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Henry Knowles Beecher and the Development of Informed Consent in Anesthesia Research

Vincent J. Kopp, M.D.

AT the end of the twentieth century, guaranteeing patients’ rights and the rights of participants in clinical research are viewed as inextricably linked to the protection of all fundamental human rights. This has not always been the case. Beginning with the Nuremberg Code of 1947, global attention began to be focused on the rights of participants to freely consent and freely withdraw from any human research project. In the aftermath of World War II, the victors regarded the need to guarantee these rights as a duty that applied to the vanquished societies more so than to their own. For years after the war tribunals, conduct of government-funded research in the United States did not always satisfy the principles enunciated in the Nuremberg Code. It was largely through the efforts of one person, Henry Knowles Beecher, that the US research community recognized the need to change its attitudes and practices toward human research participants.

David Rothman, in Strangers at the Bedside: How Law and Bioethics Transformed Medical Decision Making, begins chapter four stating:

The career of Henry Beecher provided few clues that he would be the one to expose in most compelling fashion how the researchers in the post-World War II decade abused their discretion. Unlike many whistle blowers, Beecher stood at the top of his profession. 1

A detailed look at Beecher’s life and work reveals many signs of a durable concern for the rights of patients, human subjects, and scientific purity in the conduct of research. In this article, I identify and discuss antecedents to Beecher’s interest in informed consent in clinical research, review his early work on the subject, discuss the landmark article “Ethics and Clinical Research,” and show its impact on medical research in general and on anesthesia research in particular.

Antecedents

Henry Knowles Beecher, first Henry Isaiah Dorr Professor of Anesthesia Research and Chief Anaesthetist at Harvard, had many interests during his long and illustrious career. The origins of his concern for the ethics of human research had deep scientific and humanitarian roots. His scientific concerns related to his advocacy for placebo use in randomized, prospective research trials. His humanitarian concerns related to his abhorrence of the human experiments conducted by Nazi doctors.

Beecher was among the earliest investigators to note the placebo effect. Observing the inexplicable decreased need for morphine among wounded soldiers awaiting evacuation at Anzio Beachhead, he hypothesized that the body, in particular the mind, produced physiologic effects that might otherwise be wrongly ascribed to an administered drug. 2 This observation led him to advocate placebo use in a “double-blind” technique and “randomization of administration of the agents tested” in clinical investigations of drugs in humans. 3 Although he
was not the only proponent, he was perhaps the most persistent advocate of placebo use.

A second early Beecher interest was human experimentation by Nazi doctors. After World War II, Beecher reviewed classified military documents for the US Army about human experimentation in Nazi concentration camps. He kept detailed records of these atrocities in his personal files to serve, perhaps, as a constant reminder of the actual and potential magnitude of humanity’s inhumanity during the pursuit of scientific knowledge.

The following excerpt, from a declassified report by Dr. (then Col.) Esmond R. Long, about Buchenwald Concentration Camp, is among Beecher’s papers at the Francis A. Countway Library of Medicine, Harvard University. It illustrates Beecher’s interest in how science gone awry constituted a particularly horrific form of depravity:

Near the building used as a hospital was a pathological laboratory. I saw specimens of pulmonary tuberculosis, carcinoma of the lung and tattooed [sic] skin. These were put up in regular museum jars, and were unusual in no way. It was evident, however, from the attention they excited, that they were looked upon by non-medical visitors as illustrations of the depravity of the German doctors. . . In this building, however, it seems clear that ruthless experiments on live human beings were carried on. Dr. Ding, a well-known German clinician, is said to have tested a typhus vaccine here on human beings, by inoculating them with a vaccine and injecting them with a live virulent culture later. The experiment was unsuccessful. One report was that 900 were inoculated and 700 died. Whatever the numbers, there appears no question about the basic facts. . .

From his writings, it is clear Beecher’s interest in the ethics of human experimentation sharpened as a result of his work on placebos and his review of Nazi crime records. He followed the Nuremberg trials and was familiar with the Nuremberg Code. He questioned the science behind Nazi experiments conducted in concentration camps and extended the question to those conducted by other physicians and scientists. In doing so, he became convinced that a study, to be scientifically valid, must be ethical from its inception. At the same time, he came to believe that science’s values were neither the highest ones to which all other orders of value are subordinate, nor that ethical considerations should be subordinated to the scientific value of any given experiment.

These beliefs, then, subtended his future actions as a whistle blower who would reveal his fellow researchers’ ethical transgressions, relying, as he did, on the scientific and moral authority he had gained by being at the top of his profession to advance his arguments.

From “Experimentation in Man” to the Brook Lodge Symposium

By 1958, Beecher’s thoughts on consent in human experimentation had crystallized. As early as February 10, 1958, Dr. Beecher addressed members of the Executive Committee of the Committee on Research at Harvard in a memorandum and Dean George P. Berry in a letter, expressing his concerns:

It has long seemed to me that we, in common with most other similar institutions, have not faced up to the problems surrounding experimentation in man. As I have pointed out in the attached review, such errors as I at least have encountered have all been based upon ignorance or thoughtlessness or inexperience and never upon willful or unscrupulous attitude toward patients or subjects . . . These matters are much too complex, it seems to me, to permit the establishment of rigid rules in most cases. I do believe, however, that a great deal can be done to correct nearly all abuses by disseminating information on past experience and thinking in this complicated field. Curiously enough, no review has heretofore been made which attempted to deal with all facets of the problem, but in the attached review I have attempted to cover all aspects.

The review mentioned by Beecher became an article, “Experimentation in Man” published in JAMA on January 31, 1959, as a Report to the AMA Council on Drugs, as adopted by the Committee on Research. In it, he stated the report’s aims, reviewed the history and scope of human experimentation, gave suitable characteristics for human subjects and investigators, distinguished between permissible and nonpermissible forms of human experimentation, reviewed moral and ethical aspects of human experimentation, raised emerging legal considerations, detailed the extant “codes” available to guide the ethical conduct of human experiments, and made recommendations to investigators on the conduct of experiments in humans. Widely disseminated and widely praised before and after publication as a report and as a small book, Beecher, with the benefit of hindsight, reflected on “Experimentation in Man” at a later stage in his career, saying “. . . it has all the impact of a feather in a high wind.” It was failure to gain immediate and broad-

† Unless otherwise noted, quoted materials are from the Henry K. Beecher collection, Francis A. Countway Library of Medicine, Harvard University.

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based acceptance of his position that set up the next phase of his crusade.

After “Experimentation in Man,” Dr. Beecher continued to write about ethics in clinical research, particularly informed consent and the use of placebos in therapeutic comparison studies. In 1962, “Some Fallacies and Errors in the Application of the Principle of Consent in Experimentation,” appeared in Clinical Pharmacology and Therapeutics. Here he enunciated the “two problems in the field of human experimentation which in any hierarchy of human experimentation are at the top level of difficulty.” In the article he identified these as, first, “... the problem of consent, seemingly so simple and straightforward...” and second, “the problem of the ethical justification for experimentation on one subject which cannot in any way be construed as for his benefit but is for patients in general.”

In the printed asterisk footnote to this statement, Beecher commented further on justification, stating that “Experimentation in one patient, not for his benefit but for patients in general, poses problems. Many are in the painful position of not rejecting the benefits obtained from this source but of rejecting the means which produced the benefits. To me, this is indistinguishable from the view that ends justify means.” By making this statement, Beecher acknowledged the intrinsic conflict in ethics that exists for the clinician who is also a researcher, a conflict that took some time to be broadly acknowledged by investigators even at such research facilities as the National Institutes of Health.

Dr. Beecher further developed his ideas on consent and placebo use in “Ethics and Experimental Therapy,” an editorial published in the November 30, 1963 issue of JAMA. Beecher discussed the role of sham and placebo operations and advocated their use in surgical clinical trials. Referring to a proposed study on thymectomy, he cautioned that “Such a study could be carried out only with consent, when all patients had the situation fully explained to them and were told that they might or might not have a thymectomy, that half would be kept in ignorance of what was done until the study was completed.” Citing the example of internal mammary artery ligation procedures, he maintained “It is no use to say this cannot be done,” noting “... two groups have already carried out such controlled studies” and thus proved that ligation of the internal mammary arteries in management of angina pectoris resulted in “... great (and transient) improvement...” which was “... as great after the sham procedure as after ligation.” He further noted that “... this useless and dangerous operation (the death rate was appreciable) was completely discredited in only 2 years after its enthusiastic introduction into this country...” as a result of the placebo-controlled surgical trial.

Perhaps fortified with the scientific certainty his surgical example provided and the moral authority afforded by the passage of The Declaration of Helsinki by the 18th World Medical Assembly in 1964, which addressed, in part, the subject of humans in research, Dr. Beecher moved forward with his mission to publicize abuses of researchers’ discretion. He made his boldest expression of concern about consent in clinical research on March 22, 1965 during a presentation at the Brook Lodge Symposium for Science Writers, sponsored by Upjohn Company in Kalamazoo, Michigan. At Brook Lodge, Dr. Beecher presented 18 examples of clinical investigations wherein no study participant consent was obtained before patients were enrolled in experiments from which they received no direct benefit. For the first time, Henry K. Beecher spoke publicly about a subject that, here-to-fore, had been aired yet barely heeded in the medical research community.

Reactions to Beecher’s revelations were swift and not confined to medical participants at the conference. In a letter to George Burch, June 27, 1966, Beecher later reported, “I really was subjected to the most humiliating experience,” when Dr. Thomas Chalmers and Dr. David Rutstein, both colleagues at Harvard Medical School, “called a press conference to refute what I said without finding out whether or not I could be present.” The New York Times, the Wall Street Journal and regional newspapers, such as the San Jose Mercury, carried the story, evoking comments such as this unsigned letter sent by a San Jose reader directly to Dr. Beecher, dated April 5, 1965, and which is among his personal files at the Countway Library:

Dear Dr. Beecher,

I am sending you this airtical [sic] of my paper, rather than writing you a long note.

I just want you to know how much I enjoyed this airtical [sic], and know there are many, many more people who feel the same way. We need more, a lot more Doctors like you who will tell the people the honest truth. But try and find them to-day. It is really [sic] sad.

Thank you Dr. Beecher and continue to speak the truth.

God Bless you always.
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Such acknowledgment from the lay public of his position must have energized Beecher as much as the opposition he perceived from the sophisticated medical research community. After Brook Lodge, he was galvanized into action, and in 1965 and 1966 he wrote and published with greater purpose about ethical issues, all while preparing a major article based on the materials he presented at the Brook Lodge Symposium. In “Consent in Clinical Experimentation: Myth and Reality,” published in JAMA, January 3, 1966, Beecher gave a hint of how adamant he was in his views on the subject, saying “...codes dealing with human experimentation start out with the bland assumption that consent is ours for the asking.” Calling this notion “a myth,” he went on to assert that “...informed consent is often exceedingly difficult or impossible to obtain in any complete sense” and that “...difficulties inherent in this complex situation are no excuse for giving up the effort: informed consent is a goal toward which we strive...” Two months later, in another article, “Some Guidelines for Clinical Investigation,” published March 28, 1966 in JAMA, Beecher articulated his thoughts on ethical problems in research on different subject groups: normal volunteers, self-experimentation, patient volunteers, patients requiring therapy, and patients who receive no benefit but whose participation benefits others. In an unusual move, considering the public circumstances, the JAMA Editor printed a disclaimer at the end of Beecher’s article, saying, in effect, Beecher speaks alone:

Although it is not customary to print a disclaimer with a signed communication in The Journal, the comments by Dr. Beecher have been prepared in his office with consultation as determined by him. The American Medical Association has taken no official action on this important subject. Appropriate councils and committees and the staff have this subject under study and will report at a later time.

The Preparation and Publication of “Ethics and Clinical Research”

In the midst of writing and publishing the aforementioned articles, Beecher worked to achieve his prime goal: to publish a comprehensive review of medical research experiments wherein investigators breached basic standards of informed consent. His original hope was to publish an article in JAMA based on 50 examples of studies like those he presented at the Brook Lodge Symposium. On August 20, 1965, Beecher submitted such a manuscript, which he entitled “Ethics and Clinical Research.” In the cover letter to Dr. John H. Talbot, Editor, he asserted that his effort, to which he had “...given about ten years as careful thought as I am capable of giving...” had been read by people, “...including the president of the Massachusetts Medical Society who, though appalled by the information, agrees that it should be published, and the sooner the better.” Apparently not as impressed by his work as the “others” to whom Beecher referred, Dr. Talbot wrote on October 25, 1965, that he was returning the manuscript with comments from the two reviewers who reviewed it before reaching the final decision not to publish it as submitted. The reviewers’ comments noted the absence of citations for the specific studies mentioned and the overall length of the article as reasons for not publishing it in JAMA.

Not dissuaded, Beecher submitted his article to the New England Journal of Medicine on November 10, 1965, stating in his cover letter that he had “...no objection to it being divided and published in two issues.” As in his correspondence with Dr. Talbot at JAMA, Beecher struck an urgent tone in his letter to Dr. Joseph Garland, Editor, with apparent greater effect. “There is an increasing awareness of the problems described in this paper...” he began. “I believe that unless some exceedingly common and careless practices are corrected medicine will suffer greatly in the eyes of the public.” Eschewing the idea that more than education was needed to achieve corrections, he continued, “I do believe that most people need only to be alerted to the problems involved in order to correct them.”

Beecher’s faith in the persuasiveness of his examples was rewarded, no doubt in part because of his association with the Massachusetts Medical Society. Then, unlike now, anonymous peer review was not the rule. Dr. Garland sent copies of Beecher’s article to seven “thoughtful” reviewers, only one of whom thought the article should not be published in some form. Much editorial work ensued. In his January 1, 1966 letter to Beecher, Garland asked him to make the introductory pages more succinct and if “...the 20 or 25 best examples we cite, sufficiently briefly?” More importantly, Garland asked: “Could a list of references be prepared in the usual way and ‘certified’ instead of being published, to the probable discomfiture of the authors?” Beecher, anxious to comply, submitted a pared down version with 25 examples and supplied references on January 19, 1966. By March 3, 1966, Garland wrote Beecher to say he had completed his editorial work and had initi-

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ated the reference checks he required. In his letter, Garland emphasized:

Here is the result of my editorial labor, in which I have attempted to reduce your important data to a relatively unemotional statement of factual material. I have tried to omit anything accusatory or especially critical, since what we want is not an indictment but a sober and dramatic presentation of what has been done and is being done in violation of basic ethics.

To my mind this makes the message all the more impressive; "res ipso loquitur [sic]."

On June 16, 1966, "Ethics and Clinical Research" appeared as a special article in the New England Journal of Medicine. Although in 1966 the journal had neither the circulation nor the reputation it has today, Beecher was nonetheless pleased to have his important work in print. With cool precision and deliberate attention to detail, he outlined the reasons for urgency, assessed the frequency of unethical or questionably ethical procedures, and elaborated on the problem of consent. After this he presented his 22 examples under the following categories: known effective treatment withheld (3 examples), study of therapy (1 example), physiologic studies (9 examples), studies to improve the understanding of disease (5 examples), technical study of disease (3 examples), and frankly bizarre studies (1 example; table 1).

There is no doubt "Ethics and Clinical Research" hit its mark. Stories about the article appeared in the Boston Globe, the Wall Street Journal, the Saturday Review, and other major periodicals. Immediate reaction from the medical community was muted. Beecher wrote Garland on June 28, 1966, that he had not received "...a single angry letter, but many from this medical community with warm support. (I do not doubt that you may have received some hot ones.) I have been amazed at the wide coverage of the article." Despite the publicity (or perhaps because of it) Garland had received only four letters by August 23, 1966. These appeared along with Dr. Beecher’s rebuttals in the October 6, 1966 issue.

In his rebuttal, Beecher acknowledged and explained the reason for what many thought was his article’s main weakness: absence of references. On this point, Beecher defended his actions, responding:

Several have thought references to the case material should have been given. Fortunately, the editor agreed wholeheartedly that these should not be published. All references were, of course, deposited in his office and checked for accuracy of statement by the editor and two of his associates... I had no wish to point to individuals but rather to what I believed to be widespread practices. And secondly, I was assured by a distinguished lawyer that a number of the investigators involved could be held on criminal charges if discovered by the subjects. I wanted no part in such an action.

From the beginning, Beecher had held ethical high ground. The effect of his article was as far reaching as he had hoped it would be. Simply stated, outside of medicine, his work stimulated greater oversight of governmentally funded research projects and gave rise to the ultimate requirement that human research proposals be evaluated by institutional review boards. Equally simply stated, inside medicine, his work helped stimulate awareness first, then discussion of what conflicts of interest exist for physicians who are also clinical researchers. His participation in this process illustrates how awareness and discussion evolved in medicine. How this same awareness and discussion took place within the anesthesiology community is the focus of the remainder of this article.
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The Effect of Beecher’s Work on the Anesthesia Community

That Beecher simultaneously faced the issue of “experimentation on a patient not for his benefit but for that, at least in theory, of patients in general” by fellow researchers in anesthesiology, as well as by the medical research community at large, is to his everlasting credit. Two examples among the 22 given in the article were from anesthesia research teams. Based on evidence in Beecher’s papers, he had retained the original 50 examples, he would have included more, keeping the proportion of examples from anesthesiology teams at about 9% of the total.

Although not identified in the article at the time, example 7, “Cyclopropane Anesthesia. I. Cardiac rate and rhythm during steady state levels of cyclopropane anesthesia at normal and elevated end-expiratory carbon dioxide tensions,” was authored by Drs. A. A. Lurie, R. E. Jones, H. A. W. Linde, M. L. Price, R. D. Dripps, and H. L. Price and was published in Anesthesiology in 1958. Example 9, “Changes in Circulation Consequent to Manipulation during Abdominal Surgery,” was authored by Drs. A. G. Rocco and L. D. Vandam and was published in JAMA in 1957. Beecher listed these two examples under “Physiologic Studies” in his article.

No letters among the Beecher files accessible for research contained criticism of Beecher’s article by any of the authors of the two cited examples from anesthesiology teams. Further, discussion with several of Dr. Beecher’s prominent anesthesiologist contemporaries yielded no specific recollections of negative reactions in the anesthesiology community to his New England Journal of Medicine article.

A look at the anesthesiology literature after publication of “Ethics and Clinical Research” reveals, however, that Beecher and a research team comprised of Drs. G. Long, R. D. Dripps, and H. L. Price “locked horns” over the propriety of a study published in Anesthesiology in 1967. The discussion that followed was multilayered and took place in both a behind-the-scenes and public fashion, leaving no detectable signs of acrimony among the involved participants.

The study in question was “Measurement of Anti-arrhythmic Potency of Drugs in Man: Effects of Dehydrobenzperidol” by G. Long, R. D. Dripps, and H. L. Price. The study details are not germane to this article, except to say that it involved the intentional induction of arrhythmias by epinephrine infusion and their treatment with droperidol in patients anesthetized with cyclopropane. In many ways it bore similarities to the study Beecher cited as example 7 in “Ethics and Human Experimentation.”

Dr. Leroy Vandam, who was editor of Anesthesiology when the study was published, recalled that publication of this study was surrounded by controversy from the beginning. Vandam himself regarded the study as flawed and thought what was done to patients was “blatantly wrong.” He also said the authors suggested he could be “sued for libel” if he did not publish their work when he initially resisted publication of the study. One can hardly imagine such a thing happening today.

What transpired on the Anesthesiology Editorial Board side of the controversy is revealed below. What was unusual from the outset is that the Long-Dripps-Price article appeared with a statement in a footnote written by the authors to address the question of informed consent during the study of nine female patients. In it they conceded that the problem of obtaining valid consent always exists in any human experiment and that, despite meticulous preparation of subjects “...an informed consent cannot be obtained for a study of this type, because of the impossibility of transmitting to a patient both the relevant information and the background needed to analyze and evaluate such information.” By way of defense of their actions, the authors wrote:

Instead, we have accepted the role of guarantor of the patient’s rights and safety: (1) only physical status I is acceptable; (2) inhaled cyclopropane concentration must not range beyond 20–30 per cent; (3) respiratory acidosis must be prevented; (4) starting dose and rate of administration of epinephrine must be the minimal one, 3.6 mg./minute in these experiments; (5) the infusion is terminated when an arrhythmia appears.

It was perhaps an indication of the increased sensitivity to the issue of informed consent after Beecher’s 1966 article that Beecher was not the first person to respond to the researchers’ published statement. Dr. B. Raymond Fink, in a letter published in the November–December 1967 issue of Anesthesiology, was the first to criticize the study. In his letter he said that “…the problem of obtaining a patient’s valid consent for experiments on his or her person is not solved by an investigator who

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† Drs. Leroy Vandam, J. S. Gravenstein, and Elliot V. Miller gave generously of their time to reminisce about their past associations with Dr. Beecher.

§ Dr. Vandam discussed his duties as Anesthesiology Editor in an April 27, 1998 telephone conversation.
side-steps the problem and, instead, assumes “the role of guarantor of the patient’s rights.”” Assessing the logic of this claim, he continued, saying:

... there is an obvious inconsistency between the claim to guarantee the patient’s rights and the failure to honor the foremost of those rights, the right to exercise informed consent or dissent. A guarantee of this sort is nugatory. ... What is at stake is the patient’s right to her own considered decision concerning projected experiments on her person, and to the information necessary to make a decision. If the information cannot be given, the experiment should not be carried out."

In the last part of his statement, Dr. Fink echoed, perhaps without knowing it, Dr. Beecher’s position that a experiment had to be ethical from its inception if its conclusions were to be regarded as scientifically valid. The reply to Dr. Fink’s letter, printed in the same issue, was written by Dr. Dripps. “The ethics of ‘human experimentation’ is receiving much attention...” he began. “We have been involved in this for almost three decades and think that we have developed a responsible, but practical approach...” Explicating his view that informed consent is impossible to obtain and that the investigator be responsible and serve as the guarantor for the patient during general anesthesia, prepared to stop the study if danger developed, Dripps closed by asserting that he would submit one of his own children to the protocol because he believed it to be safe.

Beecher was not deaf to the controversy being played out in Anesthesiology. On December 20, 1967, he wrote Dr. Vandam stating that he had “...given a lot of thought to the Long, Dripps and Price statement in the accompanying Letter to the Editor.” Apparently, Beecher decided to weigh in on the controversy but had been reluctant to do so without thinking his position through completely. “While in many ways it would have been desirable to have replied to their statement as soon as it was published,” he continued, “I simply could not do this because it seemed to me to be such an important matter, and one to be thought through.” As a courtesy, Beecher sent a copy of his proposed “Letter to the Editor” to Dr. Dripps for review and to allow his simultaneous preparation of a reply. The ensuing exchange of letters between Beecher, Dripps, and Vandam illustrates the gentlemanly manner in which these three giants of anesthesiology handled the controversy before them.

On January 2, 1968, Dr. Dripps wrote Dr. Beecher to say that he and his coauthors “...are not offended by your letter to Vandam. Indeed, we are grateful that it gives us an opportunity to express more clearly than we have before just what we meant by the offending phrase “...role of guarantor...” Dripps continued, expressing regret for the use of the prefatory word “instead” and went on to explain five points that governed his team’s approach to consent in research:

1. we do no studies on a patient without obtaining the patient’s signed and witnessed consent;
2. we try to make this an informed consent, for as I pointed out in my reply to Fink I realize that many patients will give consent readily when they trust or like their physicians;
3. we believe it difficult to inform the patient completely, but try to do our best;
4. we promise nothing other than the best care of which we are capable;
5. we regard clinical investigation as a major responsibility, demanding the utmost in integrity.

Declining to discuss the safety issues in the study, Dripps continued, saying:

I believe that clinical research must continue. Society stands to lose much if they [sic] are banned. It is up to all of us to see that the rights of the individual are not compromised as one seeks new knowledge. If new knowledge cannot be obtained without disregarding these rights then we must stop. I hope and believe that this will not be necessary for the good of the world.

Dr. Dripps closed his letter giving Beecher permission “...to use any or all of my letter...” in association with his letter to Anesthesiology.

Beecher was not insensitive to the potential for ruffled feathers in what might become an editorial cockfight. With Dripps’ response in hand, Beecher wrote Vandam on January 19, 1968, to say: “I am trying to conform as much as I can to information and requests that Bob Dripps has made concerning my ‘Letter to the Editor,’ so will you please hold up any publication of it until I have had an opportunity to do what I can to keep peace.” In separate, brief, follow-up letters to Dripps and Vandam on February 2, 1968, Beecher thanked each for their cooperation and again encouraged Dr. Dripps to fashion a response suitable for publication at the time his, Beecher’s, letter was to appear. The reply eventually published was a slightly modified version of the letter Dripps sent to Beecher on January 2, 1968, with all personal references eliminated.

In reply to Beecher, Dr. Vandam wrote on February 7, 1968:

I have your latest letters on the Dripps’ paper. Of course we shall publish it and there will be an editorial comment.
plus reply from Dripps if he will write one. Somehow or other as I view this matter I wonder what is to be gained by a further airing of the subject. Fink’s letter called attention to the problem in adequate fashion and I am certain that Pennsylvania has learned something thereby. . . . Your views on the subject are very well known and will further be broadcast by the Lowell Lectures with a book to follow, I suspect. It almost seems in an extended correspondence such as this that the focus shifts away from the issue, to the protagonists. The cause becomes enmeshed in personalities. You might look at it from this point of view and decide what is to be gained.

Beecher pressed on with crusader-like zeal. In his published letter to the editor, he called the Long-Dripps-Price approach to consent a “revolutionary approach to the complex problem faced by all clinical investigators . . .” insisting that a reply was warranted. He began by taking the Anesthesiology Editorial Board to task, saying:

In the first place, since there is no indication to the contrary, one can only assume that the editor and the Editorial Board, or at least the majority of those on the Editorial Board, approved of the authors’ statement . . . (One can hardly assume that as revolutionary a statement as the one under discussion could have been published by the Editor supported by the minority of his Board, unless this were plainly stated. Certainly those members who might have opposed it would thus be placed in an awkward position.) This in itself is rather remarkable, for in sounding out a number of experienced investigators, I have not found a single one who agreed with the authors.

In response to this statement, an “Editor’s Note,” written presumably by Vandam, appeared at the end of the Beecher-Dripps letter exchange. Replying to Beecher’s first point only, it tersely stated:

The article was accepted for publication in July of 1966, first having been submitted in August of 1965, months before the February 1966 recommendation by the Surgeon-General concerning investigations on human subjects. Thus, the Pennsylvania group was not impelled to supply a statement on consent. Nevertheless, the article was returned for clarification and we were rewarded with the statement now under fire. Departing from usual practice, unanimous [sic] agreement was had from the Editorial Board before acceptance for publication.

Continuing in defense of the editorial actions taken, the statement continued:

It should be evident that a journal’s policies are more often than not the distillation of experience, and at this stage of the controversy we, and many another reputable periodical, have not been able to adopt an all-or-none rule concerning the printing of papers wherein human studies are at issue. Consequently we accepted a carefully worded statement on the problem prepared by a group of established senior investigators with a long and unblemished record of productive human experimentation. Their statement could not have elicited endorsement, suppression or condemnation, for any such action would have implied censorship. . . . The Journal’s attitude was the same when, in the November-December 1967 issue, the letters to the Editor of Drs. Fink and Dripps, which ordinarily might have terminated the matter for the good of all concerned, were printed. The discussion evoked has been in the best journalistic tradition and can only serve to define further the goals Dr. Beecher is striving for.

The matter, it would appear, was resolved, at least in the minds of the Anesthesiology Editors. As the first point Beecher made in his “Letter to the Editor” is the main point of interest for this article, no need exists to review Beecher’s other points. Suffice it to say, they largely pertained to clinical research in general, although specific references to anesthesiology research served as the vehicle to carry forth his ideas.

It seems the Editors hoped the Beecher-Dripps controversy would end informed consent as an issue in Anesthesiology. This was not to be. Ever vigilant to ethical missteps, Beecher wrote Vandam as Editor to criticize the lead article in the December, 1969 issue of Anesthesiology, by Y. Koska, T. Takahashi, and L. C. Mark, entitled “Intravenous Thiobarbiturate Anesthesia for Cesarean Section.” In his letter, dated December 19, 1969, he sharply asserted that “. . . patients were subjected to procedures I would not want carried out on my family, even with consent (cf. Group IV). No evidence is presented that consent was sought or obtained. Some of the stresses and risks imposed are, in my view, unacceptable.”

His closing comment, however, can only be construed as laudatory. Acknowledging the progress that had been made over 3 years time, he added: “It is a tribute to the present-day high editorial standards of Anesthesiology that the inclusion of this study comes as a surprise.” Beecher made no other published comments on the subject of informed consent in the anesthesiology community literature after this final letter.

Conclusion

In this article I have traced the course of action taken by one person, Dr. Henry Knowles Beecher, to address
the ethics of informed consent in clinical research, with an emphasis on how he also approached the dilemma within his professional cohort of research anesthesiologists. Obviously, Dr. Beecher was not the only person concerned with this vexing societal problem. As noted previously, the Surgeon General’s office had issued a statement that addressed investigator-subject relationship issues in February 1966. This statement came before Beecher’s article but after his Brook Lodge presentation. Although a temporal relationship certainly exists, it does not prove his efforts to publicize breaches of accepted informed consent standards affected sweeping regulatory changes. After “Ethics and Clinical Research” appeared, however, the same office issued revised guidelines in July 1966, which were promulgated by the National Institutes of Health (NIH) parent organization, the US Public Health Service (PHS). All federally funded research efforts were hence required to show evidence of peer-reviewed superintendence—what came to be known as Institutional Review Board or IRB approval—for all research procedures pertaining to human subjects. During this same time the Food and Drug Administration (FDA) also established firm standards for investigator behavior concerning informed consent. In August 1966, again after publication of Beecher’s article and the revised NIH guidelines, the FDA’s “Statement on Policy Concerning Consent for Use of Investigational New Drugs on Humans” was issued.¹

In medical research in general and in anesthesiology specifically, Beecher’s bold actions effected lasting change. In a 1987 article, entitled, “Ethics and Human Experimentation: Henry Beecher Revisited,” David Rothman reflected on the substantial changes in the wake of Beecher’s actions:

In short order, federal regulations mandated the creation of institutional review boards to review all protocols submitted for federal funding to make certain that subjects had given informed consent and that the risks did not outweigh the benefits. For the first time, decisions that were traditionally left to the consciences of individual physicians came under collective surveillance. … The memory of the postwar record precludes a return to a hands-off policy, and institutional review boards are now regarded as symbolically and actually valuable. At least, researchers today would not consider submitting protocols like those in Beecher’s list of 22. At most, more subjects are giving truly informed consent.²¹

That investigators consulting the Guide for Authors printed in Anesthesiology (or a similar major medical journal) find an editorial policy statement addressing legal and ethical considerations such as the one that follows is an outgrowth of Beecher’s work:

Experiments performed on humans must conform to ethical standards, and must be approved by the appropriate Institutional Review Board (IRB). A statement concerning IRB approval and consent procedures must appear at the beginning of the Methods section of the manuscripts. However, local IRB approval does not guarantee acceptability; the final decision will be made by the Editor-in-Chief.²²

This statement and the policy it represents is but one of Henry Knowles Beecher’s legacies: that informed consent be obtained in human research. Another was his insistence on scientific rigor in anesthesia research, education, and practice, especially in the university setting, a topic that has been written about in this journal.²³ A third, and arguably his most far-reaching, legacy was his role in the redefinition of death as neurologic, rather than cardiorespiratory, in nature—the essential paradigm shift required before modern attitudes toward organ transplantation could be attained. As anesthesiologists we can be proud of the role one of our own played in these momentous steps in the advance of medical practices that respect human dignity and protect basic human rights. To Henry Knowles Beecher, we owe a great debt, one which we can only repay by recording his name clearly in our professional history.

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References


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14. Fink BR. Correspondence. Anesthesiology 1967; 28:1109
15. Dripps RD. Correspondence. Anesthesiology 1967; 28:1109–10
16. Dripps RD. Correspondence. Anesthesiology 1968; 29:603–4
18. Editorial Note. Anesthesiology 1968; 29:604