Implants and Connective Tissue Disease: No Link?

BY KATE JOHNSON
Montreal Bureau

One of the largest studies to examine the long-term health effects of cosmetic breast implants has found little evidence to advance the debate about whether implants are linked to connective tissue disease.

The retrospective cohort study by the National Cancer Institute was primarily designed to assess cancer occurrence and overall mortality patterns among implant recipients.

Several published reports on that cohort showed no association between implants and subsequent risk of breast cancer or most other cancers.

However, a two- to threefold increase in the rates of respiratory and brain cancers and a four- to fivefold increase in suicide rates were found among women with implants, compared with control patients. (For references, see the NCI's fact sheet at www.nci.nih.gov/newscenter/siliconefactsheet.)

Findings linking implants with connective tissue disorders (CTDs), however, are far less conclusive.

"Given the diagnostic complexities of these diseases, excess risks, if they exist, may be beyond detection even in a study of this size," wrote principal author Louise A. Brinton, Ph.D., of the National Cancer Institute, Rockville, Md. (Am. J. Epidemiol. 2004;160:619-27).

"The design of the study did not enable us to derive any firm conclusions, but we were able to rule out very large increased risks," she told this newspaper.

Roughly half the 7,234 breast augmentation recipients (49.7%) had received silicone implants, while about 34% received double lumen implants, about 12% received saline implants, and about 4% received other or unspecified implant types.

The 2,138 control patients were of similar age and had had other types of plastic surgery not involving silicone, such as abdominoplasty or liposuction; blepharoplasty or rhytidectomy; and rhinoplasty, otoplasty, mentoplasty, or genioplasty.

Surgeries in both groups had taken place between 1983 and 1984.

Study subjects were mailed questionnaires about demographic information, subsequent plastic surgeries, current health status, and lifestyle factors that could affect their health. They were asked whether they had a physician's diagnosis of a CTD—including rheumatoid arthritis (RA), arthritis of another type, scleroderma, systemic lupus erythematosus (SLE), Sjögren's syndrome, Raynaud's phenomenon, fibrositis/fibromyalgia, vasculitis, chronic fatigue syndrome, or multiple sclerosis.

The study found that 4.8% of implant patients reported a diagnosis of one of four major connective tissue disorder, compared with 2.9% of controls.

The study found that 4.8% of implant patients reported a diagnosis of one of four major CTDs (RA, scleroderma, SLE, or Sjögren's syndrome), compared with 2.9% of controls, representing a relative risk of 2.0. This risk elevation was statistically significant, but after controlling for various confounding factors, the investigators concluded that the risks were not significant.

One limitation is that risk estimates were based on patient reports of their CTD diagnosis, rather than on a physician's report.

Two rheumatologists blinded to the implant status of the patients reviewed medical records to determine if each participant's history, physical examination, and radiographic and laboratory findings supported the CTD diagnosis. They then rated each CTD diagnosis as "likely," "unlikely," or "unable to assess."

Although the reviewers were able to access the medical records of only 30%-40% of study participants, they concluded that "most diagnoses were insufficiently supported, either because the records were incomplete or because clinical criteria were not met."

When relative risks were recalculated using only the "likely" diagnoses, the revised estimated relative risk for RA, scleroderma, and Sjögren's syndrome combined was still 2.0, and for RA alone it was 1.3, both of which were not statistically significant, given the smaller sample size.

Continued on following page

Continued from previous page

"We were relying on self-reports of these conditions that even rheumatologists have a hard time diagnosing, and … many of these conditions are extremely rare. So we ended up with very small numbers, and it was really not possible to either confirm or refute whether there is an association," said Dr. Brinton.

The investigators note that their observations of selection and reporting biases underscore the complexities of evaluating the relationship of implants and CTDs.

"Thus, future studies designed to resolve the question of a possible association between breast implants and rheumatoid arthritis or other CTDs would need to be very large and include well-validated and documented cases and unbiased assessments of exposure," they said.

"There were a lot of methodological problems with this study, and the authors did a good job of outlining them," commented Diana Zuckerman, Ph.D., president of the National Center for Policy Research for Women & Families, a Washington-based nonprofit group. "This is the latest of several red flags warning women that the risks of breast implants have not been adequately studied," she said in an interview. ■

Herb Takers' Risk of Bleeding Is Uncertain

NEW YORK — Herb-using individuals who are at risk of bleeding should be advised to use caution, despite uncertainty about the actual degree of risk that may be involved, Adrian Fugh-Berman, M.D., said at a meeting on botanical medicine sponsored by Columbia University and the University of Arizona.

"Actual, theoretical, and fanciful herbal adverse events and interactions infest the medical literature," said Dr. Fugh-Berman of Georgetown University, Washington.

Given the level of uncertainty, it is prudent to check international normalized ratio (INR) of anticoagulated patients 7-14 days after starting any herbal, dietary supplement, or weight-loss regimen. By the same token, all herbs and supplements should be discontinued 2 weeks before surgery, she said.

Many herbs contain coumarins, most of which are benign. Some inhibit platelet aggregation in vitro, but few have been associated with actual bleeding episodes.

In one study, a 10-g dose of ginger decreased platelet aggregation 4 hours later, and a case was reported in which a 76-year-old woman developed nosebleeds and showed changes in INR after eating dried ginger and drinking tea made from it for several weeks. But three clinical studies found that up to 4 g of fresh ginger daily had no effect on bleeding.

Garlic oil has been shown to decrease platelet aggregation for up to 6 hours, and two cases of excessive postsurgical bleeding have been reported in which patients had consumed garlic-laden meals the night before.

"Tell patients not to consume meals heavy in garlic within a few days of surgery," Dr. Fugh-Berman advised.

Ginkgolide B, a component of *Ginkgo biloba*, is a known platelet aggregation factor antagonist, and the herb, alone or with analgesics, has been associated with intracranial bleeding events.

Clinical studies, however, found that one standardized ginkgo preparation (EGb761) had no effect on hemostasis, coagulation, or fibrinolysis in healthy men, and another (Bio-Biloba) did not change INR in patients who had been stabilized on warfarin.

—Carl Sherman

Fingerpricking Tied to Necrosis

Fingerprick sites should be inspected regularly for skin necrosis in diabetic patients who have peripheral vascular disease, said Olivier Giannini, M.D., and Michael Mayr, M.D., of the University Hospitals of Basel (Switzerland).

The physicians reported the case of a 59-year-old diabetic man who was hospitalized for amputation of the lower right leg because of severe arterial occlusive disease. While recovering from the surgery, the patient took fingerprick blood samples to monitor his blood sugar. Within a few days, multiple small, well-circumscribed areas of skin necrosis around the fingerprick sites quickly progressed to full necrosis of the distal phalange, despite treatment with iloprost infusions, the investigators said (Lancet 2004;364:980).

Regular inspection of these sites may prevent such deterioration. If it does develop, capillary blood samples could be drawn from the thenar eminence, rather than the fingertips, they added.

—Mary Ann Moon