both clinic and ambulatory blood pressure elevated) to ICH patients and normotensive individuals. The marker they chose to compare was the intimal medial thickness of the carotid artery, as determined by ultrasound, noting that this measurement has been correlated with coronary artery disease, MI, and cerebrovascular disease.

Carotid thickening was significantly more common among patients with sustained hypertension than normotensives, but the ICH group was not statistically significantly less likely to suffer such thickening.

Zakopoulos et al conclude that ICH may not be a benign finding. ❖

Zakopoulos N, et al. Am J Hypertens 1999;12:245-250.

In Future Issues:

Relieving the Pain of Renal Colic