Liver Cancer: Homing in on the Risks

Liver cancer, one of the five leading human cancers, claims some 250,000 lives annually, primarily in Asia and Africa. Most cases can be traced to infection with the hepatitis B virus or to long-term, high-level ingestion of aflatoxins, poisons produced by a mold contaminating many crops, especially corn.

Teasing out each agent's contribution has proved difficult, because in areas where liver cancer is endemic, exposure to both tends to occur by age 2. Last week, however, researchers reported a promising marker of aflatoxin exposure and how it might be used to sort out the respective carcinogenic roles — and interaction — of aflatoxin and hepatitis.

This biomarker also opens the prospect of more effectively screening populations to find high-risk individuals for surveillance or cancer-prevention strategies, says chemist John D. Groopman of the Johns Hopkins University School of Hygiene and Public Health in Baltimore. Indeed, he says, clinical trials are already in progress to further investigate the safety of a drug expected to limit precancerous changes in individuals eating aflatoxin-rich diets.

Groopman described the new biomarker — an adduct, or chemically modified form of DNA — last week at an American Institute for Cancer Research conference in McLean, Va. Both rat and human urine can contain this characteristic adduct, whose concentrations correspond to the amount of aflatoxin consumed. Moreover, Groopman and his colleagues reported in the Jan. 15 CANCER RESEARCH, this "adduct in urine accurately reflects DNA damage at the primary [liver] site of aflatoxin-mediated damage."

Since 1986, Groopman and an international team of co-workers have been conducting a prospective study of 18,244 initially healthy, middle-aged Chinese men in Shanghai, an aflatoxin-rich region. To date, 40 liver cancers have occurred within the group. An analysis of the first 22 cases, Groopman said last week, showed that every time the DNA adduct was present in sampled urine, the risk of liver cancer "was increased two- to three-fold," compared to adduct-free men in the study of the same age who lived in the same neighborhood.

Moreover, Groopman asserts, "for the first time, we've been able to demonstrate that there is in fact an ... [apparent synergy] between hepatitis B virus and aflatoxin exposure." Preliminary data from the Shanghai trial indicate that men with urinary evidence of aflatoxin exposure *and* of previous hepatitis B infection proved 12 times more likely to develop liver cancer than men with signs of hepatitis B exposure only.

Groopman's team "is onto something valuable" with this adduct biomarker, says Leonard Cohen of the American Health Foundation in Valhalla, N.Y.

Adds R. Palmer Beasley, dean of the University of Texas School of Public Health in Houston, these "terrific" studies "support an important role for aflatoxin in liver cancer." Previously, he says, the toxin's role in human liver cancer was generally accepted — based on animal data and epidemiologic studies — but "not proven."

Last week, Groopman also reported data on a cancer-prevention trial in rats fed a high-aflatoxin diet for one month. Some of the animals also received Oltipraz — a U.S. Food and Drug Administration-approved antiparasitic drug — during that period. Though these animals excreted low levels of DNA adducts, they developed no liver tumors. By contrast, 9 percent of the animals not treated with Oltipraz developed precancerous liver nodules, and 11 percent had full-blown liver cancers.

In the body, cells convert aflatoxin into a carcinogenic epoxide. Groopman says that Oltipraz appears to protect against liver cancer by increasing concentrations of certain epoxide detoxification enzymes known as glutathione S-transferases (see p.311).

The next step "is to ask, Does this drug affect aflatoxin metabolism in people?" If it does, Groopman told SCIENCE NEWS, experimental intervention trials in highly exposed Shanghai men might get under way within five or six years.

These data suggest "there could be some hope for the people who are at high risk [of liver cancer]," Beasley says. But any such trials should focus on carriers of the hepatitis B virus in aflatoxin-rich regions, he says, because only they "would be at high enough risk [of cancer] to justify the cost or [side effects] of the drug." — *J. Raloff*

Sounding out a sharper ultrasound echo

Like a hose nozzle that squirts a central jet of water accompanied by a smaller, diverging ring of spray, conventional generators of ultrasound usually produce multiple beams that fan out from their source. The presence of side beams represents one of the factors that at present limit the definition of images produced by bouncing high-frequency sound waves off a surface and detecting the echoes.

Now Mack A. Breazeale and Dehua Huang of the University of Mississippi in Oxford have developed improved ultrasound generators, or transducers, that emit single beams at frequencies of either 375 or 332 kilohertz. Moreover, in each case, the beam's intensity peaks in the middle and tails off toward the edges, exhibiting the bell-shaped curve of what researchers call a Gaussian, or normal, distribution. Breazeale described the improved transducer design at an Acoustical Society of America meeting held this week in New Orleans.

Any kind of acoustic imaging — sonar, medical ultrasound imaging, acoustical microscopy, ultrasonic nondestructive evaluation techniques — would benefit from the availability of well-defined sound beams, he notes.

An ultrasound transducer typically consists of a circular plate fabricated from a quartz crystal. Applying an alternating electric field via metal electrodes deposited on the plate's two surfaces causes the quartz to expand and contract, making the plate get thicker and thinner. Immersed in air or water, such an oscillating plate generates high-frequency sound waves.

The trick is to shape the plate and electrodes to generate a single, Gaussian beam rather than multiple beams. "What I want to do is to have the center vibrating with large amplitude and the edges with zero amplitude," Breazeale says. "The idea actually is obvious. The trouble is trying to make it work."

In a project that has taken more than a decade, Breazeale and his collaborators have gradually lowered the frequency at which their custom-designed transducers generate single, Gaussian beams of sound waves, starting at 4 megahertz. Many ultrasound applications, however, require beams of much lower frequencies. For example, sonar usually operates at frequencies ranging from 5 to 50 kilohertz.

"We have developed a technique over the past couple of years that seems to work, so we've gotten down to around 375 kilohertz," Breazeale says. "We're going in the right direction. We're shooting for as low a frequency as we can practically arrive at."

The researchers are now working on a Gaussian transducer made from a quartz plate 6 inches in diameter, which would operate at frequencies closer to 250 kilohertz. — *I. Peterson*