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INTERNAL MEDICINE ALERT®

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Carotid Endarterectomies—When are They Indicated?

ABSTRACT & COMMENTARY

Synopsis: *Enthusiasm for this operation is justified but restraint is indicated unless patients are properly selected and sent to appropriate surgeons who are associated with appropriate surgical facilities.*

Source: Barnett HJM, et al., for the North American Symptomatic Carotid Endarterectomy Trial. *N Engl J Med* 1998;339:1415-1425.

The number of carotid endarterectomies rose by 95% between 1980 and 1985 as enthusiasm for this procedure blossomed. By 1985, 170,000 carotid endarterectomies were being performed annually in the United States; however, reports of high complication rates, questions about the appropriateness of patients selected to undergo the procedure, and the absence of data from carefully controlled clinical studies were all evaluated and summarized in two negative trials, which quickly dampened the enthusiasm for this procedure, resulting in a dramatic decrease in the volume of these procedures that were performed in that year.[1,2] A series of large and complex randomized, controlled trials were then mounted to address the many questions about the efficacy and safety of the procedure and, as the results of these trials became available, the number of carotid endarterectomies performed increased by 94% between 1991 and 1996.

Barnett and colleagues representing the North American Symptomatic Carotid Endarterectomy Trial Collaborative recently published a paper in the *New England Journal of Medicine* reporting on the results of the last remaining cohort of a large, randomized, controlled trial of symptomatic patients with carotid stenosis. They report that performing carotid endarterectomies in patients with symptomatic moderate (50-69%) carotid stenosis yielded only a moderate reduction in the risk of stroke. Patients with stenosis of less than 50% did not benefit from surgery at all, whereas patients with severe stenosis (i.e., > 70%) had a durable benefit from endarterectomy at eight years. It should be noted that the protocol included only hospitals with perioperative complication rates of 6% or less.

INSIDE

In the same issue, Tu and colleagues calculated the annual rate of carotid endarterectomies in California, New York, and in the Canadian province of Ontario.[3] They also found a dramatic fall and then rise in the rates of carotid endarterectomy in both the United States and Canada, which correlated with the publication of first an unfavorable and later favorable clinical studies. The recent increase in numbers of carotid endarterectomies was found to be similar in high mortality rate hospitals as it was in those hospitals with low mortality rates suggesting that many patients, even if they were appropriately selected, did not receive the full risk/benefit of the carotid endarterectomy procedure[3] because the surgeon and/or the hospital they selected for the procedure had a higher complication rate than did other surgeons and hospitals.

COMMENT BY HAROLD L. KARPMAN, MD, FACP

The first carotid endarterectomies were performed successfully in 1954 on patients who had symptoms suggesting that a stroke was imminent.[4] Since that time, the numbers of carotid endarterectomies performed had been a rollercoaster curve reflecting when the procedure would either fall in or out of favor. Initially, there was a great deal of confusion about the results, but over the past 14 years, a series of large and complex randomized, controlled trials have addressed the many questions about the efficacy of this procedure in both symptomatic and asymptomatic patients. These studies have demonstrated absolute risk reductions of statistically significant degrees among symptomatic patients with stenoses of 60% or greater. In asymptomatic patients, the data on efficacy is less clear; however, one major study, the Asymptomatic Carotid Atherosclerosis Study (ACAS) demonstrated a statistically significant absolute reduction of 5.9% in the five-year risk of stroke or death. The surgical complication rate in this study was only 2.3%, but, even with this low complication rate and even under the ideal circumstances of the trial, the net benefit for asymptomatic patients is much less clear than it is for the symptomatic patients.

It is obviously critical that referring physicians are fully familiar with the complication rates of the surgical team and the hospital to which they refer potential candidates for carotid endarterectomies in order to ensure that the patients receive the full benefit of the surgical procedure especially in those cases with severe symptomatic carotid stenosis. It is also essential to carefully assess whether a specific patient will benefit at all from this surgical procedure—that is, whether the patient belongs to a sub group for whom the potential benefit is remote. All risk factors should be evaluated especially for patients who are in the 50-69% stenosis range as they are being considered for an endarterectomy. These patients will benefit statistically on a long-term basis only if they are carefully selected since it has been demonstrated that the risk of stroke with medical treatment is higher for men than it is for women, for patients who have had a stroke in the past than it is for those who have had simple transient ischemic attacks, and for patients with hemispheric symptoms rather than for those who simply have retinal artery symptomatology. Also, published studies have demonstrated that the risk of perioperative stroke or death is increased in patients with diabetes, elevated blood pressure, contra-lateral occlusion, left-sided hemispheric disease or a lesion that is evident on either computed tomography scanning or magnetic resonance imaging studies.

Because the enthusiasm for carotid endarterectomy is increasing at this time, it becomes doubly important to recognize that many patients with symptomatic stenosis of less than 70% are not appropriate candidates for endarterectomy when the risk and benefits are carefully weighed. The benefits of the randomized controlled trials will not be fully realized until mechanisms have been established to ensure that those patients who are not likely to benefit from carotid endarterectomy do not undergo the procedure and that those who have been appropriately selected receive the full benefit of the procedure (but only in the proper surgical environment performed by the proper surgeons). In other words, the carotid

Internal Medicine Alert, ISSN 0195-315X, is published twice monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

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GST Registration Number: R128870672.

Second class postage paid at Atlanta, GA.

POSTMASTER: Send address changes to ***Internal Medicine Alert***, P.O. Box 740059, Atlanta, GA 30374.

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Subscription Prices

United States

$199 per year (Student/Resident rate: $100).

Multiple Copies

1-9 additional copies: $100 each; 10 or more copies: $60 each.

Outside the United States

$229 per year plus GST (Student/Resident rate: $110 plus GST).

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endarterectomies have excellent outcomes when patients are appropriately selected and when operations are performed by those surgeons who have a high volume of patients and low complication rates, but the risk of perioperative stroke or death is significantly increased for those patients in whom the indications are not appropriate and who are afflicted with complicating medical conditions such as diabetes, elevated blood pressure, contralateral carotid stenosis or occlusions, or perhaps even with those with lesions that are evident on computed tomography and magnetic resonance imaging. In conclusion, enthusiasm for this operation is justified but restraint is indicated unless patients are properly selected and sent to appropriate surgeons who are associated with appropriate surgical facilities. ❖

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Which of the following statements is true?

a. The risk of stroke with medical treatment is higher for men than it is for women.
b. The risk of stroke with medical treatment is higher for patients who have had a stroke in the past than it is for those who have had simple transient ischemic attacks.
c. The risk of stroke with medical treatment is higher for patients with hemispheric symptoms rather than for those who simply have retinal artery symptomatology.
d. All of the above

Headache Characteristics in Subarachnoid Hemorrhage and Benign Thunderclap Headache

ABSTRACT & COMMENTARY

Synopsis: *CT and LP remain essential tools in the acute evaluation and treatment of patients with thunderclap type headache.*

Source: Linn FH, et al. *J Neurol Neurosurg Psychiatr* 1998;65:791-793.

The differential diagnosis of a sudden and severe headache includes aneurysmal and nonaneurysmal subarachnoid hemorrhage (SAH) and benign thunderclap headache (BTH). The ability of the clinician to distinguish what are potentially life threatening symptoms remains one of the vexing challenges in everyday practice. In an effort to better characterize each syndrome, Linn and colleagues prospectively evaluated 102 patients referred to the emergency room for the sudden onset of severe headache with normal level of consciousness and without focal neurologic deficits. CT scans and LP were performed to confirm the presence or absence of subarachnoid blood. A detailed history was obtained by one of only two interviewers. Linn et al established the diagnosis of aneurysmal SAH in 42 patients (41%), nonaneurysmal SAH in 23 (23%), and BTH in 37 patients (36%). In comparing the three groups, it was impossible to clearly differentiate the headache types based upon clinical criteria. Seizures in three patients (7%) and diplopia in two patients (5%) were the only two symptoms that occurred solely in the aneurysmal SAH group. Otherwise, headache severity, onset, progression, associated nausea/vomiting, and transient neurologic symptoms including change in consciousness, sensory symptoms, weakness, ataxia, and speech arrest could not distinguish benign from SAH groups. Furthermore, there was no significant difference in the SAH (37%) and BTH (57%) groups with respect to previous headache history.

COMMENT BY JEFFREY REICH, MD

Previous studies have found that 25% of patients presenting with sudden, severe headache have SAH.[1] In the current prospective study, it was 65%. It is important to note that abrupt onset, severe pain, and transient focal symptoms are all compatible with BTH as well. It is unclear from their study, however, whether a previous headache history and negative CT could comfortably rule out SAH and avoid the need for LP. Nonetheless, intracranial vascular pain appears much like other visceral pain in that it is highly sensitive but lacks specificity. As such, CT and LP remain essential tools in the acute evaluation and treatment of patients with thunderclap type headache. *(Dr. Reich is Assistant Professor of Neurology, New York Presbyterian Hospital-Cornell Campus.)*

Reference

1. Linn FH, et al. *Lancet* 1994;344:590-593.

What percentage of patients did Linn et al establish nonaneurysmal SAH?

a. 36%
b. 41%
c. 23%
d. None of the above

A Kinder, Gentler NSAID?

ABSTRACT & COMMENTARY

Synopsis: *Meloxicam, at the daily dose chosen, was slightly less efficacious than diclofenac for osteoarthritis.*

Source: Hawkey C, et al. *Br J Rheumatol* 1998;37:937-945.

Nsaids are widely used for patients with osteoarthritis. There is a small risk of serious gastrointestinal (GI) adverse effects such as gastric or duodenal ulceration associated with NSAID use. Ulcerations may be further complicated by perforation or bleeding. Both the beneficial and the adverse GI effects are believed to be due to reduction in the production of prostaglandins as a result of inhibition of cyclooxygenase, an enzyme that is known to exist in at least two isoenzymatic forms. These two isoenzymes are differentially inhibited by meloxicam, an NSAID that is currently available in Europe. Meloxicam has been shown in vitro to inhibit the COX-2 isoenzyme about 10 times more effectively than it inhibits COX-1.

Hawkey and colleagues compared 7.5 mg per day of meloxicam to 100 mg per day of sustained release diclofenac. Adverse drug reactions were recorded and efficacy in controlling arthritis symptoms was assessed by comparing baseline and four-week end points. Efficacy was quantified using a pain scale, patient and physician global ratings, and patient-reported change in arthritis symptoms. Some of the 10,051 subjects who enrolled never received study drugs. Only the data on the 9323 who received a study drug were analyzed. Of those, 4635 received meloxicam and 4688 received diclofenac. The two groups had no differences in baseline demographic or arthritis variables. Overall, there were fewer adverse events in the group receiving meloxicam (27%) than in the diclofenac group (32%). Dyspepsia, nausea, vomiting, abdominal pain, and diarrhea were all less frequent in the meloxicam group. There were fewer withdrawals in the meloxicam (5.48%) than in the diclofenac group (7.96%). Serious adverse drug reactions that were ascribed to the study drug occurred in 13 meloxicam-treated subjects and in 24 of those receiving diclofenac. Though too infrequent to be statistically significant, hospitalization for GI adverse events occurred in only three subjects in the meloxicam group resulting in a total of five hospital days. The diclofenac group had 10 subjects hospitalized for a total of 121 days for GI adverse events. In the meloxicam group, there were five subjects with serious GI adverse events: one with endoscopically documented gastric ulcer, one with duodenal ulcer, one with a reported episode of hematemesis, and two with episodes of melena but no source of bleeding found by endoscopy. The diclofenac group, by comparison, had seven subjects with serious GI adverse events: two subjects with perforated duodenal ulcers, one with a bleeding duodenal ulcer, three with endoscopically documented gastric ulcers (one with bleeding), and one with an episode of melena without an identified source of bleeding. GI adverse events were the only category of events that had a statistically significant difference in incidence (13.3% for meloxicam vs 18.7% for diclofenac).

Diclofenac was more efficacious in relieving arthritis pain than meloxicam and there were more dropouts due to lack of efficacy in the meloxicam (80) than in the diclofenac group (49).

COMMENT BY JERRY M. GREENE, MD

It appears likely that highly selective COX-2 inhibitors will become available in the United States in the not too distant future. The results of this European study of a moderately selective COX-2 inhibiting NSAID, meloxicam, are encouraging and suggest that there may be some significant safety advantage conferred by avoiding inhibition of the "housekeeping" isoenzyme COX-1. Meloxicam was less efficacious and one wonders if an increase in dosage of meloxicam would have made its efficacy more nearly comparable to diclofenac. If so, would it have been at the cost of an increased number of adverse events?

Although the relative number of GI adverse events in the two groups in Hawkey et al's study only differed by about 20%, the severity of the events tended to be less in the meloxicam group, and hospital use was substantially less as a result. It will be interesting to see how the next generation of NSAIDs, which are highly selective in their inhibition of COX-2, will do in comparision to this mellifluously named NSAID, meloxicam. If their use can reduce the incidence of NSAID associated ulcers, bleeding, and perforation, while still providing symptomatic relief for arthritis sufferers, it will be sweet news indeed. ❖

When meloxicam and diclofenac were compared, which NSAID had fewer adverse events?

a. Meloxicam
b. Diclofenac

Regular Doctor Helps Glycemic Control

ABSTRACT & COMMENTARY

Synopsis: *A regular health care provider for diabetes can improve some of the more generally recognizable criteria for intensive care in glycemic control.*

Source: O'Connor PJ, et al. *J Fam Pract* 1998;47:290-297.

Evidence has suggested that intensive diabetic care is associated with better clinical outcomes. Therefore, O'Connor and associates looked at 144 health maintenance organization (HMO) members who did not have a regular health care provider vs. 1243 who did. By first adjusting for age, race, gender, co-morbidity, years of education, duration of diabetes, and type of HMO clinic, O'Connor et al then looked at some specific parameters that would suggest whether a patient was being more intensively controlled.

They found a P value of significance for the following: a special diet for diabetes, regularly monitoring their own glucose levels at home, greater frequency of glycosylated hemoglobin, more foot examinations, recommended cholesterol checks and preventive examinations.

There were no differences for dental checkups or endocrine referrals. This study was conducted in Minnesota, known as a hot bed of HMOs through a large HMO with 700,000 members.

O'Connor et al identified the patients by looking at the diabetic drugs the patients were placed on and then performed a 16-page, 61-item diabetes survey on all of the patients. By correcting for the parameters listed above, they were then able to statistically analyze whether those parameters generally thought to be an indicator of good glycemic control were being differentiated by whether a person had a regular provider. They found in multiple areas, including diet, regular monitoring of glucose level, hemoglobin A1C testing, foot examinations, and cholesterol checks, that having a regular primary care practitioner increased the chance that a diabetic would have those tests.

Having a regular provider of diabetes care can improve parameters generally thought to be correlated with intensive diabetes care.

COMMENT BY LEN SCARPINATO, DO

Ever since the release of the DCCT trial, tightly controlling diabetes has been the mantra among diabetic educators. One of the more difficult aspects of this has been the more frequent office visits, tighter control, and more frequent blood testing that must occur in patients. As a primary care physician, I have always suspected that patients did better if they had a primary care provider. What O'Connor et al have done for me in this specific area of diabetes has proven this fact.

HMOs and other organizations are looking for methods to delineate tighter control of diabetes and, therefore, reduce complications of diabetes. When a group of physicians or an organization can go to an HMO and say that their patients are more likely to spend time at a regular provider's office rather than urgent care, O'Connor et al have now shown us that those patients will likely have tighter diabetic control. Alternatively, we may see HMOs and other organizations now putting "money where their mouth is" and supporting physicians and organizations where continuity of care is emphasized with their patients.

I, for one, have been supportive of this over the years and believe it is the true and correct way to go. I will continue to re-enforce with my patients that having a regular provider of diabetes care will enhance their care and better control their diabetes. ❖

In which of the following areas did O'Connor et al find a P value of significance?

a. A patient who regularly monitors their own glucose levels at home
b. More foot examinations
c. A special diet for diabetes
d. All of the above

Persistent Disability Associated with Ankle Sprains in Athletes

ABSTRACT & COMMENTARY

Synopsis: *It is important to identify the syndesmotic ligament injury and anticipate that a substantial proportion of even athletically fit individuals will not recover quickly from what appears to be a "simple" ankle sprain.*

Source: Gerber JP, et al. *Foot Ankle Int* 1998;19(10):653-660.

A prospective observational study was carried out on all the cadets at the United States Military

Academy who presented with ankle injuries during a two-month period. A standardized treatment program for ankle sprains was performed, and all of the injured ankles were reevaluated at six weeks and six months, subjectively, by physical examination, and through functional testing. There were 104 injuries over this two-month time span, with 96 sprains, seven fractures, and one contusion. Sixteen (17%) of the ankle sprains were syndesmosis injuries—injuries of the anterior tibiofibular ligament caused by an external rotation force. This is a higher incidence than reported by others.

While 95% of the injured cadets had returned to sports activities by six weeks, 55% of them reported loss of function and the presence of intermittent pain. Twenty-three percent had some persistent functional impairment as well. Even at six months, while all had returned to full activity, 40% had residual symptoms. A surprisingly high percentage of those with residual symptoms were in the syndesmosis sprain group.

COMMENT BY JAMES D. HECKMAN, MD

The simple ankle sprain may not always be so simple. This group of extremely fit, highly competitive individuals at the United States Military Academy, despite treatment in a rigorously controlled environment, frequently had persistent symptoms as long as six months after the injury. Gerber and associates identify the syndesmotic sprain as a particular cause of prolonged disability. We usually think of the lateral ligament complex (anterior talofibular and fibulocalcaneal ligaments) as being the ligaments susceptible to injury at the time of a sprain. Often, the syndesmosis is overlooked. Injury to the syndesmosis can be easily identified by careful palpation over the area of the anterior tibiofibular ligament, performing an external rotation stress of the talus in the ankle mortise that will put tension on this ligament,[1] and by performing the "squeeze test."[2] This review indicates even a mild syndesmotic sprain may continue to be symptomatic for up to six months and suggests that more aggressive early treatment, perhaps even with the temporary use of an air cast or fracture boot, might facilitate the healing of these syndesmotic injuries. For these injuries, I do not hesitate to provide an initial period of cast immobilization for 10 days to two weeks to facilitate early soft tissue healing.

The study shows that it is important to identify the syndesmotic ligament injury and anticipate that a substantial proportion of even athletically fit individuals will not recover quickly from what appears to be a "simple" ankle sprain. (*Dr. Heckman is Professor and Chairman, Department of Orthopaedics, University of Texas Health Science Center, San Antonio, TX.*) ❖

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Not all "simple" ankle sprains heal quickly. This is particularly true of injury to which ligament?

a. Deltoid
b. Anterior talofibular
c. Calcaneofibular
d. Anterior tibiofibular

Pharmacology Update

Lyme Disease Vaccine—LYMErix (SmithKline Beecham)

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

Lyme disease is the most common vector-borne infection in the United States and the incidence is increasing, with more than 16,000 cases annually.[1] The disease, caused by the tick-borne spirochete *Borrelia burgdorferi*, can be found throughout the nation but is particularly concentrated in rural and wooded areas in the Northeast, upper Midwest, and Pacific Northwest.

Work has been ongoing for years to develop a vaccine for this potentially debilitating, multisystem disease and, in December 1998, SmithKline Beecham received approval from the FDA to market the first Lyme disease vaccine (LYMErix). The vaccine contains an immunodominant outer surface protein (OspA) of *B. burgdorferi* produced by recombinant DNA technology and expressed by *E. coli*.

Indications

LYMErix is indicated for active immunization against Lyme disease in individuals 15-70 years of age. Safety and efficacy in children has not been established.

Dosage

Primary vaccination consist of 30 mcg/0.5 mL dose given intramuscularly at 0, 1, and 12 months. LYMErix is supplied as single-dose vials and prefilled syringes.

The efficacy for this vaccine is based on administration of the second and third doses several weeks prior to the onset of the Borrelia transmission season in the local geographic area.[2]

Patients previously infected may also benefit from the vaccine, as such infection may not confer protective

immunity.[2,3] However, LYMErix should not be administered to patients with treatment-resistant Lyme arthritis, since these patients are immune reactive to OspA.[2]

Potential Advantages

LYMErix is the first vaccine found to be safe and effective for the prevention of Lyme disease. Efficacy has been shown to be 50% in the first year (after 2 doses) and 78% in the second year (after 3 doses) as defined by clinical and serologic evidence of Lyme disease.[2,4] The incidence of disease was reduced from 0.77% to 0.39% the first year and from 1.27% to 0.27% the second year. The efficacy of preventing asymptomatic disease (defined as seroconversion with no clinical symptoms) was 83% the first year and 100% the second year. The incidence of asymptomatic seroconversion was reduced from 0.23% to 0.04% the first year and 0.27% to 0% the second year.[2]

Potential Disadvantages

The currently approved regimen requires one year to complete. After two doses, the vaccine provides modest protection of 50% (CI, 14-71%). The second year protection after the third dose increased to 78% (59-88%). SmithKline Beecham is studying several shortened regimens, including 0, 1, and 2 months, which may provide optimal protection,[5] but the FDA has not approved these regimens. The vaccine has not been approved by the FDA for use in ages younger than 15 years. The percent of reported cases of Lyme disease in this population is 23%.[1]

The most commonly reported side effects of LYMErix were injection site pain (22% vs 7% for placebo). Others included chills/rigors (2% vs 0.7%), fever (2.6% vs 1.6%), myalgia (4.8% vs 2.9%), and flu-like symptoms (2.5% vs 1.7%).[2]

The duration of immunity has not been established,[2] and longer-term studies will be needed to determine whether boosters are necessary and at what interval.

The vaccine may induce a false-positive serologic test for Lyme disease. If Lyme disease is suspected in a vaccinated patient due to a positive ELISA assay, a Western blot test should be performed.[2]

Comments

LYMErix is the first vaccine marketed against Lyme disease. The vaccine stimulates the production of antibodies against the OspA. *B. burgdorferi* express OspA while in the midgut of the tick and are generally undetectable when the spirochete is injected into the human host. The vaccine-induced human antibodies must be taken up by the tick during its blood meal and interact with the *B. burgdorferi* in the midgut of the tick to prevent transmission of the spirochete to the human host.

The efficacy of the vaccine was determined in a multicenter, double-blind, randomized, 20-month trial involving more than 10,000 subjects who lived in endemic areas in the United States.[4] Study sites were in Connecticut, Maine, Massachusetts, Rhode Island, Delaware, Maryland, New Jersey, New York, Pennsylvania, and Wisconsin. Since the vaccine does not prevent all cases of Lyme disease, individuals at risk of exposure must be encouraged to take standard preventive measures such has wearing long-sleeved shirts, pants, treating clothing with tick repellent, and checking for and removing ticks. In addition, the vaccine does not prevent other tick-borne infections such as babesiosis or ehrlichosis. LYMErix is about $50 per injection or about $150 per course.

Clinical Implications

Lyme disease is a multisystem inflammatory disease. It usually, but not always, begins with erythema migrans (including the "bull's-eye rash) and may be accompanied by flu-like symptoms. Weeks later, characteristics of early dissemination includes secondary skin lesions, neurologic involvement (e.g., meningitis, facial palsy), cardiac involvement (e.g., atrioventricular block), or migratory musculoskeletal pain may develop. Late dissemination includes episodes of arthritis and neurologic or psychiatric symptoms.[1,6,7] The disease is frequently misdiagnosed, overdiagnosed, and overtreated, but it is also under reported and is a public health concern in endemic area.[8,9] Lyme disease prevention, detection, and treatment are associated with substantial health care resources, and the disease can result in long-term morbidity.[6,8,10]

In the Northeast and Midwest the main vector is the deer tick (Ixodes scapularis) while in the west the vector is the western black-legged tick (Ixodes pacificus). Most cases result from bites by the nymphs which most commonly occur in late spring-summer, although infection is possible at any time of the year. The high-risk season may vary annually according to local weather conditions. The incidence varies from state to state but most cases are reported in the Northeast and upper Midwest. The highest reported cases (per 100,000 population) in 1996 occurred in Connecticut (94.8), Rhode Island (53.9), New York (29.2), Pennsylvania (23.3), Delaware (23.9), and New Jersey (27.4). Moderate incidence in states such as Oklahoma, Kansas, Missouri, and Oregon (0.52-1.40 cases per 100,000) and low in California (0.3 cases per 100,000).[1,2] The vaccine offers another strategy to prevent Lyme disease along with personal protection, insecticides, and wildlife management. Individuals mostly likely to benefit from vaccination are those who live,

By Louis Kuritzky, MD

work, or spend their leisure time in endemic areas with frequent and prolonged exposure to wooded or grassy areas infested with Ixodes ticks. Widespread and routine use of the vaccine is not indicated. ❖

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Which is true about LYMErix:

a. The duration of immunity has not been established.
b. It is approved for use in adults and children.
c. The vaccine is 95% effective after the third dose.
d. The vaccine prevents tick bites.

Oral or Parenteral Therapy for B_{12} Deficiency

Vitamin b_{12} deficiency is most commonly treated with parenteral vitamin B_{12}. A survey of 1991 Minnesota clinicians reported that most (90%) believe intramuscular injections are necessary to treat pernicious anemia; indeed, 95% of physicians surveyed did not know that oral preparations for pernicious anemia are effective or available. In 1998, a controlled trial indicated that oral cobalamin is at least as effective as parenteral therapy, and in other nations such as Sweden, such therapy has been widely used.

Although every medical student learns about the classical system of B_{12} absorption that requires intrinsic factor, other transport systems are functional. When given in large oral doses (300-100,000 mcg), about 1% of B_{12} is absorbed, substantially above the daily requirement of 1-2.5 mcg. Indeed, a comparison trial of oral B_{12} 1000 mcg bid vs. IM B_{12} on days 1, 3, 7, 10, 30, 60, and 90, showed that both regimens were comparable as far as hematologic and neurologic responses were concerned. The serum concentrations attained with the oral regimen were actually more than three times higher than the parenteral regimen.

Given that parenteral B_{12} is painful and may be associated with noncompliance due to failure to obtain the injection, and that contrary to propagated opinion, oral B_{12} is efficacious in pernicious anemia, Elia suggests an increased opportunity for the use of oral B_{12}. Since mild cobalamin deficiency affects up to 15% of senior citizens, much restorative opportunity is at hand. ❖

Elia M. Lancet 1998;352:1721-1722.

Effect of Tragus Clips on Gastric Peristalsis: A Pilot Study

Clinical observations as early as 1977 noted that needles placed in the ear tragus assisted in weight loss by producing early satiety. Barium swallow studies have shown delay in gastric emptying subsequent to needle placement. In theory, vagus nerve stimulation is responsible for these effects. Acupuncture points have shown effects on gastric motility and pyloric sphincter pressure.

Ear clips are earring-like devices intended to clamp onto the tragus without cutaneous puncture. This trial (n = 11) measured the effect of tragal ear clips on the duration of gastric peristalsis in normal healthy volunteers. Peristaltic wave time was defined from the first observable gastric contraction to the end of the wave at the pylorus, as measured with dilute barium sulfate.

Within minutes of application of the ear clips, peristalsis was reduced by about one-third. One patient had complete cessation of peristalsis, which only resumed after clip cessation. Subjects underwent four cycles of ear clip application and removal seven minutes later, with consistent reductions in gastric peristalsis during each application. Choy and Eidenschenk conclude that reduction in gastric emptying induced by tragus ear clips results in a sense of fullness, hence, early satiety. This technique may prove valuable in weight control therapy. ❖

Choy DS, Eidenschenk E. J Altern Complement Med 1998;4(4):399-403.

In Future Issues:

Nephrolithiasis and the Risk of Hypertension in Women

A National Survey of End-of-Life Care for Critically Ill Patients

Fish Oil and Glycemic Control in Diabetes: A Meta-Analysis

Fish oil supplementation has demonstrated beneficial effects on hypertriglyceridemia and in the prevention of cardiovascular disease. Diabetes, both Type 1 and Type 2, is disproportionately associated with both factors. Friedberg and associates performed a meta-analysis to evaluate the relationship of fish oil supplementation to glycemic control. Main outcome measures included fasting glucose, hemoglobin A-1-C, triglycerides, cholesterol, HDL, and LDL. The meta-analysis included 26 trials.

Although fish oil supplementation did significantly increase fasting blood glucose among Type 2 diabetics and reduced it in Type 1 diabetics, neither impact was sufficient to have an effect on hemoglobin A-1-C. Triglycerides were reduced by more than 25% in both Type 1 and Type 2 diabetes. The dose of fish oil used contained 1.8 g of eicosapentaenoic acid and 1.2 g of docosahexaenoic acid.

Cardiovascular deaths remain the most prominent cause of demise for diabetic patients. Reduction of triglycerides in diabetic patients by fish oil supplementation may have a favorable effect on cardiovascular end points. ❖

Friedberg CE, et al. Diabetes Care 1998;21(4):494-500.