Aggressive ovarian cancer in patients frequently correlates with the presence of thrombocytosis and a poorer response to treatment, according to scientists at the Women's Cancer Research Institute at Cedars-Sinai Medical Center, Los Angeles, Calif. The findings may enable better selection of treatment approaches and development of more targeted modes of therapy.

Researchers reviewed the records of 183 patients with and without thrombocytosis who had undergone surgery for advanced ovarian cancer. Of 183 patients, 41 had thrombocytosis before surgery as well as higher CA-125 levels, higher-grade tumors, more advanced stage of disease, and a greater tendency of cancer to spread to the lymph nodes. Further, surgery removed most cancer in 87% of all patients; however, nearly half of patients with thrombocytosis had increased postoperative residual cancer, compared with only 4 patients without thrombocytosis who had postoperative residual cancer greater than 1 cm. Finally, women with ovarian cancer who also had thrombocytosis had survival times that were 15 months shorter than women who had ovarian cancer but who did not also have thrombocytosis.

Scientists anticipate that further research will investigate whether thrombocytosis is a reaction to a more aggressive ovarian cancer or whether thrombocytosis exacerbates the cancer.

Findings were presented at the annual meeting of the Society of Gynecologic Oncologists in March 2002.

Scientists have identified a gene that triggers death in leukemia cells, according to results of a study conducted by researchers at Dartmouth Medical School, Hanover, NH. The gene is activated by treatment with retinoic acid (RA), a vitamin A derivative used in cancer therapy.

All-trans-retinoic acid induces remission in patients with acute promyelocytic leukemia, a rare and lethal leukemia, by degrading an abnormal RA receptor created by the disease. Scientists found that the gene, ubiquitin-activating enzyme E1-like (UBE1L), mimics the retinoic acid response, triggering degradation of the abnormal receptor and inducing apoptosis in leukemia cells.

The report can be found in the March 12, 2002, issue of the *Proceedings of the National Academy of Sciences.*

Postmenopausal women who stop hormone replacement therapy do not appear to have accelerated bone loss but resume bone loss at a rate similar to women who never had the drugs, according to researchers at Wake Forest University School of Medicine, Winston-Salem, NC.

Results of the 4-year follow-up of 800 women who participated in the 3-year Postmenopausal Estrogen / Progestin Intervention study also indicate that while bone mass increased substantially during the first 3 years after women initiated hormone replacement therapy, there was little annual change in bone mass after that (−1.01% hip and −1.04% spine).

Researchers note that the follow-up indicates the consequences of remaining on estrogen or stopping estrogen after 3 years—critical information as sustained use of hormone replacement therapy over many years may increase a woman's risk of breast cancer.

The report can be found in the March 25, 2002, issue of *Archives of Internal Medicine.*

Study results strongly suggest the value of using stress tests (treadmill exercise tests) to detect heart disease in middle-aged men and women who do not present with symptoms of the disease, while a 20-year study follow-up indicated that patients with no history of heart disease who had irregularities or inconclusive results on stress tests had higher mortality rates. (Women with irregular or inconclusive results were 2.6 times more likely and men were twice as likely to die of cardiovascular disease as patients who had normal results.) Researchers therefore suggest that physicians give stress tests and subsequent aggressive risk-factor modification treatment to patients known to be at higher risk for heart disease, including people with high blood cholesterol levels or heart problems. The treadmill test—besides indicating how well the heart handles physical exertion—also indicates if there is a lack of blood supply through the arteries that go to the heart.

Researchers studied death rate and cause data for 3775 men between the ages of 30 and 79 years and 2001 women between the ages of 40 and 80 years who participated in the Lipid Research Clinics Prevalence Study conducted between 1972 and 1976. Participants underwent treadmill exercise tests at the beginning of the study and were followed for an average of 20 years.

Thirty percent of women with abnormal test results died during the follow-up period, compared with 22% who had inconclusive test results and 13% who had normal test results. In addition, women with abnormal and inconclusive test results were 2.4 and 2.6 times more likely to die from cardiovascular disease as those with normal test results, and 1.4 and 1.7 times more likely to die from any cause, respectively, adjusting for age and other known cardiac risk factors.

Ten percent of the men tested positive for cardiovascular disease. During the follow-up, 45% of men who had positive test results died, compared with 32% of men who had inconclusive test results and 13% of men who had normal test results.

Men aged 60 years and older who regularly used nonsteroidal anti-inflammatory drugs (NSAIDs) were half as likely to have prostate cancer over a 5-year follow-up as men who did not regularly use NSAIDs, according to a study by researchers at Mayo Clinic, Rochester, Minn. The likelihood of having prostate cancer was further decreased among men 70 years of age and older who regularly used NSAIDs. Scientists attribute the greater benefit in this population to the possibility of increased dosages to treat inflammatory conditions, such as arthritis, or because drugs have a cumulative effect over time. Previous studies have linked patient use of NSAIDs to lower levels of colon and breast cancer.

The cohort study involved 569 partici-

pants who were regular NSAID users—assumed to be following a program for preventing heart disease—more than three quarters of whom were taking aspirin alone.

Researchers note that study results are too preliminary to use as a basis for treatment recommendations.

The report can be found in the March 2002 issue of *Mayo Clinic Proceedings.*

Patients with heart disease who had abnormalities during a psychologic stress test were three times more likely to die within 5 years of the study's completion as their counterparts who had no abnormalities, according to cardiologists at the University of Florida Health Science Center. Researchers note that the magnitude of difference is similar to that posed by any other risk factor for heart disease, such as cigarette smoking.

Previous study results linked mental stress and psychologic factors, such as anger, to adverse cardiovascular-related events, including increased risk of myocardial infarction. The current study is the first to single out an independent association between mental stress and cardiovascular disease–related death.

Scientists evaluated data for 196 patients with coronary artery disease who participated in the Psychophysiological Investigations of Myocardial Ischemia study. Radionuclide angiograms given at baseline indicated that all patients had reduced blood flow to the heart during physical exercise. Patients received a second angiogram during a psychologic stress test that required them to speak for 5 minutes about a hypothetical, stressful situation. One fifth of the patients had abnormalities on the angiograms; most were women, and most were likely to have diabetes.

Of 17 patients who died within 5 years of the study's completion, nearly half had new or worsened abnormalities on the angiogram given during the speech test, compared with only 19% of the survivors. Scientists note that patients with an acute stressor may have increases in heart rate and blood pressure level, increasing the heart's need for oxygen, yet less oxygen is supplied in part because coronary arteries constrict, while patients under a chronic state of psychologic stress have physiologic changes that promote atherosclerosis and increases in blood pressure.

The report can be found in the March 25, 2002, online issue of *Circulation*.

Patients at high risk of stroke who were treated with the angiotensin-converting enzyme inhibitor, ramipril, reduced risk of stroke by 32%, despite only a modest reduction in blood pressure, compared with risk among patients in the placebo group, according to researchers at McMaster University, Hamilton, Ontario. Further, the relative risk of fatal stroke was reduced by 61% in the group who received ramipril.

The international, randomized trial involved 9297 patients with vascular disease or diabetes, plus an additional risk factor, who were followed up for 4.5 years. The cohort was part of the HOPE study in which participants were randomly assigned to groups that received ramipril 10 mg or less, 400 IU of vitamin E, both ramipril and vitamin E, or placebo. Outcome measures included incidence of stroke, transient ischemic attack, and cognitive function.

Participants who received ramipril had significantly reduced risk of stroke and fatal stroke, while reduction in blood pressure was modest (3.8 mm Hg systolic and 2.8 mm Hg diastolic). In addition, significantly fewer patients who received ramipril had cognitive or functional impairment, compared with the placebo group. Benefits were consistent regardless of baseline blood pressures, drugs used, and subgroups defined by the presence or absence of previous stroke, coronary artery disease, peripheral arterial disease, diabetes, or hypertension.

The report can be found in the March 23, 2002, issue of the *British Medical Journal.*

In the adult population of a Minnesota county, the incidence of myocardial infarction in women increased by 36% and decreased in men by 8% between 1979 and 1994, according to researchers at Mayo Clinic, Rochester, Minn.

To investigate how the incidence and rate of death from myocardial infarction changed between 1979 and 1994, researchers reviewed hospital records to identify patients who had myocardial infarction, their subsequent treatment, and the number of hospital deaths due to myocardial infarction. In addition, researchers reviewed county records to identify patients who died within 1 month of hospitalization for myocardial infarction.

Besides increases in percentages in women and men, greater numbers of myocardial infarction were seen in older people and fewer in younger and middle-aged people. Survival rates following myocardial infarction improved in people younger than 75 years but did not change in people older than 75 years. Finally, more patients who had myocardial infarction received medications that included aspirin, reperfusion, and beta-blockers.

Researchers note that increased myocardial infarction among women and older people may be attributable to increased cigarette smoking among women and the fact that prevention efforts have been aimed at middle-aged men, seen as primary candidates for myocardial infarction.

The report can be found in the March 5, 2002, issue of the *Annals of Internal Medicine.*

An oral drug, hexadecyloxypropyl-cidofovir (HDP-CDV), that appears to be effective against the smallpox virus—the most dreaded potential agent of biological terrorism—has been developed by a researcher at the Veterans' Affairs Medical Center, San Diego, Calif. The pill is an altered form of an antiviral medication that now must be given intravenously. The oral drug form will make it possible for scientists to strategize large-scale treatment.

The new compound, HDP-CDV, appears to be more effective than the intravenous form, cidofovir, because cells absorb it more readily, therefore requiring significantly reduced concentrations to achieve the same effect. Results of animal studies indicate its effectiveness against a disease similar to smallpox.

The findings were presented at the 15th International Conference on Antiviral Research in Prague.◆