Sweet route to heading off colon cancer

In recent years, a host of studies have identified a broad spectrum of medical attributes in honey – including antifungal, antibacterial, anti-inflammatory, antiproliferative, and cancer-drug-potentiating properties. Now, researchers at the American Health Foundation in Valhalla, N.Y., have uncovered another. In the Sept. 15 CANCER RESEARCH, Bandaru S. Reddy and his co-workers describe the ability of honey-derived caffeic esters to inhibit the development of precancerous changes in the colon of rats given a known carcinogen.

These esters come from the propolis – the brown, resinous, tree-derived material that honeybees use to cement together their hives. Reddy's group considers three derivatives of the caffeic esters promising enough to use in longer-term animal studies of colon cancer.

Tamoxifen slashes serum cholesterol . . .

Tamoxifen is the most widely used and effective drug for preventing the recurrence of breast cancer (SN: 2/22/92, p.124). In 1990, researchers at the University of Wisconsin-Madison showed that it can also yield a "durable" (two-year) 12 percent average decrease in cholesterol. But the researchers didn't know how quickly cholesterol concentrations in blood serum fall once tamoxifen treatment begins. Now, in the Aug. 18 JOURNAL OF THE NATIONAL CANCER INSTITUTE, Richard R. Love and his co-workers at Wisconsin show that serum cholesterol plummets immediately after treatment starts. It took only two weeks for total cholesterol levels to drop an average of 32 milligrams per deciliter of blood – roughly 12 percent – in the seven cancer survivors studied.

Many women starting tamoxifen therapy complain about the onset or exaggeration of menopausal side effects – chiefly hot flashes and vaginal dryness. Such symptoms can prove disturbing enough for some women to discontinue treatment. But if doctors could point to a reduction in a major risk factor for heart disease, Love says, they might convince women to stick with the drug a little longer. And that may be all that's needed. In the April 21 JOURNAL OF THE NATIONAL CANCER INSTITUTE, Love's team reported finding that the severity of hot flashes peaks at about six months and then wanes.

. . . but shows link to 'bad' uterine cancers

A potent hormone-like drug, tamoxifen poses some risks of its own. The leading one: development of endometrial cancer, a malignancy of the uterine lining. However, many researchers have all but brushed off the importance of tamoxifen-induced uterine cancers, charging that because they seldom kill, "it's no big deal" (SN: 4/25/92, p.266). A pair of new studies now forcefully challenges that assessment.

Elvio G. Silva, a pathologist at the University of Texas M.D. Anderson Cancer Center in Houston, examined tissues from 71 breast cancer survivors who later developed uterine cancer. He says his unpublished analysis indicates that, compared with the 56 women who did not take tamoxifen, the 15 who did were 4.7 times more likely to develop serous carcinoma, almost twice as likely to develop mixed mullerian tumors, and 50 percent more likely to develop clear-cell carcinoma. The prognosis for any of these three uterine cancers is poor. The tamoxifen users also proved three times as likely to exhibit additional precancerous polyps in the uterus.

"I don't want to scare everybody with this," Silva told SCIENCE NEWS, noting that the development of uterine cancer among tamoxifen users remains a fairly rare occurrence. However, he adds, the data now indicate that once a tamoxifen user does develop a uterine cancer, there is a strong likelihood it will be "bad" – that is, likely to spread and kill.

That's also the conclusion of a study of uterine malignancies in 53 breast cancer survivors, conducted at Yale University School of Medicine. Again, 15 were tamoxifen users.

Estrogen can foster endometrial cancer. But when it does, says Yale pathologist Maria Luisa Carcangiu, such hormone-induced malignancies tend to be low-grade – that is, unlikely to spread and therefore "curable" through surgery. As a result, she says, "everybody used to say that since tamoxifen acts like an estrogen, any endometrial cancers [it causes] will be low-grade." Her data now refute that.

The interval between the diagnosis of breast and endometrial cancers averaged 12 years in women who had *not* been treated with tamoxifen, but was only five years for those who had. Moreover, 67 percent of tumors in tamoxifen users were high-grade, compared with 24 percent in the other women. Because the cells of uterine tumors in tamoxifen users also proved uncharacteristic of estrogen-linked malignancies, they may trace to "a different mechanism of action of tamoxifen on endometrial cells," Carcangiu's group concluded in the March JOURNAL OF CLINICAL ONCOLOGY.

She hopes these new data convince physicians that in tamoxifen patients, "endometrial cancers *can* kill. In our experience, they did so frequently."

Retallying tamoxifen's risks and benefits

Last year, the National Cancer Institute initiated a disease-prevention trial that will dispense tamoxifen to 8,000 healthy women who are at high risk of developing breast cancer (SN: 5/9/92, p.309). Though the treatment poses some risks, expected benefits of the drug far outweigh them, the trial's designers have said. But that weighing of the pros and cons underestimated the frequency of some reported complications and failed to account for several others altogether, according to two epidemiologists at Johns Hopkins University in Baltimore.

In the just-released EPIDEMIOLOGIC REVIEWS (Vol.15, No.1), Trudy L. Bush and Kathy J. Helzlsouer reevaluate the drug's trade-offs. Their conclusion: For this population, the trial is as likely to prove tamoxifen a net detriment as a benefit.

Planners of the tamoxifen trial have estimated that their five-year program will prevent 62 breast cancers and 52 heart attacks, Bush and Helzlsouer note. However, on the basis of the age of the study recruits and the heart risks faced by women of similar age, the Hopkins researchers assert that tamoxifen should avert only about 13 heart attacks. They also suggest that, given the age of the recruits, the trial would likely prevent only 52 cases of breast cancer.

Furthermore, they say, data on endometrial cancer in tamoxifen users suggest that the drug probably triples – rather than doubles – the usual incidence of this malignancy. If so, then the trial might foster between 39 and 57 such uterine cancers, somewhat more than the 38 anticipated by the trial's designers.

Moreover, the Hopkins group points out that the designers' risk-benefit analysis included only anticipated deaths from blood clots. Given the potential for damage from even nonlethal clots – which can cause strokes, for example – these should also be part of any risk accounting, Bush and Helzlsouer argue. When the Hopkins researchers factored in nonlethal clots, they estimated that the cancer-prevention trial could achieve anything from a small net benefit (preventing eight more health problems than it induced) to a moderate negative effect (fostering 17 more problems than it prevented).

Finally, recent reports have linked tamoxifen use with eye toxicity (SN: 7/4/92, p.12). When Bush and Helzlsouer included such ophthalmic complications in the risk equation, they estimated that the trial would have a solidly negative impact, causing 31 to 57 more adverse outcomes than it prevented.