Science News of the Week

Geneticists and gene transplants: A historic call for a ban on research

It was an action rarely precedented in science. A group of molecular biologists, with the backing of the National Academy of Sciences, last week acted to limit a "potentially harmful" line of genetic engineering research. Eleven NAS members, including four directly involved in the research effort, made their move at "auto-regulation of the scientific community" by publishing a letter in SCIENCE, NATURE and the NAS PROCEEDINGS, and by holding a press conference at the NAS headquarters in Washington, urging a temporary ban on further research in three specific areas.

In only two other cases in recent memory have similar appeals been made to the scientific community. Non-German physicists in the early 1940's called for a ban on published reports on atomic research, to deny the Germans defense information (but the research itself went ahead). And in 1969, a team of Harvard scientists foreshadowed the current appeal by warning against Government misuse of their contribution—the first isolation of a pure gene from a bacterium.

The recent publication of simplified techniques for combining foreign animal, viral and bacterial DNA with the DNA of bacteria caused the group to venture outside slow-moving NAS study channels and publish the appeal. The panel believes potential hazards exist in three specific types of experiments. It urged members of the world scientific community to defer researching them until the National Institutes of Health, the NAS and the members of a conference to be held next February attempt to quantify the risks involved and establish research guidelines.

The research in question has been



Roblin, Baltimore, Berg meet the press.

reported in several major journals during the past six months (SN: 6/1/74, p. 348; 7/6/74, p. 5). A newly discovered class of enzymes called "restriction enzymes" can now be manipulated to remove a particular gene from one organism's genetic material and anneal it to a type of genetic material called bacterial plasmid DNA. When this hybrid sequence is introduced into the bacterium *Escherichia coli*, the characteristic coded for by the foreign gene is expressed. Frog, mouse and fruit fly genes have been successfully transplanted and expressed in *E. coli*.

The technique holds promise for many research areas. The gene for insulin production, for example, could theoretically be removed from human DNA, placed in bacterial DNA, and start producing the insulin molecule in the new system. It could then be harvested and used for cheap, efficient drug production. The gene for nitrogen-fixation could be added to nonnitrogen-fixing bacteria or plants, and of course, genetic manipulation could conceivably correct human genetic disorders.

But, the committee emphasizes, the

In a letter entitled "Potential Biohazards of Recombinant DNA Molecules," the panel members warn of possible risks and describe specific types of experiments to avoid. By combining the DNA from viral, animal and bacterial sources, the result would be "the creation of new types of infectious DNA elements whose biological properties cannot be completely predicted in advance." They also expressed concern because the well-studied receptor bacterium E. coli commonly resides in the human intestinal tract. The bacteria are "capable of exchanging genetic information with other types of bacteria, some of which are pathogenic to man. Thus, new DNA elements introduced into E. coli might possibly become widely disseminated among human, bacterial,

plant or animal populations with unpredictable results." The threat of easy,

efficient cultivation of biological war-

fare agents therefore exists.

potential risks overshadow the promises.

The high-powered committee, under the chairmanship of Paul Berg of Stanford University, includes Stanley Cohen, Ronald Davis and David Hogness, also of Stanford: David Baltimore of MIT; Richard Roblin of Harvard Medical School; Norton Zinder of Rockefeller University; Daniel Nathans of Johns Hopkins; James D. Watson of Harvard; Herbert Boyer of the University of California; and Sherman Weissman of Yale. They asked scientists to join them in voluntarily deferring two types of experiments and in carefully weighing the risks of a third. One type might result in the addition of genes for antibiotic resistance or the addition of genes for the formation of toxins to bacterial strains that lack these properties in nature. A second type of experiment would involve linking DNA from cancercausing or noncancer-causing animal viruses to bacterial plasmids. Such recombinant DNA could be more easily disseminated and could possibly increase the incidence of cancer or other diseases. The third type of experiment about which they urge caution is the combining of animal cell DNA with bacterial DNA. Many types of animal cell DNA's contain base sequences common to RNA tumor viruses, they state, and such recombinants could be dangerous.

During the press conference, Berg said that "probably no more than five laboratories" in the United States are

Construction of Biologically Functiona LETTERS (R factor/restriction enzyme/transformation/a-Potential Biohazards of dication and Recombinant DNA Molecules *Departme University (Genome Construction Between Recent advances in techniques for Expression of Staphylococcus P the isolation and rejoining of segments on) tion/R plasmid/antibiotic resi of DNA " Replication and Transcription of Eukaryotic DNA in Escherichia coli (restriction/plasmid/transformation/recombination/ribosomal DNA) JOHN F. MORROW*†‡, STANLEY N. COHEN†, ANNIE C. Y. CHANG†, HERBERT W. BOYER§, HOWARD M. GOODMAN, AND ROBERT B. HELLING Departments of *Biochemistry and † Medicine, Stanford University School of Medicine, Stanford, California 94305; and Departments of §Microbiology and †Biochemistry and Biophysics, University of California, San Francisco, Calif. 94143 Communicated by Joshua Lederberg, January 4, 1974

Journal articles announcing the research results that led to the biologists' fears.

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involved in recombinant experiments, and "no lab known to us now is planning type one or two experiments." The third type is more common, he says.

In addition to their specific warnings, the group requested that an NIH committee oversee studies on the potential hazards of the three types of experiments, develop ways to contain such recombinants if created and to set up guidelines for future recombinant experiments. They also requested the February conference.

Examination of this issue first started at the 1973 Gordon Research Conference on Nucleic Acids, where "a very large number of people brought the problem to the attention of the NAS through a letter," Berg says. The NAS asked Berg to establish a committee. and he and the 10 others met in April. They decided an international conference should be convened, but were unable to put the conference together before next February. They became alarmed at the progress in simplifying the techniques reported in the May PROCEEDINGS and decided to issue a joint statement which the NAS then agreed to endorse.

During the press conference, Roblin emphasized that the hazards are potential and not demonstrated at this point. "But with the rapid development of the technology, we suspect that research might be done by those more chemically oriented and not used to thinking about infectious organisms." About the possibility of the deferment setting back beneficial applications, Berg says: "First of all, we are talking about a six month deferral—that should not in itself set back any research efforts significantly. I don't know of any alternate methodologies for isolating specific genes, but a large number of beneficial experiments can still go forward. With some relatively small changes, we hope we can make the procedure safe."

Will the scientific community accept their appeal? Says Berg: "We feel the scientific community should be given a chance to regulate itself. If this attempt at auto-regulation is successful, it will be an extremely important precedent. If not, it could lead to restrictive legislation." Peer pressure is an important motivating force, he says, and "it is likely if a person tried to talk about or publish this type of work, he would have to answer" to critical peers. A funding and publication ban may be instituted after the February meeting.

Could this research lead to more effective biological warfare? Baltimore says yes. The Department of Defense may express an interest in this research but "this is a challenge we must meet. Many of us grew up with the question of the moral correctness of the atomic bomb," and moral feelings greatly influenced the group's decision, he says. \square

Test-tube babies: Reaction sets in

The announcement last week by a physician in England that test-tube procreation in humans has now been achieved (SN: 7/20/74, p. 37) has, as might be expected, caused a world-wide flurry of comment and controversy. To review briefly, professor Douglas Bevis reported that one baby in England and two in Western Europe had been conceived in test tubes. Eggs had been removed from would-be mothers, fertilized in the laboratory, then placed back in the mothers' wombs to develop to birth.

What effect will the capability have on human reproduction and society?

First there is the question of whether the report was really true since Bevis initially would not say who did it, although he has since admitted that he was one of the participants. Scientists working in the field of human reproduction, though, think it probably was true. Efforts at test-tube reproduction had already been successful in animals (SN: 2/24/73, p. 124). So if test-tube reproduction is indeed now possible in people, what are the chances of it going awry and deforming offspring? As a National Academy of Sciences report being prepared on the subject puts it: "Although there have been no reports of gross deformities at birth following successful transfer in mice and rabbits, the number of animals so far produced in this way is too small to provide reassurance.

The academy report also points out that the chances of test-tube reproduction succeeding are as low as four percent—a far from acceptable rate if couples really hope to produce a baby.

There have been efforts to thwart human test-tube procreation, at least in the United States. The National Institutes of Health will fund animal testtube research, but it will not fund human test-tube research. The American Medical Association asked for a moratorium on human test-tube research two years ago (SN: 5/6/72, p. 295). And when Landrum B. Shettles tried to carry out human test-tube research, Columbia University's College of Physicians and Surgeon's "confiscated" his material. But as the achievement reported from England points out, efforts to stop human test-tube procreation were not successful, nor will they probably be in the future. All it takes is one scientist willing to defy conventions and clever enough to do it.

Some believe the event emphasizes that public discussion of what scientists should or shouldn't do too often has little impact on them. Daniel Callahan, a director of the Institute of Society, Ethics and Life Sciences at Hast-

ings-on-Hudson, N.Y. points out, "The fact that people talked about this—some for, some against—seems in the end not to have made any difference. This raises some basic problems for science and society."

So what can the public do? If nothing more, it can try to get human test-tube reproduction in perspective. There is little doubt that test-tube procreation is a misnomer. Only six days of the fetus's life are spent outside the womb; the other 260 days are spent within. And as for dehumanizing procreation, the test-tube technique is no more disruptive than artificial insemination and probably even less so because the woman has the option of having her egg fertilized by her husband's sperm, not by sperm from an outside donor. People who endorse artificial insemination but condemn test-tube procreation are, in the opinion of Andre Hellegers, an obstetrician with the Georgetown University School of Medicine, exhibiting "male chauvinistic piggery." That is, they argue that one can exteriorize sperm from the male, as in artificial insemination, but one cannot exteriorize eggs from the female, as in test-tube procreation.

Will test-tube procreation threaten natural procreation? Most scientists don't think so. They think it will be used mostly when women cannot reproduce because of blocked oviducts. Says Hellegers: "I don't see that a woman would prefer to have her ovum taken out of her and fertilized *in vitro*, then see a doctor again and have it reinjected if she can reproduce by intercourse. I don't think that test-tube reproduction will endanger the family because I don't think there is going to be a big market for it."

Famine fears rise, battle lines form

Again the rains are failing in the two most populous countries on earth. In China, lack of water now threatens crops at the height of their growing season, particularly in the northern central plains where irrigation is not available. Along the fertile river valleys of northern India, the monsoons began four weeks late and even now appear spotty. In pictures taken by weather satellite, the Himalayas stand barren of clouds, portending little runoff from melting snows to sustain agriculture in northern India during the dry season. Already conditions in the area are worse than in 1972 when crop failures brought India to her knees and when

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