Estrogenic agents leach from dental sealant

For 30 years, dentists have used a class of plastic resins to seal teeth from decay-causing bacteria and to help repair teeth that have developed cavities. Now, a new study reports that significant quantities of bisphenol A, a chemical building block of these resins, can leach into the saliva of treated patients.

In the body, this chemical can emulate the female sex hormone estrogen. Exposure to estrogenlike agents—especially during fetal or early postnatal development—can trigger gender-bending changes (SN: 7/15/95, p. 44) or reproductive havoc (SN: 1/22/94, p. 56). They may also foster cancer in reproductive organs such as the breast (SN: 7/3/93, p. 10).

Researchers at the University of Granada in Spain applied about 50 milligrams of a bisphenol-A-based dental sealant to the molars of 18 college-age volunteers. The scientists then hardened the material using a curing process that links individual molecules of bisphenol A into a chainlike polymer.

Because studies by others had shown that such curing fails to harden all of the bisphenol A, the Granada group looked for leaching of this chemical or of small, partial chains known as bisphenol A dimethacrylate. They took saliva from each of the volunteers before and 1 hour after they had been treated and compared the samples.

In the just-published March ENVIRONMENTAL HEALTH PERSPECTIVES, Nicolás Olea and his coworkers report finding between 90 and 931 micrograms of bisphenol A in the roughly 30 milliliters of saliva obtained from each person after, but not before, treatment. The researchers also found some dimethacrylate in the saliva of three volunteers after treatment. The scientists then confirmed the estrogen-mimicking ability of bisphenol A and dimethacrylate in a test of human breast cancer cells.

"This study seems very well done and well controlled," says Jack L. Ferracane, chairman of biomaterials and biomechanics at Oregon Health Sciences University in Portland. However, while he observes that "we don't know a lot about these resins," he says the leaching of bisphenol A here "seems at odds with other studies, which don't show this [leaching]."

Though some of the never-cured molecules "will come out," he acknowledges, "that happens relatively quickly and doesn't provide a constant source of exposure." So "the seriousness of this issue seems limited," he concludes.

"It's premature to say that," counters endocrinologist Ana M. Soto of Tufts University School of Medicine in Boston, a coauthor of the new study. "We have some evidence that bisphenol A is still leaching after 2 years." To determine how common long-term leaching is, her group has collected 6-month follow-up samples of saliva.

Soto notes that dental resins also wear away in time and are ingested. While there are no data on how much of this material crosses the stomach lining and enters tissues, "this is something that should be studied," she maintains.

Frederick S. vom Saal of the University of Missouri-Columbia agrees. Though the Granada study indicates that it takes 10,000 times as much bisphenol A to elicit the same effect in human cells as the body's natural estrogen, his work indicates that such cell culture studies underestimate the potency of this estrogen mimic.

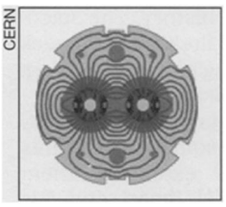
Much estrogen in the body is bound to blood proteins and cannot enter cells. Vom Saal's recent experiments with cells in culture suggest that bisphenol A does not bind to these proteins as well as estrogen does. So proportionally more bisphenol A would be available to interact with cells.

"Our studies show that estrogens operate at a trillionth of a gram per milliliter of blood," he says. The bisphenol A measured in saliva during the Granada study is "100 million times higher than the amount of estrogen that is biologically active in the human fetus." But as yet there is no indication of how much bisphenol A in saliva would actually enter the blood.

Although fetuses are unlikely to be exposed to bisphenol A, vom Saal worries that such environmental hormones might cause serious, irreversible problems during other periods of development, including puberty.

Indeed, he says, based upon the amounts of bisphenol A being reported by Olea's group, "I would be concerned about the possibility of high levels of this chemical getting into a child. And until we learn more about its biological effects, as a parent I would therefore err on the side of caution" when it comes to using dental sealants. —*J. Raloff*

Toward a U.S. role at CERN's new collider



Representation of the magnetic field that confines and bends a pair of proton beams inside a superconducting magnet at the Large Hadron Collider.

Tracking the particles created in high-energy, head-on collisions between protons requires massive detectors that can record particle paths to within a millimeter and can precisely measure the energy of these scattered fragments.

Physicists and engineers have teamed up to design and build two such detectors for the Large Hadron Collider (LHC), under construction at the European Laboratory for Particle Physics (CERN) near Geneva (SN: 1/7/95, p. 4). Several hundred U.S. physicists have already formed collaborative groups to participate in this effort.

"Our scientists are heavily involved with their European counterparts in determining the detailed design of both detectors," says John R. O'Fallon, head of the high-energy physics division at the U.S. Department of Energy.

Last week, officials from DOE, the National Science Foundation, and CERN reached agreement on the approximate scale of U.S. involvement in building not only the detectors for the LHC but also the collider itself. The agreement calls for funding from DOE in the range of $400 million to $500 million, divided equally between the collider and detector projects and spread out over 8 to 10 years. The NSF contribution to detector work would be about $80 million over the same period.

Overall, the LHC is expected to cost about $2.7 billion to build, and the cost of its two main detectors would total $1 billion.

The new agreement represents a significant step toward putting U.S. participation in the LHC effort on a firm legal and financial basis. Now, it's up to negotiating teams to work out the technical details of how these funds would be used.

"We think this is positive progress, and we're very pleased to be at this stage of the game," says Martha A. Krebs, director of DOE's energy research office. However, "we are far from finished. There are lots of issues that are going to face us in these negotiations in order to get the best possible arrangement for the U.S."

The LHC is slated to go into CERN's existing tunnel, some 27 kilometers in circumference, which now houses an electron-positron collider. The proposed

LHC design requires more than 1,000 high-powered superconducting magnets to accelerate protons to nearly the speed of light and bend their paths to keep them on a steady course around the ring.

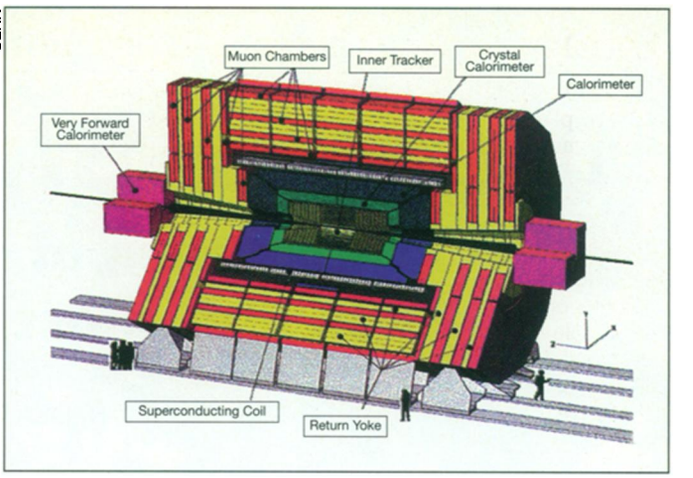
When the LHC's two adjacent proton beams, circulating in opposite directions around the ring, are brought together, protons collide at a combined energy of 14 teraelectronvolts. This energy should be high enough for researchers to detect the postulated Higgs boson. Theorists have proposed that this particle is responsible for determining the masses of other fundamental particles, but no one has detected any traces of it at the energies now accessible to particle accelerators.

The builders of both the LHC and its two main detectors face a number of formidable technical challenges. For instance, the collider's magnets must maintain larger magnetic fields than those used previously in accelerators, and they must operate at a frigid 1.9 kelvins, about 300°C below room temperature and even colder than liquid helium. Moreover, the LHC's detectors must be able to withstand intense radiation yet rapidly and precisely measure the trajectories and energies of hundreds of millions of photons, electrons, and muons per second.

Officials of DOE hope to reach a final agreement with CERN by November, before preparing the department's 1998 budget for congressional consideration.

— I. Peterson

CERN



This cutaway view of the Compact Muon Solenoid particle detector shows the instrument's layered structure. A large superconducting coil generates a uniform magnetic field of 4 teslas at its core. The detector itself measures 14.6 meters wide and 21.6 m long. Collisions between protons traveling in opposite directions spray debris into the detector's walls, where calorimeters and other devices record the arrival of the scattered particles.

Bringing bold color to chromosomes

When television executives colorize classic black-and-white films such as *Casablanca*, howls of protest from movie purists fill the air. In contrast, a report announcing the colorization of human chromosomes has raised a hue and cry of delight among geneticists—24 hues, in fact.

By attaching fluorescent markers to carefully chosen DNA sequences, investigators have learned how to paint a color-coded picture of all 24 human chromosomes (the sex chromosomes X and Y and the 22 chromosomes present in pairs).

This newly developed artistic ability should improve diagnosis of the many chromosomal abnormalities that cause cancer or other genetic diseases.

"It offers the promise of greatly improving the efficiency, as well as potentially the accuracy, of both clinical and research chromosome analysis," says Huntington F. Willard of Case Western Reserve University School of Medicine in Cleveland.

The color-coding technique is described in the April NATURE GENETICS by Michael R. Speicher, Stephen Gwyn Ballard, and David C. Ward of Yale University School of Medicine. It is "a beautiful (scientifically and literally) study," observes Michelle M. Le Beau of the University of Chicago in an accompanying commentary.

Researchers studying chromosomes traditionally stain them to reveal distinctive black-and-white banding patterns. By painstakingly analyzing the bands, a task difficult to automate, scientists can often spot chromosomal irregularities.

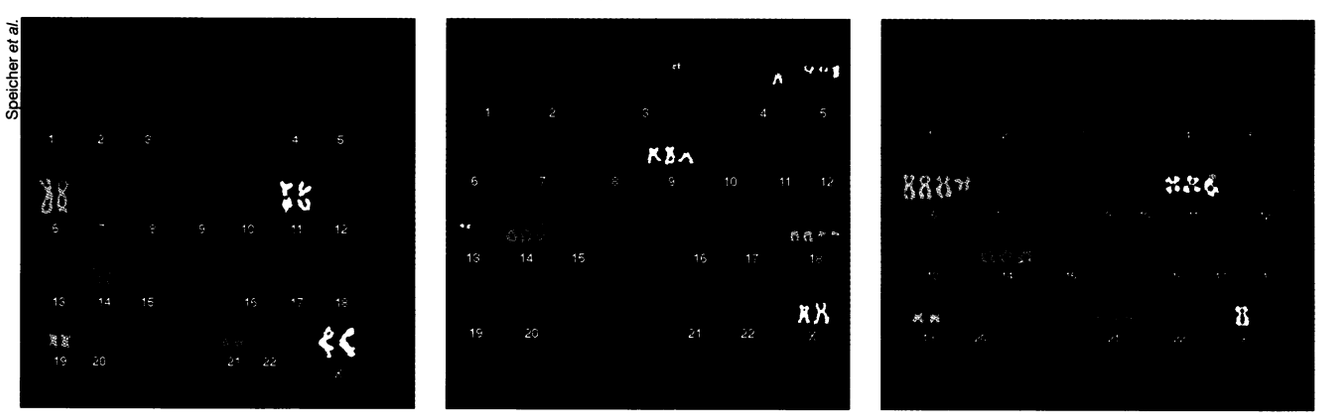
To improve the odds of finding abnormalities, and to make possible the automation of such analysis, researchers have experimented with linking fluorescent markers to known DNA sequences. These DNA-based probes attach only to specific sites within the human chromosomes.

By labeling thousands of chromosome-specific DNA sequences with five different fluorescent markers, the Yale group was able to produce unique spectral fingerprints for each of the 24 chromosomes. Using these fingerprints, they assigned a different color to the computer image of each chromosome.

This method has made it easier for researchers to detect abnormalities such as translocations, in which pieces of chromosomes exchange places with one another. "That's very important for tumor cytogenetics. Many of these rearrangements can't normally be deciphered," says Speicher.

Other research groups are working on variations of the Yale technique, ones they hope will be less costly or even easier to automate. *— J. Travis*

Speicher *et al.*



A new analytical technique colorfully shows the differences between the chromosomes in a normal cell (left) and those in cancer cells (center and right). In dividing cancer cells, parts of chromosomes inappropriately trade places and extra chromosomes persist.