

BREAST CANCER UPDATE

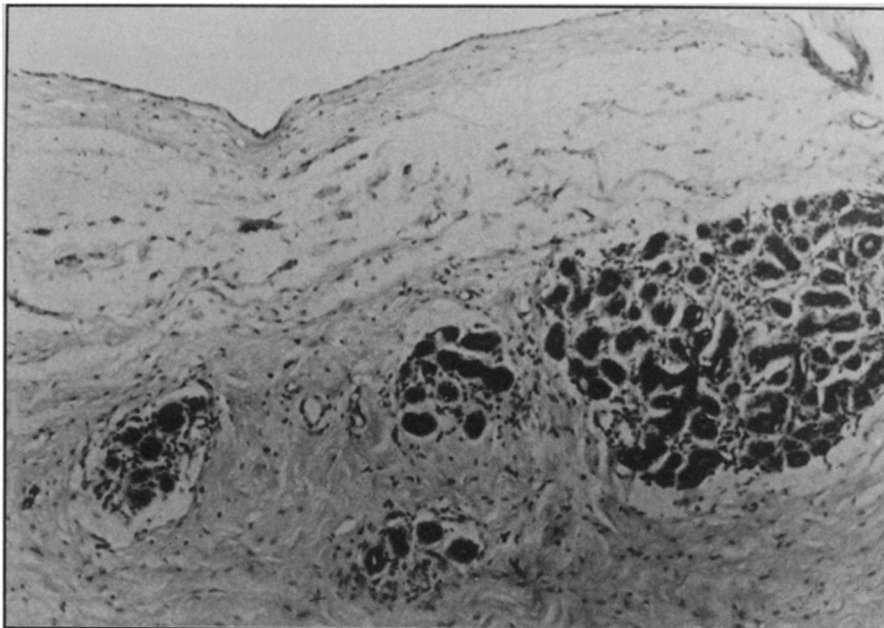
Major progress lies in identifying precancerous tissue and in using more limited surgery

BY JOAN AREHART-TREICHEL

Although rapists, muggers and male chauvinists number among women's formidable foes these days, there is still a more ruthless enemy from a health viewpoint. It strikes 89,000 American women each year. More than 32,000 of these victims die from it annually, making it the number one cancer killer of American women. Even those thousands of women who survive it often suffer from psychologically devastating surgery and live in dread of its return, because it can still kill them 15 or 20 years later. Their nemesis is breast cancer.

A number of cancer scientists are vigorously trying to get at the cause or causes of this rampant disease, to diagnose it earlier and to treat it more effectively. The progress they are making in these areas was recently highlighted at an international symposium sponsored by the White House, the National Cancer Institute and the American Cancer Society in Washington. The symposium's message, in brief, is that while the pathogenesis of breast cancer continues to elude scientists and while efforts to diagnose breast cancer earlier have been somewhat disappointing, striking advances are being made in determining whether precancerous breast cells will become cancerous or not. Progress is also being made in saving lives without resorting to cosmetically destructive surgery.

As for the cause or causes of breast cancer, numerous studies have shown since the 1940s that a woman's risk of developing breast cancer is two to three times greater if she has a mother or sister with it. These results suggest that genetic factors may play a role. A culprit gene may code for some hormonal imbalance that sets the stage for breast cancer. Some research suggests that the female hormone estradiol might be a culprit. Still other evidence suggests that lack of the female



Normal human breast tissue. The dark globules, or channels, are mammary ducts.

hormone progesterone might allow estrogens to overstimulate breast cells, thus creating a favorable milieu for breast cancer. Perhaps another female hormone, prolactin, might be the villain.

But 90 percent of women with breast cancer have no relatives with it, points out N.L. Petrakis of the University of California at San Francisco, suggesting that an exogenous rather than an endogenous substance is the cause. That a surprisingly low number of women with cancer of one breast go on to develop cancer of the other breast also points toward an environmental determinant.

What environmental substance or gene might be the malefactor? A virus continues to be a possibility since viruses can trigger breast cancer in mice and possibly monkeys, and immune cells from breast cancer patients react against these viruses in the test tube. But some sinister interplay between genes in a breast cell and a breast cancer virus appears to be necessary for the expression of the virus, at least in animals. Jeffrey Schlom of the National Cancer Institute has shown that mouse breast cancer viruses can be transmitted as genetic information via an infectious (but not contagious) process. He also notes the strong interactions in animal systems between viruses and other factors such as environmental chemicals, radiation and hormones. These studies may help explain why some types of breast cancer in women follow genetic trends, whereas others do not.

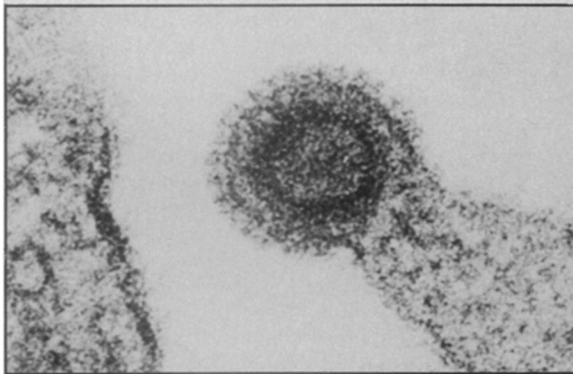
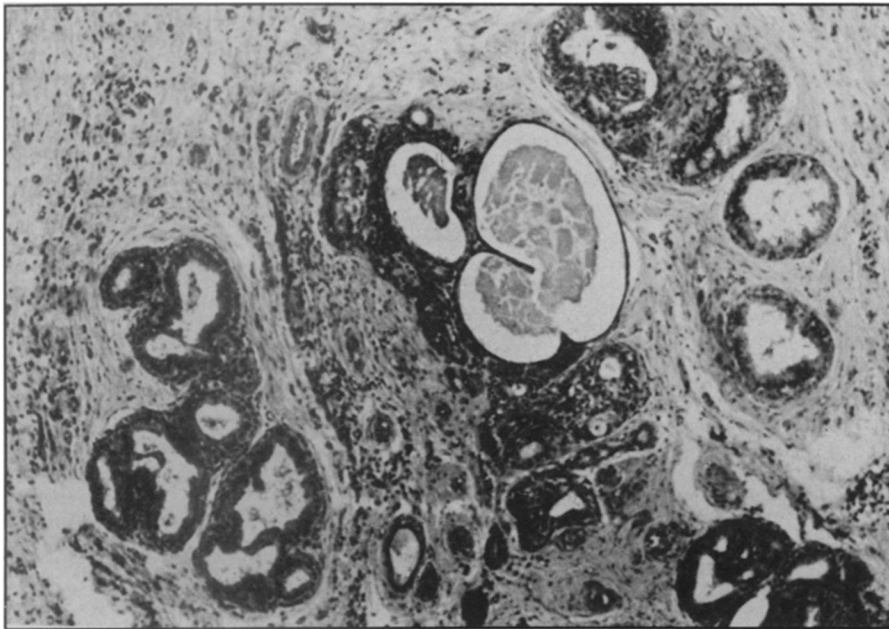
Numerous efforts have been made to see whether oral contraceptives might be a cause of breast cancer, since they consist of female hormones that could be cancer causing. Until recently, no connection could be found. In fact, the pills were linked with a decreased risk of benign breast disease. Then last August, Robert Hoover of the NCI and his colleagues

reported an increasing incidence of breast cancer in women who had received menopausal estrogens for a decade. Whether these drugs are really a factor in breast cancer will only become evident as women continue to use them over the next few years.

Just as mystifying as the cause of breast cancer is how it gets established in breast tissue. A breast cancer cell may double every 24 hours or every 250 days. Only when it has multiplied into 100 million cells does it comprise a detectable tumor. Why does breast cancer develop so rapidly in some women, yet so slowly in others? Cancer scientists do not know. Nor can they say when breast cancer cells will decide to multiply. But they *do* now recognize precancerous breast tissue under the microscope. Such lesions have been identified in a number of species, including humans, reports R.D. Cardiff of the University of California at Davis. The next challenge, he says, is to find some way of determining which precancerous lesions will become cancerous and which will not. Such a marker may have finally been found by Pietro M. Gullino of the NCI.

Evidence from Gullino's lab suggests that progressions from a precancerous to a cancerous state can be predicted if breast tissue forms new blood vessels in host tissue in the test tube. If the predictive value of this finding is confirmed in a prospective clinical trial, Gullino explains, it will be a powerful tool for identifying and removing precancerous tissue before it really causes disease.

Until such a tool becomes available, however, physicians can only try to diagnose breast cancer early—before a small tumor becomes a large one and spreads into the lymph nodes under the armpits and from there, throughout the body. They have had some success in achieving



Breast tissue (above) that may be on the border of becoming cancerous because of an increasing number of skin cells (dark areas), which in turn erode the mammary ducts (various circular channels). The question is: Will the increasing number of cells go on to become a tumor? Left: mouse breast cancer virus.

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this aim in women over age 50. A study in the 1960s by the Health Insurance Plan of New York City (HIP) showed that mammography—low-dose X-ray screening—is indeed effective in detecting breast cancer early in women over age 50. A follow-up of that study nine years later, to 1975, also showed that this early detection saved 30 percent more lives than if the patients had not had early detection by mammography.

Yet the same study did not find that mammography could help diagnose early breast cancers in women under age 50. Nonetheless, since the technique has become more sensitive during the past several years, the National Cancer Institute and the American Cancer Society decided to make mammography screening available to women under age 50 as well as over, at 27 cancer centers throughout the United States. Before any definitive results could accrue from this screening, though, an NCI task force decided that the risks of mammography to younger women probably outweigh the benefits (SN: 8/7/76, p. 90). As a result, the NCI now advises the centers to no longer screen younger women, reports John C. Bailar III, editor of the JOURNAL OF THE NATIONAL CANCER INSTITUTE. However,

many of the centers persist in screening younger women in spite of the NCI's new position. So another NCI task force will further examine the benefits and risks of mammography, and their results should become available some time this year.

The status of mammography? "Besieged, and maybe in battle," declares Gerald D. Dodd of the M.D. Anderson Hospital and Tumor Institute in Houston.

Meanwhile, women under age 50 who are wary of the risks of mammography, may diagnose breast cancer in its early stages, advises Maureen Henderson of the University of Washington, by examining their own breasts and armpits regularly for any unusual lumps. The HIP study showed that palpation by a physician detected small breast tumors three out of four times. Self-examination, she says, is easy to learn, and a woman who examines her own breasts over and over again is more likely to detect any subtle changes than a person less familiar with them.

As increasing numbers of women undergo screening procedures that can detect small breast cancers or find small breast cancers themselves through monthly examination, cancer scientists are attempting to see whether treatment less drastic than a radical mastectomy can be carried out

and still arrest the further spread of cancer. A radical mastectomy, the most common method of treating breast cancer, consists of removing not only the entire breast but also the underlying chest muscles and the nearby lymph nodes.

Preliminary study results look encouraging. Several large multicenter trials in Great Britain, for instance, reported by A.P.M. Forest of the University of Edinburgh, suggest that a simple mastectomy (removal of the breast only) coupled with X-ray therapy for any recurrent disease in the lymph nodes is as effective as a radical mastectomy. From 1971 to 1974, trials were conducted at 34 American centers to see whether a simple mastectomy without postoperative X-ray therapy is as effective as a radical mastectomy for women with cancers believed to be confined to the breast. Thus far, some three years after treatment, there has been no difference in recurrence of cancer or death from cancer in the three groups of patients, reports Bernard Fisher of the University of Pittsburgh and project chairman.

An even less drastic treatment—removal of only part of the breast—is being explored at Italy's National Cancer Institute in Milan, in conjunction with lymph node removal and postoperative radiation therapy. Although the study will not be completed until the end of this year, preliminary results so far show no difference in recurrence rates. "We believe that the conservative approach has a definite place in breast cancer therapy," says J. Veronesi of Italy's NCI.

If breast cancer spreads to another area of the body, surgery and radiation of the breast area is no longer enough to arrest it. That is where surgical adjuvant chemotherapy comes in. It, too, looks promising and will probably result in a long-term remission rate. Fisher and his colleagues at the 34 centers have found a 36 percent reduction in death two years after giving patients the drug L-PAM as an adjunct to a radical mastectomy. Gianni Bonadonna and his colleagues at Italy's NCI continue to find that cyclophosphamide, methotrexate and fluorouracil can prevent relapses in women who have had a radical mastectomy (SN: 2/21/76, p. 117).

Whether these less drastic, new treatments can really save lives remains to be seen as patients are followed over a longer period of time. Even then, the ultimate cure for breast cancer has yet to be found. Meanwhile, thousands of women must worry about reaching the so-called five-year cure period and even after that, about whether breast cancer might still invade their bodies. The psychological trauma that such patients experience is succinctly summed up by one patient who has experienced cancer remission for over a decade now—38-year-old Sylvia Capetillo of Pasadena, Tex. "I cannot help but feel that in my body, there are some dormant cancer cells just waiting for their time." □