be extremely difficult to prevent doctors from prescribing them widely, says Anderson. He and others urged the RAC, which advises NIH director Harold Varmus, to treat such proposals with caution until ethical concerns such as fair distribution and the potential for eugenics can be addressed.

For the moment, the big safeguard against misuse of gene therapy—and against the world depicted in *GATTACA*, in which choice jobs are reserved for the genetically enhanced—is that the technology doesn't work very well. Seven years after the first gene-therapy trial in humans, the technique has yet to produce a definitive cure for a single patient. Although more than 200 gene-therapy experiments are under way, researchers are having trouble delivering DNA into target cells and getting transplanted genes to work for more than a few months. Genetic therapies for complex traits are even more distant. "We don't yet know the genes involved in any of these characteristics," geneticist Huntington Willard of Case Western Reserve University in Cleveland told the conference.

For now, those uncertainties make it "difficult to contemplate enhancements where we can predict the outcome," says Willard. To Anderson, they make gene therapy for enhancement "medically hazardous, morally precarious, and philosophically debatable."

But all that may change, said panelist Theodore Friedmann of the University of California, San Diego. "Technology will make enhancement therapy feasible," he told the conference, and although there will be serious ethical questions to consider, he predicted that some aspects of the practice will eventually be socially acceptable. Social historian Sheila Rothman of the Columbia University College of Physicians and Surgeons in New York City agreed. Once gene therapy shows its first success, she warned, broader applications will not be far behind. The use of human growth hormones, hormone replacement therapy for menopause, and broad use of psychiatric drugs such as Prozac and Ritalin suggest that there is a very blurry line between treatment and enhancement, she says.

Most panelists recommended that the RAC take an open but cautious stance. Several suggested that any therapy with potential applications in healthy people be held to stricter standards than those designed as a last-chance therapy. Other panelists recommended that the RAC should "flag" such experiments, warning the Food and Drug Administration, which has the power to approve or reject individual proposals, to proceed with caution. "We're going to be on the slippery slope of enhancement without knowing it unless we—the RAC, the FDA, and the public—stay alert," said Anderson. A slope that could eventually bring *GATTACA* closer than your local theater.

–Gretchen Vogel

EPIDEMIOLOGY

A Plan to Register Unpublished Studies

It is considered one of the insidious problems in clinical research: Researchers tend to publish the results of trials that show an intervention works, while not even submitting those that don't. As a result, systematic reviews of the literature to determine the efficacy of a particular treatment or preventive measure are likely to be biased, and doctors may end up prescribing useless or even harmful medications to their patients. Now, the editors of 100 journals around the world have proposed a novel way to deal with this problem.

Editorials in this week's issues of the *British Medical Journal* (*BMJ*) and *The Lancet* call for "an amnesty" for unpublished trials. The idea, explains Richard Smith, editor of the *BMJ*, is to get researchers to register the existence of trials they have completed but never published, and post the registry on the World Wide Web. Then, when other researchers perform a systematic review of the literature, they can track down the unpublished results to see if they should be included in the review.

The amnesty idea was initiated by Ian Roberts, director of the Child Health Monitoring Unit at The Institute of Child Health in England. Roberts has been reviewing the effectiveness of interventions in the treatment of brain and spinal cord injuries for the Cochrane Collaboration (*Science*, 5 April 1996, p. 22), an international network of medical researchers who prepare, maintain, and disseminate systematic reviews of the effectiveness of treatments and preventive measures. He realized that unpublished results could skew his analysis. "It's quite clear from the work we've been doing," says Roberts, "that unpublished trials pose a major threat to the validity of systematic reviews."

Other epidemiologists have come to similar conclusions. Over the past decade, says University of Maryland epidemiologist Kay Dickersin, researchers have done five studies assessing the percentage of clinical trials that are completed but never published. "The final publication rate varies from 50% to 90%," says Dickersin, "and on average it is probably closer to 50." David Naylor, a clinical epidemiologist at Ontario's Institute of Clinical Evaluative Sciences, says the bulk of unpublished studies will simply be inconclusive. But he agrees that researchers are more likely to publish results that suggest a treatment works than that it doesn't, resulting in "an unduly inflated and excessively precise estimate of the treatment effectiveness in meta-analyses."

> **"Unpublished trials pose a major threat to the validity of systematic reviews."**
>
> **—Ian Roberts**

The amnesty idea will be discussed at the International Conference on Biomedical Peer Review, a gathering of journal editors from around the world being held this week in Prague, Czech Republic. Although the editors of 100 journals have already endorsed the proposal, Smith says he hopes others will sign on and help disseminate the call for unpublished work throughout the world. "We want to make it as easy as possible for people to be able to say 'Well yes, this study did happen.' And anybody can report one of these trials. It doesn't have to be the person who did it. It can be any trial you know about that's unreported. We're quite prepared to have the same trial reported more than once."

The idea has not won universal approval in the biomedical publishing world, however. The editor of one journal that is not involved suggested it would "encourage a vast *gemische* of junk." He questions the logic of inviting studies that have never been peer reviewed to be included in systematic reviews. Even Naylor, who wrote the editorial in the *BMJ* introducing the amnesty, wonders whether there is any real incentive to register unpublished trials, as they won't count toward a researcher's publication record. Moreover, he says, a disproportionate number of unpublished inconclusive or negative trials may have been sponsored by pharmaceutical companies that may not want the results publicized.

Naylor suggests that editors should increase the incentives by offering to review trials as submissions and publishing them annually in an electronic supplement. "The amnesty is a nice altruistic idea," he says, "and it's a sign of increasing activism of medical journals to improve the standards of reportage of clinical research. But some kind of more tangible benefit may be needed for this to have a real impact."

–Gary Taubes