Biomedicine

Kathy A. Fackelmann reports from Phoenix, Ariz., at the American Cancer Society's science writers' seminar

The caffeine-chemotherapy connection

In the attack on cancer, physicians must estimate the highest chemotherapy doses their patients can tolerate without life-threatening side effects. Oncologists using the experimental cancer drug amonafide face a particularly precarious balancing act, because different people metabolize the drug in different ways. While some can take the "standard" amonafide regimen with no problems, others develop potentially lethal infections as their bodies convert the drug into large amounts of a toxic metabolite that damages the immune system.

Noting that the body metabolizes amonafide and caffeine similarly, Mark J. Ratain and his colleagues at the University of Chicago devised a caffeine test designed to predict a person's risk of amonafide toxicity.

The team studied 18 people with colon, breast or other types of cancer. They instructed the volunteers to drink a cup of caffeine-containing coffee or cola and to collect urine samples four to six hours later. In analyzing the samples, they discovered that seven people metabolized caffeine in a way that suggested a predisposition to amonafide toxicity. Later, when each of the 18 participants received a standard dose of amonafide, signs of drug-related toxicity emerged in the same seven people, including three who responded with a severe decline in white blood cells, Ratain says.

Among the remaining 11 participants — whose caffeine tests had suggested a low risk of drug-related toxicity — seven showed no significant toxicity from the amonafide dose.

People whose caffeine tests indicate low risk should receive larger-than-average amonafide doses for a more potent blast against cancer cells, Ratain suggests, while those who appear vulnerable to amonafide toxicity should receive less than the standard dose or switch to another treatment.

Ultimately, he notes, the test's value will depend on whether amonafide — which is showing some antitumor promise in U.S. clinical trials — proves an effective cancer-fighter.

Preventive tamoxifen: Safe so far

Healthy women with a family history of breast cancer live with the knowledge that they face an increased threat of the disease. While physicians can use mammograms to detect emerging tumors, they have no way to prevent such tumors from developing.

British researchers are now exploring the effects of tamoxifen — a synthetic, hormone-like drug already used to treat breast cancer — in a trial of healthy women at risk of developing the disease. Animal studies, including an April 3 report in the JOURNAL OF THE NATIONAL CANCER INSTITUTE, suggest that tamoxifen prevents breast cancer. However, many scientists worry about the danger of giving this drug to healthy women.

But Trevor Powles and his co-workers at the Royal Marsden Hospital in Surrey report some good news regarding tamoxifen's safety. In an ongoing study of about 500 cancer-free women receiving 200 milligrams of tamoxifen or placebo each day, they have detected no serious drug-related side effects, Powles says. After monitoring the women for up to three years, the team reports that about 15 percent of those taking tamoxifen — which binds to estrogen receptors — have reported mild, menopause-like symptoms such as hot flushes.

Powles cautions that it's too soon to predict long-term safety. For at least another five years, the researchers will continue to monitor the women for toxic reactions to the ongoing treatment and for endometrial cancer, tentatively linked to tamoxifen in previous studies. Ultimately, the study should also yield data on the drug's protective potential.

U.S. researchers plan a similar trial involving about 16,000 healthy women, says Bernard Fisher of the University of Pittsburgh, who will lead the multicenter trial.

Earth Sciences

Rain raises Parkfield quake alert

The San Andreas fault near Parkfield, Calif., shifted suddenly last month, prompting officials to issue a level B earthquake alert for that section of the fault. Scientists have predicted a strong shake for Parkfield sometime in the next few years, and the recent alert, which expired after three days, represents the highest level announced since the monitoring program began there in 1985. Researchers suspect, however, that the recent surface shifting resulted from heavy rains, and not from changes indicating the predicted quake is nigh.

As part of a multimillion-dollar experiment, the U.S. Geological Survey (USGS) keeps close tabs on the San Andreas near Parkfield in hopes of issuing a short-term prediction minutes to days before the quake. The USGS has established five alert levels, ranging from E to A, to describe the near-term likelihood of an earthquake. Information from monitoring instruments serves as the basis for determining the alert status. When the USGS calls a level A alert, officials will issue a warning to residents of Parkfield and nearby areas.

According to the rating system, a level B alert signifies an 11 to 37 percent chance the expected temblor will strike in the next three days. The USGS issued the March 19 alert after two instruments detected a substantial acceleration in the normally slow surface creep along the fault. The opposite sides of the fault slipped 5 millimeters past each other in 16 hours.

That slip, while sufficient to trigger a level B alert, did not truly indicate a state of heightened seismic risk, scientists believe. The recently heavy rains, which dumped more than 3 inches on the area, probably weakened the soil at the surface, allowing it to creep faster, says Evelyn A. Roeloffs, head of the Parkfield experiment. Other instruments indicate that similar movement did not occur on deeper sections of the fault, where the quake is expected to start.

To prevent a repeat of last month's debatable alert, the USGS now plans to alter its rating criteria, Roeloffs says.

Sound sent halfway around the world

After traveling 18,000 kilometers through the deep ocean, sound signals transmitted near Antarctica arrived, faint but clear, at the East and West coasts of North America. The successful experiment raises hopes that scientists can use this technique over the next decade to gauge whether the expected greenhouse warming has started.

U.S. and Australian researchers tested the idea in late January during a trial experiment near remote Heard Island in the Antarctic Ocean. An underwater transmitter emitted periodic signals about as loud as a foghorn, and 17 receiving stations around the globe listened for the weak sound (SN: 1/26/91, p.53). Scientists hope to use the timing of the signals' arrival to make precise measurements of the speed of the sound, and then monitor future transmissions for any change in speed. A widespread increase in the sound speed over several years would indicate an oceanic warming.

Project coordinator Robert Spindel, an engineer with the University of Washington in Seattle, says almost all the listening stations picked up the signal. The sound took about 3.5 hours to reach its most distant destinations, the North American stations. The researchers are now conducting tests to determine whether the received signals came in clearly enough to allow a sufficiently accurate measurement of the sound speed. "It looks like the answer is yes," Spindel says.

Spindel and his colleagues hope to install the first of several permanent underwater transmitters in 1993, and then add several more transmitters around the globe as part of a long-term monitoring program. Because various ocean regions will respond differently to climate change, the researchers will need widespread coverage to catch signs of a global warming.