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It's True! Beans Really ARE Good for Your Heart

ABSTRACT & COMMENTARY

Synopsis: *There is a significant inverse relationship between eating legumes and the risk of coronary heart disease.*

Source: Bazzano LA, et al. *Arch Intern Med.* 2001;161:2573-2578.

This was a 19-year prospective study of 9632 people. at baseline (1971-1975), subjects were 25-74 years old and free of cardiovascular disease. Legume consumption was assessed by 3-month food diaries. People were asked how often they ate "dry beans and peas like pinto beans, red beans, black-eye peas, peanuts, and peanut butter." Data about lifestyle and cardiovascular risk factors including smoking, age, gender, diabetes, activity level, education, alcohol use, and total energy intake were collected and controlled for. Cardiovascular disease and coronary heart disease (CHD) data were collected from nursing home and hospital records and from death certificates.

Some interesting facts about legume eaters emerged: people with high bean intake tended to be younger, male, more physically active, less overweight, and less educated than people with low bean intake. High bean eaters were also more likely to smoke and to eat more saturated fat, but tended to have lower cholesterol levels, less hypertension, and lower rates of diabetes than their bean-eschewing counterparts.

Controlling for all these risk factors, frequency of bean consumption was significantly and inversely related to the risk of CHD ($P = 0.002$). People who ate beans at least 4 times a week had a 22% lower risk of CHD compared with those who ate beans less than once a week. There was also a significant inverse relationship between eating beans and cardiovascular disease; eating beans 4 times a week lowered this risk by 11%. The protective effect of bean eating was more important in those older than 60 than in those younger than 60 at baseline.

■ COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

Talk about bean counting! The NHANES study is an important, ambitious project, which tells us a lot about the lifestyle and health

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of Americans.¹ Because of the wealth of data collected at baseline and the long follow-up, products of this study are worth serious consideration. It also includes both men and women, which many previous studies of cardiovascular disease failed to do.

Since CHD is the No. 1 killer of Americans, interventions that reduce its risk are noteworthy. What I found interesting about bean eating is that it seems to be something that people who may not have sterling health habits to begin with (smokers, those with less education, higher unsaturated fat consumers) seem to be likely to do. Further, beans are inexpensive and quite filling.

Bazzano and colleagues speculate that increased fiber,^{2,3} soybean protein,⁴ folate,⁵ or some other component of beans may contribute to their protective effect. For now, maybe we just need to encourage folks to remember that beans are “The magical fruit.” ❖

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The High Prevalence of Multidrug Resistant Salmonella in Food—An Important Public Health Concern

ABSTRACT & COMMENTARY

Synopsis: Twenty percent of samples of ground meats from Washington DC area stores contained salmonella. Eighty-four percent of the isolates were resistant to at least 1 antibiotic.

Source: White DG, et al. *N Engl J Med*. 2001;345:1147-1154.

Salmonella is a leading cause of foodborne illness. The emergence of antimicrobial-resistant salmonella is associated with the use of antibiotics in animals raised for food; resistant bacteria can be transmitted to humans through foods.

In this study, salmonella was isolated from samples of ground chicken, turkey, beef, and pork purchased at 3 supermarkets. The isolates were characterized by serotyping, antimicrobial-susceptibility testing, phage typing, and pulsed-field gel electrophoresis.

Of 200 meat samples, 41 (20%) contained salmonella, with a total of 13 serotypes. Eighty-four percent of the isolates were resistant to at least 1 antibiotic, and 53% were resistant to at least 3 antibiotics. Sixteen percent were resistant to ceftriaxone, the drug of choice for treating salmonellosis in children. Bacteriophage typing identified 4 isolates of *Salmonella enterica* serotype typhimurium definitive type 104 (DT104), 1 of DT104b, and 2 of 208. Five isolates of *S enterica* serotype agona had resistance to 9 antibiotics and 2 of the isolates of serotype typhimurium DT208 were resistant to 12 antibiotics. Electrophoretic patterns of DNA which were indistinguishable from each other were found in isolates

from different meat samples and different stores. Eighteen isolates, representing 4 serotypes, had integrons with genes conferring resistance to aminoglycosides, sulfonamides, trimethoprim, and beta-lactams such as ceftriaxone.

Resistant strains of salmonella are common in retail ground meats. These findings provide support for the adoption of guidelines for the prudent use of antibiotics in food animals and for a reduction in the number of pathogens present on farms and in slaughterhouses. National surveillance for antimicrobial-resistant salmonella should be extended to include retail meats.

■ COMMENT BY RALPH R. HALL, MD, FACP

This study, in itself, is cause for concern but added to this information are the data from other recent studies.

A second study by McDonald and colleagues in the same issue found that 17% of chickens from supermarkets in 4 states had strains of *Enterococcus faecium* that were resistant to a new antimicrobial agent, quinupristin-dalfopristin, that has recently been approved for use in humans.¹ This is apparently related to the use of a similar antibiotic used in chicken feed.

A third study in the same journal examined glycopeptide-resistant and streptogramin-resistant strains of *E faecium*, isolated from chicken obtained at a grocery store.² A previously reported study by Manges and colleagues suggests that antibiotic-resistant strains of *Escherichia coli* responsible for an epidemic of urinary tract infections may be the result of contaminated food.³

Two excellent editorials, by Stamm⁴ and Gorbach⁵ point out that a “multidisciplinary and worldwide” approach is needed to solve this problem. The antibiotics given to food animals for infections and growth promotion need more effective regulation and perhaps should only be given under the direction of veterinarians. Gorbach suggests that subtherapeutic use of these agents be banned since there is evidence that improvements in animal husbandry, the quality of feed, and hygiene can prevent any economic losses for the animal food industry.

Gorbach sites a report by The Union of Concerned Scientists that estimated that each year 24.6 million lbs of antimicrobials are given to animals for nontherapeutic purposes, 2 million lbs are given to animals for therapy, and that 3 million lbs are given to humans.⁶

White and colleagues point out that ceftriaxone is commonly used to treat children with salmonella infections because of its favorable pharmacologic properties and low prevalence of resistance. Ciprofloxacin, a fluoroquinolone, and trimethoprim-sulfamethoxazole are also used for therapy in children with serious salmonellosis. The recent prophylactic use of ciprofloxacin for the pre-

vention of anthrax will undoubtedly add to our problems of selecting treatment for these serious infections. ❖

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Fecal Occult Blood Testing for Colorectal Cancer Screening: Use the Finger

ABSTRACT & COMMENTARY

Synopsis: *Fecal occult blood testing (FOBT) using a specimen obtained at digital rectal examination has the same positive predictive value as occult blood testing on spontaneous passed stools (SPS).*

Source: Burke CA, et al. *Am J Gastroenterol.* 2002;96:3175-3177.

Digital rectal examination should be done as part of routine physical examinations, and occult blood testing of the specimen from the examining glove is desirable and useful for identifying patients at increased risk of colorectal neoplasia.

It has been recommended that all patients over age 50 should have FOBT annually, but this is actually accomplished in a small minority of cases. Part of the explanation for this involves guidelines for FOBT that mandate occult blood testing on 3 spontaneously passed stools, a prior specialized and restrictive diet, and avoidance of NSAIDs. In the past, physicians often performed occult blood testing on fecal specimens obtained from the examining glove at the time of digital rectal examination. However, there was some concern that this technique might result in anal trauma or otherwise increase false-positive occult blood tests. This paper included reviews of records from patients who underwent colonoscopy for positive FOBT results in the Department of Gastroenterology at the Cleveland Clinic Foundation. One hundred sixty-five patients with a mean age of 61 years were examined. Twenty-nine percent of the

patients with positive results from SPS testing had colorectal neoplasia, and 33% of those with positive occult blood tests on digital rectal examination had neoplasia. There were no differences in adenomas or invasive carcinomas between the groups.

■ **COMMENT BY MALCOLM ROBINSON, MD,
FACP, FACC**

Colorectal cancer screening by FOBT is known to reduce mortality from colorectal cancer by 33%, but less than 35% of Americans underwent such screening in the past 5 years. It is estimated that there will be 130,000 colorectal cancer cases this year and 56,000 deaths. Reasons for not testing stools for occult blood are varied, but the inconvenience of testing SPS certainly plays a role. Another large study confirmed that stool testing for occult blood from rectal exam vs. SPS did not result in divergent results in terms of colonic neoplasia (49.4% vs 44.3%).¹ Since many patients are seen in physicians' offices for routine examinations, and since rectal examination is easily done in that setting, a strong argument can be made for the widespread use of FOBT on finger-obtained stool specimens. This should result in significant decrements in colorectal cancer incidence, morbidity, and mortality. ❖

Reference

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What Does a Low Cholesterol Mean?

ABSTRACT & COMMENTARY

Synopsis: Serum albumin and HDL cholesterol levels predict prognosis in elderly people with low serum cholesterol values.

Source: Volpato S, et al. *J Am Geriatr Soc.* 2001;49:1142-1147.

Volpato and colleagues from the national Institute on Aging had previously published results from the Established Populations for Epidemiologic Studies in the Elderly (EPESE) which showed that the association of low cholesterol levels and adverse coronary events was spurious and based on failure to adjust for comorbidity and frailty.¹ Their study suggested that serum albumin was a marker for poor health. The same group studying the same population had earlier shown that low high-density lipoprotein cholesterol (HDL-C) levels were associat-

ed with mortality from coronary heart disease.² This study's goal was to determine whether combining albumin and HDL-C levels could stratify the mortality risk among elderly people with low serum cholesterol. During the sixth annual follow-up of the EPESE, blood was drawn from 4128 subjects (mean age, 78.7 years, 64% women). These people were followed for up to 6 years (median, 4.9 years). The outcome of interest was time until death. During the follow-up period, 1117 participants died (27%). Nonfasting blood samples were assayed for total cholesterol, HDL-C, and albumin at baseline. The subjects were classified into 3 groups, low cholesterol (≤ 160 mg/dL), normal-to-borderline high cholesterol (161-239 mg/dL), and high cholesterol (≥ 240 mg/dL). Those in the low cholesterol group numbered 393 (9.5%). (One of these subjects was taking a lipid-lowering agent.) Not surprisingly, low-cholesterol subjects had higher all-cause mortality (170 deaths or 43%) than the other 2 groups (29% and 17%, respectively).

To examine the interplay of HDL-C and albumin, the participants were assigned to 1 of 4 categories, low HDL-C/low albumin, high HDL-C/low albumin, low HDL-C/high albumin, and high HDL-C/high albumin. The definitions were as follows: high HDL-C ≥ 47 mg/dL and high albumin > 38 g/L. After adjusting for age, sex, race, body mass index, smoking, alcohol use, and blood pressure, those participants with high albumin had a lower relative risk (RR) of death than those participants with low albumin (RR = 0.57, 95% CI, 0.41-0.79). When the high albumin group was subdivided by HDL-C level, the RR of death for low HDL-C/high albumin subjects was 0.68 (95% CI, 0.47-0.99). For high HDL-C/high albumin the RR was even lower, 0.38 (95% CI, 0.20-0.68). Surprisingly, a high HDL-C level did not confer any benefit to individuals with low albumin.

■ **COMMENT BY ALLAN WILKE, MD**

This article addresses one of the paradoxes of medicine: in some studies when mortality is plotted against serum cholesterol levels, a U-shaped curve is produced. In 1990 the National Heart, Lung, and Blood Institute convened a conference to investigate why this happens.³ The conference concluded that there is a direct relationship between death from coronary artery disease and cholesterol levels, and there is an inverse relationship for a host of other diseases (eg, lung cancers, respiratory disease, digestive disease, and trauma). A study from the Framingham project showed that while low cholesterol levels in people younger than 50 years were associated with longevity, in people older than 50, the association was less clear.⁴ What confounded the association were those people with spontaneously falling cholesterol val-

ues, who were in poor health.

As physicians, we seem to handle this paradox well. We work to lower our patients' cholesterol levels, all the while knowing that low cholesterol levels are associated with poor outcome in certain patients. Who are these patients? This study makes it clear. They are those folks who also have low albumin levels. ❖

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4. Anderson KM, et al. *JAMA.* 1987;257:2176-2180.

Lack of Symptom Relief Following Presumptive *H pylori* Eradication Therapy in Primary Care

ABSTRACT & COMMENTARY

Synopsis: *The eradication of Helicobacter pylori in primary care does not produce long-term benefits in terms of the avoidance of future need for antisecretory therapy.*

Source: Williams D, et al. *Aliment Pharmacol Ther.* 2001; 15:1769-1775.

Dyspepsia is extremely common and is said to account for 2-3% of all primary care consultations in the United Kingdom.¹

“Ulcer-healing” drugs, largely prescribed for gastroesophageal reflux disease (GERD) and dyspepsia, account for a full 10% of all British drug costs, and US data are quantitatively similar. Once ulcer disease and *Helicobacter pylori* were etiologically linked along with an apparent association between *H pylori* infection and dyspepsia, empirical eradication of *H pylori* in uninvestigated dyspepsia has been widely encouraged.

This study assessed a large prescription database in Ireland to identify patients who received *H pylori* eradication therapy. It was then determined whether such patients subsequently received further antisecretory therapy. In Ireland, 3847 primary care patients received 3851 prescriptions for one of the standard *H pylori* eradication regimens. Median follow-up was 8 months in the overall group. The overall “failure rate” (ie, need for further antisecretory therapy) was 49% with no significant differences between various eradication regimens. Par-

ticularly high failure rates were seen in elderly patients, those previously receiving antisecretory therapy prior to an eradication regimen, and in patients on NSAIDs.

■ COMMENT MALCOLM ROBINSON MD, FACP, FACC

More than half of all patients receiving *H pylori* eradication therapy in primary care settings require further antisecretory medications. Some of these patients might have received therapy in the absence of clearly documented *H pylori* infection, and the precise indications for therapy were not known in this particular study. Nevertheless, this study provides no evidence whatsoever that would support the use of *H pylori* eradication therapy in primary care settings as a means of averting the future need for antisecretory therapy. Patients older than age 65 and those on aspirin were particularly likely to fail in this setting. Thus, the hoped for and promised fiscal benefits from eradication therapy seem unlikely to be realized. All in all, most studies of *H pylori* eradication in dyspepsia continue to show the futility of this approach. ❖

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ACE Inhibition for High-Risk CAD Patients

ABSTRACT & COMMENTARY

Synopsis: *One must consider adding ramipril (or possibly 1 of the other ACE inhibitors) to the list of pharmacologic agents now prescribed for most high-risk coronary artery disease patients.*

Source: Dagenais GR, et al. *Circulation.* 2001;104:522-526.

Activation of the renin-angiotensin-aldosterone in the system has been demonstrated to increase the risk of developing acute ischemic heart disease.¹ The results of 3 large trials conducted in patients with heart failure or left ventricular dysfunction revealed that the long-term use of an ACE inhibitor reduced cardiac mortality and hospitalizations for congestive heart failure (CHF) and, in addition, decreased the incidence of acute myocardial infarctions (MIs).²⁻⁵

The Heart Outcomes Prevention Evaluation (HOPE) study demonstrated significant benefits using an ACE inhibitor, ramipril (Altace), in high-risk persons without

known heart failure or left ventricular dysfunction.⁶ Dagenais and associates, on behalf of the HOPE investigators, expanded the observations of the initial HOPE study by providing greater details on a broad range of coronary events including fatal and nonfatal MIs, types of MIs, unexpected death, unstable angina, coronary revascularization, and worsening or new angina. During the mean follow-up period of 4.5 years, the use of ramipril resulted in a trend toward fewer fatal MIs and unexpected deaths and was associated with a significant reduction in nonfatal MIs. Although ramipril had no effect on hospitalizations for unstable angina, it reduced the risk of worsening and/or new-onset angina and coronary revascularizations in this high-risk cohort of 9297 high-risk men and women over the age of 55 with known previous cardiovascular disease and diabetes.

■ **COMMENT BY HAROLD L. KARPMAN, MD, FACC, FACP**

Traditionally, ACE inhibitors have been used primarily for control of vascular hypertension, but more recently they have also been used to reduce preload, afterload, and neurohumoral factors associated with congestive heart failure. In addition, recently published data¹ suggested that ACE inhibition may have a positive effect on the vascular wall by reducing endothelial dysfunction and, therefore, it would appear to be unlikely that only the modest blood-pressure-lowering effect of ramipril noted in the Dagenais et al study was the sole mechanism responsible for reducing the frequency of ischemic events among the HOPE participants. In fact, it is much more likely that the endothelial vascular protective effects of ramipril were responsible for reducing the frequency of ischemic events by virtue of the drug's beneficial effects on the atherosclerotic process, on thrombogenesis, and/or on the endothelium resulting in the observed decrease in frequency of ischemic events.

From a clinical point of view, multiple studies have clearly demonstrated that high-risk coronary artery disease patients should be treated with antiplatelet agents, beta blockers, and lipid-lowering drugs of the statin variety. It would now appear that one must consider adding ramipril (or possibly 1 of the other ACE inhibitors) to the list of pharmacologic agents now prescribed for most high-risk coronary artery disease patients in order to reduce the risk of developing acute MIs, worsening or new angina, and in order to diminish the frequency of coronary revascularizations. ❖

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Pharmacology Update

Norelgestromin/Ethinyl Estradiol Transdermal System—Ortho Evra—Ortho Pharmaceuticals

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

The fda has approved the first hormonal contraceptive skin patch. Ortho-McNeil's Ortho Evra patch is a small (one-and-three-quarter-inch square) patch that delivers ethinyl estradiol and norelgestromin transdermally. The patch is worn for 1 week, then replaced. Similar to oral contraceptives, the patch is used for 3 weeks, then left off for the fourth week each month. Although the patch was developed by Ortho-McNeil, it will be marketed by RW Johnson.

Indications

The norelgestromin/ethinyl estradiol (NGMN/EE) transdermal system is indicated for the prevention of pregnancy.

Dosage

The patch is applied each week for 3 weeks. The fourth week is patch free. Every new patch should be applied on the same day each week. The start day may be during the first 24 hours of the menstrual cycle or on the first Sunday after menstruation begins. If therapy begins after the first day of the menstrual period, a back-up contraception should be used concurrently during the first 7 days of the first treatment cycle. The patch should be applied to clean, dry, intact, healthy skin on the buttock, abdomen, upper outer arm, or upper torso. It should not be applied to the breast. If the patch is partially or completely detached for more than 1 day or for an unknown period, a new cycle should be started immediately. Back-up contraception should be used for the first week of the new cycle. If the patient forgets to change her patch, she should consult the

detailed patient labeling for instructions. Patients switching from oral contraceptives should wait until menstruation occurs.¹

The patch delivers 150 µg of norelgestromin (progestin) and 20 µg of ethinyl estradiol (estrogen) (NGMN/EE) every 24 hours. It is supplied as cartons of 1 cycle (3 patches).

Potential Advantages

The NGMN/EE patch has been reported to have a higher rate of compliance than an oral contraceptive (levonorgestrel 125 µg/ethinyl estradiol 30 µg—Triphasil).² The mean percent of patients with perfect compliance, patch vs. oral contraceptive, was 88.2% and 77.7%, respectively. Overall percentage of cycles with perfect compliance was 88.7% and 79.2%, respectively.² About 60% of oral contraceptive users in this trial were recent users.

Potential Disadvantages

The NGMN/EE patch may be less effective in women with a body weight greater than 198 lbs. The most common side effect is skin reactions. About 3% of patients withdrew from the clinical trials due to this reaction. Greater increases in total cholesterol (15.8 mg/dL vs 8.1 mg/dL; $P < 0.001$) and triglyceride (9.7 mg/dL vs 0.9 mg/dL; $P = 0.008$) were observed with the patch compared to an oral contraceptive (levonorgestrel/ethinyl estradiol). An overall higher occurrence of breast discomfort was also observed with the patch, primarily with the first and second cycles.² The incidence of the breakthrough bleeding and spotting (but not breakthrough bleeding alone) was higher with the patch in the first 2 cycles only. The incidence of patch becoming detached varied from 2-6%.¹⁻³ In a clinical trial, about 5% of all patches were replaced for either complete or partial detachment.²

Comments

NGMN/EE is the first contraceptive patch to be marketed. The progestin component, norelgestromin, is the primary active (17-deacetylated) metabolite of norgestimate and is responsible for the progestogenic properties of norgestimate.⁴ The latter is in Ortho-Cyclen and Ortho-Tri-Cyclen. NGMN/EE patches have been tested in more than 3000 women world wide.¹⁻³ A recent North American study compared NGMN/EE with levonorgestrel/ethinyl estradiol (Triphasil) on the basis of efficacy (Pearl Index and probability of pregnancy), cycle control, and safety. Subjects were randomized to the patch or oral contraceptive for 6 or 13 cycles. There was no statistical difference in efficacy in terms of over-

all Pearl Index between NGMN/EE patch and the oral contraceptive (1.24 vs 2.18), method-failure Pearl Index (0.99 vs 1.25), or the cumulative probability of pregnancy. The Pearl Index was defined as the number of pregnancies per 100 person-years of use. Method-failure pregnancy includes those where there was apparent dosing error (ie, compliance). Probability of pregnancy was estimated using the Kaplan-Meier method. In terms of cycle control, breakthrough bleeding and/or spotting were higher for the patch in cycle 1 and 2 only.

The cost of Ortho Evra is currently not available.

Clinical Implications

NGMN/EE provides an alternative to other methods of contraception but should not be used in patients with body weight greater than 198 lbs. Once-weekly administration may improve compliance in some patients. ❖

References

1. Ortho Evra Product Information. Ortho Pharmaceuticals, Inc. November 2001.
2. Audet MC, et al. *JAMA*. 2001;285:2347-2354.
3. Smallwood GH, et al. *Obstet Gynecol*. 2001;95(5 pt 1):799-805.
4. Henzl MR. *J Reprod Med*. 2001;46:647-661.

CME Questions

47. Legumes:

- a. are more likely to be eaten by women than by men.
- b. include beans, peas, and peanuts.
- c. do not appear to confer health benefit when consumed.
- d. may be a risk for hypertension when consumed in excess.

48. In the Cleveland Clinic study, significant colorectal neoplasia was found in what percentage of patients who were found to have positive fecal occult blood testing?

- a. 15-20%
- b. 5-10%
- c. 75-80%
- d. 33-36%

49. Among elderly patients with low serum cholesterol levels, the combination of HDL cholesterol and albumin levels that has the best prognosis is:

- a. low HDL-C/low albumin.
- b. low HDL-C/high albumin.
- c. high HDL-C/low albumin.
- d. high HDL-C/high albumin.

50. Eradication of *H pylori* should be done in which of the following settings?

- a. Documented gastric or duodenal ulcer patients
- b. Uninvestigated dyspepsia
- c. Symptoms strongly suggesting GERD
- d. Patients taking aspirin for cardiovascular prophylaxis

By Louis Kuritzky, MD

Cost Implications of Using an Alternative Treatment for Patients with OA of the Knee in Managed Care

Management of osteoarthritis (OA) occupies an important position in day-to-day practices of clinicians. Commonly used tools for appropriate pharmacologic management include NSAIDs, opioid analgesics, physical therapy, glucocorticoids, and alternative medicine regimens. Viscosupplementation—instillation of hyaluronic acid (HYL) or its derivatives intra-articularly—is much less frequently used as a foundation treatment for OA.

Waddell and colleagues calculated the cost savings associated with use of hyaluronic acid (Hylan G-F 20) incorporated into the treatment pathway for OA of the knee. The hypothetical clinical scenario included persons followed for 3 years in a managed care setting.

The clinical benefits in symptom reduction following viscosupplementation average approximately 1 year. Such treatment forestalls, or sometimes obviates, the need for total knee replacement. Waddell et al calculate that adding at least 1 course of HYL to a treatment pathway for OA of the knee results in an estimated savings of \$4706 per patient over a 3-year period.

Clinicians have been slow to adopt viscosupplementation into the typical OA therapeutic plan. HYL may be both clinically effective and cost saving when included as basic management in persons with OA of the knee. ❖

Waddell D, et al. *Am J Manag Care.* 2001;7:981-991.

First-Line vs. Second-Line Antibiotics for the Treatment of Acute Uncomplicated Sinusitis

Recent data suggest that sinusitis is the fifth most common diagnosis for which clinicians prescribe antibiotics in the ambulatory setting. At a time when bacterial resistance, which may be related to outpatient antibiotic prescribing, is an ever-growing dilemma, considerations of when to prescribe and which agent to prescribe become increasingly relevant. Piccirillo and associates examined antibiotic use, efficacy, and cost based upon data obtained from the Express Scripts Patient Treatment Episode registry, which includes 29,102 antibiotic prescriptions for sinusitis in adults.

The 3 most commonly prescribed antibiotics (in descending order of frequency) were amoxicillin, trimethoprim-sulfamethoxazole (TMP-SMX), and clarithromycin. Approximately one third of subjects received antibiotics not FDA-approved for sinusitis. For the purposes of this study, first-line antibiotics are defined as amoxicillin, TMP-SMX, and erythromycin.

Primary care physicians were more likely to prescribe first-line antibiotics than specialists. The success rates for treatment were essentially identical between first- and second-line treatments (90.1% vs 90.8%); relapse rates were similarly indistinguishable (3.3% vs 3.5%). On the other hand, the mean cost per patient of first-line therapy (\$68.98) was approximately half that of strategies using second-line agents (\$135.17).

This analysis demonstrates that there no significant demonstrable added clinical

benefit to using second-line antimicrobial agents, which cost almost twice as much as first-line agents. ❖

Piccirillo JF, et al. *JAMA.* 2001;286:1849-1856.

Treatment of Acute Hepatitis C with Interferon Alfa-2b

The disease management model of the HIV virus suggests that early intervention may allow host defenses to subsequently control viral replication. Delay in clearing viral load may result in deletion of virus-specific CD4 T cells and CD8 T cells, rendering the host less able to respond to culprit virus.

The current trial evaluated the effect of daily interferon alfa-2b (IA2b) on acute hepatitis C (HCV). Subjects had known/suspected HCV exposure in the past 4 months, documented seroconversion, or new abnormal liver function tests (LFTs), coupled with positive HCV virus RNA testing. Patients received IA2b daily for 4 weeks, followed by thrice weekly subcutaneous doses for 20 further weeks (traditional therapy has been thrice-weekly without initial daily dosing).

All patients (n = 44) achieved undetectable HCV RNA levels by 12 weeks of therapy, and 98% continued to undetectable levels at 24 weeks. LFT abnormalities normalized within 11 weeks after initiation of treatment and remained so through 24 weeks of treatment. All but 1 patient tolerated treatment well. Jaeckel and colleagues conclude that an early intervention for patients with acute hepatitis C. ❖

Jaeckel E, et al. *N Engl J Med.* 2001;345:1452-1457.