

unique to its region.

Scientific isolation. Indeed, Chinese scientists feel their isolation within their own country keenly. When Young toured Chinese labs 2 years ago, he recalls, "the first thing people wanted us to tell them is not what's going on in the U.S., but what's going on elsewhere in China. Their ears were just burning." La Roche's Hong, who left China in 1980, says, "It's harder for Chinese to cooperate. We have less experience in dealing with win-win situations. It's our culture."

Whether culture has anything to do with it or not, leaders in Shanghai, a stronghold of life sciences, have decided to try to break down the barriers that divide scientists. Last year, they set up the new Shanghai Research Center of Life Science to administer and fund research that promotes closer ties among two dozen life science labs scattered among the CAS institutes, universities, and medical colleges in Shanghai. "We want to organize research in frontier areas, provide good conditions for young researchers, promote interdisciplinary and international collaboration, and improve the research management system," says Xu Zhihong, one of the center's co-directors.

But a scientist familiar with the center's



Open field. Nanjing trials with *Bt* toxin improve cotton yields.

activities says that "right now it doesn't work well, because Chinese scientists traditionally do not have good experience collaborating on one project. It's basically an opportunity to ask for more funding from the local government." And even then, the funding has not had quite the impact the founders might have envisioned. The \$350,000 spent by the center so far on genome mapping, gene diagnosis, and gene therapy has been carved up among several groups, which have ended up working independently.

An equally serious impediment to progress in biotechnology, says Hong, is Chinese scientists' isolation from the global cutting edge. "I'm surprised at the depth of biotech research the Chinese do," he says. "But the

problem is they don't know the current state of research, or how to focus on promising areas. They're very active, but not well organized." What's more, he adds, Chinese scientists still have much to learn about conforming to international scientific standards.

But if Chinese biotech researchers can develop a more open, globally competitive outlook, their work could begin to pay off. Consider the possibilities of China's rice genome project. By the researchers' own admission, their mapping efforts fall far behind a much larger, well-funded Japanese effort (*Science*, 18 November 1994, p. 1186). But "the portions aimed at applications are moving well," says Rockefeller's Toennissen. "Chinese scientists need to find an important niche that isn't duplicated elsewhere. I think that niche will be to link advanced tools to applications. There are all kinds of genes for disease resistance waiting to be discovered."

China still has a long way to go in biotechnology, but its biotech pioneers such as Mang Keqiang and Li Baojian have helped put the foundations in place. Li has lived apart from his children, now grown, for nearly a decade, but he has few regrets. "We are developing China's agriculture and helping farmers," he asserts. "At first, we didn't have many labs, and now we have many. My task now is to fill them with young scientists."

—June Kinoshita

EPIDEMIOLOGY

China's Unique Environment Favors Large Intervention Trials

BEIJING—The residents of Linqu, a poor county in Shandong Province in east-central China, have little formal education. But they know gastric cancer is killing them at a higher rate than anywhere else in the world. So when epidemiologist You Weicheng explained that they had a chance to participate in an experiment that could increase understanding of the disease and, maybe, save their lives, he had no shortage of volunteers.

The experiment that began in September is the world's first randomized intervention aimed at inhibiting or preventing the development of gastric cancer. It extends earlier work by the 43-year-old You, who has spent almost 20 years exploring the origins and progression of the disease in China, at the Beijing Institute for

Cancer Research, and the U.S. National Cancer Institute (NCI). The trial also builds on a large-scale nutritional intervention trial, which ended in 1991, in Linxian Province in north-central China, a region with one of the world's highest rates of esophageal cancer. The Linxian study, conducted by a team of U.S. and Chinese scientists, provided the first clear evidence that a nutritional supplement in pill form could arrest or prevent the development of a human cancer.

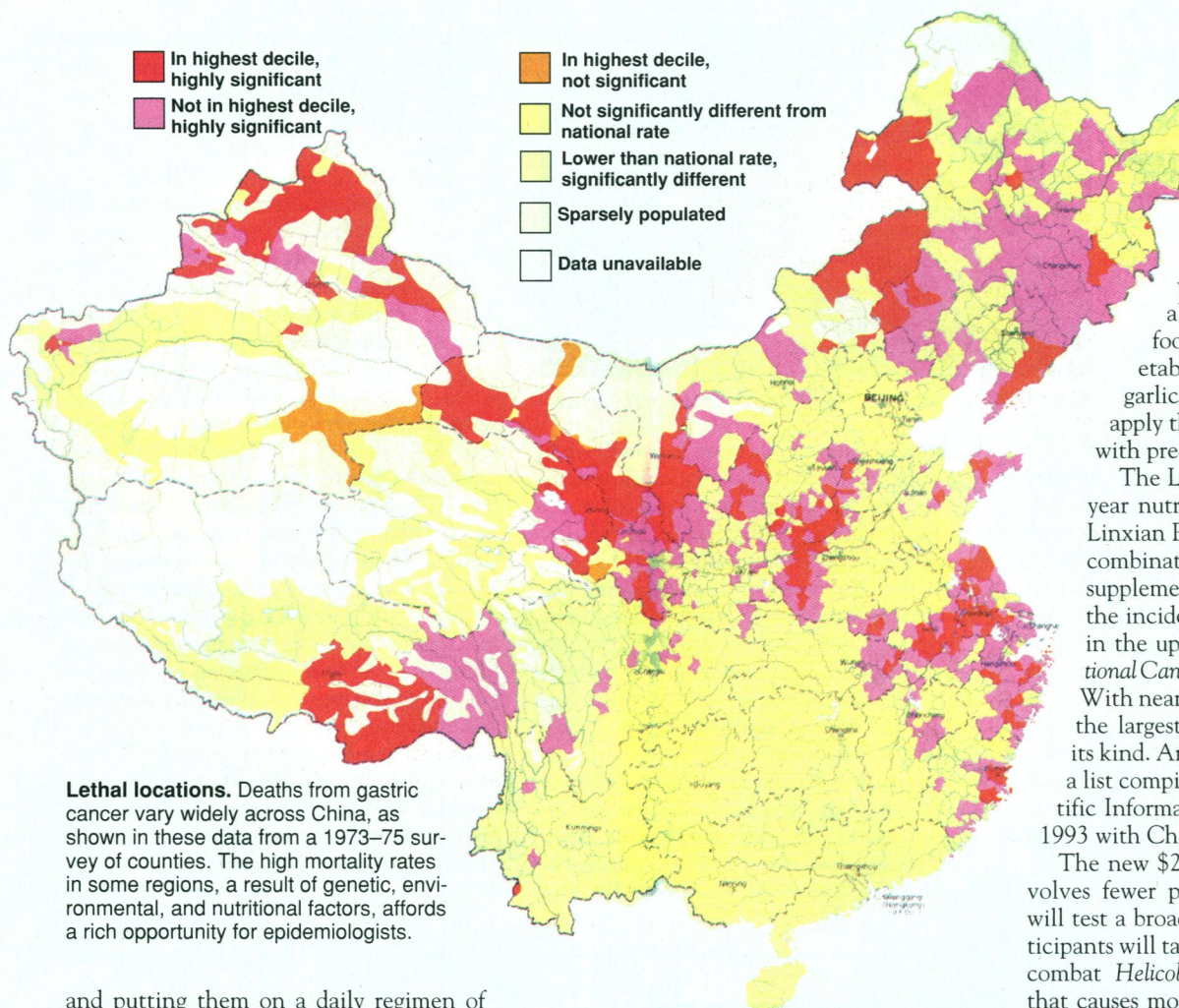
It's no accident that China is providing epidemiologists with some of the best data on ways to lower rates of diseases like gastric cancer. "China provides a tremendous opportunity for case-control and intervention studies," says Joseph Fraumeni, acting head of NCI's division of cancer epidemiology and genetics, which is funding the Linqu

trial as well as projects in other parts of China. "There are striking variations in the incidence of various cancers and several extremely high-risk populations," he says. "For example, esophageal cancer just doesn't occur here often enough to get good results, but it's widespread in parts of China." Cultural and demographic factors also make it easier to conduct major epidemiological studies in China. "Its population is more compliant than in the West," notes Fraumeni, "which leads to very high participation rates. The studies are much cheaper to carry out—practically nothing compared to what a similar trial would cost in the U.S. And the population is more stable, so follow-up is much easier."

All these factors are evident in perhaps the largest intervention trial now under way anywhere in the world. It is aimed at reducing the high rate of neural tube defects in China, in particular spina bifida and anencephaly (SBA). Each year nearly 100,000 children in China are born with SBA, but small daily doses of folic acid, taken before and during the first weeks of pregnancy, are thought to be capable of lowering that number by at least half. So in 1993 the Chinese Ministry of Public Health, in conjunction with the U.S. Centers for Disease Control and Prevention, began signing up hundreds of thousands of women in three provinces



Cancer killer. You Weicheng hopes that NIH trial will improve health of rural Chinese.



Lethal locations. Deaths from gastric cancer vary widely across China, as shown in these data from a 1973–75 survey of counties. The high mortality rates in some regions, a result of genetic, environmental, and nutritional factors, affords a rich opportunity for epidemiologists.

and putting them on a daily regimen of folic acid at the same time that they registered for marriage with local authorities. Enrollment ended in September, and the first results are expected next spring. The entire cohort of women will be followed through the birth of their first child.

The grandfather of prevention trials in China is a 10-year study of 80,000 children in the Shanghai suburb of Qidong who received shots of the hepatitis B vaccine at birth in an effort to lower rates of adult liver cancer, which are among the highest in the world. "We know that [the vaccine] brings down the number of chronic carriers," says immunologist Zongtang (T) Sun of the Cancer Institute, Chinese Academy of Medical Sciences, in Beijing. "The big question is whether it can reduce incidence of chronic hepatitis in children, which leads to adult liver cancer." Enrollment was ended in 1990 when the vaccine became widely available, and the researchers—a team of Chinese and British scientists—are now writing up results from the original cohort on the incidence of chronic hepatitis.

For You, who became the Beijing institute's youngest full professor 2 years ago, the political and economic changes in his country were a big factor in his ability to wage war on gastric cancer. You was in medical school in the 1970s, for example, when China com-

pleted the country's first comprehensive mortality survey and opened up the field of epidemiology. Within a few years, China had started to emerge from the self-imposed isolation of the Cultural Revolution, sending researchers abroad and giving Western scientists a chance to learn more about these data sets. You spent 2 years as a postdoctoral fellow at Mount Sinai School of Medicine in New York City working with the late Irving Selikoff and E. Cuyler Hammond. He wasn't alone: During most of the 1980s, more than a quarter of the institute's faculty at any one time was working and studying abroad.

While most Chinese scientists chose to remain in the West after their training, You returned to Beijing in 1982. "I thought that there would be opportunities for me because things were changing in China," he recalls. While there were plenty of opportunities, there wasn't always enough money to take advantage of them. The government turned down the institute's proposal for a cancer incidence survey of 5 million people, for example, citing the high cost. So You and his colleagues approached NCI's Fraumeni and William Blot, then head of the institute's cancer prevention studies branch, with four proposed studies.

NCI said yes, and after some initial work in other areas, the joint team decided to examine the major risk factors contributing to the high prevalence of stomach cancer in Linqu. They found that sour pancakes, a local staple, were a major contributor, along with an excess of salted foods and a dearth of vegetables, particularly onions and garlic. The intervention trial will apply these findings to a population with precancerous lesions.

The Linqu trial follows up on a 5-year nutritional intervention trial in Linxian Province, which found that a combination of vitamin and mineral supplements was effective in reducing the incidence and mortality of cancer in the upper stomach (*Journal of National Cancer Institute*, vol. 85, p. 1483). With nearly 30,000 participants, it was the largest nutritional intervention of its kind. And the paper ranks second on a list compiled by the Institute of Scientific Information of most-cited papers in 1993 with Chinese co-authors.

The new \$2 million, 42-month trial involves fewer people—3400 adults—but it will test a broader range of substances. Participants will take a mixture of antibiotics to combat *Helicobacter pylori*, the bacterium that causes most stomach ulcers, as well as four vitamin and mineral supplements, and garlic extract. It is based on You's previous work suggesting that gastric cancer, which has a very low survival rate, is the end of a multistep progression of increasingly severe conditions. In particular, it will test whether nutritional and medical interventions can block that progression in a high-risk population. "Gastric cancer is the second most common cancer worldwide, and the most common in China," says You. "If we can inhibit the lesions, we can prevent gastric cancer."

The study has powerful institutional backing, including \$400,000 from the U.S. National Institutes of Health (NIH) and significant contributions from U.S. drug companies. But that doesn't eliminate the problems of working in a developing country. You's earlier study, for example, involved performing endoscopies on 3400 adults at walk-in clinics using local anesthesia. In addition to working under conditions that would be anathema to Western scientists, You and his colleagues had to assemble and train the technical staff.

For the current trial, You is most concerned about achieving high levels of compliance among a population not accustomed to taking pills. So he has enlisted a cadre of primary students, hand-picked by their teach-

ers, who will visit 25 to 30 villagers on their way home from school each day and remind them to take their medicine.

The results are expected to clarify some of the findings from the Linxian study, which was far from conclusive on the effects of such supplements as beta-carotene, vitamins A and E, and selenium. Last year a Finnish study co-funded by NIH (*New England Journal of Medicine*, vol. 330, p. 1029) reported an unexpected

increase in lung cancer among male heavy smokers who received beta-carotene, leaving epidemiologists scrambling for an explanation. Even so, most scientists remain convinced that such supplements can be effective in lowering cancer rates. They expect that faith to be validated next year in results from the first of two large, long-term U.S. trials among health professionals in the Boston area—22,000 male physicians who have been tak-

ing beta-carotene for a dozen years to reduce the incidence of epithelial-cell cancers.

Most intervention studies are too costly to run for such a long time, and there will still be plenty of unanswered questions when the Linqu trial is completed. But the trial is off to a good start, says You, and that is good news for both the residents of Linqu county and epidemiologists around the world.

—Jeffrey Mervis

ENVIRONMENT

National Monitoring Network Does Science—and a Lot More

BEIJING—Ouyang Hao took on a daunting collection of responsibilities when he left the Chinese Academy of Sciences' (CAS's) Institute of Botany here earlier this year to set up shop 1400 kilometers away in a rural part of southern Jiangxi Province. An expert on nutrient cycling in forest ecosystems, Ouyang is measuring the extent of deforestation—a serious problem in the region—and identifying alternative fuel sources. After that, he intends to teach local residents how to implement his findings. And that's just part of his job. He's also monitoring the environmental impact of water cycles, natural disasters, and the emission of greenhouse gases.

Ouyang's heavy load reflects the broad sweep of an ambitious new program called the China Environmental Research Network (CERN), a collection of 29 field sites spread across the country. As a rising population and a booming economy place increasing demands on limited resources, CERN researchers like Ouyang are gathering long-term ecological data on China's growing environmental problems. The network also is expected to set the standard for new data management techniques and pioneer procedures for sharing information among government agencies and with researchers around the world.

CERN's 29 stations, managed by CAS and run by individual CAS institutes, have been equipped and staffed over the past 5 years with \$16 million from the World Bank and \$10 million from the Chinese government. The sites, selected from among the 52 stations of an older, less sophisticated network, cover a variety of ecosystems: 16 focus on agro-ecosystems, with the rest tracking lake, sea, grassland, and forest ecosystems.

A large share of CERN's budget has been devoted to data management. Some \$3 million from the World Bank has gone to pay for computers, with a similar amount paying for training. More than 40 CERN scientists have already traveled abroad, including visiting sites that are part of the U.S. Long-

Term Ecological Research (LTER) network funded by the National Science Foundation. Although the U.S. program emphasizes data collection over the short-term implementation of results, scientists familiar with both programs say China has avoided some of the problems of the 15-year-old LTER program.

"One of the big mistakes we made and that the Chinese seem to have learned from was the neglect of data management," says University of Washington ecologist Jerry Franklin, who ran LTER for 12 years and is now a member of CERN's international scientific advisory committee. "Like scientists everywhere, we tried at first to do it on the cheap. The people at CERN have done the right thing by investing in data management from the beginning."

That investment includes a commitment to standardization to make sharing data technically feasible. Potential government users include China's National Environmental Protection Agency (NEPA), the State Meteorological Administration, and the Ministries of Forestry and Agriculture, each of which has a representative member on CERN's data management committee. CERN administrators have also suggested making data available to those doing economic or historical research, and even to businesses. But this commitment to openness runs counter to the Chinese bureaucratic tendency to hoard potentially valuable information. And that makes some observers skeptical.

"Whether that will be truly possible in the context of the Chinese system is not clear,"

says Susan Shen, a senior ecologist in the World Bank's East Asia and Pacific Division. "It is not a secrecy issue, but a commodity issue. A lot of CAS institutes have had to become self-sufficient in recent years, and one of the ways they pay their own way is to sell useful data that they gather. Well, if you share it you can't sell it, can you?"

A staffer at NEPA's policy research center confirms that the problem has the potential to be quite serious. "CERN is supposed to be collaborating very closely with us, but so far they have not been," says the staffer, who requested anonymity. "They have not yet established procedures for informing us of their research results."

Even if CERN does live up to its promises, however, some environmental scientists doubt that it can greatly improve China's chances of heading off ecological disaster. Environmental degradation costs China at least 10% of its gross domestic product each year, says geographer Vaclav Smil of the University of Manitoba in Canada, who has written extensively on China's environmental problems, and there are few signs that the trend will be reversed.

"If they could get it together scientifically, which is a questionable assumption to begin with, priorities elsewhere among the

On the ground. A network of monitoring stations brings Chinese scientists in touch with a variety of environmental conditions.

