

## Breast cancer versus bones

An unusual and distressing aspect of breast cancer — its ability to invade bones — has led scientists to initiate a new approach in the search for potential treatments. John Eisman of the University of Melbourne in Australia reports that breast cancer cells possess the mechanism to detect and respond to the active metabolic form of vitamin D. He suggests that antagonists to 1,25-dihydroxyvitamin D<sub>3</sub> could prolong the lives of women with advanced breast cancer.

Breast cancers are among the few malignancies that invade bones. To do so the cancer cells must destroy the bone around them, releasing calcium into the blood. Eisman says that bone breakdown in breast cancer patients causes severe pain and weakens the bones. Eventually the high blood calcium level affects nerves and muscles and is often the cause of death.

Eisman suggests that the bone-invading ability of breast cancers stems from the breast's natural involvement in calcium transport, which is required for producing milk. The metabolite 1,25-dihydroxyvitamin D<sub>3</sub> plays an important role in maintaining calcium levels in the body. So Eisman does not find it surprising that cells derived from breast tissue have a means to sense that metabolite.

Breast tissue taken from both malignant and benign breast tumors have the 1,25-dihydroxyvitamin D<sub>3</sub> receptors, Eisman and colleagues find. The receptor is "virtually identical" biochemically to the receptor in chicken intestine, which is known to stimulate calcium transport there. Eisman suggests that normal breast tissue, which is more difficult to study, also has the receptors and that its calcium transport is stimulated appropriately by 1,25-dihydroxyvitamin D<sub>3</sub>. In breast cancer cells, the metabolite might stimulate bone destruction or cancer cell growth.

Eisman finds receptors for the vitamin D metabolite in 85 percent of the breast cancers examined so far. He points out that in about 80 percent of women with advanced breast cancer, the cancer invades the bones. "Thus it is possible that certain breast cancer cells may respond to this hormone and be stimulated to transport calcium and destroy bone," he says. Antagonists, yet to be developed, to 1,25-dihydroxyvitamin D<sub>3</sub> might block further growth of the cancer cells in bone. Eisman envisions such treatment paralleling current therapy in which antagonists to estrogen are used to prolong the lives of women whose breast cancer cells contain estrogen receptors.

## Reducing prolactin

A new thread is weaving through the tangled biochemistry that regulates reproductive processes — the role of catechol estrogens. These substances, short-lived natural metabolites of estrogens, bind to a cell's estrogen receptors but do not mimic estrogen's biological activities. Instead they affect the metabolism of catecholamines, another class of hormones and nervous system transmitters.

The "first, genuine clinical result" with the principal catechol estrogen, 2-hydroxyestrone, was reported by Jack Fishman of Rockefeller University. He infused the purified compound into normal young women during the first half of the menstrual cycle. The catechol estrogen caused a sharp drop in blood levels of a hormone called prolactin, which promotes lactation and is also involved in normal ovarian function. Three days after the infusion, the prolactin level was still below normal. The catecholamine dopamine is the only other compound known to reduce prolactin levels. In contrast, estrogen would be expected to raise the level of prolactin. Fishman expects 2-hydroxyestrone to be useful clinically to reduce prolactin levels in cases where a surplus causes reproductive problems.

## Intrapatent transplantation

In some organ transplants a single patient is both the donor and the recipient, perhaps with a freezer as an intermediary. Parathyroid gland "autotransplants" currently outnumber transplants from patient to patient, says Samuel A. Wells of the University of North Carolina. He reports on 36 patients who since 1973 have had autotransplants of their parathyroid glands. The glands were moved from their original neck location to the forearm. In each case all four parathyroid glands had been enlarged and were producing too much hormone, which along with vitamin D regulates calcium and phosphorus balance in the body. The common treatment for the condition, called hyperparathyroidism, is surgical removal of portions of the glands. If too much tissue is removed, however, the patient sometimes suffers from a deficiency of hormone resulting in dangerously low calcium and high phosphorus blood levels.

In the autotransplant approach, Wells removes all four glands from the patient's neck, slices them into small sections and replants some of the slices into pockets of muscle in the forearm. The slices of gland produce the required parathyroid hormone in their new location. The tissue slices can also be preserved by special freezing techniques, so should a patient later have calcium levels that are too low, additional slices of gland can be thawed and implanted.

The hormone level can rise again after two or three years, necessitating removal of more tissue. Previously in such instances, major surgery on the neck was again performed. However, if the tissue has been transplanted to the forearm, removal of an additional portion is a simple procedure.

## Vive la différence?

The higher incidence of heart attacks in men is well documented but little understood. Many researchers have been looking for the answer in the activity of male and female hormones.

University of Texas researchers have followed up their finding of receptors for male hormones on the heart muscles of monkeys and baboons (SN: 2/23/80, p. 117) with the discovery that human heart and artery cells also have these receptors. The presence of these receptors indicates that circulating male hormones can affect the cells.

The findings provoked a word of caution from the San Antonio researchers. "Since the heart is a muscle, androgen may increase the size of the heart in man, as has been demonstrated in rats," says Peter Sheridan.

"Physicians should know that adding sex hormones, such as contraceptive agents for women or muscle-building androgen for male athletes, to what the body produces naturally may have a profound effect on the cardiovascular system," he says.

## Another form of growth hormone

The human growth hormone found in its mother gland, the pituitary, is not identical to the growth hormone that circulates in the blood, according to researchers at the Scripps Clinic and Research Foundation in La Jolla, Calif.

The scientists questioned why greater amounts of circulating hormone could be detected by using measurements of biological activity than by immunological tests and found that growth hormone in the blood is actually a "clipped" version of the pituitary form. Growth hormone plays an important role in controlling metabolism and skeletal growth, and characterization of the circulating hormone is important because of its potential use in treating growth disorders such as short stature and gigantism.