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Does Physical Exhaustion Cause Heart Disease?

ABSTRACT & COMMENTARY

Synopsis: *The results of a prospective observational study confirm that a frequent sense of exhaustion appeared to be independently associated with increased risk of CHD mortality in men.*

Source: Cole SR, et al. *Am J Cardiol* 1999;84:1401-1405.

Vital exhaustion, a combination of fatigue, lack of energy, feelings of hopelessness, loss of libido, and increased irritability, has been suggested to be a significant risk indicator for the development of coronary artery heart disease (CAD).[1] The age-adjusted relative risk of developing an acute myocardial infarction in patients afflicted with vital exhaustion has been reported[2,3] to be 2.3 ($P > 0.001$). However, it has been unclear as to whether or not an association existed between vital exhaustion and the development of CAD in those individuals independent of other potentially significant factors such as associated depression, sleep disturbances, and/or physical inactivity.

Cole and associates from the Division of Preventive Medicine of the Brigham and Women's Hospital and the Harvard Medical School evaluated the degree of vital exhaustion among 5053 male college alumni who were free of cardiovascular disease, cancer, and chronic pulmonary obstructive disease on a health survey in 1980. The subjects were asked, "How often do you experience a sense of exhaustion (except after exercise)?" During a 12-year follow-up period, 15 men died of a variety of illnesses and 25% of these were found to have died of CAD. After adjustment for age, body mass index, smoking status, and history of physician-diagnosed diabetes and/or hypertension, a frequent sense of exhaustion was associated with a two-fold increase in coronary heart disease (CHD) mortality. The significance became somewhat blunted when adjustments were made for insomnia, sleep duration, use of sleeping pills and/or tranquilizers, physical inactivity, history of physician-diagnosed depression, and the degree of regular alcohol intake.

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INSIDE

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

A previous prospective study has demonstrated that vital exhaustion was associated with an age-adjusted relative risk of 2.3 for myocardial infarction.[2,3] A second prospective study of 3365 men followed over a period of 9.5 years revealed that those individuals who reported that "at the end of the day I am completely exhausted mentally and physically" were at risk of cardiac death in a time-dependent fashion with risk ratios of CHD death of 8.96, 6.33, 4.47, and 3.16 for the first 10, 20, 30, and 40 months respectively of the study ($P > 0.05$ for each risk ratio).[4]

The results of the prospective observational study reported by Cole et al confirm that a frequent sense of exhaustion appeared to be independently associated with increased risk of CHD mortality in men. Although several previous studies have suggested that sleep complaints have been associated with increased risk of myocardial infarction and CHD mortality,[6,7] adjustment for insomnia did not appear to attenuate the association between exhaustion and CHD mortality. In addition, Cole et al's findings suggested there was no association between exhaustion and CHF mortality in patients regardless of whether they were depressed or not.

It has been hypothesized that a sense of exhaustion may effect CHD end points by decreasing heart rate variability, increasing platelet aggregability, and/or by altering health behaviors. Altered heart rate variability has been implicated as a potential pathway through which anxiety, social psychological stresses, and/or depression may effect the incidence of symptomatic CHD however, it must be clearly recognized that the available data regarding the association between exhaustion and heart rate variability is not conclusive at this time. There has been some suggestion that fibrinolytic capacity is reduced in exhausted patients, but there has been no hard data on the association between exhaustion and fibrinolytic activity or between exhaustion and CHD end points. Finally, it should be recognized that a sense of exhaustion may actually be a sign of subclinical heart disease and may be present before the onset of cardiac symptomatology occurs.

It would seem that regardless of whether a sense of exhaustion causes CHD or simply suggests that subclinical disease of a silent nature is present, the significant findings on this prospective study lend support to previously reported studies suggesting that there is an increased risk of CHD in patients who complain of pervasive exhaustion. Further, well controlled studies in both men and women are certainly indicated. It goes without saying that it is incumbent upon physicians to properly counsel their patients to acquire an adequate amount of sleep and, if they continue to feel exhausted despite having adequate sleep, a complete cardiac workup would be in order to rule out the presence of silent ischemic heart disease and/or the presence of incipient congestive heart failure. ❖

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Classic Teaching About Intussusception in Adults Needs Revision

ABSTRACT & COMMENTARY

Synopsis: *Intussusception can be encountered as an incidental finding at CT and MR imaging of adults. Contrary to conclusions drawn from surgical data, the majority of such intussusceptions in adults are not due to a mass acting as a lead point.*

Source: Warshauer DM, et al. *Radiology* 1999;212:853-860.

For years, standard radiologic dictum has stated that no cause for intussusception is generally found in infants—allowing nonsurgical therapies such as a fluoroscopically monitored enema to be used as definitive therapy in many cases. In contrast, intussusception in adults has been said to frequently have a lead point, thus often requiring surgical exploration for definitive evaluation and treatment. Modern cross-sectional imaging techniques are demonstrating the characteristic findings of intussusception (e.g., a bowel-within-bowel configuration, typically with mesenteric fat included within it) with increasing frequency, even in patients in whom that diagnosis is unsuspected and seemingly dissonant with clinical findings.

To assess the clinical significance of intussusception detected at computed tomography (CT) or magnetic resonance (MR) imaging in adults, Warshauer and colleagues from the University of North Carolina School of Medicine retrospectively reviewed the clinical records and CT and MR images of 33 patients who had one or more intussusceptions shown on those images. The 33 patients (24 male, 9 female) ranged in age from 18 to 84 years (median age, 41 years). Twenty-nine patients had abdominal symptoms at the time they were imaged, including 24 with abdominal pain. The intussusception was enteroenteric in 29 patients and involved the colon in four others. Only 10 (30%) patients, including all four with intussusception involving the colon, were shown to have a neoplastic lead point; seven of the lead points were malignant, and three were benign. In nearly half (48%) of the patients in whom no lead point was identified, the intussusception was considered to be idiopathic.

Warshauer et al found some statistically significant differences in the imaging appearances of enteric intussusceptions: those without a lead point were shorter (median length, 4 cm vs 10.8 cm) and smaller (median diameter, 3 cm vs 4 cm), and they less often caused obstruction (4.3% vs 50%). Warshauer et al suggest that not all intussusceptions discovered at imaging require further work-up—particularly those in younger patients with a transient, small, enteroenteric intussusception that does not obstruct the bowel.

COMMENT BY DAVID M. PANICEK, MD

This study was reportedly undertaken in an attempt to reconcile a discrepancy between classic radiologic teachings and Warshauer et al's clinical experience with intussusception. My own experience has been similar: none of the radiologic tests that I recommended for several patients with unsuspected intussusceptions shown on CT in adult patients in recent years has demonstrated a mass that could have been a lead point—even though virtually all of the patients in my practice have cancer, placing some of them at risk for metastasis to bowel.

The findings of this study are an excellent example of how conclusions can be markedly affected by the manner in which the underlying data are collected. When examined from the perspective of findings at surgery, the majority of cases of adult intussusceptions have been found to be due to a lead point. However, cross-sectional imaging now allows us to discover a larger number of intussusceptions, including those that apparently occur as a transient phenomenon and that are not associated with a mass acting as a lead point. Such intussusceptions may produce intermittent symptoms or none at all. As a result of this new perspective, it is no longer necessary to recommend intensive work-up of every intussusception that is incidentally demonstrated at CT or MR imaging in an asymptomatic patient. (*Dr. Panicek is Professor of Radiology, Department of Radiology, Memorial-Sloan Kettering Cancer Center, New York, NY.*) ❖

Gabapentin vs. Propranolol for Essential Tremor

ABSTRACT & COMMENTARY

Synopsis: *A statistically significant treatment effect was shown for gabapentin and propranolol compared to placebo with regard to tremor, motor task performance, functional disability, and subjective assessment by the patient.*

Source: Gironell A, et al. *Arch Neurol* 1999;56:475-480.

Essential tremor (et), one of the most common movement disorders, is characterized by tremor dur-

ing the maintenance of posture and active movement. Although ET is commonly perceived to be benign, some patients suffer significant disability, and a larger number suffer substantial embarrassment.

The efficacy of primidone and B-adrenergic antagonists (e.g., propanolol) has been demonstrated, but many patients fail to respond, suffer intolerable side effects, or have contraindications to these medications. Previously, an open-label trial of gabapentin (Neurontin) suggested efficacy for ET,[1] but a double-blind, placebo-controlled study of adjunctive gabapentin in 20 patients found no improvement at a dose of 1800 mg/d compared to placebo.[2] The current study was undertaken in the neurology clinic in Barcelona, Spain. Sixteen patients with moderate to severe bilateral ET and no other neurological disorders were enrolled. Exclusion criteria included cardiac failure, asthma, peripheral vascular disease, diabetes mellitus, and active treatment with tremor-inducing or alleviating drugs.

After a two-week washout period, participants were given gabapentin 400 mg tid or propranolol 40 tid for two weeks in a double-blind, placebo-controlled, crossover trial. A one-week washout period occurred between treatments. Assessment measures included the Tremor Clinical Rating Scale (TCRS), accelerometric (neurophysiological) recordings done on the index finger of the most affected hand, and a 25-item self-reported disability scale. The TCRS includes four examinations rated on a 0-4 scale: 1) tremor of the hands, legs, head, and trunk; 2) motor task performance; 3) functional disability; and 4) subjective assessment by the patient. Analysis of variance (ANOVA) was used to test the effect of medication on tremor. Paired comparisons were analyzed by the test after control for inflation type I errors.

A statistically significant treatment effect was shown for gabapentin and propranolol compared to placebo with regard to tremor, motor task performance, functional disability, and subjective assessment by the patient on the TCRS. No statistical differences were found between gabapentin, propranolol, and placebo in terms of the accelerometric (neurophysiological) recordings; baseline variability may have been too great to see a treatment effect. In terms of the self-reported disability scale, neither drug was statistically better than placebo. All patients completed the study; no serious adverse events occurred. Limitations included a small sample size, fixed dosing (which limited meaningful titration), performing accelerometric recordings only on the most affected hand (potential bias, rather than an average of both hands), and a single study site (which limits generalization of the results).

COMMENT BY DONALD M. HILTY, MD

The origin of ET is unknown. A central mechanism involving the inferior olive is incriminated by most experimental data,[3] though some modulation may occur from the cerebellum, thalamus, motor cortex, and brainstem nuclei.[4] Gabapentin may work by increasing gamma-aminobutyric acid (GABA) levels and reducing intracortical excitability. Gabapentin is extremely well tolerated, even in geriatric patients.[5] A large, multicenter trial is indicated to further study gabapentin for ET. (*Dr. Hilty is Assistant Professor of Clinical Psychiatry, University of California, Davis, Sacramento, CA.*) ❖

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Another Promising New Antistroke Treatment

ABSTRACT & COMMENTARY

Synopsis: *These data from the PROACT study suggest that intra-arterial r-proUK may extend this therapeutic window for acute ischemic stroke to six hours.*

Source: Furlan A, et al. *JAMA* 1999;282:2003-2011.

Thrombolysis with intravenous tissue plasminogen activator (tPA) has been shown to be beneficial when given within three hours of acute ischemic stroke. These data from the PROACT study suggest that intra-arterial (IA) recombinant prourokinase (r-proUK) may extend this therapeutic window to six hours.

A total of 180 patients were randomized in a ratio of 2:1 to receive up to 9 mg of IA r-proUK plus heparin (n = 121) or heparin only (n = 59). In the primary analysis, 40% of r-proUK patients and 25% of control patients had a modified Rankin score of 2 or less (P = 0.04). This was a 58% relative benefit. Recanalization rates were 66% for the r-proUK group and 18% for the control group (P < 0.001). Other secondary outcome measures at 90 days, such as Barthel Index of 90 or more or NIH Stroke Scale of 1 or less showed insignificant trends toward benefit. The overall hemorrhage rate was 35% with r-proUK compared to 13% in controls, while

symptomatic hemorrhage occurred in 10% and 2%, respectively. There were no differences in mortality.

COMMENT BY ALAN Z. SEGAL, MD

Although total hemorrhage rates were high for r-proUK (often small and seen on a mandatory post-procedure CT scan), the symptomatic rate was only 10%. This is not enormously higher than in the NINDS-tPA trial (6.3%). Furthermore, the r-proUK patients were treated later and had larger strokes, both factors known to increase hemorrhage risk.

IA thrombolysis should be strongly considered for patients presenting with MCA occlusion within 3-6 hours of symptom onset. IA therapy for basilar artery occlusion might be considered up to 12 hours post-stroke. In the 0- to 3-hour time window, IV tPA remains the standard of care. However, in centers where it is available, combination IV followed by IA therapy should be considered.

r-proUK is not currently FDA approved. Current options for IA therapy include nonrecombinant urokinase (which is currently out of production) or tPA (which may be given in IA doses of approximately 20-30 mg). (*Dr. Segal is Assistant Professor, Department of Neurology, Weill-Cornell Medical College, Attending Neurologist, New York Hospital.*) ❖

Venlafaxine for Diabetic Neuropathy

ABSTRACT & COMMENTARY

Synopsis: *The current series of cases suggest that extended release venlafaxine (Effexor XR) may be useful in the treatment of of diabetic neuropathy.*

Source: Davis JL, Smith RL. *Diabetes Care* 1999;22(11): 1909-1910.

Despite many advances in the treatment of diabetes mellitus, diabetic neuropathy (DN) remains a common clinical dilemma. Even when maintaining tight glycemic control, patients may develop DN, which can be difficult to treat. Pharmacotherapy for DN involves many different types of agents, including aldose reductase inhibitors, mexiletine, capsaicin, gabapentin, carbamazepine, and tricyclic antidepressants (TCAs). However, in many cases these medications either fail to provide adequate relief or are difficult to tolerate. The current series of cases suggest that extended release venlafaxine (Effexor XR) may be useful in the treatment of DN.

The first case involved a 41-year-old man who was diagnosed with diabetes after presenting with mild nocturia. He was found to have blood glucose levels of approximately 200 mg/dL. Approximately seven months after treatment with dietary modification and glipizide 10 mg/d, he developed severe burning paresthesia around the mid-tibial region, necessitating that he not wear shoes. He experienced no relief from acetaminophen, codeine, or amitriptyline. The patient was started on venlafaxine extended release capsules at 75 mg/d and experienced 95% relief within five days. The pain recurred five days after discontinuing venlafaxine and remitted once again approximately three days after restarting the drug.

Due to the remarkable response shown in this patient, 10 additional patients (age 35-71) were initiated on venlafaxine 37.5-75 mg/d. The duration of diabetes for this group varied from 2-25 years. All patients had been treated with oral hypoglycemics alone or in combination with insulin. All patients, who had failed previous trials of medications such as TCAs, experienced approximately 75-100% reduction in pain within 3-14 days after the initiation of venlafaxine. Extended release venlafaxine was well tolerated by all subjects.

COMMENT BY MICHAEL F. BARBER, PharmD

The current article suggests that venlafaxine extended release capsules may be effective and well tolerated in the treatment of DN. Since this was a non-randomized study, a placebo response cannot be ruled out. However, the reported results were striking, especially since the participants had failed previous trials of other agents. Venlafaxine is an antidepressant that inhibits the reuptake of serotonin, norepinephrine, and, to some extent, dopamine, in a dose-dependent manner. Tricyclic antidepressants also inhibit the reuptake of serotonin and norepinephrine, but tend to have more side effects because of additional effects on alpha adrenergic, muscarinic, and histaminic receptors. Davis and Smith hypothesized that the patient's mixed neuotransmitter profile is associated with greater efficacy in treating DN compared to prior studies with fluoxetine, which is more selective for serotonin reuptake. However, in the relatively modest doses used in this series, the primary effect of venlafaxine would be inhibition of the reuptake of serotonin. As such, there may be a more complex reason for the differences in response between venlafaxine and fluoxetine if such a difference is indeed demonstrated in head-to-head randomized studies. Venlafaxine is usually well tolerated, particularly when the

extended release capsules are used. One of the more concerning side effects of venlafaxine is an increase in blood pressure. This effect is dose-dependent, with clinically important blood pressure increases usually only taking places in doses of 225 mg/d or higher.

In conclusion, while venlafaxine may be effective in the treatment of DN, controlled trials are required before venlafaxine can be considered as a front-line agent. However, venlafaxine should be considered when other agents are unsuccessful in the treatment of DN. (*Dr. Barber is Assistant Professor of Clinical Sciences and Administration, University of Houston College of Pharmacy, Houston, Texas.*) ❖

Pharmacology Update

Ciclopirox Topical Solution 8% (Penlac Nail Lacquer)

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

The fda has approved ciclopirox, a topical broad-spectrum antifungal agent, for the treatment of fungal infections of the fingernails and toenails. Ciclopirox is formulated in a 8% topical solution and will be marketed as Penlac Nail Lacquer by Dermik. It is manufactured by Aventis in Germany where it is already available. The vehicle contains volatile (flammable) solvents such as isopropyl alcohol and ethyl acetate that vaporize after application. Daily application results in a build up on the nail which must be removed on a weekly basis. Ciclopirox has also been marketed worldwide for years in cream, lotion, and gel formulations.

Indications

Ciclopirox topical solution is approved as topical treatment of mild to moderate onchomycosis of fingernails and toenails without lunular involvement, due to *Trichophyton rubrum*. Treatment should be a component of a comprehensive management program that includes removal of the unattached, infected nails as frequently as monthly by a trained health care professional.[1]

Dosage

Ciclopirox should be applied once daily evenly over the entire affected nail plate. Application is preferable at bedtime or eight hours before washing. Where possible, the solution should be applied to the underside of the nail and to the skin beneath it.[1] Daily application should be applied over the previous coat. Layers should be removed with alcohol every seven days.

Potential Advantages

Bioavailability studies in human volunteers suggest that ciclopirox formulated as an 8% nail lacquer can penetrate the nail.[2] In vitro studies demonstrated penetration up to a depth of about 0.4 mm.[1] Efficacy with nail lacquers appears to be better than other topical therapy.[3] Microbiologic cure has been reported in the range of 29-36% after 48 weeks of therapy.[1]

Potential Disadvantages

Complete clear nail may not be achieved with ciclopirox nail lacquer even after 48 weeks of therapy along with the comprehensive nail care program which

includes weekly trimming of the nails by the patient and monthly removal of unattached nail by a professional.[1] Less than 12% of patients with oychomycosis of the great toenail achieve either a completely clear or almost clear toenail. Common side effects include rash-related side effects (periungual erythema and erythema of the proximal nail fold), 5%.[1]

Comments

Ciclopirox is a hydroxy-pyridone that is chemically distinct from the azoles or other antifungals. It has a broad spectrum of action including fungicidal activity against *T. rubrum*.[4] Ciclopirox has been available as a cream and solution for many years as a 1% strength. The 8% nail lacquer has been available in Europe and has now been introduced in the United States. The nail lacquer appears to improve nail penetration and is well tolerated. However, in patients with 20-65% involvement of the great toenail plate, complete cure was less than 10% and mycological cure ranged from 29% to 36% after 48 weeks based on intent-to-treat and last observation carried forward. Relapse rates have not been reported. There does not appear to be any published comparative trials with other topical or oral regimens. Dermik is expected to launch Penlac within the next few months.

Clinical Implications

Onychomycoses, or infections of the nail, are common, and can be caused by a number of organisms including dermatophytes, yeast, or molds. Dermatophytes with *T. rubrum* as the major pathogen are responsible for about 90-95% of the infections.[3] Pharmacologic treatment involves oral and topical routes.

Topical therapy, which has the advantage of few systemic side effects, is generally limited by diffusion of the drug through the horny layers of the nail which may be enhanced with lacquer formulations. Ciclopirox in a nail lacquer formulation is reported to enhance nail penetration, but its long duration of therapy may be problematic. Oral therapy with antifungals such as fluconazole, itraconazole, and terbinafine are more effective and involve shorter courses of therapy. For example, the cure rates for terbinafine (250 mg daily) range from 60% to 80% after three months of therapy and that of fluconazole (150-450 mg weekly) 77-86%.[3] A recent comparative study (n =137) suggested that terbinafine (250 mg for 12 weeks and evaluated at week 60) was more effective than fluconazole (150 mg weekly for 12 or 24 weeks).

Mycological cure was 89% vs. 51% and 49% and complete clinical cure was 67% vs. 21% and 32%.[5] As for topical therapy, it may be reasonable for less severe infections (e.g., involvement of < 30% of the nail).[3]

Combined topical and systemic therapy is also being evaluated. ❖

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CME Questions

13. Based on the current study, which of the following is true?
- a. Gabapentin is more effective than propranol for the treatment of essential tremor.
- b. Gabapentin is less effective than propranol for the treatment of essential tremor.
- c. Gabapentin and propranol are equally effective for the treatment of essential tremor.
- d. There is no effective treatment for essential tremor.

14. Published data supporting the use of venlafaxine in the treatment of diabetic neuropathy include:
- a. both case reports and double-blind studies.
- b. a single double-blind study.
- c. a case series only.

15. Intussusception in adult patients:
- a. is usually due to a lead point in the bowel.
- b. may often be a transient phenomenon.
- c. should be aggressively worked-up when shown at CT or MR imaging.
- d. usually involves the colon.

16. Which of the following statements is *not* true regarding ciclopirox topical solution (Penlac)?
- a. It must be applied daily.
- b. Unattached, infected nails do not need to be removed.
- c. Treatment may be needed for 48 weeks or more.
- d. Layers should be removed once a week.

By Louis Kuritzky, MD

Weight Loss Intervention on Antihypertensive Medication

The hot study was a prospective randomized trial in hypertensive patients to determine if achieving diastolic blood pressures of 90, 85, or 80 were differentially associated with outcomes. One subgroup in this study population (n = 112) was selected on the basis of BMI more than 27 and were randomized to weight loss intervention, or control, in addition to the same stepwise antihypertensive therapy that all subjects received. Weight reduction intervention consisted of counseling by a registered dietitian, advice about food selection, and a diet of restricted calories with decreased fat intake. There were periodic contacts at least every 3-6 months throughout the study. Those in the control group were told that weight loss should be achieved, but received no further input in that regard.

At the six-month point, the intervention group had lost more weight than the control (approximately 1.4 kg), but at the 30-month point, no difference was seen.

The mean number of medications needed to achieve goal diastolic blood pressure was lower at the six-month point (2.9 vs 3.5 medications) for the intervention group than the control group; furthermore, this difference in medication requirement remained significantly lower for the duration of the 30 month trial, despite the regained weight in the intervention group, and despite the fact that at the end of the trial, there was no significant difference in weight loss between the groups. Jones and colleagues are unable to explain the persistent beneficial effect on blood pressure by an initial weight loss, but encourage renewed enthusiasm for early weight loss as a tool to potentially reduce the number of medications needed for blood pressure control, thus enhancing compliance, and reducing expense. ❖

Jones DW, et al. Am J Hypertens 1999;12:1175-1180.

Urgent Colonoscopy

Although there have been case reports of successful evaluation and acute treatment of diverticular bleeding by urgent colonoscopy, there have been no studies to evaluate issues such as the complication or recurrent bleeding rate using this intervention. Urgent colonoscopy was defined as being performed 6-12 hours after hospitalization and within one hour of colonic sulfate purging (i.e., Golytely, Colyte). This report details experience from two separate studies.

In the first study (1986-1992), 17 of 73 diverticulosis patients with severe bleeding had diverticular hemorrhage as the etiology. In the second study (1994-1998), 10 of 48 patients had definite diverticular hemorrhage as the cause, 14 had presumptive diverticular hemmorhage, and 24 had incidental diverticulosis.

In the second study, all patients with definite diverticular hemorrhage received colonoscopic treatment, consisting of local epinephrine injection or local tamponade for actively bleeding vessels, and bipolar coagulation for nonbleeding visible vessels.

In the group treated medically without colonoscopic treatment (e.g., transfusions), bleeding, requiring hemicolectomy, did occur in six patients, of whom two sustained surgical complications. Endoscopic treatment did not result in any complications or recurrent bleeds, and none of the endoscopically treated patients required surgical intervention. Even during the long-term follow-up (18-49 months), only one patient, a patient with presumptive diverticular hemorrhage on warfarin, rebled. Based upon these data, Jensen and colleagues suggest using surgical intervention only for those patients with definite or presumptive diverticular hemorrhage in whom medical or colonoscopic treatment has failed or produced complications. ❖

Jensen DM, et al. N Engl J Med 2000;342:78-82.

Instability of Atherosclerotic Plaques

The major complications of atherosclerosis are apparently related to stability of atheromatous plaques, not just extent of atherosclerosis. Unstable angina, MI, stroke, and TIA have all been associated with irregular or ruptured plaques. Although local factors like sheer stress and plaque structure are felt to be important, systemic factors like autoimmunity and infection, resulting in plaque inflammation and hemorrhage, also appear to play a role.

One important issue evaluated in this study was the relationship between plaque-surface irregularity and MI in subjects of the European Carotid Surgery Trial (n = 3007) for persons with symptomatic carotid stenosis. Evaluations included comparisons of carotid angiograms (bilateral) and carotid pathology specimens for the subgroup which underwent carotid endarterectomy (n = 1671). There is no information in this trial about markers of infection or inflammation, such as CRP.

The risk of non-stroke vascular death (i.e., essentially coronary artery disease death) was significantly higher in persons with plaque surface irregularity (RR = 1.67). Additionally, persons with surface irregularity in one carotid were more likely to have the same in the contralateral artery. Jenson and colleagues comment that traditional risk factors (HTN, cholesterol, smoking, Diabetes) do not account for which persons will develop the demonstratedly higher risk irregular plaques. ❖

Rothwell PM, et al. Lancet 2000; 355:19-24.

In Future Issues: The DHEA Controversy