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INSIDE

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Cancer or Heart Disease? Drinkers May Need to Choose

ABSTRACT & COMMENTARY

By Mary Elina Ferris, MD

Clinical Associate Professor, University of Southern California

Dr. Ferris reports no financial relationship to this field of study.

Synopsis: *Moderate alcohol intake was associated with longer survival and better quality of life scores for Australian women age 70-75 years old, while non-drinkers had greater risk of death and poorer health-related quality.*

Source: Byles J, et al. A Drink to Healthy Aging: The Association Between Older Women's Use of Alcohol and Their Health-Related Quality of Life. *J AM Geriatr Soc.* 2006:54;1341-1347.

USING SELF-REPORTED SURVEY DATA FROM THE AUSTRALIAN Longitudinal Study on Women's Health, 11,800 women aged 70-75 years who were randomly selected from the national insurance database completed questionnaires from 1996 through 2002 at three year intervals. These were used to measure alcohol consumption and health-related quality of life, and the computer database provided information on mortality as well as risk behaviors. Low-to-moderate alcohol intake was defined as 1-14 drinks/week, and this group was further subdivided into 4 subgroups depending on weekly quantity. Sequential surveys found there was little quantity change over the years in the 69% who drank rarely or at low levels.

Higher mortality (death rate, 0.019/person-year) was found in the 29% of women who rarely or never drank alcohol, compared to women with low regular intake (lowest death rate, 0.010 for 3-12 drinks/week) after adjustment for smoking, comorbidity, education, BMI, and area of residence. High intake of 15 or more drinks/week had the highest death rate (0.024/person-year). Individual questionnaires provided eight subscales of health status and quality of life that were averaged into one score that also showed the same associations with quantity of alcohol consumed.

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COMMENTARY

Is it surprising that we continue to be interested in showing benefit from alcohol drinking? Regular drinkers may rejoice in this Australian study of older women which not only shows better quality of life in moderate drinkers, but also suggests non-drinkers are more likely to die, and if they survive do not enjoy life as much as drinkers.

While other studies have also supported lower cardiovascular risk and many other benefits with moderate alcohol drinking in both men and women, others point out that alcohol use is only an association and not a cause of these outcomes.[1] Non-drinkers may have other health problems or take medications contraindicated with alcohol, and studies are not randomized. Not all results agree, and there are many problems with underreporting of alcohol consumption when self-report is used.

Unfortunately the benefits of alcohol consumption do not seem to apply to cancer prevention. The American Cancer Society has just issued nutritional guidelines that limit alcohol to one drink or less daily for women (two for men) to prevent cancers of the mouth, pharynx, larynx, esophagus, liver, colorectum, and breast.[2] A drink is defined as 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits. They point out that cardiovascular disease can be reduced in many other ways, and that there is no reason for non-drinkers to begin drinking. ■

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Exercise and Restless Legs Syndrome

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

Residency Program Director, Associate Professor of Family Medicine, University of Alabama at Birmingham School of Medicine—Huntsville Regional Medical Campus

Dr. Wilke reports no financial relationship to this field of study.

Synopsis: *A program of resistive exercise and treadmill walking reduced the severity of restless legs syndrome symptoms.*

Source: Aukerman MM, et al. Exercise and restless legs syndrome: a randomized controlled trial. *J Am Board Fam Med.* 2006;19:487-493.

Restless legs syndrome (RLS) is a movement disorder, characterized by four features:

1. An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. (Sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs.)
2. The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.
3. The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
4. The urge to move or unpleasant sensations are worse

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in the evening or night than during the day or only occur in the evening or night. (When symptoms are very severe, the worsening at night may not be noticeable but must have been previously present.)[1]

All four criteria must be met to make the diagnosis, which is clinical. Risk factors for RLS are age, multiparity, sedentary lifestyle, obesity, and family history. It is also associated with iron deficiency, pregnancy, chronic renal disease, neuropathy, and medications, such as antipsychotics, tricyclic antidepressants, selective serotonin reuptake inhibitors, and metoclopramide; this is termed secondary RLS. The mainstay of treatment is drug therapy with dopaminergics, anticonvulsants, benzodiazepines, and opioids.

Although activity helps relieve symptoms, there are reports that exercise performed near bedtime can increase the risk of RLS. To confuse matters even more, there are data suggesting that lack of exercise contributes to RLS.[2] Aukerman and colleagues devised a study to determine the effect of a conditioning program on RLS. The program consisted of thrice weekly lower body resistance exercises and walking on a treadmill. Exclusion criteria were inability to exercise, a recent coronary event, uncontrolled hypertension, chronic renal disease, and anemia. The exercise group and the control group both received education about modifiable RLS risk factors: cigarette smoking, alcohol use, excessive caffeine use, and sleep hygiene. At the baseline visit, subjects were examined by a physician to confirm the diagnosis of RLS and to obtain laboratory work, including hemoglobin and creatinine. Subjects were again seen at six and twelve weeks, and had telephone contact at three and nine weeks. The primary outcome measures were scores on the International RLS Study Group Scale and on an overall RLS severity 1-to-8 scale. The International Restless Legs Severity Scale (IRLS) is a validated, 10-item scale with a maximum score of 40. For both scales, the greater the score, the greater the severity.[3] These scales were rescored at 3, 6, 9, and 12 weeks.

Forty-one (41) subjects were available for randomization. However, due to scheduling problems, 13 participants dropped out before the study began. At week 6, there were 11 subjects in the exercise group and 17 in the control group. At Week 12, only 12 participants remained in the study group. The average age of the subjects was 53 years. Despite randomization, the exercise group was taller (statistically significant) and had more males and were heavier (not statistically significant). At baseline the two groups had equivalent IRLS scores (20.6 for the exercise group, 22.5 for the control group) and severity scores (4.0 and 4.8, respectively). By week 6 the IRLS and severity scores diverged: 12.6 and 1.7 for the exercise group and 20.8 and 4.1 for the control group. The scores then remained steady: 12.1 and 2.0 for the exercise group and 21.5 and 4.3 for the control group. The difference in the scores at weeks 6 and 12 were statistically significant.

COMMENTARY

This is not the definitive study of exercise as a treatment for RLS. It was too small and there were too many drop-outs. It does suggest, though, that exercise could be useful, either alone or as an adjunct to pharmaceutical therapy. As the authors point out, exercise has other benefits for older individuals, so there is little to lose by advising it (after proper medical clearance, of course) while we await larger, more robust studies.

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The Nose Knows

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

Professor of Medicine, University of Kentucky; Director, Sleep Disorders Center, Samaritan Hospital, Lexington

Dr. Phillips serves on the speaker's bureau of Cephalon, Boehringer Ingelheim, Merck, ResMed, and GlaxoSmithKline, and is a consultant for Boehringer Ingelheim, Wyeth-Ayerst, and ResMed.

Synopsis: *People who have symptoms of allergic rhinitis report more sleep complaints, including daytime sleepiness, than do those without allergic rhinitis.*

Source: Leger D, et al. Allergic rhinitis and its consequences on quality of sleep: An unexplored area. *Arch Intern Med*. 2006;166:1744-1748.

This report comes from a cross-sectional study of patients recruited by French otolaryngologists. The study was entitled DREAMS (Etude Descriptive des RhinitES Allergies et des Modifications du Som-

meil). Eligible patients were those aged 18 to 50 with a score of 7 or higher on the Score for Allergic Rhinitis questionnaire[1] who had symptoms for at least a year. Subjects were assigned a point score based on their responses to the following items on the allergic rhinitis questionnaire:

- Blocked/runny nose or sneezing in the past year (nasal symptoms)
- Duration of symptoms (perennial vs seasonal)
- Nasal symptoms PLUS itchy eyes
- Triggers
- Perceived allergic status
- Previous allergy tests
- Previous medical diagnosis of allergy
- Family history of allergy

People with nasal septal deviation or polyps were included. A French version of the Sleep Disorders Questionnaire[2] and the Epworth Sleepiness Scale[3] were used to assess sleep symptoms. The investigators assembled a fairly well-matched control group from general practice clinics. Altogether, there were 591 allergy patients and 502 control subjects. Their mean age was about 40 and most were nonsmokers, though there were slightly more smokers in the control group. Their BMI was about 24 Kg/m^2. In their analysis, the authors controlled for age and gender. In this study, persistent moderate-to-severe allergic rhinitis was the most frequent type of allergy (about 60%), and 85% of patients with this condition were being treated for it. Almost a quarter of those with allergic rhinitis had asthma, compared with only about 2% of the control group.

Patients with moderate-to-severe allergic rhinitis were more likely to have severe insomnia, hypersomnia, snoring, witnessed apneas, and daytime sleepiness. In general, patients with allergic rhinitis were more likely to use sedative drugs and alcohol. The authors estimated, based on symptoms of snoring and sleepiness, that sleep apnea was more prevalent in patients with allergic rhinitis than in the control group.

Patients with allergic rhinitis also reported more symptoms of morning headache, anxiety, and impaired memory and mood than did the control group.

The authors identified other factors that were predictive of sleep disturbances in this group of patients. Not surprisingly, male patients were more likely to be at risk for symptoms of sleep apnea, and those with insomnia were more likely to take anxiolytic drugs. They also noted that those with asthma were more likely to report severe insomnia.

COMMENTARY

Intéressant, n'est ce pas? Although these French authors subtitled their report "an unexplored area," there is actually quite a bit known about allergies and sleep. A substantial body of literature demonstrates increased sleep complaints in individuals with respiratory disease all of all types, including asthma, rhinitis, and chronic obstructive pulmonary disease. The relationship is probably multifactorial, including disturbances related to trying to breathe, depression, medication effects and coughing due to secretions.

Particularly, allergic rhinitis and sinusitis are strongly associated with daytime fatigue. There are two schools of thought about this. The first is that fatigue results from the chronic activation of immune mediators (evil substances such as interleukins, interferons and tissue necrosis factor) in people who have chronic airway inflammation.[4] The second idea is that the increased inspiratory airflow resistance associated with upper airway inflammation results in significant sleep-disordered breathing, a/k/a sleep apnea.[5] Indeed, nasal obstruction is associated with an increased risk of sleep apnea.[6] The strongest evidence that rhinitis impairs sleep by contributing to sleep apnea comes from studies of the use of nasal steroids in patients with rhinitis and sleep disturbance. Much of the work in this area has been done by Craig and colleagues,[7] who have demonstrated in several placebo-controlled trials with at least 3 different nasal steroids (budesonide, flunisolide, and fluticasone) that these agents can decrease nasal congestion, sleep complaints, and sleepiness in treated patients with allergic rhinitis. Further, there is a correlation between reduction in nasal congestion and an improvement of sleep and daytime somnolence. Measured improvement in the severity of sleep apnea has been demonstrated with use of nasal steroids for both adults[8] and children,[9] and the Cochrane Database has recently noted that fluticasone, in particular, is a promising agent for pharmacologic treatment of sleep apnea.

Rhinitis and sinusitis are extraordinarily common, as are complaints of fatigue, insomnia, and snoring. The relationship between these problems is robust and probably not coincidental. Since sleep apnea kills, it's important to consider it in the patient with fatigue and nasal congestion. If sleep apnea turns out not to be the problem, nasal steroids are safe, effective, and relatively cheap. ■

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Cluster Headaches

ABSTRACT & COMMENTARY

By Michael Rubin, MD

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Dr. Rubin is on the speaker's bureau for Athena Diagnostics, and does research for Pfizer and Merck.

Synopsis: *Cluster headache may be accompanied by a variety of neurological manifestations, and responds well to triptans and oxygen therapy.*

Source: Schurks M, et al. Cluster Headaches: Clinical Presentation, Lifestyle Features, and Medical Treatment. *Headache*. 2006;46:1246-1254.

Using international headache society criteria to establish a diagnosis of cluster headache (CH), 246 such patients were recruited from the Headache Clinic at the University Hospital in Essen, Germany, to characterize the clinical features and medical treatment of CH. Student's t-test, the Chi-square test, and Fisher's exact test were used for statistical analysis.

Most (77.6%) were men and had episodic (74.7%) rather than chronic (16.7%) CH. Nine percent were newly diagnosed, with no established pattern. Mean age of onset was 36.9 years for both men and women. Strictly unilateral pain, albeit changing sides between attacks, was seen in 97.2%. Seventy-nine percent were always strictly unilateral and 2.8% were bilateral, remaining predominantly one-sided but radiating to the contralateral side. Pain was usually sharp (61.8%) or pulsating (31.3%), and usually lasted 45-180 minutes (67.9%). Twenty-four percent experienced attacks of 2-45 minutes in duration and, in 7.3%, it lasted longer than 3 hours. Cranial autonomic features, including ptosis, miosis, ipsilateral facial sweating, nasal congestion and/or rhinorrhea were present in almost all (98.8%), with many experiencing restlessness during the attack (67.9%) and photophobia and phonophobia (61.2%). Twenty-three percent experienced migrainous aura of fortification spectra, tunnel vision, hemiparesis, hemisensory symptoms, dysarthria, or dysphasia, and physical activity worsened the pain in 21.7%. Men and women shared these clinical characteristics.

Alcohol consumption was more frequent in patients with episodic than chronic CH and, in 53.5%, alcohol (red wine [70.5%] or beer [23%]) triggered an attack, usually within 1 hour (65.2%), with a shorter latency in men than women. Sixty-six percent were current smokers, and 29% had never smoked.

Acute abortive therapy most often comprised triptans (77.6%) and oxygen (71.1%), with 71.7% and 76.6% experiencing relief, respectively. Ergots (32.1%) and lidocaine nasal spray (22.8%) were used less frequently, and almost 60% used unproven medication, including nonsteroidals, caffeine, and opioids. Prophylactic medication was used in 84.6%; usually verapamil (70.3%, with 65.3% efficacy) or corticosteroids (57.7%, with 73.2% efficacy). Lithium was effective in 37%, but valproic acid in only 20%. Once properly recognized and diagnosed, appropriate treatment is usually effective for CH.

COMMENTARY

More recently described treatments for CH include hypothalamic stimulation, where 13 of 16 intractable CH patients were pain-free or almost so, with no persistent side effects, following 23 months of follow-up, and the remaining 3 were improved.[1] Among 53 CH patients who had experimented with psilocybin or lysergic acid diethylamide (LSD), 22 of 26 noted that psilocybin aborted attacks, 25 of 48 noted that it terminated the cluster period, and 18 of 19 reported that it extended their remission period.[2] Cluster

headache period termination was reported in 7 of 8 LSD users, and extended remission in 4 of 5. Clozapine, testosterone, and pramipexole have also been reportedly successful. Clearly, more research is needed to determine the most effective and safest treatments for this disabling and common disorder. ■

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Pharmacology Update

Posaconazole Oral Suspension (Noxafil®)

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

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; Assistant Clinical Professor of Medicine, University of California, San Francisco; Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Chan and Elliott report no financial relationships to this field of study.

THE FDA HAS APPROVED A NEW ANTIFUNGAL AGENT FOR the prevention of Aspergillus and Candida infections in at-risk individuals. Posaconazole is an oral triazole, broad spectrum, antifungal chemically similar to itraconazole. It is marketed by the Schering Corporation as Noxafil®.

Indications

Posaconazole is indicated for prophylaxis of invasive Aspergillus and Candida infection in patients (13 years or older) who are at high risk of developing these infections. These include severely immunocompromised patients such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.[1]

Dosage

The recommended dose is 200 mg (5 mL) three times a day with a full meal or with a liquid nutritional supplement for those who cannot eat a full meal. The duration of therapy is based on recovery from neutropenia or immunosuppression.[1]

Posaconazole as Noxafil is available as a 4-ounce suspension with each mL containing 40 mg of posaconazole.

Potential Advantages

Posaconazole is the most active among the triazoles against Candida species and filamentous fungi (eg, Aspergillus species, Zygomycetes) including isolates resistant to other triazoles.[2,3] Clinical efficacy has been demonstrated in patients who are refractory or resistant to other antifungals.[4,5] It may be less susceptible than fluconazole or voriconazole to mutations of CYP51, the target enzyme for antifungal activity.[4] In vitro data suggest synergy with caspofungin against Aspergillus species.[4] Posaconazole is not metabolized significantly by the cytochrome P450 enzyme system and does not inhibit these isoenzymes except for CYP3A4.[4,5]

Potential Disadvantages

Patients with severe diarrhea or vomiting should be monitored for breakthrough fungal infection.[1] Coadministration of posaconazole and rifabutin, phenytoin, ergot derivatives, quinidine, and cimetidine should be avoided. Liver functions should be monitored at the start, and during the course of therapy. The dose of midazolam, cyclosporine, tacrolimus, and sirolimus should be reduced and patients monitored if posaconazole is initiated.[1] Common adverse events associated with posaconazole are similar to those of fluconazole or itraconazole. Common adverse events include nausea (9%), vomiting (6%), abdominal pain (5%), headache, diarrhea, rash, and elevation of ALT or AST (each 3%). Serious adverse events include nephrotoxicity, adrenal insufficiency and prolongation of QTc.[4] Resistant isolates of Candida species have been reported.[1] Posaconazole is not available in a parenteral form.

Comments

Posaconazole is a new triazole antifungal agent that is highly active against a broad spectrum of fungi. Posaconazole (200 mg three times a day) is at least as effective as fluconazole (400 mg once daily) or itraconazole (200 mg twice daily) for the prophylaxis of invasive fungal infections in patients who are receiving chemotherapy for acute myelogenous leukemia or myelodysplastic syndrome or those with HSCT with GVHD.[1] In one study (n = 602), treatment failure (breakthrough invasive fungal infection, death, or systemic antifungal therapy) was 27% for posaconazole and 42% for fluconazole/itraconazole. All cause mortality at 100 days was in favor of posaconazole, 14% vs 21%. In a second study (n = 600) proven or probable invasive fungal infection was 5% for posaconazole and 9% for fluconazole. All-cause mortality was 19% and 20% respectively.[1] Posaconazole has shown effectiveness in patients who are intolerant of other agents or whose fungal infections

are refractory to other antifungals as well as in salvage therapy and CNS infections.[2,4] Posaconazole is generally well tolerated. The adverse reaction profile appears similar in those treated for less than 6 months or those treated for longer than 6 months.[4] The cost of posaconazole suspension is $480 for 4 ounces.

Clinical Implications

Invasive mold infections, particularly Candida species and Aspergillus species are the major cause of morbidity and mortality in immunocompromised patients such as hematopoietic stem cell transplant recipients.[6] Prophylaxis in high-risk individuals has been recommended and antifungal options include azoles, amphotericin, and caspofungin.[7] Posaconazole provides an option with good in vitro antifungal activity including isolates resistant to other agents. ■

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CME Questions

22. Which amount of weekly alcohol intake for older Australian women was associated with lower mortality and better health-related quality of life?
a. < 1 drinks/week
b. 1-15 drinks/week
c. 15-28 drinks/week
d. > 28 drinks/week
e. None of the above
f. All of the above

23. Choose the *incorrect* answer. When compared to the control group, the exercise group with restless legs syndrome:
a. had more males.
b. were taller.
c. were lighter.
d. had a decrease in the severity of their symptoms.

24. Which of the following statements about sleep and airway symptoms is most true?
a. Both allergic rhinitis and asthma are associated with sleep complaints.
b. Neither allergic rhinitis nor asthma is associated with sleep complaints
c. Allergic rhinitis is associated with sleep complaints, but asthma is not.
d. Asthma is associated with sleep complaints, but allergic rhinitis is not.

Answers: 22 (b); 23 (c); 24 (a)

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CME Objectives

The objectives of *Internal Medicine Alert* are:

- to describe new findings in differential diagnosis and treatment of various diseases;
- to describe controversies, advantages, and disadvantages of those advances;
- to describe cost-effective treatment regimens;
- to describe the pros and cons of new screening procedures.

Clinical Briefs

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

Global Consequences of Smoking

In the United States, COPD is the 4th leading cause of death. Widespread public education about smoking toxicity has not decreased COPD mortality, and since 2000 the number of women who die from COPD has eclipsed men.

Worldwide, more men than women suffer toxicity from smoking, with an average life shortening of 22 years for those who succumb to smoking-related disease. Currently, persons in developing countries comprise 82% of all smokers worldwide.

The INTERHEART study is a case-control study which recruited participants from 52 countries in Asia, Europe, the Middle-East, Africa, Australia, and the Americas. The cohorts compared were persons with first acute MI (n = 15,152) and age/sex-matched controls.

The odds ratio for non-fatal MI in current smokers was approximately 3 times that of non smokers. After smoking cessation, this risk was almost halved by 3 years time, but was never reduced to the level of risk of lifelong non-smokers.

Second-hand smoke was also directly associated with increased risk for MI in a graded fashion: even a 'low' level of exposure (1-7 hours/week) was associated with a 24% increased odds ratio for MI, and persons in the highest quartile of exposure (more than 22 hours/week) had a 62% increased odds ratio. Developing countries do not have well established policies to educate the public about health risks of smoking. The majority of life lost in the decades to come will be in developing countries; development of effective cessation programs, public education to prevent the acquisition of a tobacco habit, and heightened public awareness of risks to non-smokers are critically needed. ■

Teo KK, et al. Lancet. 2006;368: 647-658.

Celecoxib for Prevention of Sporadic Colorectal Adenomas

The knowledge that colonic adenoma express tumorigenic cyclooxygenase-2 (COX-2), whereas healthy colonic mucosa does not, led to clinical trials in high-risk populations which have confirmed that COX-2 inhibition reduces colorectal cancer (CCA). For persons with familial adenomatous polyposis, a population with exaggerated CCA risk, celecoxib has shown antitumor activity. Whether the antitumor activity of celecoxib might be useful in prevention of new adenomas for persons who have already had one adenoma detected—but do *not* have familial adenomatous polyposis—was the subject of this trial.

Patients (n = 2,035) were randomized to receive celecoxib (200 mg b.i.d. or 400 mg b.i.d.) or placebo and were followed for three years, with colonoscopy at years one and three.

Celecoxib was associated with statistically significant reductions in new adenomas: a 33% relative reduction at 200 mg b.i.d., and 38% reduction at 400 mg b.i.d. compared to placebo. Attesting to the elevated risk of new adenomas in this population is the > 60% incidence of new adenomas amongst the placebo group.

Unfortunately, an increase in cardiovascular risk (2.6-3.4 risk ratio increase) was seen in this middle aged population (mean age = 59 years). Although risk reduction for new adenomas is evident, competing cardiovascular risk must temper enthusiasm for these favorable results. ■

Bertagnolli MM, et al. N Engl J Med. 2006;355:873-884.

Trends in Herpes Simplex Prevalence

Early thinking about herpes simplex virus (HSV) simplified pathology into anogenital lesions, which were caused by HSV type 2 (HSV-2), and orofacial lesions which were caused by HSV type 1 (HSV-1). Increasingly, it became clear that either virus could cause lesions at either site, although the preponderance of pathogen-specific sites was still consistent with the earlier thinking. The use of HSV typing was based upon the observation that HSV-1 anogenital lesions have a less frequent recurrence pattern. Although genital HSV-2 is usually sexually transmitted, either type of HSV may be acquired by non-sexual means, and most acquisition is asymptomatic.

Since 1994, overall HSV-2 seroprevalence has declined almost 20% and HSV-1 seroprevalence has decreased 6.9%. On the other hand, there has been a more than four-fold increase in the percentage of individuals whose anogenital HSV is attributable to HSV-1 (ie, they have been diagnosed with genital herpes, but are HSV-2 seronegative), albeit the absolute percentage remains low.

Highly effective antiviral therapies to reduce HSV transmission and recurrences are available, and promising results for an HSV vaccine have been reported. Because HSV-2 infection is associated with increased risk for HIV acquisition, enhanced methods for HSV prevention are a priority. ■

Xu F, et al. JAMA. 2006;296:964-973.

In Future Issues: ¿Qué Pasa, Acetaminophen?