Pummeling tumors with localized therapies

By taking better aim with both chemical and radiation treatments, cancer researchers have discovered they can pack more power into their antitumor punches—enough, they hope, to beat back hard-to-treat liver and pancreas cancers.

In an approach called brachytherapy, oncologists first inject microscopic clumps of the protein albumin into a tumor, positioning the needle with the aid of a CT scanner. They then add radioactive phosphorous through the same needle. For at least several hours, albumin clumps clog the capillaries, says Stanley E. Order of the Robert Wood Johnson Medical School in Camden, N.J.

Meanwhile, because cells take up and use phosphorous, the tumor quickly absorbs this radioactive version of the element. By the time the capillaries open again, no phosphorous remains to escape to—and possibly harm—other cells in the body, Order adds.

"It's quite simple in concept, and yet it delivers huge amounts of radiation," comments Harmon Eyre, vice president for medical affairs and research at the Atlanta-based American Cancer Society (ACS).

In a preliminary study, Order and his colleagues treated 23 people diagnosed with inoperable pancreatic tumors. After each group of three patients, they increased the phosphorous dose. Even at more than 500,000 rads, they saw no toxic side effects, he reported in Tucson this week at the annual ACS science writers seminar.

Weeks later, the radioactive material remained inside the tumor, doing its deadly job, he added.

A different strategy, this one for liver cancer, has enabled researchers to increase the dose of anticancer drugs. Steven A. Curley and his colleagues at the University of Texas M.D. Anderson Cancer Center in Houston limit the spread of drugs away from the liver in two ways.

First, they have developed a relatively simple surgical procedure for inserting a narrow tube, called a catheter, and two balloons into body. In this way, blood leaving the liver can be diverted out of the body and through a filter that screens out the anticancer drugs, which would harm noncancerous tissues.

"He's been able to make a major improvement in terms of increasing the amount of drug [used]," Eyre says.

This system made it possible to inject up to three times the usual concentration of the drug doxorubicin into the livers of 10 patients. "Seven patients had a marked reduction of their tumors," Curley reports. In two, the tumors shrank enough that surgeons could remove the remaining malignancy.

To add even more killing power to this therapy, Curley's group packages an anticancer drug in a gel of collagen and two other structural proteins common in the body. With this gel matrix, they have managed to increase concentrations of cisplatin to 50 to 100 times the doses possible through conventional drug-delivery routes, Curley says.

In a preliminary study, this matrix-drug complex caused at least a 50 percent reduction in the volume of the liver tumors in all 15 patients treated. However, he cautions that additional therapy is needed: Tumors do return, sometimes with the ability to resist the killing effects of the anticancer drug used.

Another team fights liver cancer by combining radiation with chemicals that make cells more susceptible to radiation. Because liver tumors usually cause no symptoms at first, all but about 15 percent of them are too big, too spread out, or too close to important ducts or blood vessels for surgeons to remove them and still preserve liver function, says Theodore S. Lawrence of the University of Michigan Medical Center in Ann Arbor.

Also, the amount of radiation needed to destroy liver tumors far exceeds the amount the rest of the liver can tolerate. To get around this problem, Lawrence's group first exploits the fact that liver tumors get their blood supply primarily through the hepatic artery, while much of the rest of the liver depends on the portal veins. Injecting radiation-sensitizing chemicals into that artery enables the team to concentrate these chemicals in malignant cells, he reported at the ACS seminar.

Then they use a technique called three-dimensional radiation treatment planning to figure out the best way to aim three radiation beams so they intersect at the tumor. In this way, they can concentrate a powerful dose on the tumor and hit as little normal liver as possible.

In an early trial of 26 people with liver cancer, the researchers found that the technique works best if the tumors aren't too widespread or near any key ducts or vessels. The median survival of these patients doubled or quadrupled, Lawrence reports. *—E. Pennisi*

Fouling the air: Not just a modern problem

Greece gave the world philosophers and timeless tragedies. Rome bequeathed Latin and enduring architecture. But that's not all that came out of these ancient societies. Lake sediments in Sweden contain evidence of air pollution that drifted over the skies of Europe even as Socrates and Seneca paced through marble halls.

"Most people believe that there was no air pollution in preindustrial times," says Ingemar Renberg, an environmental scientist at the University of Umeå in Sweden. Yet he and his colleagues detected signs of lead pollution in Swedish lakes going back at least 2,600 years. "This is the clearest evidence so far presented for preindustrial airborne pollution," says Renberg.

The Swedish researchers measured concentrations of lead in sediment cores pulled from 19 lakes. Using radiocarbon dating, they pinpointed important changes, which they describe in the March 24 NATURE.

Lead amounts remained low and showed little variation between 10,000 and 3,000 years ago. Around 2,600 years ago, they started to rise, reaching a small peak 2,000 years ago at five times the natural amount of lead. Concentrations then dropped but began to rise steeply 1,000 years ago. They jumped even more during the 1800s and crested in 1970.

The rise and fall of lead concentrations in the sediments appear to parallel the history of lead production in the ancient world, according to Claire Patterson, a geochemist at the California Institute of Technology in Pasadena who studies preindustrial use of metals. Patterson notes that lead pollution started to appear in Swedish lakes at roughly the time when Greece began coining silver, which was obtained by melting down lead ores.

Lead mining increased until approximately 2,000 years ago, when the Roman Empire exhausted its principal deposits in Spain. During Roman times, people used lead for water pipes, cisterns, and even as an additive for wine, says Patterson. Such heavy reliance on lead by the Romans has prompted some to speculate that lead poisoning contributed to the empire's fall.

The lead increase 1,000 years ago correlates with rising silver production and lead use in Germany.

Renberg's team argues that lead in the lakes came from air pollution because the changes in lead concentration occurred at the same time all over Sweden, ruling out the possibility that local fires caused the spikes in lead values. The lakes also show a gradient, with the smallest amounts of lead in the north and the largest in the south—the region closest to early Roman cities in England and northern Europe.

By today's standards, ancient air pollution was modest: Lead concentrations 1,000 years ago only reached a tenth of modern values in the sediments, says geochemist Stephen Norton of the University of Maine in Orono. But because lead use has such a long history, pollution added at least as much lead to the environment during ancient times as it has since the industrial revolution, says Renberg. He believes preindustrial air pollution also contained other heavy metals. *—R. Monastersky*