Cell Videos Catch Asbestos in the Act

Molecular moviemakers have produced the first graphic evidence suggesting why the size of an asbestos fiber plays a key role in its toxicity. Another research team has shown that asbestos can activate a versatile enzyme present in all living cells, turning on cell proliferation. Together, the new findings provide important clues to how needle-like asbestos fibers trigger cancer.

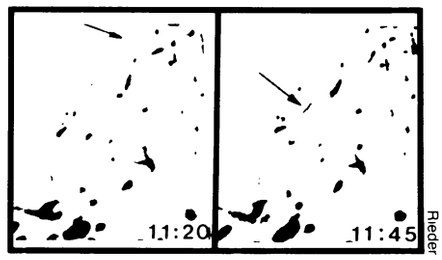
Asbestos, a potent carcinogen, has long eluded attempts to discover its biological mode of action. Several hints have emerged in recent years, however. For instance, unlike most carcinogens, asbestos fibers do not cause cells to mutate. And many studies indicate that straight asbestos fibers – especially long, thin ones – are more carcinogenic than curly ones (SN: 2/3/90, p.79).

New videos of lung cells exposed to needle-like crocidolite asbestos now suggest why. Conly L. Rieder and his colleagues worked with cells from newts. "There's no way the studies we're doing right now could be conducted in human or rat cells because they're too little," explains Rieder, who directs the NIH Biological Microscopy and Image Reconstruction National Resource at the Wadsworth Center for Laboratories and Research, in Albany, N.Y.

The team's live-action movies, described in the Sept. 15 CANCER RESEARCH, show that a lung cell incorporates crocidolite fibers by encapsulating each in a membrane sac called an endosome.

The researchers found that endosomes carrying crocidolite fibers 5 micrometers or smaller quickly begin speeding toward the cell nucleus via microtubules – elaborate, filamentous roadways along which the cell shuttles its inner "vehicles." Endosomes holding larger fibers never make it onto these roadways; instead, they slowly move toward the nucleus through Brownian motion.

Rieder's group worked with cultured, nondividing cells. However, he says, the new findings suggest that in a dividing cell, endosomes with small asbestos fibers would continue to scoot along the tubule roadway, but away from the region of the dividing chromosomes. If so, this could spare the chromosomes from potentially carcinogenic asbestos-induced changes, he says. Because the microtubules appear to ignore endosome-enclosed fibers larger than 5 micrometers, Rieder says he suspects that any such fibers near the nucleus when a cell begins to divide will stay there – ideally placed to "gum up" chromosome division. It's something he hopes to film in follow-up investigations of dividing cells.



Video frames taken 25 seconds apart show a small asbestos fiber (arrow) moving rapidly along an unseen microtubule.

Rieder's study "is a very elegant demonstration of the mechanisms by which asbestos fibers are incorporated into cells – one that I think will yield new insights into our understanding of the consequences of asbestos exposures and perhaps the importance of fiber size," says J. Carl Barrett, a molecular biologist at the National Institute of Environmental Health Sciences in Research Triangle Park, N.C.

In new work at the University of Vermont College of Medicine in Burlington, scientists have shown that "mechanistically, asbestos acts through a pathway which turns on cell proliferation – like a classic tumor promoter," says study coauthor Brooke T. Mossman. Using hamster lung cells, her team observed that crocidolite can activate an enzyme, protein kinase C (PKC), in the cell's outer membrane. When activated, PKC signals the cell to begin proliferating. However, unlike "classic" chemical tumor promoters such as phorbol esters, asbestos "does not appear to activate PKC by a receptor-like interaction," the researchers report in the September CARCINOGENESIS. The insoluble asbestos fibers may instead trigger PKC activation by some unknown change in the membrane, they say.

The new studies suggest that multiple mechanisms contribute to asbestos carcinogenesis, says Barrett, whose own work focuses on the activation of cancer-causing genes and inactivation of tumor-suppressor genes in an asbestos-induced cancer known as mesothelioma.

– J. Raloff

Clues emerge from vowels of the brain

The unusual spelling problems of two Italian-speaking men who suffered brain-damaging strokes in 1990 suggest that the brain uses separate mechanisms to identify vowels and consonants, according to a report in the Sept. 19 NATURE. The distinction between vowels and consonants may reflect "a psychological reality" rather than just a formal property of written languages, concludes psychologist Roberto Cubelli of Maggiore Hospital in Bologna, Italy.

Both men suffered damage on the left side of the brain and displayed marked difficulties with written vowels. In an examination two weeks after his stroke, one man omitted all vowels when writing his name, the town he lives in and the names of common objects, leaving blank spaces between correctly written consonants. For instance, instead of "Bologna," he wrote "B l gn ." Although aware of his spelling errors, the man still could not come up with any vowels. This vowel-specific disturbance – never before identified in a brain-damaged patient, Cubelli says – largely improved in the week following testing.

The other man wrote vowels as well as consonants but made an overwhelming number of spelling errors involving vowels. Most of the time, he either replaced a vowel with an incorrect alternative vowel or transposed two vowels in the same word. For example, he wrote "dietro" (the Italian word for "behind") as "diatro," and "caro" (Italian for "dear") as "cora." The high proportion of vowel errors applied to both common and unusual words. Moreover, the error pattern appeared whether the man spelled the words aloud, wrote them by hand or used a typewriter. Yet when single vowels and syllables were read to him, he wrote them down without error.

Cubelli proposes that the representation of any word in the brain may include a breakdown of each letter's status as a consonant or vowel. Brain damage in the first man produced a total inability to pluck vowels from the cerebral vowel organizer, whereas in the second man it led to incorrect vowel choices, Cubelli maintains.

The contrast between vowels and consonants in the two men's writing problems remains unexplained, argues psychologist John C. Marshall of Radcliffe Infirmary in Oxford, England. A reversal of the first man's problem – an omission of all consonants from words – probably could not occur, he says.

In a commentary accompanying Cubelli's report, Marshall writes, "One might reflect tht whn y wrt wtht vwls the message is still fairly clear, but e ou ie iou ooa. . . ."

– B. Bower