

Panel Wants to Break R&D Barrier

Hundreds of millions of couples worldwide lack adequate contraception, despite the worldwide success of the pill and other modern contraceptives, and this situation leads to over 50 million abortions each year, according to a new report by the U.S. Institute of Medicine (IOM). Yet pharmaceutical companies have all but abandoned R&D programs in this area, forced out by towering political, economic, and cultural obstacles.

Staring at this bleak picture, a 17-member IOM panel recommends several ways for the U.S. government, industry, and organizations already involved in providing population services to break this impasse. They include: reforming U.S. product liability law, including contraceptives in health insurance coverage, and pooling contraceptive purchasing funds from international health agencies to create a large market. These several steps, taken together, might prod new research efforts, says Allan Rosenfield, the dean of the Columbia University School of Public Health in New York City, chair of the committee that produced the report. But both Rosenfield and outside observers acknowledge that most of these recommendations will face stiff opposition.

Even though dozens of new potential drug targets for contraceptives have been identified in recent years (see table), the number of major pharmaceutical companies involved in contraceptive research dropped from a dozen in the 1960s to just four by the mid-1980s. Company officials were worried about entering a market where safe, effective, and cheap alternatives (such as the pill) already exist, where there is a high potential for lawsuits should unforeseen side effects arise, and where the sale of such products could draw them into debates on abortion and appropriate sexual behavior (*Science*, 2 December 1994, p. 1489).

So Rosenfield and his colleagues recommend that Congress pass a product liability reform bill that would shield contraceptive manufacturers from some liability once their product had been approved by the Food and Drug Administration. "It would make a fantastic difference," says Nancy Alexander, who heads the contraceptive development branch at the National Institute of Child Health and Human Development's Center for Population Research. "There really is a reticence on the part of industry to develop new contraceptives," she says, particularly new drugs as opposed to barrier devices, because of the difficulty of gauging their long-term health effects. Yet hopes for such reform in the near future are dim, Alexander and Rosenfield

admit, noting that President Clinton vetoed a liability reform bill earlier this year.

The IOM panel also urges insurance companies to add contraceptives to their standard coverage as a way to boost access and demand. But here again, the recommendation is likely to encounter opposition, says Henry Gabelnick, director of the Contraceptive Research and Development Program in Arlington, Virginia. He notes that while covering contraceptives is likely to save insurance companies money in the long run by reducing costs associated with pregnancies, those companies typically balk at such suggestions for fear of being branded as supporting promiscuity.

Other recommendations are aimed at boosting economic incentives for new contraceptive research. One proposes a joint purchasing pool for international agencies that distribute contraceptives to developing countries—such as the U.S. Agency for International Development (AID)—in the hope that commitments to buy large volumes of contraceptives would induce companies to develop low-cost products. Yet Jeff Spieler, head of research at AID's Office of Population, says that it would be hard for agencies with annual budgets to make commitments extending for several years. Another avenue the report recommends may be less fraught with difficulties: cooperative ventures between private foundations, such as the Consortium for Industrial Collaboration in Contraceptive Research, whose grants to researchers are matched by drug companies.

SOME STRATEGIES FOR NEW CONTRACEPTIVES

Near-Term

- ♂ Stopping sperm production with injections of progestin-androgen combinations
- ♀ Inducing menses with a combination of antiprogesterins, antiestrogens, and inhibitors of enzymes involved in steroid synthesis

Medium-Term

- ♀ Preventing sperm passage by modifying mucous secretions from cervical epithelial cells

Long-Term

- ♂ Preventing sperm maturation by inhibiting epididymal function
- ♂ Preventing fertilization by causing sperm cells to prematurely release enzymes that otherwise break through the egg's protective coat
- ♀ Inhibiting ovulation using a combination of a nonpeptide gonadotropin-releasing hormone antagonist and hormones
- ♀ Preventing fertilization or the implantation of a fertilized egg in the uterine lining with various vaccines

SOURCE: "CONTRACEPTIVE RESEARCH AND DEVELOPMENT: LOOKING TO THE FUTURE" (INSTITUTE OF MEDICINE).

While these recommendations may face an uphill battle, Rosenfield says the report is important to show drug companies the massive need and potential market for new contraceptives and to underscore the need for continued public funding of research in the area. The recommendations, Gabelnick agrees, can "bring awareness to the public of the need for new contraceptives and that the private sector can't do it alone."

—Robert F. Service

MARINE POLLUTION

Science Intrudes on Brent Spar Saga

LONDON—This time last year, the environmental group Greenpeace scored a David-and-Goliath victory over the giant Shell Oil company. Greenpeace activists, playing to a worldwide television audience, boarded an oil storage buoy called the Brent Spar and temporarily halted Shell's plan to scuttle it in the deep Atlantic off the west coast of Scotland. Greenpeace claimed that the sunken rig—a 141-meter-long vertical steel tube that had served as a holding tank in the North Sea for 15 years—would pose a toxic threat. The publicity prompted a widespread consumer boycott of Shell products, particularly in Germany, as a result of which the company gave up and towed the Brent Spar to Erfjord in Norway.

Last week, a panel of scientists passed judgment on Greenpeace's claims—and both sides are claiming vindication.

The panel, chaired by oceanographer John Shepherd, director of the Southampton Oceanography Centre, concluded that Brent Spar, by itself, would have a very small impact on the marine environment. "Any adverse effects would be confined to the immediate vicinity of the wreckage," the report says—an area of only a few square kilometers—and sea-floor wildlife would recover after 2 to 10 years. The only real danger would come from exotic materials, such as polychlorinated biphenyls (PCBs), but as Shepherd told *Science*, "Brent Spar probably contains less of these than the average



Limited threat. Greenpeace made Brent Spar famous.

* "Contraceptive Research and Development: Looking to the Future," Institute of Medicine, 1996.

pumped-out oil tanker." Shepherd's committee did not advocate dumping as a standard practice, however. It pointed out that repeated scuttling of similar structures with a low impact could accumulate into a large overall impact.

The scientific analysis was commissioned by Britain's Department of Trade and Industry (DTI), which issues licenses for deep-sea dumping. In the wake of the Brent Spar spectacle, DTI asked Britain's Natural Environment Research Council to look into the risks of deep-sea disposal and compare them with other options. Shepherd assembled a group of scientists and engineers specializing in deep-ocean biology, oceanography, environmental toxicology, chemistry, geology, and engineering. The group's first report, based on analysis of the literature and computer modeling of the area, simply seeks to characterize the deep sea-floor environment and the impact of a structure such as the Brent Spar, without comparing such disposal to other methods. It will do that analysis when Shell declares what methods it is considering.

Shell welcomed the report last week, as it confirmed the company's studies that the environmental impact of dumping the Brent Spar would be small. But Greenpeace also gave it a warm reception. The panel's warning about the possible cumulative effects of repeated dumping, Greenpeace says, means the DTI's case-by-case approach to licensing such dumping is inadequate.

At a press conference last week, Shepherd said that more research is needed into the impact of "analogs" to such dumps, such as shipwrecks and waste sludge disposal, as well as natural processes, including slumps and hydrothermal vents. He also put great emphasis on the group's "attempt to reduce confusion and improve public understanding [of the issue]." Deep sea-floor biologist and group member Tony Rice of the Southampton Oceanography Centre says that the most useful outcome of the report would be more openness in the selection of sites and licensing of dumps—one of the report's main recommendations. Last year Shell kept many of its studies secret, and when they were made public scientists soon spotted flaws—most notably in the company's estimation of the ocean currents at the chosen site and its level of biodiversity. "Had the process been more open, some of these events might not have happened," Rice says.

In the meantime, Shell is still wondering what to do with the most famous oil-storage buoy in the world. Last October, it put out a request for proposals to deal with Brent Spar and has so far received 419, from members of the public as well as the oil industry. The company is trying to winnow the pile down to a short list of six for full project studies. Deep-sea disposal may be among them, but for the meantime the company is keeping details secret.

—Daniel Clery

RUSSIA

Academy Fights to Maintain Research in the "Wild East"

VLADIVOSTOK, RUSSIA—In July, 30 Russian, American, and Japanese scientists are scheduled to set sail from here on a Russian research vessel to study the biodiversity of a scientifically fascinating region: the Kuril Islands off Japan's northern tip. These islands, which were off-limits to foreigners for decades because of their strategic importance to the former Soviet Union, have a unique biological heritage, including species that have developed in isolation for up to 70 million years. This important expedition is the latest example of the trans-Pacific alliances that have been forged since Russia opened up its far eastern coast to the outside world. But it is also a symbol of a different kind. It is the only expedition the Far Eastern Branch (FEB) of the Russian Academy of Sciences can afford this year, and as *Science* went to press, it still faced an embarrassing hurdle: The academy was scrambling to pay a dock fee that would allow the ship—the *Professor Bogorov*—to leave harbor.

In the 1980s, the FEB led up to three dozen international expeditions a year on eight ocean-going vessels, while another seven ships operated close to shore. "We have the biggest and best ships for biology in the world," says Alexey Zhirmunsky, former director of Vladivostok's Institute of Marine Biology. But this once-proud fleet is now in dire straits. Several vessels are rusting away in disuse, while others are leased out for commercial ventures, such as transporting television sets from Japan, simply to keep their crews employed until better times arrive. As a result, dozens of scientific projects are floundering. "The FEB's overall research quality ... has decreased dramatically," says chemist Victor Vaskovsky of the Pacific Institute of Bio-Organic Chemistry (IBC) in Vladivostok.

Just a few years ago, Vladivostok looked set to become a research boomtown, not a ghost town. During the Soviet era, most of the region was closed to foreigners because of its numerous military bases—the Russian Navy's Pacific Fleet, for instance, is based in Vladivostok. But in 1990, the Soviet Union

opened up the Far East, and scientists from Pacific Rim countries such as China, Japan, and Korea, as well as from Alaska and the U.S. Pacific Northwest, began streaming in to forge new ties. Best known for its biology and environmental sciences, the FEB hosted visits from nearly 700 foreign scientists in 1992. The influx fueled a rapid rise in joint expeditions on both land and sea, from 17 in 1992 to 64 in 1993.

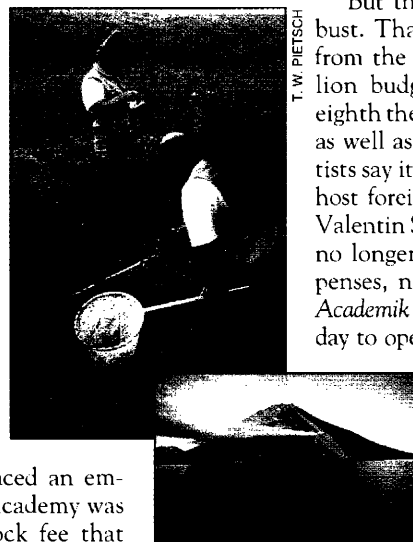
But the boom quickly turned to bust. Thanks to dwindling support from the state—the FEB's \$36 million budget for 1996 is just one-eighth the amount it spent in 1980—as well as high inflation, FEB scientists say it is nearly impossible now to host foreigners. IBC deputy director Valentin Stonik says his institute can no longer afford to pay visitors' expenses, nor can it run its ship, the *Academik Oparin*, which costs \$7000 a day to operate. "Now it's very rare to have visits," he says.

This year's Kuril expedition has managed to stay afloat, so far, because it has substantial overseas support. The U.S. National Science Foundation's biotic surveys and inventories program has budgeted \$75,000 for the expedition. The FEB will pay \$35,000—a sum already

in hand—for items such as fuel, food, and crew salaries. The Japan Society for the Promotion of Science will pay \$20,000 for the expenses of six Japanese researchers, and the Japanese TV station NHK is currently negotiating a deal to pay up to \$20,000 for fuel and an NHK documentary team.

The expedition is part of a 6-year, \$1.2 million effort to map the biological diversity of this Russian chain of 56 islands that stretches from the southern tip of Russia's Kamchatka peninsula to the northeastern coast of Japan's Hokkaido island. The Soviet Union strictly limited access to the Kurils, where it kept military garrisons during the Cold War, all but excluding the islands from scientific study. But when they were opened up in the early 1990s, they yielded rich scientific harvests.

On the first two expeditions, scientists identified nearly 60 new species of spiders, mollusks, and other organisms. "We have



Diverse bounty. Earlier expeditions to the Kuril Islands have identified nearly 60 new species of spiders, mollusks, and other organisms.