

# Clinical Digest

### **O**NCOLOGY

### Friends, Family, and IL-6

Good relationships with friends and family may help women with ovarian cancer beat the odds. Levels of interleukin-6 (IL-6), a proinflammatory cytokine closely linked to prognosis, rise in the later stages of ovarian cancer. But the stronger the patient's social network, the lower the levels of IL-6, according to results of a study conducted by researchers at the University of Iowa (UI) and UI Hospitals and Clinics, both in Iowa City; Hartford Hospital, Hartford, CT; and M. D. Anderson Cancer Center, Houston, TX.

In the study 61 women with International Federation of Gynecology and Obstetrics (FIGO) stage 3 or 4 cancer completed assessments of social support, distressed mood, and quality of life before therapeutic surgery. A subset of 36 women completed a survey about whether they felt their current relationships provided a sense of worth, belonging, intimacy, and being needed. The researchers drew samples of the patients' peripheral blood before the operation, and, for a subset of patients, assayed ascites samples. Fifty three women, who also were undergoing surgery for either a suspected ovarian malignancy or FIGO stage 1 or 2 cancer, served as a reference group for IL-6 values.

The patients with advanced-stage cancer showed elevated levels of IL-6 in the peripheral blood and in the ascitic fluid. After adjusting for age and cancer stage, social attachment was significantly related to IL-6 levels: Women who reported low social attachment had 1.7 times more IL-6 in the peripheral blood and 2.5 times more IL-6 in their ascitic fluid than did women

who reported high social attachment. Depression and anxiety were not related to peripheral IL-6 levels, though women who reported a history of depression had higher ascitic IL-6 levels. Poorer physical and functional well-being and greater fatigue also were associated with higher levels in the peripheral blood, beyond the effects of age and disease severity, with a similar trend in ascites.

In vitro studies have shown that IL-6 stimulates proliferation, attachment, and migration of ovarian tumor cells and, therefore, may play a role in metastasis, the researchers note. Elevated IL-6 levels have been linked to larger tumors, faster progression, reduced effectiveness of chemotherapy, poorer clinical disease status, relapse, and shorter survival. Significantly higher levels of IL-6 also have been found in people with chronic stress, posttraumatic stress disorder, and depression.

Source: Cancer. 2006;104:305-313.

#### PRIMARY CARE

## Macular Degeneration and Stroke

It has been suggested that similar pathogenic mechanisms exist between age-related macular degeneration (AMD) and stroke. Few studies, however, have examined the relationship directly, say researchers from the University of Melbourne, Victoria, Australia; University of Wisconsin, Madison; University of Sydney, Sydney, Australia; University of North Carolina, Chapel Hill; and Johns Hopkins University, Baltimore, MD. In order to clarify the risk, they conducted the Atherosclerosis Risk in Communities

Study, a prospective cohort study involving 10,405 patients living in Minnesota, Maryland, Mississippi, and North Carolina between the ages of 49 and 73 with no history of stroke or coronary heart disease.

Both AMD and stroke were relatively rare in the study group. Based on retinal photographs taken over a two-year span, the researchers found 498 early-stage and 10 late-stage cases of AMD. They also found that, over a 10-year period, 241 people had strokes.



People with early-stage AMD had a higher incidence of stroke than those without AMD (4.08% versus 2.14%, respectively). They also had a higher risk of stroke: after adjustment for stroke risk factors, the risk ratio was 1.87.

The overall incidence of AMD and stroke varied by ethnicity and geographic location. White patients in North Carolina and Maryland had the highest prevalence of AMD (5.6% and 5.4%, respectively) and black patients in Mississippi had the lowest prevalence (3.3%). At 3.75%, the incidence of stroke was highest in the black patients residing in Mississippi, compared with 1.82% in North Carolina, 1.92% in Minnesota, and 2.22% in Maryland.

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The association of early-stage AMD and stroke also varied by race and location. Among the patients with early-stage AMD, white patients in Minnesota and black patients in Mississippi had the highest risk of stroke. The researchers say they have no adequate explanation for the site-specific differences in the association between the two conditions.

Because of the limited number of study participants found to have latestage AMD, the authors do not speculate a correlation between late-stage AMD and stroke. But they do provide a few possible explanations for the association between early-stage AMD and stroke. First, they mention that atherosclerosis may have an effect on choroidal circulation or the Bruch membrane. Second, inflammation or microvascular disease may be a pathogenic mechanism in AMD development. And third, they make the point that genetic factors may contribute to both AMD and stroke, as both conditions have been associated with Alzheimer disease.

Source: Ann Intern Med. 2006;145:98-106.

#### **N**EURLOGY

### Rediagnosing "False" Essential Tremor

About one in three patients with tremor is misdiagnosed as having essential tremor (ET), according to results of a recent study.

The researchers, from the department of neurology at Columbia University, New York, NY, identified 71 patients who consecutively underwent a neurologic evaluation at the Neurological Institute (NI) of New York, NY between 2001 and 2005 with a preevaluation diagnosis of ET. Of those, only 45 (63%) had true ET.

The most common actual diagnosis was Parkinson disease (PD). Nearly one in four patients diagnosed falsely

with ET had either PD only or both ET and PD. The parkinsonian signs were often subtle, the researchers say, such as a slight unilateral decrease in arm swing or mild hypomimia. Their findings highlight the need for physicians to look out for these subtle signs, they note, as almost half of the 71 patients had been seen by more than one physician before their evaluation at the NI.

The second most common diagnosis among patients with false ET was dystonia. Although the researchers acknowledge that it's possible for a patient to have both ET and dystonia, they point out that all six patients with dystonia had nonrhythmic tremor restricted to the body region affected by dystonia.

Investigators identified several characteristics that call into question the diagnosis of ET, including unilateral arm tremor, isolated head tremor, tremor directionality, isolated thumb or leg tremor, and nonrhythmic tremor. While some of these might seem self-evident, the researchers say that the high proportion of misdiagnosed ET cases demonstrates that the characteristics "may not always be fully appreciated."

Source: Arch Neurol. 2006;63:1100-1104.

### INFECTIOUS DISEASE

## What Are the Atypical Presentations of Anthrax?

Inhalational anthrax disease may present with a broad spectrum of atypical symptoms, warn researchers from the VA Palo Alto Health Care System, Palo Alto, CA and Stanford University, Stanford, CA.

They evaluated all of the published case reports of anthrax in the medical literature from 1900 to 2005, excluding all cases in which the port of entry (either cutaneous, gastrointestinal, or inhalational) was known. They found

42 cases of atypical anthrax. In most of these cases, the researchers suspected the port of entry to be inhalational. Descriptions of typical inhalational anthrax usually include the symptoms of cough, dyspnea, and chest pain and the clinical finding of abnormal lung examination with pleural effusions or enlarged mediastinum. This wasn't the case, however, for most of the patients in this study.

Patients with atypical presentations that fell into the categories of primary nasopharyngeal or primary meningoencephalitis anthrax experienced less nausea and emesis than those with typical inhalational anthrax. Patients with primary nasopharyngeal involvement reported more nasal symptoms, such as rhinorrhea, nasal congestion, or epistaxis (67% versus 14%, respectively). And patients with primary meningoencephalitis were more likely to report nonheadache neurologic symptoms (88% versus 43%, respectively).

The mortality rate for patients with atypical anthrax did not differ from that of patients with typical inhalational anthrax. Patients with primary meningoencephalitis anthrax, however, had a 97% mortality rate, compared with the 100% mortality rate reported for patients with typical inhalational anthrax who develop meningoencephalitis.

The good news is that when the researchers applied a screening protocol, published in 2003, to the patients with atypical presentations, it correctly identified anthrax 91% of the time. This means that clinicians using a similar recent algorithm could recognize most anthrax cases—even the atypical ones. For the remaining percentage of patients, however, clinicians will need to pay close attention to other clues. Notably, the mortality rate in those patients not identified by the screening protocol was significantly lower than the rate in identified patients.

Source: Ann Emerg Med. 2006;48:200-211.