

New cancer treatment promising



DALLAS (AP) — Synchronizing cancer treatment with the body's own internal rhythms appears to give ordinary chemotherapy drugs a much stronger punch, perhaps even doubling their power to fight tumors, a major new study shows.

Typically, cancer medicines are given in single injections or in steady infusions that remain constant day and night. The new approach varies the way these drugs are released, depending on the body's natural circadian cycles through a 24-hour day.

Some drugs, it seems, work best when given at gradually peaking and ebbing doses through the night, while other seem more potent when taken during the day.

The strategy, called chronotherapy, has been discussed for at least 20 years. Until recently, however, no practical way existed to test it in significant numbers of patients.

The development of programmable infusion pumps, devices roughly the size of hardcover books that hang from shoulder straps and can be worn at home, enabled a European team to try the idea for the first time. Patients were randomly assigned to get either standard treatment or the new approach.

Dr. Francis Levi of Paul Brousse Hospital in Villejuif, France, presented the results Monday at the annual meeting of the American Society of Clinical Oncology.

The study was conducted in France, Italy and Belgium on 186 people with advanced colon cancer. Tumors shrank by at least half in 51 percent of the chronotherapy patients, compared with 28 percent of those getting steady doses of drugs.

The idea of treating patients this way "has been around for years, but perhaps its time has come," said Dr. Bruce Cheson of the National Cancer Institute in Bethesda, Md. "This is the first randomized trial, and the fact that it's positive should be very exciting."

"It shows us that circadian rhythm really does have an impact on how drugs work," said Dr. Margaret Kemeny of North Shore University Hospital in Manhasset, N.Y.

The body works on a 24-hour cycle governed by the Earth's rotation. The release of hormones, the activity of different organs and the response of blood cells all fluctuate, depending on the time of day or night.

Various studies on animals and people suggest that chemotherapy drugs are more potent and produce fewer side effects if they are coordinated with

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these natural rhythms, although why this is so is largely a mystery.

For instance, the bone marrow's production of new blood cells peaks around midnight. So the doctors take this into account when they program the release of 5-fluorouracil, a drug that has the undesirable side effect of suppressing bone marrow activity.

In this study, the doctors gave a combination of three drugs — 5-fluorouracil, oxaliplatin and folinic acid. They set the infusion pumps to deliver 5-fluorouracil and folinic acid starting at 10 p.m. with a peak rate at 4 a.m., when blood cell production is at its lowest point. Oxaliplatin was diffused throughout the day, with a maximum rate at 4 p.m.

The two major side effects, mouth ulcers and numbness of the fingers and feet, were significantly less in those patients receiving the circadian doses.

The doctors found that 14 percent of patients getting the fluctuating doses suffered serious mouth ulcers, compared with 76 percent in the standard treatment group. Numbness bothered 30 percent getting standard therapy but only 15 percent on the experimental approach.

With side effects reduced, doctors were able to increase drug dosages in the chronotherapy group, which they hope increases the chance of having a lasting impact on the cancer. Levi said chronotherapy is also being considered for testing on other tumors, including breast, lung and pancreatic cancer.

Most humans' circadian cycles are the same, but researchers have noticed that cycles seem to be out of sync in cancer patients. These differences may need to be taken into account when tailoring individual treatment schedules.

Levi said it was too soon to say whether the new approach actually increased survival in the gravely ill patients in the study. So far, however, the European team has treated about 400 patients using various fluctuating dose schedules, and cancer has completely disappeared in 4-5 percent of them.

"It gives us some hope of the potential curability of this disease," he said.

Demand for two-car garages rises in 90s

NEW YORK (AP) — A drive through some of the country's newer neighborhoods shows few homes are built these days without a garage, and that the garage rarely is meant for anything less than two cars.

Builders and real estate folks know that two-car garages, once considered luxury items, are in strong demand today, and that to offer anything less is to invite wariness on the part of buyers.

You can skip the basement and the attic, but you must leave room for cars. And year by year, Americans are more and more adamant about it. More families than ever own two cars, and they want garages for them.

In 1978, only half the new homes had room for at least two vehicles. Last year it was up to 77 percent. In the span of those years, only in 1991 did the percentage fail to rise, and that was followed by a spurt a year later.

So strong is the attachment to larger garages that space for two cars isn't even enough for some people.

As recently as 1991, the National Association of Home Builders didn't bother even to count the number of super-size garages — three cars or more — and when it began, it found 11 percent of garages were that size.

In themselves, these facts might be merely interesting. Or maybe not. But another observation made during the same drive provokes a serious question: Why is a car sighted in almost every driveway — outside the garage?

What is inside those garages?

Builders really don't have the answer to the question, nor do real estate people. What they do know is that anything less than a two-car structure is as price-deflating as a new home without central air.

In 1978, only 58 percent of new homes were built with central air conditioning, but last year the percentage had risen to 78, making that characteristic even more in demand, but less a puzzle, than larger garages.

Air conditioning is considered essential in new homes almost everywhere in the country and, in fact, in some areas is considered more necessary than a furnace. About 97 percent of new homes in the South had it in 1993. But the rising demand for air is easily understood: People use it.

Even less of a puzzle are two other housing trends — larger homes and more baths.

Twenty-nine percent of new homes built nowadays are of at least 2,400 square feet. Only 14 percent of new homes qualified in 1978, when almost half the houses were of less than 1,600 square feet, many of them a good deal less.

In that year, only 25 percent of new homes had at least 2.5 baths, but that percentage has almost doubled since then, and 14 percent even have three baths or more. Buyers today like bedrooms too; 30 percent now have four or more.

The demand for space is easily understood: This is home, and the space is used to live in. The extra bedroom may become the computer room or office, a trend gaining in popularity but too new to be measured statistically.

There is no mystery to this desire for more living space. The mystery is out there in the garage. Garages are for cars, but the cars — or at least one of them — seem to be left in the driveway.

The word garage is derived from the French, to protect or preserve. What's being preserved in those suburban garages? And just as mysteriously, for what reason?

U.S. will test abortion drug in fall

WASHINGTON (AP) — The French manufacturer of the abortion drug RU486 has agreed to donate the drug to the Population Council, which will begin testing it in American women this fall, U.S. officials announced today.

Roussel Uclaf agreed to give up its patent rights to the Population Council, a not-for-profit corporation. It will begin testing the drug in 2,000 American women in Oregon and about a dozen other sites around the country this fall, Rep. Ron Wyden announced just before a congressional hearing on the issue.

"American women who waited far too long for this drug will now see the days of stalling and foot dragging are over," Wyden said.

RU486 has long been controversial. Abortion opponents say it could encourage women to have abortions and may not be safe anyway.

The Bush and Reagan administrations opposed the drug's testing here.

The pill, long an alternative to surgical abortions in Europe, will be given to U.S. women through the seventh week of pregnancy, Wyden said.

The Food and Drug Administration has agreed to expedite testing of the drug, completing its review six months after it receives the test data, because it has access to information about RU486's use in 150,000 European women, Wyden said.

That means the U.S. testing

will mainly be to determine the proper procedures for giving RU486, as opposed to safety tests.

But Health and Human Services Secretary Donna Shalala cautioned that FDA's agreement did not mean it would merely rubber stamp the drug.

"FDA's decision will be based solely on the scientific and medical evidence about the safety and efficacy of the product," she said.

Rep. Pat Schroeder, co-chair of the Congressional Women's Caucus, said the fight against RU486 has kept the drug's other medical uses, such as a potential treatment for brain tumors, from being explored.

"The medical McCarthyism affecting women and their organs has now disappeared," she said.

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