CONTRACEPTION R&D

Barriers Hold Back New Contraception Strategies

Amidst the breakneck pace of new discoveries in medicine, fueled by the ongoing revolution in molecular biology, one area is lagging far behind: new strategies of contraception. "Research in contraception has been markedly slowed over the last 20 years," says Wayne Bardin, the director of the center for biomedical research at the Population Council in New York City. Though there have been new developments in contraceptive vaccines (see p. 1484), much of today's contraceptive technology—such as the birth control pill—comes from work done in the 1950s and '60s.

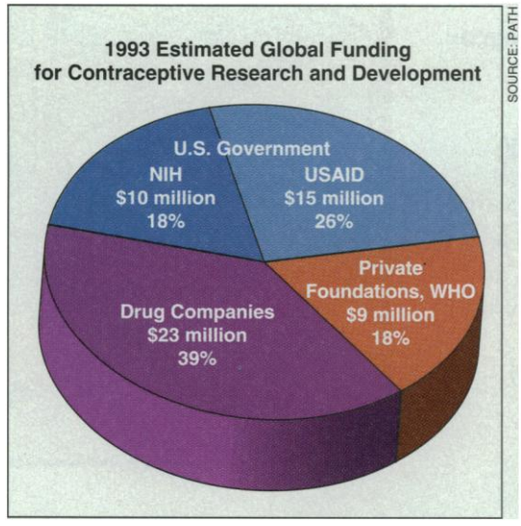
Yet it is easy to make a case that old approaches are not doing the job. Concerns continue to be raised over the long-term safety and effectiveness of current contraceptives. And according to a report released earlier this year by the World Health Organization (WHO), one quarter of pregnancies worldwide are unwanted, of which roughly 50 million a year end in abortion.

Given this apparent need for new technology, what's holding back its development? The answer seems to be that the two sectors likely to produce such advances—drug companies and federal funding agencies—perceive little demand on the part of the public for such developments. And therefore they are not putting resources into development programs. "There really isn't any constituency that is talking to their congressmen saying 'we need new research in contraception,' " says Nancy Alexander, who heads the contraceptive development branch at the National Institute of Child Health and Human Development (NICHD).

In the private sector, "companies look for areas where people perceive a big problem, where you can introduce a new product that is cheaper, more effective, or has less side effects," explains Jonathan Fleming, a partner in the Boston-based venture capital firm of MVP Ventures, which specializes in capitalizing new biotechnology start-ups.

But in the case of contraception, since they don't have such a product, why not develop it themselves? According to a report released last year by the Program for Appropriate Technology in Health (PATH), a Seattle-based international nonprofit health research organization, which surveyed executives at 14 drug companies, executives said they believed the market was well-served by the current contraceptives. They also worry about product liability, regulatory hassles, and the high cost and long time needed to develop new contraceptives. "When you throw everything into the balance, companies decide to work on other things," such as developing new drugs against cancer or heart disease, says Richard Douglas, the vice president for corporate development for Genzyme, a biotechnology firm based in Cambridge, Massachusetts. Of the dozen major pharmaceutical companies involved in contraceptive research in the 1960s, only a handful remain, according to a recent Rockefeller Foundation internal report.

With the downturn in drug company interest in contraceptive research, the bulk of the R&D in the area is carried out by nonprofit research organizations, such as the Population Council, and U.S. and international agencies, such as NICHD and WHO



Cash for contraception. Not much drug company money is going into contraceptive R&D.

(see chart). But here too progress is largely limited to modifications of existing contraceptives, concludes PATH. There are novel approaches in the offing, such as halting membrane changes to the heads of sperm cells necessary for fertilization or preventing sperm from binding to the outer coat of eggs, known as the zona pellucida. But these approaches are in their most basic stages, according to a report published in a June special issue of *Human Reproduction*, and are not developed to a point where a private company will pick them up.

Because private contraceptive developers are not willing to pursue potential leads with their own research dollars, that creates a problem, says Michael McClure, who heads the Center for Population Research's (CPR's) reproductive sciences branch at NICHD. The federal government, says McClure, is "now looked at as a far greater source to provide basic research funding," but federal funding for reproductive biology has long been hard to come by. In contrast to the billions of dollars spent on diseases such as cancer and AIDS, notes McClure, the budget for CPR's reproductive sciences branch, which funds much of U.S. basic research in reproductive biology, is a mere $89 million. "Contraception is not AIDS," says University of Colorado molecular biologist Jonathan van Blerkom. "It's not a big issue in this country."

Another obstacle, say McClure and others, is the 13-year-old NIH ban on federal dollars spent on research involving the creation of human embryos for research purposes. This, they say, has played a major role in preventing much contraceptive research from advancing to the point where companies would be willing to pick it up. Creating such embryos is necessary, for example, in figuring out ways to stop the sperm cells from penetrating the egg, says John Eppig, a reproductive biologist at the Jackson Laboratory in Bar Harbor, Maine. "If you want to prevent fertilization, you have to study fertilization," he says.

There is some hope that a thaw in the freeze may be approaching. NIH Director Harold Varmus is currently considering lifting the moratorium on some types of embryo research (*Science*, 19 August, p. 1024). And this month an Institute of Medicine committee, funded by a partnership of U.S. governmental agencies and private foundations, will begin looking at the application of biotechnology to contraception in hopes of stimulating interest among drug companies and biotech start-ups.

But even if new breakthrough technologies do arise, that's no guarantee they will find rapid commercialization, says Bardin. Anti-progestins, such as the controversial abortion pill RU 486—developed by the French drug maker Roussel-Uclaf—represent the only breakthrough in fertility control developed in 20 years, Bardin says. But when it came to testing and marketing the drug in the United States, "every pharmaceutical company in the country turned it down," for fear of being targeted by a political backlash, he says.

So new technologies aren't enough, Bardin says. What companies really want, he continues, "is a blockbuster technology that is totally noncontroversial." Since that may be hard to come by in such a politically charged arena as contraception, it's likely, he concludes, that publicly funded research organizations such as his are going to remain the main contraceptive developers for years to come.

–Robert F. Service