Combination cancer therapy salvages bladder

An experimental approach to invasive bladder cancer may spare the bladder yet save the patient.

For the past 20 years, surgeons have treated such malignancies by removing the entire bladder. Although that traditional approach results in a 50 percent survival rate after five years, patients must live with the discomfort of urine-collecting bags that never quite work the way a healthy bladder does.

Oncologist Donald S. Kaufman and his colleagues at the Massachusetts General Hospital in Boston didn't want to jeopardize their patients' survival, but they did want to avoid radical surgery if possible. So they devised a regimen designed to preserve the bladder while launching a blitz on the cancer.

This year, an estimated 52,300 people in the United States will develop bladder cancer. About 30 percent of that group would be candidates for the experimental regimen, Kaufman estimates.

The Boston team recruited 53 people with invasive bladder cancer, in which the disease has spread to the bladder's muscular wall. All 53 then underwent a procedure called transurethral resection, in which surgeons guide a slender fiberoptic scope through the urethra to the bladder. Aided by a video display of the bladder's interior, surgeons then manipulate tiny instruments to remove the tumor. Afterwards, patients received an initial blast of several different types of chemotherapeutic drugs, as well as radiation therapy.

For patients who showed any signs that their cancers had not responded, the team recommended complete removal of the bladder, the traditional operation known as radical cystectomy. Rather than risk a recurrence of cancer, eight patients opted for this operation.

In 34 cases, patients either responded well to early therapy or couldn't tolerate such a drastic operation. They went on with the experimental treatment, which consisted of more chemotherapy and radiation, the researchers report in the Nov. 4 New England Journal of Medicine.

Eleven other patients couldn't complete the experimental regimen. Some couldn't tolerate the harsh chemotherapy or radiation therapy, and others refused to undergo a radical cystectomy when doctors advised such a course.

Overall, out of the 53 patients studied, 28 (53 percent) were alive after about four years, when a follow-up examination was conducted. In addition, 24 of the 53 (45 percent) showed no visible evidence of a recurring tumor, the researchers note.

Of the 34 who completed the experimental protocol, 28 tolerated the full doses of chemotherapy and radiation. Of these, 25 (89 percent) remained free of bladder cancer, the team reports. These patients all had the added bonus of a functioning bladder, Kaufman points out.

Overall, the results of this pilot study suggest that this attempt to spare the bladder compares favorably with the surgeon's knife. Yet Kaufman points out that the study didn't include a control group and thus the survival statistics might be influenced by an unknown bias.

These results may force oncologists and surgeons to reevaluate their approach to invasive bladder cancer, comments oncologist Howard I. Scher of the Memorial Sloan-Kettering Cancer Center in New York City. The findings argue against "the automatic reaction of many people, which is to just remove [any] bladder with signs of muscle invasion," Scher says.

In the future, doctors may base their decisions about a bladder cancer regimen on the tumor's molecular characteristics, Scher adds. People with highly aggressive tumors may get a cystectomy, whereas others will start with a bladder-salvaging approach. Scher wrote an editorial that appears in the same issue.

Meanwhile, the Boston researchers continue to monitor their patients. Will some of these same people remain cancer-free for eight years or longer? "All I can say is that I'm hopeful," Kaufman says. —*K.A. Fackelmann*

Oxygen-extinction theory draws counterfire

It seems fitting that a team of researchers chose the week before Halloween to bring a controversial theory back from the dead. The scientists made news last week when they proposed that the dinosaurs died out because of a drop in the atmosphere's oxygen concentration 65 million years ago. Portions of that theory attracted intense criticism when first advanced six years ago, and researchers familiar with the work are showing even less charity this time around.

"It isn't cold fusion, but it has that kind of ring to it," says geochemist Harmon Craig of the Scripps Institution of Oceanography in La Jolla, Calif.

Gary P. Landis of the U.S. Geological Survey in Denver and his colleagues base their extinction theory on analyses of gas bubbles found in amber, a fossilized form of tree resin. They propose that the bubbles contain samples of air from the age of the dinosaurs.

At a meeting of the Geological Society of America in Boston, Landis and coworkers reported that the amber bubbles show a sharp drop in the atmosphere's oxygen concentration at the end of the Cretaceous period, from a high of 35 percent down to 29 percent. The researchers speculate that the oxygen decline — caused by changes in volcanic activity and sea level — killed off the dinosaurs because these reptiles had poor respiratory systems. This theory stands in contrast to the prevailing view that the dinosaurs and many other forms of life died out at the end of the Cretaceous at least in part because a huge asteroid or comet slammed into Earth.

Landis first raised the idea of analyzing air in amber in 1987 in a report with Robert A. Berner of Yale University. Landis and Berner came under attack from several scientists, who reported evidence that amber cannot trap air for millennia (SN: 8/27/88, p.141). Berner has since disassociated himself from this research and has refused to comment on the new work.

Many researchers were surprised that the amber studies have continued. "I'm just absolutely mystified that it could get this far again," says Harold B. Hopfenberg, a chemical engineer at North Carolina State University at Raleigh.

Hopfenberg, who specializes in diffusion studies, reported in 1988 that results of an experiment with propane molecules showed amber to be relatively porous, with a diffusion coefficient for propane of 10^{-13} square centimeters per second (cm^2/s). Because the main components of air are much smaller than propane, they should pass even faster through amber. Hopfenberg estimated that oxygen could permeate a chunk of amber within weeks, indicating that the gas trapped inside was hardly ancient air.

Craig and a colleague reached a similar conclusion in 1988, reporting that amber cannot contain air for long. Their experiments suggest that amber had a diffusion coefficient for oxygen of approximately 10^{-10} cm^2/s, in line with Hopfenberg's findings.

Many researchers thought such results sealed the debate on amber's permeability. But Landis remains convinced that amber can trap air for millions of years. His own experiments with argon gas suggest that amber has a much lower diffusion coefficient, less than 1.5×10^{-18} cm^2/s, he told Science News. This figure is eight orders of magnitude smaller than that reported by Craig — a disparity roughly equal to the difference between the length of a dollar bill and the diameter of Earth.

Hopfenberg takes issue with Landis' experiment: "He still confuses where, when, and how diffusional phenomena occur in amber." Craig says he too questions Landis' results. "You just don't have the feeling this is very believable," he says. If Landis and his colleagues cannot find stronger evidence to support their claims about amber, the scientific community may write off their dinosaur extinction theory as just hot air. —*R. Monastersky*