on from there" to expand the discovery into other areas of physiology and possible medical applications. "It's all very well to make suggestions," says Vane. "It's different to make the actual discovery."

Believing that it was "unjust and unfair" to omit Moncada from the prize, Vane wrote a letter, before the prize was announced, to the Albert and Mary Lasker Foundation, hoping to influence the announcement—or at least draw attention to the narrowness of the selection. He also circulated copies among members of the U.S. National Academy of Sciences, of which he is a member. Others have also expressed concern, including Gertrude Elion, a Burroughs Wellcome scientist who won the Nobel Prize in 1988 for a variety of drug discoveries, including acyclovir, and Max Perutz of Cambridge University, winner of the 1962 Nobel for structural studies of globin proteins. Elion declined to comment. Perutz described Moncada as "the chief pioneer of the physiologic function of nitric oxide." Perutz wrote to the Lasker prize committee, too, and says he received a routine response noting that the prize decision was reached by a "large and competent committee." But, Perutz adds, "I don't agree with it."

Furchgott declined to comment on the dispute, although he called Moncada "a brilliant scientist," and noted that France's Roussel-UCLAF prize in 1994 was awarded to himself, Ignarro, and Moncada. Moncada, who was elected to the National Academy of Sciences in 1994 on the basis of his research on nitric oxide, also declined comment.

As for the Lasker group, neither the director of the prize, Jordan Gutterman of the M.D. Anderson Cancer Center in Houston, nor the leader of the jury in this case, Joseph Goldstein of the Southwestern Medical Center at the University of Texas, Dallas, would comment on how it selected the two winners this year. But Gutterman stated that "important work done later by other investigators is not precluded from other awards."

A U.S. member of the National Academy of Sciences familiar with the case commented on condition of anonymity that "there were a lot of people who made contributions" to the pioneering work in nitric oxide physiology: "A very good case can be made that Moncada was an important contributor, and a very good case could be made that the way the [prize committee] formulated it was equally appropriate." He added, "a good case can be made that [Ignarro] should be included" as well, particularly because of his fundamental studies on how nitroglycerin is converted to nitric oxide, and how it acts to relax the blood vessels. Awarding credit is "very tricky," he says, noting that he regards the whole affair as "an honest difference of opinion."

–Eliot Marshall

EPIDEMIOLOGY

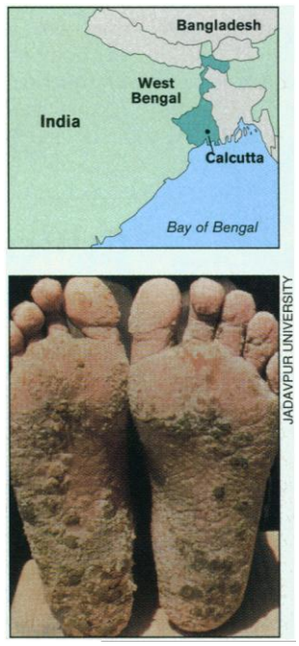
India's Spreading Health Crisis Draws Global Arsenic Experts

NEW DELHI—A potentially devastating health crisis is quietly unfolding in West Bengal, India, where high levels of arsenic have leached from natural underground sources into thousands of village wells. More than 1 million Indians are drinking arsenic-laced water, and tens of millions more could be at risk in areas not yet tested for contamination. An estimated 200,000 people already have arsenic-induced skin lesions, and many of them also have hyperkeratoses, hardened patches of skin that may develop into cancers.

The immense scale of the human tragedy has begun to attract the attention of scientists from around the world. They see in this grim event an unprecedented chance to learn more about the health effects of arsenic, a known carcinogen. "We're talking about numbers [of arsenic-poisoning victims] that have never been seen before in the world," says University of California, Berkeley, epidemiologist Allan Smith.

What is learned in West Bengal could help other countries, including Chile, Taiwan, and Mongolia, cope with arsenic-tainted drinking water. It could also help regulators decide what constitutes an acceptable level of arsenic in drinking water. New legislation requires the U.S. Environmental Protection Agency (EPA), for example, to revise the maximum arsenic level in water by the year 2000. It is considering reducing the current standard by 90%, a change that could be very costly for many small communities.

The exact mechanism behind this widespread poisoning is still uncertain, and it is not clear how the water supply can be made safe. "There's a clear division of opinion about what ought to be done, what the problem is, and how much research should be devoted to it," says one foreign scientist who requested anonymity. "It's a very difficult question in a resource-starved country." Debabar Banerji, professor emeritus at the Centre of Social Medicine and Community Health at the Jawaharlal Nehru University in New Delhi, says that "there has been a certain lethargy in the intellectual intelligentsia, because of which so many questions still remain unanswered."



Deadly trail. Seven districts in West Bengal have been hit hard by arsenic poisoning from tube wells along the Indian-Bangladeshi border. *(Above)* Nodular keratoses on a victim's feet.

How it began. The first cases of arsenic poisoning in West Bengal turned up in the early 1980s, and water from tube wells was quickly fingered as the culprit. These wells, which reach down anywhere from 20 to 150 meters, were dug beginning in the early 1960s to provide year-round support for a new, irrigation-intensive kind of rice that fueled the so-called Green Revolution. Although the arsenic-tainted water at first came mainly from the middle of three aquifers in West Bengal, researchers now believe the problem is more extensive. "No tube well of any depth is safe in the arsenic-affected villages," says chemist Dipankar Chakraborti of the School of Environmental Sciences at Jadavpur University in Calcutta, whose team has worked on the problem for nearly a decade.

Drill cores from Chakraborti's team have yielded layers of arsenic-rich sediments in which the arsenic seems to be associated with pyrite (iron sulfide). However, more detailed boring and analysis is needed before researchers can be certain about the form of arsenic that is to blame, as well as the geochemical process by which it is released. "Identifying the exact source of arsenic is still a ticklish question," says Narayanaswamy Kittu, a member of the Ministry of Water's Central Ground Water Board.

Chakraborti and others suspect that the problem is related to the large-scale withdrawal of ground water. The seasonal fluctuation of the water table results in rapid and regular intake of oxygen within the pore space of the sediments, he says. This inflow breaks down sulfides in the arsenic-laden pyrite rock through oxidization and thus releases arsenic into the water. Hydrogeologist Sukumar Mallick of the Council of Scientific and Industrial Research says that the rapid

flow of water causes the wells to act like a spoon in a teacup, mixing the arsenic and oxygen in a process that would unfold naturally over thousands of years.

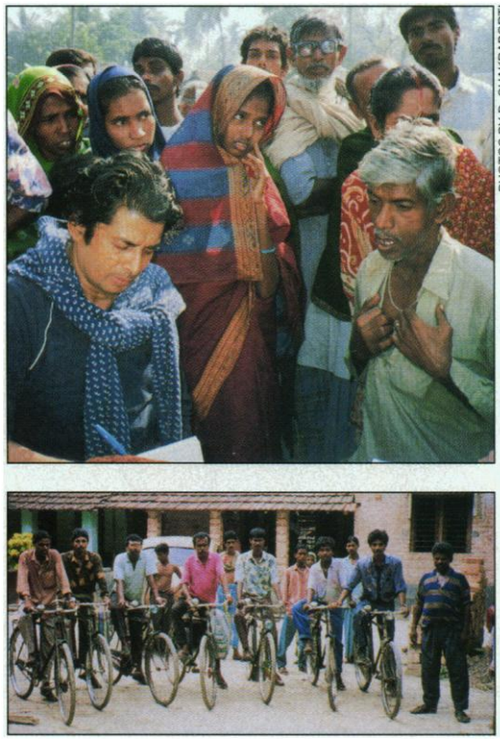
Other researchers offer different explanations. Environmental scientist Arup Sengupta of Lehigh University suggests that phosphorus—an ion similar to arsenic—may help displace arsenic from the pyrite in which it is encased. High levels of phosphorus are also found in the ground water, he notes, probably from fertilizers. And a team led by Prosun Bhattacharya and Gunnar Jacks of the Royal Institute of Technology in Sweden speculates that the arsenic may be released not from pyrite, but from iron oxide coatings on grains of sand. This would happen through reduction rather than oxidation—that is, electrons may be added to the iron compound, not taken away. Jacks suggests that the rising number of flooded fields created by farmers to grow more crops is speeding up the leaching process by hindering the diffusion of oxygen into the ground.

Once in a lifetime. Chakraborti's team has analyzed 20,000 tube-well waters for arsenic and found that 62% have an arsenic content above the World Health Organization (WHO) permissible limit of 0.01 milligrams per liter (mg/l), with some as high as 3.7 mg/l. Hair, urine, skin, and nail samples from people drinking the water show that many have ingested high levels of arsenic. Scientists who attended a conference organized by Chakraborti in February 1995 were stunned by the numbers of villagers with arsenic-induced lesions, pigmentation, and keratoses on their palms and the soles of their feet. "Chakraborti told me, 'You'll never see anything like this again in your lifetime,' " Herman Gibb of the EPA recalls. "It was a good comment. I doubt that I ever will."

Scientists would like to supplement the epidemiologic data collected by Chakraborti's team with more intensive studies of the affected population's size, age, exposure levels, and symptoms. Another key researcher, gastroenterologist D. N. Guha Mazumder of the Institute of Postgraduate Medical Education and Research in Calcutta, has gathered data from 6000 people on the poison's health effects that they now plan to analyze together with Smith. But a more comprehensive survey would be needed to gauge the full scope of the problem. Gibb thinks better epidemiology would also encourage outside public health experts to respond to the crisis. "If there were a little more scientific data, people would take it more seriously," he says.

This kind of information would also be critical for determining dose-effect curves. "This is a tragedy, but there are also some things we can learn," Gibb says. Arsenic experts would like to know, for example, whether the Indian victims' risk of skin cancer is comparable to that of a Taiwanese population exposed to arsenic-contaminated drinking water between 1910 and 1965. Eventually, they also want to develop a dose response based on internal cancers, a better indicator of risk than skin cancers because of higher fatality rates.

Studies in India could fill in other knowledge gaps as well. "We're still getting an idea of what diseases are caused by arsenic," says environmental scientist Willard Chappell of the University of Colorado, Denver, who heads an international task force on arsenic poisoning. The West Bengal arsenic victims appear to experience lesions at lower levels of exposure than Chileans do, for example, Smith says. Indian scientists have also found symptoms not usually described in association with arsenic, such as liver effects and respiratory problems. Some researchers believe part of the answer may lie in the poor diet of some West Bengalis, or in a genetic susceptibility.



PHOTOS BY D. CHAKRABORTI

Spreading the word. Chakraborti meets with arsenic patients in Deganga, West Bengal, and uses a bicycle brigade of local patients to conduct door-to-door surveys to collect more data.

Understanding the health effects could help resolve a debate in the United States and other Western countries over what constitutes acceptable exposure levels. Although the EPA now sets a maximum level of 0.05 mg/l, for instance, a more recent analysis co-authored by Gibb based on studies of skin cancer in Taiwan has led the agency to consider a more stringent level, perhaps one-tenth the current standard. Achieving that level in some communities in the western United States, where mining has introduced arsenic into ground water, could cost "billions of dollars per year," says Chappell.

Is help on the way? Despite mounting concern by scientists, India's official response to the tragedy has been low-keyed. Last year the federal government approved a $25 million project to supply piped water to the Malda district, but so far there has been little progress. The West Bengal government wants $200 million to supply arsenic-free piped water from the river Ganges to the affected regions, but experts say such a project could take up to 20 years to implement and would provide no short-term relief.

As an immediate measure to curb the use of deep-well water, 2 years ago a panel of experts recommended to the West Bengal government that rice be replaced with crops that require less irrigated water. To date, however, no steps have been taken to implement the plan. There are also efforts to develop treatments for the well water, such as a method Chakraborti is planning to patent that could be used at home. But Chakraborti says such efforts are hindered by the government's reluctance to explore the extent of the contamination. "We have many examples where arsenic was not present [in tube-well water] at the beginning of the study but got contaminated in the course of time. Even today the bureaucracy and policy-makers have not realized the seriousness of the problem," he says.

A few international collaborations to help study the cause and gauge the extent of the poisonings could soon be under way. Pauline Smedley of the British Geological Survey, for example, leaves next year to do more geological and hydrogeochemical studies in western Bangladesh, which shares West Bengal's arsenic problems, and Jacks is seeking funding from the Swedish government for similar work. Smith has asked the EPA for funds to help complete Mazumder's study. Gibb hopes the EPA might also collaborate in a broader international project in West Bengal. Such proposals may get a boost from a WHO team expected to call for joint research by the Indian government and international researchers.

Arsenic experts are watching and waiting. "It's a very large public health problem that needs attention," says Gibb. "You come back [home] and you feel almost helpless."

–Pallava Bagla and Jocelyn Kaiser

Pallava Bagla is a science writer in New Delhi, India.