Heavy exposure to solvent linked to cancer

The chemical solvent trichloroethylene has a bad reputation these days. The popular nonfiction book *A Civil Action* (1995, Jonathan Harr, Random House) and its movie version relate how residents of a Massachusetts town came to blame a set of leukemia cases on trichloroethylene and other chemicals in the town's water supply.

In Europe, scientists know trichloroethylene well. During studies of various cancers, they have analyzed patients' exposure to the solvent. While the work hasn't yet produced hard proof that the chemical causes malignancies, German researchers now report strong evidence linking excessive trichloroethylene exposure to cancer via a specific gene mutation.

For decades, metal-processing workers in Germany used trichloroethylene as a degreaser—breathing its fumes in poorly ventilated rooms, washing floors with it, even scrubbing their hands and arms with the chemical. To gauge the cancer risk these practices imparted, scientists scrutinized a gene called *von Hippel-Lindau (VHL)*, which normally suppresses the disease.

Mutations in this gene cropped up in 33 of 44 kidney cancer patients who had been exposed to trichloroethylene in the workplace, researchers report in the May 19 JOURNAL OF THE NATIONAL CANCER INSTITUTE. In general, about half of kidney cancer patients have a mutated *VHL,* says coauthor Hiltrud Brauch of the Margarete Fischer-Bosch Institute of Clinical Pharmacology in Stuttgart.

The intensity of exposure to trichloroethylene varied among the former factory workers, and those getting heavier doses of the solvent over many years were more likely to have multiple *VHL* mutations. Of the 17 cancer patients with the greatest solvent exposures, 11 had two or more mutations in *VHL*.

The *VHL* gene is a string of hundreds of nucleotides, the components of DNA. At nucleotide 454, the scientists identified a potential weak link in the molecular chain. In 13 of the trichloroethylene-exposed cancer patients, a defect showed up at this precise location. In contrast, none of 107 people with kidney cancer who had not been exposed to trichloroethylene and none of 97 healthy volunteers had a mutation at nucleotide 454. Of 14 patients with multiple *VHL* mutations, 9 had a defect at the 454 spot.

"I think this is a very important, exciting study," says W. Marston Linehan, a urologist at the National Cancer Institute in Bethesda, Md. While researchers suspected a link between trichloroethylene and kidney cancer, "there was no molecular basis for it until this study," he says.

However, the study data don't establish whether such a mutation is merely a marker of trichloroethylene overexposure or instead a risk factor for kidney cancer, says toxicologist Laura C. Green of Cambridge Environmental, a consulting firm in Massachusetts. Further tests on animals may clarify this point, she says.

Also, the study concentrates on gross overexposure to the chemical and so contributes little to the debate behind *A Civil Action.* The German workers encountered trichloroethylene doses that "are thousands of times greater" than the amounts people typically come across in contaminated air or drinking water, Green says.

The researchers have produced "a good paper," says toxicologist Steven R. Tannenbaum of the Massachusetts Institute of Technology. However, he cautions that the work on *VHL* mutations, and particularly the 454 nucleotide site, is far from conclusive. He notes that the majority of the heavily exposed workers with kidney cancer had an intact 454 site.

The cancer tracked in this study, clear-cell renal carcinoma, accounts for roughly 85 percent of kidney cancer cases, Linehan says. Kidney cancer itself ranks 13th in frequency among malignancies in the United States. It is diagnosed in roughly 27,000 people annually and accounts for about 12,000 deaths every year. —*N. Seppa*

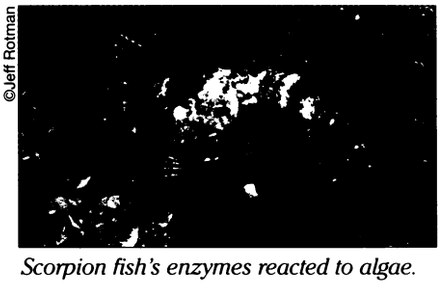
Rogue algae may harm Mediterranean fish

Since it got loose in the mid-1980s, an aquarium-derived variant of a tropical seaweed has been spreading over the bottom of the Mediterranean Sea like a dense shag carpet. A new study now shows that this alien form of *Caulerpa taxifolia* may do damage beyond usurping floor space. The alga alters the activity of a fish's chemical-detoxification enzymes, even in fish that don't eat the weed.

This alga is an abnormally large, fast-growing variant of a species found naturally in tropical waters. Unlike the natural *Caulerpa,* which grows in small clumps and would never survive the Mediterranean's cool winters, the weedy variant has been choking out native flora and fauna (SN: 7/4/98, p. 8). Lack of natural predators in its new home aids this *Caulerpa's* advance.

Scientists in Montpellier, France, recently teamed up to probe the Mediterranean alga's effect on finfish. They housed locally caught scorpion fish, *Scorpaena porcus,* in aquariums for 4 weeks. One group of fish had no exposure to the alga. Another group ate mussels that the researchers had injected with ground-up *C. taxifolia.* The third group shared a tank with the *Caulerpa,* but not being algae eaters, these fish didn't consume the weed.

At the end of the 4 weeks, the researchers killed the fish and extracted their cytochrome P-450 enzymes, which break down chemicals. Then, they incubated these enzymes with the hormone progesterone. Christian Larroque of INSERM, the French Institute of Health and Medical Research, uses such hormones to assay the activity of an animal's detoxification system.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Scorpion fish's enzymes reacted to algae.

Exposure to *Caulerpa* through ingesting the alga or merely sharing a tank altered the fish's P-450 enzyme activity, Larroque's team reports in the May 15 ENVIRONMENTAL SCIENCE & TECHNOLOGY. Enzymes from the exposed fish produced only 25 percent as much of the major breakdown product of progesterone as enzymes from unexposed fish did. On the other hand, the enzymes from exposed fish produced unusually high amounts of a second breakdown product.

"We now plan to cage fish with *Caulerpa* in the sea to see if they respond the same way," Larroque says.

He adds that it's too early to say how the *Caulerpa* triggered the changes. However, his team suspects the effects may trace to caulerpenyne, a toxin made by the weed. In preliminary tests, caulerpenyne indeed appeared to inhibit fish P-450 enzymes, Larroque told SCIENCE NEWS.

Though the observed enzyme changes may not be deleterious, they raise a concern that affected animals might not be able to quickly clear a variety of chemicals from the body before they cause toxicity, Larroque notes. It "adds to concerns about what a dastardly weed this is," says *Caulerpa* biologist James N. Norris of the Smithsonian Institution's National Museum of Natural History in Washington, D.C.

Last October, a group of scientists recommended a ban on the weed's importation into the United States (SN: 11/21/98, p. 332). In record time, the federal government complied. Last month, it listed the alien form of *C. taxifolia* under the Federal Noxious Weed Act—the first marine plant banned under this law.

Photos of the alien alga have been circulated to agents of the Animal and Plant Health Inspection Service (APHIS). From now on, explains Polly P. Lehtonen of APHIS in Riverdale, Md., any plant labeled as *C. taxifolia* or resembling it will be barred from entry to the United States, unless experts show it is the noninvasive tropical form of the species. —*J. Raloff*