Informed Consent for Research

The Achievements of the Past and the Challenges of the Future

In his historical account of the development of informed consent in anesthesia research, Dr. Vincent Kopp tells an engaging story about the issues and personalities prominent in the early debates about the protection of human research subjects. The description of Dr. Henry K. Beecher’s role in this controversy illustrates just one of the many ways that he has earned the distinction of being one of the founding fathers of bioethics. As anesthesiologists, we should be proud that “one of our own” was able to have such a profound impact in changing the way that medicine is practiced and in defining the relationships between clinicians, researchers, and patients.

Although Beecher’s work helped lay the foundations of research ethics, the structure is still far from complete. Serious concerns about our current system of oversight have been noted, from within academia as well as from within the government. These reports have voiced disturbing questions about the ability of Institutional Review Boards (IRBs) to effectively accomplish their mission. For example, a recent report from the Inspector General of the Department of Health and Human Services outlined several reasons why changes in the research environment have outpaced the ability of IRBs to adjust and respond.

Chief among these are the increasing number of protocols and the extreme time constraints faced by many IRBs. A 1996 survey reported that some committees spend only one or two minutes reviewing each protocol. Not surprisingly, solutions for this and other problems would require a significant increase in financial support for IRBs, and various organizations have therefore objected to many of the Inspector General’s recommendations, both because they represent an “un-funded mandate” and because they have the potential to interfere with the typically collegial relationship between IRBs and investigators. Nevertheless, if even a modest portion of the anticipated bonanza of increased federal funding for clinical trials in the coming years were devoted toward these goals, substantial progress could be made.

In addition to these concerns about the function of IRBs, another area wherein Beecher’s pioneering work is being refined concerns the requirements for informed consent. The developments in this area have been fascinating as in some cases the demands for informed consent are perceived as too lax, whereas in other areas they are seen as being unnecessarily restrictive.

Phase I trials are a good example of the former type of criticism. The problem here involves the “therapeutic misconception,” i.e., the belief by subjects that participation in a trial is likely to benefit them directly. Although the therapeutic misconception is a problem with all types of research, it is particularly difficult in phase 1 studies, which are explicitly designed not to benefit the subject, but to measure toxicity. The individual benefits of such trials are low. In one phase 1 trial of 1,248 cancer patients, for example, just 2% of subjects showed a significant beneficial tumor response and only 2 subjects (0.16%) achieved complete remission. Because of these concerns, one research group recently recommended that all phase 1 consent forms should include the phrase, prominently displayed in bold type on the first page, “This medical research project is not expected to benefit you.”

Overreliance on consent forms, however, is yet another facet of the problem. As numerous studies have demonstrated, subjects rarely display an adequate understanding of consent forms, and often do not even understand the meaning or implications of randomization. Nevertheless, IRBs have not focused on methods for monitoring or improving the actual practice of informed consent, but have instead continued to concentrate on the content of consent documents. As a result, IRBs tend to emphasize the letter rather than the spirit of informed consent. The solution to these
problems is active monitoring of the consent process by IRBs and development of procedures to assess whether the goals of informed consent are met by the actual practice. In contrast to concerns about the inadequacies of informed consent, there may be other situations wherein informed consent is an obstacle to the completion of important research without also being necessary to ensure the protection of the research subject. These possible "exceptions" to informed consent raise many concerns because they potentially threaten some of the hard-won gains in respect for patient’s rights championed by Beecher. As Kopp demonstrates, Beecher strongly challenged the view of Dr. Robert Dripps that an investigator may take on the role of "guarantor for the patient's rights" in cases in which informed consent is difficult to obtain. Yet despite Beecher's worries about unjustified paternalism in formulating exceptions to the mandate of informed consent, there may be situations in which the requirements of informed consent are counterproductive or even harmful. This view was recently acknowledged in the new federal guidelines pertaining to research during emergency conditions. For many years, research on emergency treatments was virtually paralyzed by the impossibility of obtaining informed consent. For new therapies like thrombolytic agents in acute myocardial infarctions or new methods of performing CPR, systematic clinical trials could not be undertaken. In 1996, the Food and Drug Administration and the Department of Health and Human Services endorsed a waiver of informed consent for this type of research under certain limited circumstances. Details of this approach were recently reviewed in Anesthesiology.

We have recently considered other situations wherein exceptions to the requirement for informed consent should be considered and have proposed criteria for evaluating these situations. Consider, for example, a randomized controlled trial comparing two brands of disinfectant soap for prepping patients before surgical skin incision, in which half of the operating rooms would use one brand and the other half the other brand. Assume that both brands have been in standard use and that the purpose of the trial is simply to assess which brand is associated with the lowest rate of postoperative wound infection. In this case, it would be difficult to understand why any patient would have objections to being enrolled in this trial, and it is difficult to see the value of obtaining specific informed consent from the patient under these circumstances. Yet requiring informed consent in such a trial would significantly increase the logistical difficulties of performing the trial, without any clear benefit to the patient. Dilemmas such as this are occurring more frequently within the context of "quality improvement" initiatives and bring interesting challenges to the traditional view of informed consent in research.

Beecher's work and influence were of monumental importance in changing the culture of medicine in many areas, from the definition of brain death to informed consent. One can only wonder how he would respond to the contemporary pressures that threaten the protection of human subjects. To preserve and maintain Beecher's legacy, we must remain constant to his overriding principle, that the rights and welfare of patients in research are of paramount importance. A better understanding of the pressures faced by Beecher in his quest to protect research subjects can only help us in our efforts to ensure that this ideal continues to be respected in the future.

Robert D. Truog, M.D.
Director
MICU, Children's Hospital, Boston
Associate Professor, Anesthesia (Pediatrics)
Harvard Medical School
Children's Hospital FA-108
Boston, Massachusetts 02115
Robert Truog@childrens.harvard.edu

Walter Robinson, M.D., M.P.H.
Assistant Director
Division of Medical Ethics
Harvard Medical School
Staff Physician
Division of Respiratory Medicine
Children's Hospital, Boston
Instructor in Pediatrics
Harvard Medical School

References