

## Animal cancers from popular drugs

Three important drug ingredients join the list of chemicals suspected of causing cancers. Experiments with rats and mice at the National Cancer Institute have associated tumors with ingestion of compounds found in drugs to lower high blood pressure, over-the-counter sleeping aids and anti-dandruff shampoos.

Epidemiological studies led scientists to laboratory animal tests of reserpine, a component of drugs used by about 1 million Americans to control mild high blood pressure. The International Agency for Research on Cancer recently reviewed 12 large epidemiological studies and concluded that reserpine may increase human breast cancer risk by 50 to 100 percent, says Harriet Kennedy of NCI.

In NCI animal experiments mice and rats were fed high doses of reserpine. Breast cancer was detected among the female mice and tumors of the seminal vesicles and adrenal gland among the males. Kennedy says that tumors of the seminal vesicle, a temporary sperm storage sac, are normally very rare in mice. She finds the data especially significant in that all three types of tumors detected involve the endocrine system. Usually the tumors found in animal tests involve the liver, the body's detoxification center.

The pharmaceutical division of Ciba-Geigy Corp., which makes one of the most widely used reserpine drugs, sent out news releases saying the NCI studies were flawed and the conclusions not supported by the data. The Ciba-Geigy statement notes that the NCI data show a significant reduction in certain tumors in reserpine-treated male mice, a result not discussed in the report summary. Kennedy says the Ciba-Geigy criticisms result from a naive way of looking at statistics. She says the decrease in incidence of some tumors appears because the mice developed a different type of tumor and died early from it. Kennedy flatly denies the charges that the report's summary is inaccurate and does not reflect its own data.

The Food and Drug Administration has called an advisory meeting for June 22 to review the reserpine findings. Meanwhile they say that people should not abruptly halt use of reserpine drugs, but rather could discuss alternatives with their physicians. FDA and NIH officials stress that the risk of untreated high blood pressure "far exceeds" reserpine's potential cancer risk.

An ingredient found in a long list of non-prescription drugs also causes tumors in rats, NCI scientists discovered in preliminary studies of methapyrilene. That anti-histamine goes into over-the-counter sleeping aids, sedatives, nasal sprays and decongestants. About 10 million Americans use products containing that ingredient.

Last week the Environmental Defense Fund petitioned the FDA to stop the sale

of methapyrilene-containing over-the-counter drugs. The fund cites studies at Oak Ridge National Laboratory, as well as at NCI, indicating the chemical causes liver cancer. The petition says that normal use of methapyrilene products poses a great threat to human health. EDF associates calculated the amount of methapyrilene per kilogram body weight ingested by a consumer taking four sleeping pills a month for 25 years. They find that intake to be one-fourth to one-fifth the dose that induced liver tumors in the laboratory experiments in half the treated animals.

The petition says there are satisfactory substitutes for methapyrilene for relieving allergy symptoms. It also points out that the effectiveness of the products as sedatives and sleep-aids has been seriously questioned by the FDA, the National Academy of Sciences and the American Medical Association. Last June the FDA

proposed a ban on nonprescription sedatives with methapyrilene, but has not enacted it yet. At that time it found the drugs without benefit and possibly harmful (by making people drowsy) and said methapyrilene was a "possible" carcinogen. The FDA now is waiting for a final report by the NCI panel.

Selenium sulfide is the ingredient of widely used antidandruff shampoos also charged with causing cancer in NCI tests. When high doses of selenium sulfide were given to rats and mice, liver cancer was found in both species and lung cancer in the female mice.

These animal experiments are part of the NCI Carcinogenesis Testing Program, which is currently examining more than 100 different chemicals, Kennedy estimates. She says the program aims to test 100 each year. In the program's early days, it focused on pesticides and herbicides, but now chemicals are selected for a variety of reasons, the most important being the degree of human exposure. □

## Getting set for Skylab

Skylab's end is near. The North American Air Defense Command's Space Defense Center, which tracks the more than 4,500 manmade objects now orbiting the earth, estimated this week that there is a 90 percent chance of the huge space station reentering earth's atmosphere sometime from June 20 through July 4, with the likeliest specific date being June 26.

NORAD's predictions, which are being distributed by the National Aeronautics and Space Administration, will be updated weekly until less than two weeks remain; thereafter they will be updated daily, and issued finally with 24, 12, 6, 4 and 2 hours to go. Predicting just where the 77.5-ton object will hit, however, is virtually impossible according to NORAD. "Because of many factors that can change the course of a returning satellite," says a NORAD statement, "it may come down thousands of miles from any predicted point. Thus, no precise advanced impact warning can be given to populated areas in the re-entry path of the decaying satellite." Such factors include gravitational variations over land and water, unexpected solar flares, irregularities in atmospheric density and limitations in NORAD's radar coverage. In addition, a given object may skip one or more times after hitting the atmosphere, or it may start tumbling erratically and reach "final decay" earlier than expected.

NORAD's predictions are not for time of impact on the earth, however, but for the time when an object reaches a point about six miles up in the atmosphere where it has lost most of its forward velocity and is starting a steeper downward course. Yet even there, the uncertainties are great. As little as six hours before the object's arrival at that point, NORAD says, its point of impact could still be anywhere along a

41,400-mile portion of the reentry path. With two hours to go, the uncertainty is still about 13,800 miles, and even after the impact, space tracking data alone cannot pinpoint the impact along the path to closer than about plus or minus 300 miles.

The difficulties were demonstrated in a recent rehearsal of the procedures to be followed when Skylab is actually on its way down. A Soviet rocket stage used in the 1971 launching of Cosmos 461 reentered the atmosphere on April 29, and the NASA-NORAD team that will be monitoring Skylab's descent used the Soviet craft's reentry to practice their procedures. NORAD's prediction with only two hours to go was in the vicinity of Pitcairn Island in the south Pacific. The last update, computed with just one minute remaining, showed the actual splashdown to be somewhere northwest of Hawaii, about a sixth of the way around the planet.

NASA now estimates that about 25 tons of material from Skylab will reach the ground, in about 500 pieces. The biggest are a 5,175-pound airlock shroud, a 3,901-pound lead-lined film vault, six 2,736-pound oxygen tanks and a 1,578-pound bulkhead. "It is not expected that there would be any impact craters [larger than the objects themselves] resulting when the pieces hit the ground," says a NASA document, "because the impact velocities are relatively low." The film vault, for example, fastest-hitting of the objects in one NASA analysis, is predicted to hit at 405 feet per second.

Meanwhile, the possibility of actively controlling Skylab to prolong its life an extra orbit or two (to let it get over less-populated regions) became less certain on April 23 when one of the facility's remaining control-moment gyros failed. □