the country's police departments to adopt a mandatory arrest policy. Another striking, although longer term, payoff has been found from research in Ypsilanti, Michigan, on Headstart programs. Although the programs were not shown to have a significant impact on school performance, they led to reduced rates of social dysfunction including unemployment, drug abuse, teen pregnancy, and crime.

The immediate application of knowledge about career criminals is elusive. A major change, called for by James Stewart, head of the Justice Department's National Institute of Justice, would be to allow the courts easier access to an adult offender's juvenile records. These are ordinarily sealed and often disposed of when an individual reaches adulthood.

The career criminal concept affords more guidance but also more complexity to the problems of prediction about future criminal behavior. There is much debate now, for example, on maximum desirable sentences and the extent to which high risk—as opposed to the nature of the crime at hand—should determine sentence length. There are traditionally two philosophical approaches to sentencing: the "just deserts" approach (make the punishment fit the crime), and the utilitarian approach (based on deterrence). The career criminal paradigm suggests a third approach that depends on reasonably accurate prediction of risk, based on the criminal's record and circumstances (such as drug abuse and employment history) as well as on the severity of the offense at hand.

The data on drugs and crime are being taken very seriously by this drug-conscious administration. Stewart pointed out at the conference that self-reports of drug use are extremely unreliable and recommended that all those arrested be given drug tests as a "diagnostic" measure. He also said that when abstinence from drugs is made a condition of bail, offenses during pretrial release are reduced. He called for a "national drug index" to track trends in drug use around the country.

As the conference participants noted, crime research has too often borne little relation to practice. But the career criminal concept seems to offer a practical model relatively invulnerable to the winds of political ideology. The NRC report says a broad get-tough approach might reduce crime by 5% to 10%, but at the cost of doubling the prison population. In contrast, longer sentences for career criminals could, under optimal conditions, result in the same reduction of crime with only a 10% to 20% increase in prison populations. ■

CONSTANCE HOLDEN

NIH Asked to Tighten Gene Therapy Rules

But a group studying the proposal recommends against changes, saying sound policies are already in place

WHEN the National Institutes of Health's Recombinant DNA Advisory Committee (RAC) meets later this month, it will be asked to expressly prohibit certain kinds of human gene therapy experimentation that has already been declared off limits. Specifically, the RAC will be asked to ban for the indefinite future any tests of gene therapy "not aimed solely at the relief of a life-threatening or severely disabling condition," and to forbid gene therapy that "could alter germline cells."

Existing policy documents drafted by the RAC's subcommittee on human gene therapy already state that neither form of experimentation would meet with NIH approval at present, but the Boston-based Committee for Responsible Genetics (CRG) has proposed additional regulatory language anyway, arguing that the "restrictive provisions" it favors should be spelled out in legally binding form and not be left solely as a statement of policy in documents that are merely advisory. CRG, an activist group that includes many scientists who have long opposed recombinant DNA research, asks not only that the experimentation be prohibited but also that the RAC refuse to even review such experimentation should a proposal be forthcoming. At an open meeting last month at which a number of important policy issues were reexamined, the subcommittee voted to recommend that the RAC reject the CRG proposal.

The first experimental test of human gene therapy is on the horizon. It is possible that the first protocol will be submitted to the National Institutes of Health for approval within the next few months; it may turn out to be longer in coming. But it is certain that medical researchers are close to being ready for a pioneering study and, in anticipation, an elaborate system of reviews has been put in place.

Policy makers, ethicists, researchers, and others have been debating the social and technical facets of human gene therapy for several years. Congress has held hearings; the congressional Office of Technology Assessment (OTA) has conducted a thorough, wide-ranging study (*Science*, 1 February 1985, p. 493); the RAC and its gene therapy subcommittee have examined the issues in open meetings. Both the RAC and the subcommittee contain members who represent the public.

Before the first experimental attempt at human gene therapy can legally begin, it will have to be cleared at the local level by the research center's Institutional Biosafety Committee, which looks at procedures for the safe handling of recombinant organisms, and by the Institutional Review Board, which concerns itself with the protection of the patient and such matters as informed consent. At the national level, the experiment will be reviewed in open session by the gene therapy subcommittee, which has spelled out a host of technical and ethical considerations in a document called "Points to Consider," which is, itself, constantly being reviewed. The experimental therapy protocol will have to be described in lay language and published in the *Federal Register* so any member of the public can comment. The full NIH Recombinant DNA Advisory Committee must approve the protocol. And, finally, it must be approved by the director of NIH.

But the Committee for Responsible Genetics does not have confidence in this elaborate series of safeguards. Thus, it proposed that the RAC refuse to even consider those aspects of research of which the CRG does not approve. As discussion at the subcommittee meeting revealed, the CRG actually raised two issues: one speaks directly to the substance of research that will be permitted or prohibited; the other, equally important if a bit more arcane, is a procedural question that speaks to the role NIH committees should play in the ongoing public debate.

First, the substantive issues. The CRG has proposed adding the following language to the NIH's official Guidelines for Research Involving Recombinant DNA molecules: "The RAC will not review and the NIH will not approve any human genetic therapy (i) that is not aimed solely at the relief of a life-threatening or severely disabling condition, or (ii) that could alter germline cells. Furthermore, the RAC will not review and the NIH will not approve any in vitro recombinant DNA experiments that alter human

germline cells or early human embryos."

The CRG argues that the more restrictive language is necessary because the Points to Consider define "a process for reviewing protocols but set no limitations and place no boundaries on human gene therapy experiments and on research on human germline cells."

This interpretation is arguable. The Points to Consider do say, for example, that "The RAC and its subcommittee will not at present entertain proposals for germ-line alterations. . . . " In effect, the CRG wants to delete the phrase "at present." The subcommittee, however, does not wish to foreclose the possibility that germline therapy may one day be appropriate in a few carefully chosen cases.

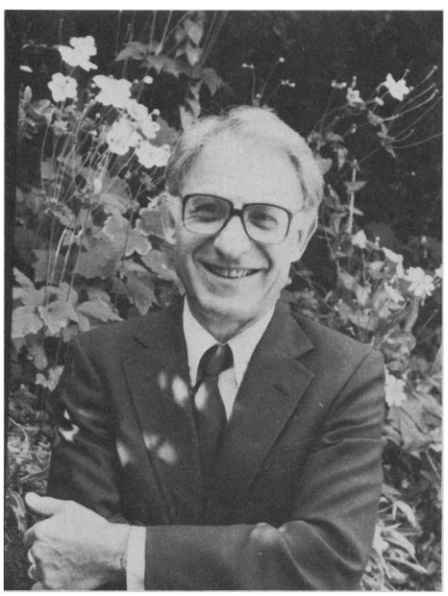
Nor did it wish to categorically prohibit any human genetic experimentation in which germ cells might be inadvertently affected as an unavoidable side effect of beneficial medical treatment. Making the point that this is quite different from experimentation intentionally directed at germ-cell alteration, subcommittee members cited examples in current medical practice in which germ cells are affected. Certain forms of radiation and of chemotherapy for cancer, for instance, are known to affect germ cells, but no one argues that life-sparing treatment should be denied on that account.

The gene therapy subcommittee also argued against the CRG's proposed language limiting the therapy to "life-threatening or severely disabling" diseases. Arno G. Motulsky of the University of Washington was among those who spoke against a flat-out prohibition. "If it should turn out that human somatic gene therapy is practically feasible to ameliorate or cure serious genetic diseases without untoward side effects, a good case can be made for no additional limitations on this mode of therapy," he said. "Apart from reasons of public policy to assure the public that all safeguards are taken when DNA is used, there is no scientific rationale in my opinion to consider somatic DNA therapy differently from any other new medical therapy."

Gene therapy can be thought of in two main categories: Somatic and germline. Somatic (or body) cell therapy, which will be the goal of initial experiments, is aimed at correcting a serious medical disease by repairing the defective gene that is the cause of the disorder. The genetic therapy of certain severe immune deficiency diseases is an example. Because of a faulty gene, the body fails to produce a protein that is essential for normal immune system function. In theory, by altering or repairing the gene, one could cure the disease. Technical problems and the need for further animal testing must be resolved before the first test of somatic cell therapy, but almost no one objects to it on ethical grounds. Somatic cell therapy is directed only at body cells that are not part of the germline.

Germline therapy, by contrast, would correct defects in reproductive cells, thereby not only alleviating disease but doing it in a way that means the corrected genes would be passed on to an individual's children.

Another category of potential future gene therapy is so-called "enhancement therapy," whose aim would be to alter a gene in order to affect some feature such as eye color or height. (It can be seen as a form of somatic cell therapy.) The prospect of tampering with the gene for growth hormone, in order to custom-grow basketball players, for instance, is often cited as an undesirable potential use of gene therapy. But, as Motulsky pointed out, there are easier ways to "enhance" someone than genetic manipulation. Even now, "stimulation of growth to enhance stature [can] be achieved more readily by administration of growth hormone than by the complicated implantation of the gene for growth hormone."



Arno Motulsky. *There is no scientific rationale for thinking gene therapy in somatic cells is any different from any other new medical therapy.*

If anything, the gene therapy subcommittee seemed a bit perplexed by CRG's proposals because it saw them as redundant. Robert F. Rich of the Institute for Government Public Affairs at the University of Illinois, Urbana, seemed to capture the subcommittee's feeling when he said, "We have been sympathetic already to the points they make. We've addressed their points in our Points to Consider. So I'm left wondering just what it is the Committee for Responsible Genetics wants us to do."

The one member of the subcommittee who showed some tendency to support the CRG was Clifford Grobstein of the University of California at San Diego. The CRG's rationale for more restrictive language was based in part on the premise that "adequate public debate [on extended uses of gene therapy] has not taken place." Although he said he did not accept the exact language of the CRG proposal, he was sympathetic enough to it as "interim public policy," to suggest alternative wording. The RAC would limit its purview to proposals for somatic therapy of life-threatening diseases "pending suitable national review and recommendation on broader policy," Grobstein suggested.

Subcommittee member Alexander M. Capron, of the Law Center at the University of Southern California, took strong exception to the suggestion that a concept as "vague" as "suitable national review" be written into regulations without spelling out exactly what that means. Grobstein's proposed wording is "an invitation to disaster," said Capron, noting that gene therapy could be stalled for years in court while opposing sides argued about "how many public forums it takes to constitute a full public debate."

The idea that either the RAC or the gene therapy subcommittee should announce that it would categorically refuse to even discuss certain types of experimental protocols also came in for rebuttal. Subcommittee member Susan Gottesman of the National Cancer Institute said such a restriction could actually "harm public debate." Robert Cook-Deegan, who was staff director for the OTA gene therapy report and who attended the subcommittee meeting as an observer, objected in even stronger terms. It would, he said, "undermine the very function of the RAC and the subcommittee which are meant to be part of the public debate. Refusing to review would just foreclose debate in important national forums."

In the end, the subcommittee voted to recommend that the RAC reject the provisions proposed by the Committee for Responsible Genetics. Taking them one by one in a letter it submitted to the RAC, the subcommittee concluded that "the suggested limitations [on what it will review] would diminish the flexibility that is one of the strengths of the RAC's function of providing advice" and that virtually all of the other items cited by the CRG are already dealt with as a matter of subcommittee or RAC policy.

The RAC meets on 29 September. ■

BARBARA J. CULLITON