Psychological Stress Linked to Cancer

As if the sagging economy and rush-hour commuting weren't stressful enough, here comes a provocative pair of studies to add to your worries. They indicate that psychological stress may increase an individual's risk of developing certain cancers.

Two years ago, Australian researchers reported that stressed-out individuals might face an increased risk of colorectal cancers — malignancies that each year strike an estimated 152,000 people in the United States alone. Hoping to verify that link, Joseph G. Courtney of the University of California, Los Angeles (UCLA), School of Public Health and his co-workers joined forces with researchers in Sweden who had access to a large database on Stockholm-area patients with colorectal cancer.

The researchers recruited 569 of these men and women for their study, along with 510 randomly selected cancer-free adults. Each of the study's participants then answered a series of questions about stressful events.

In the September EPIDEMIOLOGY, Courtney's team now confirms that severe on-the-job aggravation appears to put people at increased risk of developing colon and rectal cancers. Those who reported a history of workplace problems over the past 10 years faced 5.5 times the colorectal-cancer risk of adults who reported no such problems.

That association held even after the researchers accounted for diet and other factors that had previously been linked to these malignancies. Unpublished research by the UCLA team also hints that individuals who toil in high-pressure situations while possessing little or no control over workplace decisions face the highest risks.

In a second new study, Japanese researchers report finding cellular changes in psychologically stressed animals that may explain how anxiety might foster cancer.

For their investigations, Shuichi Adachi and his co-workers at Saitama Medical School in Moroyama caged sets of 30 young rats in a "communications box." The box is laid out like a checkerboard, with half the rodents — those in the chambers corresponding to the red squares, for instance — receiving periodic electrical shocks over a 5- to 10-hour period. The study then monitored how nonshocked animals, in cages corresponding to the black squares, responded biochemically to the psychological stress induced by watching, listening to, and smelling the torment of their neighbors.

In terms of the amount of altered DNA in their tissues, nonshocked rats that had completed one day of tests were no different from animals that had never participated in the psychological testing. But nonshocked rats that endured two to four days of such tests developed sharply elevated concentrations of 8-hydroxy-2′-deoxyguanosine in the DNA of their livers.

This oxidative change, known as a DNA lesion, occurs spontaneously in the target organs of animals exposed to carcinogens, radiation, or an overabundance of free radicals — biologically damaging chemical agents possessing one or more unpaired electrons.

The stress-induced increase in the number of lesions in liver DNA "must be interpreted as [caused by] excess generation of reactive oxygen species," Adachi's team concludes in the Sept. 15 CANCER RESEARCH. As such, they report, it constitutes "the first evidence that oxidative damage to nuclear DNA is induced by psychological stress."

The rats appeared to be able to repair most of the stress-induced lesions within an hour. However, numerous studies have shown that as animals age, they tend to accumulate such oxidative lesions in their DNA. And in the Sept. 1 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, Bruce N. Ames and his co-workers at the University of California, Berkeley, review the cancer significance of those lesions. If present when a cell divides, they note, "an unrepaired DNA lesion can give rise to a mutation" — and ultimately a malignancy.

Nor is the liver the only organ vulnerable to stress-mediated cancers, Adachi's team reports. The Saitama researchers note that mice psychologically stressed every other day for four months proved more susceptible to urethane-induced lung tumors than unstressed animals exposed to this carcinogen.

The Japanese study offers a "superior model" of psychological stress in humans, Courtney told SCIENCE NEWS.

Scientists know that stress can trigger the body's "fight-or-flight" response, in which the adrenal glands churn out powerful hormones that divert blood flow from internal organs (such as the intestines or liver) to the brain, muscles, and heart. Once the danger subsides, blood rushes back into the oxygen-starved internal organs, Courtney says. That burst of oxygen-rich blood may lead to increased production of free radicals — and DNA lesions.

In addition, stress weakens the immune response, Courtney says. A vigorous immune response should kill damaged cells. However, if the immune system is compromised, a malignant cell might escape, spawning a tumor, he suggests. *— K.A. Fackelmann and J. Raloff*

New gene study enters human origins debate

In a finding that captured the imagination of scientists and the public alike, researchers announced in 1987 that an analysis of mitochondrial DNA — genetic material located outside the cell nucleus and inherited only from the mother — traced the maternal lineage of all humans back to an African "Eve" who lived about 200,000 years ago. A computer-run statistical analysis of mitochondrial DNA samples drew an evolutionary tree with African roots lying at mitochondrial Eve's feet, suggesting modern humans originated in Africa and rapidly spread elsewhere.

Fatal statistical flaws in this approach later emerged and researchers dropped genetic arguments for the "Out of Africa" theory (SN: 2/22/92, p.123). However, a new type of mitochondrial DNA analysis, described in the August-October CURRENT ANTHROPOLOGY, now presents a more complicated picture of human evolution.

In this scenario, a small subgroup of *Homo erectus* evolved into modern humans — probably in Africa — and slowly trekked to several parts of Europe and Asia beginning around 100,000 years ago. About 50,000 years later, geographically isolated human populations experienced dramatic growth and expansion fueled by the appearance of many cultural innovations.

Genetic analysis offers weaker support for the multiregional evolution theory, a competing view of human origins, contend Henry C. Harpending, an anthropologist at Pennsylvania State University in University Park, and his colleagues. The multiregional theory holds that modern humans evolved simultaneously in several parts of the world for around 2 million years, with contact between separate populations along the way.

Rather than constructing evolutionary trees out of genetic data, Harpending's group analyzed the differences in sequences of mitochondrial DNA both within and between human groups now living in Africa, Asia, and Europe. According to the researchers, these differences preserve a record of ancient population expansions and separations, which they modeled in computer simulations of mitochondrial DNA change in pairs of populations.

"In living populations, between-group mitochondrial DNA differences far out-

pace within-group differences," Harpending holds. But this pattern of change in the structure of mitochondrial DNA does not characterize his computer models of single populations that rapidly grow and split into separate clusters. "Groups of archaic humans apparently remained isolated from each other for tens of thousands of years," Harpending says.

The dating of humanity's common mitochondrial ancestor does not show that our species suddenly evolved around 200,000 years ago, Harpending says. The mitochondrial DNA evidence simply cannot illuminate the structure of human populations before that time, he asserts. But his group estimates that the number of human females at the time mitochondrial Eve lived ranged from 1,000 to no more than 10,000.

This relatively small population shows genetic signs of slight size expansion in Africa around 100,000 years ago, with major size increases occurring on that continent approximately 80,000 years ago, the researchers maintain. Population growth blossomed in Asia and Europe about 50,000 to 40,000 years ago, according to the mitochondrial DNA comparisons.

Up until these growth spurts, stone tools and other artifacts found at sites throughout Eurasia displayed many similarities; soon thereafter, sophisticated regional cultures appeared, Harpending and his co-workers note. Indeed, cultural change may have sparked marked population increases in dispersed human groups, they argue.

Alan R. Templeton, an evolutionary biologist at Washington University in St. Louis, regards the new analysis of mitochondrial DNA with considerable skepticism. He provided the statistical critique that chopped down earlier evolutionary trees derived from mitochondrial DNA.

"This study is a step in the right direction," Templeton remarks. "But the computer models of population expansion are pretty simple and only test the Out of Africa theory, not multiregional evolution."

Harpending acknowledges that large margins of error exist in his simulations: "We all feel that we need to move beyond mitochondrial DNA as a locus of study."

In a report in the March AMERICAN ANTHROPOLOGIST, Templeton found no evidence for a definite geographic origin for a common mitochondrial ancestor, whom he dates to around 800,000 years ago. Current mitochondrial DNA variations come from dispersed, ancient populations, he contends.

Using a computer program that analyzes the geographic distribution of DNA differences, Templeton concluded that humans experienced size expansions largely within continents, with periodic contact across continents.

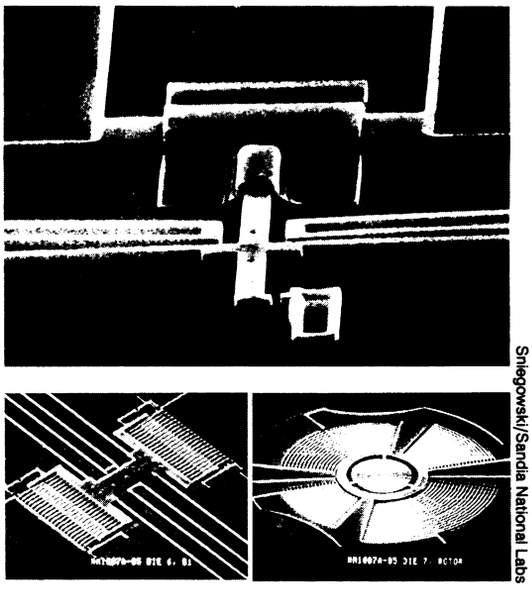
—B. Bower

Micro steam engine makes forceful debut

For some time now, microelectronics engineers have been chugging along, struggling to build a pinhead-size engine capable of doing some real work on the tiniest scale. The goal is to hook a micromotor to some minitools and move speck-like objects around. But until recently, state-of-the-art engines just haven't had enough oomph.

Now, a new motor has come onto the scene: a steam engine small enough to sit on a computer chip, yet powerful enough to do useful work.

Invented by Jeffry J. Sniegowski, a physicist at Sandia National Laboratories in Albuquerque, and his colleagues, the engine measures all of 6 microns long and 2 microns wide. Perched on a polycrystalline silicon wafer, it sports "a single piston that slides in and out of a silicon sleeve, moved by a bubble of water vapor that expands and contracts as it's heated," Sniegowski says.



Sniegowski/Sandia National Labs

Micron-scale motors: Above, a new steam engine; below, two electrostatic motors.

What distinguishes this engine from the more common types of micromotors — called electrostatic comb devices — is its strength. It can deliver up to 100 times more power than the electrostatic motors, with a peak force of roughly half a micronewton. Unlike electrostatic actuators—which use electrical charge rather than water vapor pressure to do their work — this steam engine could potentially open and close gates and cut, move, and probe objects smaller than a single human blood cell.

"One of the biggest problems with microactuators is producing enough force to do the work you need done," says Paul McWhorter, an electrical engineer at Sandia who helped develop the steam engine. "The existing devices, mostly electrostatic comb motors, look very impressive when they're running. But they don't deliver much force, which is a problem. In some cases, the force generated is only a little more than the internal friction generated by the device itself. This [steam] engine uses a fundamentally different type of actuation."

Sniegowski originally developed the steam engine to move an optical sensor inside a nuclear weapon, but he is now looking for more general civilian applications. "We want to build a set of microtools, which means coupling this steam engine to small tweezers, scalpels, probes, or sensors. Since it generates enough force to do work, the question is, what useful work should it do?"

Possibilities include microsurgery or any other delicate operation that requires sensitively positioning objects as small as a single cell. "Eye surgery, neurosurgery, certain areas of brain surgery come to mind," says McWhorter. "Right now we're looking for neurosurgeons and eye surgeons to tell us what they really need."

Other potential applications include use in fiber optics, lasers, electron microscopy, and semiconductor manufacturing — "basically, any area of science or medicine where very precise alignment is a critical factor," says McWhorter. Even sensors. "It turns out that these devices make excellent accelerometers and pressure sensors, which are useful for cars, boats, planes, or any vehicle that needs a navigation system. Since they can detect subtle motion changes, they may also be useful in geological research as seismic monitors."

Another advantage of the miniature steam engines is that "they're cheap to make," says McWhorter. "You can fabricate them in a facility for making high-density electronic memories for less than $10 apiece. For about $50,000 you can produce 20 wafers, each with 1,000 steam engines on it. When you figure in production costs and throw away the engines that don't work, the end price would be between $5 and $10 apiece. And, of course, as the volume rises, the price falls. This is a much simpler structure to build than a computer chip."

Both Sniegowski and McWhorter say they have entertained some far-off applications as well.

"People have talked to us about powering microrobots, microrefrigeration systems for computer chips, devices that float in a person's bloodstream," says McWhorter. "But for now, the next step is to build the microtool kit by coupling the engine to pumps, valves, and tweezers."

—R. Lipkin