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## The Use of Placebos in Randomized Clinical Trials

by Robert J. Levine

Most discussions of the ethical problems presented by the use of placebos in randomized clinical trials focus on the problem of deception. As I shall demonstrate, this focus is misplaced; it reflects a lack of appreciation of the differences between placebo usage in medical practice and in randomized clinical trials. One class of placebo usage in randomized clinical trials presents peculiarly difficult ethical problems—that is, clinical trials in which placebo is compared with an active

agent, the purpose of which is to mitigate that component of a disease process that leads to lethal or disabling complications. I shall argue that in this class of clinical trial placebo administration should be regarded as a non-therapeutic procedure that presents more than minimal risk.

### Deception

In medical practice, the use of placebos is almost invariably associated with the physician's deception of the patient. Physicians use suggestion to enhance or to reinforce the placebo effect. They tell patients that the pill or injection they are about to receive is very powerful and very likely to relieve the patient's symptoms. Those who use placebos in medical practice wish to produce as great a placebo effect as possible.

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In a placebo-controlled randomized clinical trial, the situation is much different. Each prospective subject is told that there is, for example, a 50-50 chance that he or she may receive an inert substance.<sup>1, at p.113</sup> Each subject is told further that neither the physician-investigator nor the subject will know whether he or she is receiving the placebo or the presumably active agent. In the context of randomized clinical trials, great care is taken to minimize deception. Although this is done in the interests of informed consent, it also minimizes the likelihood and magnitude of the placebo effect. In most cases such minimization serves the interests of the investigator, who usually wishes to show the superiority of the active agent to placebo in producing the desired effect.

Thus, in the placebo-controlled randomized clinical trial, there is generally no deception about whether the subject will receive a placebo. Prospective subjects are invited to agree to remain ignorant of which of two—or in some cases, more—agents they might receive during the course of the randomized clinical trial. To remain ignorant for a finite period of time with full knowledge that that is what one is doing is ethically much less problematic than to be deceived.<sup>2</sup>

Some types of research involving placebos do entail deception about the nature of the substance to be administered to the subject. For example, research on the nature of the placebo effect ordinarily requires deception of the subject in order to produce the placebo effect. These types of research are outside the scope of this discussion.

### The Null Hypothesis

It is generally agreed that ethical justification for beginning a randomized clinical trial requires that the investigators be able to state an honest null hypothesis.<sup>3, at pp.126-129;4</sup> In a randomized clinical trial comparing therapy A with therapy B, the investigators must state that there is no scientifically validated reason to predict that therapy A will be superior or inferior to B. Further, there must be no therapy C that is known to be superior to either A or B unless there is good cause to reject therapy C, e.g., the population of research subjects will consist of either those in whom therapy C has been tried and failed or individuals who are aware of therapy C, and for various reasons, have refused to accept it.

The ethical requirement for a bona fide null hypothesis notwithstanding, generally placebo-controlled ran-

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domized clinical trials are not begun until there is some preliminary evidence that the agent to be compared with placebo is more effective than placebo in bringing about the desired consequence. There are important practical reasons for this.<sup>3, at p.127</sup> Not the least of these reasons is that randomized clinical trials are expensive and those who finance such trials do not, in general, wish to make major investments in studying agents that are not likely to be superior to placebo. Moreover, in the period before beginning a randomized clinical trial, studies are done that are designed not only to establish preliminary evidence of efficacy but also to determine the optimum dose to be studied during the randomized clinical trial.<sup>5, at p.224</sup>

Quite commonly at the time a randomized clinical trial is begun, the investigators have available quite a bit of evidence about the agents to be tested. In the United States, for example, the results of extensive experience with new drugs obtained during clinical investigations or in medical practice in other countries are often available. Moreover, proposals to repeat clinical trials in which the null hypothesis was rejected are not uncommon; usually in such cases the investigator or the industrial sponsor claims that either the design or the conduct of the first clinical trial was inadequate.

Thus, in the practical world, the ethical standard seems to be that there be no scientifically validated reason to predict that the agent to be compared with placebo is superior to placebo. For purposes of further discussion, I shall assume that each time one plans to initiate a placebo-controlled randomized clinical trial there exists at least some preliminary evidence that the active agent to be compared with placebo is effective in producing the desired consequence. Moreover, as I have noted, in many cases there is a substantial body of such "preliminary evidence."

#### Classes of Clinical Trials

It is important to distinguish two classes of placebo-controlled randomized clinical trials. The distinction is based on the purpose of the active agent against which placebo is to be compared. In the first class of clinical trial, the purpose of the active agent is to mitigate that component of a disease process that leads to lethal or disabling complications. In the second class, the purpose of the active agent is to relieve symptoms without altering the rate of development of lethal or disabling complications.

The second class of placebo-controlled randomized clinical trial is exemplified by comparisons between pain-relieving agents and placebo. This is the class of activities characterized by Beecher as presenting "no discernible risk."<sup>1, at p.291</sup> Although this class of placebo usage may present important ethical problems, I shall not discuss it further here.

In order to understand the problems presented by placebo usage in the first class of clinical trials, let us consider in some detail two diseases in which placebo-controlled clinical trials are commonly done: peptic ulcer and essential hypertension. For each of these diseases there are therapies known to be safe and effective—therapies that substantially retard the development of disabling or lethal complications.

Data available on the natural history of peptic ulcer were derived from naturalistic observations of large groups of patients.<sup>6</sup> Those who compiled the data did not, in general, know how many of these patients were being treated with various forms of therapy, whether they were complying with medical advice about therapy, or if they were receiving no therapy at all. Consequently, these estimates of the rates of complications are imprecise. Since at least some of the observed patients were being treated for peptic ulcer, these are probably underestimates of the true incidence of these complications in untreated patients.

Three of the most common serious complications of peptic ulcer are hemorrhage, perforation, and obstruction of the gastric outlet. Such complications may lead to disability or death; major emergency surgery often is required for their treatment.

During a 15-25 year period of follow-up, 15-20% of patients with peptic ulcer will have at least one hemorrhage. This means that approximately one in 100 patients with peptic ulcer will hemorrhage each year. Moreover, during these 15-25 years, perforations will occur in approximately 5-11 percent of patients and gastric outlet obstruction in slightly less than 5 percent. Thus, if one wishes to justify starting a placebo-controlled randomized clinical trial in patients with peptic ulcer, one must defend the claim that it is worth the risk of permitting one of these major complications at a rate of 1.5 times per 100 control subjects per year.

In patients with essential hypertension, the rate of complications is directly proportional to the diastolic blood pressures of the patients measured before the study begins.<sup>7</sup> For example, if we let the mortality rate of

those having diastolic blood pressures of 85-88 equal 100 percent, the mortality rate for those having diastolic blood pressures of 89-93 is 126 percent and for those having diastolic blood pressures of 94-103, 151 percent.

Information is available on morbidity and mortality rates in patients with untreated essential hypertension that is much more precise than that for untreated peptic ulcer. Such information may be found in the reports of the Veterans Administration Cooperative Study Group on Antihypertensive Agents, a long-term placebo controlled randomized clinical trial of anti-hypertensive therapy in men.<sup>8,9</sup>

The first report presents their findings in 143 men with initial diastolic blood pressures of 115-129.<sup>8</sup> These men entered the study between April 1964 and December 1966 and observations were concluded in May 1967. The men who received placebo were observed for an average of 15.7 months while those who received active therapy were observed for an average of 20.7 months; this discrepancy reflects the much higher complication rate in the placebo group and the policy of the Study Group to discontinue the involvement of those who sustained certain severe complications. Of the 70 men who received placebos, 27 had severe complications (e.g., stroke, malignant hypertension, heart failure) and four died. Of the 73 men who received active therapy, only two had severe complications and none died. From these data we derive the following estimates: Men with initial diastolic blood pressures of 115-129 who are treated with placebo have an approximately 28 percent chance of a severe complication or death per year. Similar men who receive active treatment for their hypertension have an approximately 1.6 percent chance of a severe complication per year.

The second report of the VA Study Group presents their findings in 210 men with initial diastolic blood pressures of 105-114.<sup>9</sup> Men entered the study between April 1964 and September 1968 and observations on these men ended in October 1969. Thus, the time in the study for these men ranged from 1.0-5.5 years, the average being 3.2 years for those receiving active therapy and 3.3 years for those receiving placebo. "Terminating morbid events," complications so severe (including death) as to require the removal of the subject from the protocol, occurred in 35 (19 deaths) of the 110 men who received placebo and in 9 (8 deaths) of the 100 men who received active therapy. Life-table analysis

yielded these estimates: the cumulative incidence of serious morbid events over a five-year period was 55 percent in the placebo control group and 18 percent in those who received active therapy.

### Placebo Administration as a Nontherapeutic Procedure

In a randomized clinical trial in which placebo is compared with an active agent, the purpose of which is to mitigate that component of a disease process that leads to lethal or disabling complications, the administration of the placebo must be viewed as a nontherapeutic procedure. Attempts to justify placebo administration in this context in terms of the benefit it might yield for the patient-subject are generally without legitimate warrant. Such attempts usually cite experience with placebo usage derived either from clinical practice or from research conditions simulating clinical practice. I do not dispute the power of the placebo to produce salutary effects when it is administered as is customary in clinical practice. As I have discussed, however, placebos are administered in the randomized clinical trial in ways that are designed to minimize their effects, especially their beneficial effects.

Some commentators argue that placebo administration may benefit the subject indirectly. Lasagna, for example, observes: "Too often the placebo-treated patients turn out to be the lucky ones in such a trial, 'deprived' only of a toxic and ineffective chemical."<sup>10</sup> at p.506 Such reasoning may be applicable at times but only in those unusual circumstances in which there is little or no preliminary evidence indicating the safety and efficacy of the active agent to be compared with placebo.

When we consider placebo-controlled randomized clinical trials in the treatment of patients with diseases such as peptic ulcer or essential hypertension, it is necessary to recognize that placebo usage is not only a nontherapeutic procedure but also one that presents the patient-subjects with more than minimal risk.\* In many cases it is possible to develop reasonably accurate estimates of the risk involved. Thus, for example, if one wishes to justify starting a placebo-controlled randomized clinical trial in patients with peptic ulcer, one must defend the claim that the knowledge to be gained is worth the risk of permitting one of the three major complications of peptic ulcer at a rate of 1.5 times per 100 patients per year. To put

this in perspective, we commonly see heated controversies over the ethical justification of performing certain invasive diagnostic procedures for research purposes. This rate of serious complications with placebo usage in patients with peptic ulcer is substantially greater than the risk of similarly serious complications with, for example, liver biopsy.<sup>11</sup>

Justification of placebo-controlled randomized clinical trials of antihypertensive drugs should be even more difficult. The knowledge to be pursued must be worth the risk of permitting a severe complication at a rate of approximately 26 per 100 control subjects per year (patients having initial diastolic blood pressures of 115-129) or 37 per 100 control subjects per 5 years (patients having initial diastolic blood pressures of 105-114).<sup>\*\*</sup>

In the past, those who subscribed to the legitimacy of the distinction between therapeutic and nontherapeutic research labeled all clinical trials, including those that were placebo-controlled, therapeutic research and justified them accordingly. As I have argued elsewhere,<sup>3</sup> at pp.6-8 this is a spurious distinction that ought to be abandoned because its use inevitably confounds ethical reasoning; fortunately, most North American commentators on research ethics have discarded this distinction. Labeling a placebo-controlled clinical trial "therapeutic research" and evaluating it accordingly is to commit the "fallacy of the package deal"; that is, to justify the entire clinical trial as therapeutic research because one of its major components is

therapeutic—the administration of active therapy. Instead, what is called for is a separate analysis of the various components. Nontherapeutic components should be justified as such—their risks must be reasonable in relationship to the benefits one hopes to secure for the collective, not for the individual subject.

In order to assess the risks to a placebo-control group of subjects, it is necessary to have reliable information on the natural history of the disease in its untreated or placebo treated state. The data do not have to be as precise as those available for essential hypertension; I believe that the information available on peptic ulcer is adequate for these purposes. Data of similar quality are probably available for most major diseases in which one might consider placebo-controlled randomized clinical trials.

Are there any diseases with such grave prognoses that placebo controls should never be considered? Yes, there seems to be a consensus that it would be unethical to conduct a placebo-controlled trial of a new therapy for a uniformly lethal disease such as rabies if there was cause to predict that the new therapy might be successful in even a small percentage of cases.<sup>12</sup> Not too long ago a placebo-controlled trial of adenine arabinoside in the treatment of herpes simplex encephalitis, a disease that is lethal in approximately 70 percent of untreated cases, precipitated a controversy that was both heated and illuminating.<sup>13,14</sup>

In some situations, the benefits to be pursued by a placebo-controlled clinical trial may be so small that little or no risk can be justified. Chief among such clinical trials are those designed to repeat trials in which the null hypothesis has been rejected. Those who wish to repeat such clinical trials often point to some flaw in the design or conduct of the earlier study to justify repetition. Others simply appeal to the scientific tradition of not accepting the results of research until they have been confirmed independently. Such justifications for repetition of clinical trials must be considered skeptically. Perhaps the flaws in the earlier trial were serious, but often they were minor. If independent confirmation of clinical trials is necessary, then one may avoid many problems by conducting two or more simultaneously.

### Further Implications

My conclusion is this: In a randomized clinical trial in which placebo is compared with an active agent, the

\*As I have argued elsewhere, "minimal risk," a standard designed as threshold for ethical justification for certain procedures performed to serve the interests of research in children, is unsuitable for autonomous adults.<sup>3</sup> at pp.26-27 A more suitable standard for autonomous adults is one I have labeled "mere inconvenience." Research presenting mere inconvenience is characterized as presenting no greater risk of consequential injury to the subject than that inherent in his or her particular life situation.

Placebo administration in randomized clinical trials designed to compare placebo with an active agent the purpose of which is to mitigate that component of a disease process that leads to lethal or disabling complications presents a burden of risk to the patient-subject that exceeds either threshold—"minimal risk" or "mere inconvenience." Therefore, use of the "minimal risk" standard in this discussion yields the same conclusions that would be reached using the "mere inconvenience" standard.

\*\*Complication rates for control subjects with hypertension were calculated from data reported by the VA Cooperative Study Group; complication rates for subjects receiving active treatment were subtracted from complication rates for placebo-control subjects to yield the "excess complication rates" presented in this paragraph.

purpose of which is to mitigate that component of a disease process that leads to lethal or disabling complications, the administration of the placebo must be viewed as a nontherapeutic procedure that presents more than minimal risk. The most conspicuous implications of this conclusion are, as discussed in the preceding section, in the area of assessing the balance of harms and benefits. The risks of using a placebo control—exposing subjects to the threat of death or disability—must be justified in terms of the benefits one hopes to secure for the collective, not for the individual.

I shall mention only briefly some other implications of my conclusion; space does not permit their full elaboration.

There are clear implications for the informed consent process. There should be a forthright disclosure of the perils of withholding active therapy. To the extent that important "preliminary evidence" indicates efficacy of the active agent, there should be an increasing presumption of a requirement to inform prospective subjects of the preliminary evidence and its implications.\* In those cases in which there

has already been one randomized clinical trial which rejected the null hypothesis, this, too, should be disclosed.

If the subjects are to be vulnerable persons, various ethical codes and regulations call for special protections for the subjects when one plans to perform nontherapeutic procedures that present more than minimal risk.<sup>15</sup> And, finally, serious consideration should be given to providing free medical therapy and compensation for injury to subjects in such placebo-controlled randomized clinical trials. As concluded by the President's Commission, compensation is due those who are injured in the service of the collective.<sup>16</sup> at pp.61-63

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- <sup>15</sup>See, for example, the regulations of the United States Department of Health and Human Services governing research involving children (45 CFR 46, Subpart D). These were published as "Additional protections for children involved as subjects in research." *Federal Register* 48 (No.46): 9814-9820, Tuesday, March 8, 1983. For a commentary on these regulations, see: Levine, R.J. Research involving children: An interpretation of the new regulations: *IRB: A Review of Human Subjects Research* 5 (No.4): 1-5, July/August, 1983.
- <sup>16</sup>President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research: *Compensating for Research Injuries: The Ethical and Legal Implications of Programs to Redress Injured Subjects*. Washington, 1982.

\*This assertion may seem inconsistent with a conclusion I reached earlier, that preliminary data developed during the conduct of a randomized clinical trial may and should be withheld from subjects.<sup>3</sup> at pp.132-133 There are, however, some relevant distinctions. In the present case, for example, the preliminary data are already known to the physician-investigator and probably also to others. Thus the physician-investigator may be called upon to lie to the subject and this lying behavior may be exposed (to the detriment of all concerned).

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#### COMMENTARY:

### The Randomized Clinical Trial: For Whose Benefit?

by Arthur Schafer

When is it ethically justified to undertake a randomized clinical trial?

According to Robert Levine, "It is generally agreed that ethical justification for beginning a randomized clinical trial requires that the investigators be able to state an honest null hypothesis."

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That is, the investigators must be able to tell the potential research subjects that whether they are randomly assigned to treatment arm A or treatment arm B, they will be receiving the best available treatment. The argument might be put as follows. The physician-investigator is able honestly to say to a patient-subject, "You will be receiving the best known therapy," because prior to completing the trial there is no scientifically validated reason to predict that therapy A will be superior to therapy B (and there is no fur-

ther alternative, C, which is known to be better than A or B). Consequently, for a physician-investigator to recruit patients as subjects for a randomized clinical trial is not inconsistent with the physician's duty to provide the best possible treatment for his or her patients.

This argument represents an attempt to resolve an apparent conflict between the obligation to patients and the obligation to advance scientifically validated knowledge. On closer examination, however, the argument can be



seen to fail. There is an unresolved (and perhaps irresolvable) ethical conflict.

As Levine notes, "It is the general rule that placebo-controlled randomized clinical trials are not begun until there is some preliminary evidence that the agent to be compared with placebo is more effective than placebo in bringing about the desired consequences." And he adds, "in many cases there is a substantial body of such 'preliminary evidence.'" This is true, however, not only for placebo-controlled randomized clinical trials, but for randomized clinical trials in general. Because randomized clinical trials are typically expensive to conduct (both with respect to financial cost and human resources), they are not usually initiated unless clinical experience and/or preliminary data (from uncontrolled trials or from earlier, less-than-satisfactory, randomized clinical trials) are favorable. Thus, most physicians will have a treatment preference, based on these (admittedly) incomplete data prior to commencing a randomized clinical trial.

When patients are told that it is not known which treatment is best, this statement is misleading at best, deceptive at worst. Very few patients are aware that by the phrase "scientifically validated knowledge" the physician-investigator means "confirmed by a controlled trial meeting the standard significance of  $P < 0.05$ ." Is it not somewhat arbitrary (as well as misleading) to claim that one achieves knowledge of the comparative value of competing treatments only when the results of one's experiments are 95 percent certain? This statistical convention is just that, a mere convention. It asks an underlying value judgment of patients, if they were to become aware of it, might choose to reject.

Patients have been led by the medical profession to expect that when physicians advise them as to the most reasonable course of action, they (the physicians) will indicate their treatment preferences, even when these are based on evidence that has not yet been scientifically validated. To conceal from patients (or potential research subjects) such information about treatment preferences because the evidence which it is based is merely probable rather than 95 percent certain, is to state the physician's traditional commitment to act univocally in the patient's best interests. Even when the physician's treatment preference falls short of "knowledge," even when it consists of an intuitive hunch or is based upon uncontrolled clinical experience or data from poorly designed

earlier trials, one could argue that the patient's right to give informed consent imposes on the physician the obligation to share all materially relevant information with the patient.

This line of reasoning leads us to the following problem: if physicians will seldom be truly indifferent to the alternatives being tested by the randomized clinical trial and if they inform their patients of their "intuitive" treatment preferences (perhaps supplying the preliminary evidence on which this preference is based), how likely is it that the patient will then consent to participate in the trial? Many investigators share the not unreasonable apprehension that once patients learn that their physician has a preference with respect to available treatments, they will then refuse to participate in any clinical trial in which—because of randomization—an alternative treatment may be substituted. Levine appears to accept this outcome with equanimity. In his concluding comments he favors "forthright disclosure" as part of the consent process.

Earlier he takes the even stronger position that investigators should not even attempt to recruit patients for a clinical trial unless the knowledge to be pursued is "worth the risk." The judgment as to what sort of knowledge is worth what degree of risk to patient-subjects is one that Levine appears to believe ought properly to be made by the investigator. But since this is a value issue rather than a purely scientific issue, why should one accept that the physician-investigator's values should be authoritative? Is there a danger, perhaps, that the judgments of some researchers may be biased on this issue by considerations of career self-interests? When Levine writes that "if one wishes to justify starting a placebo-controlled randomized clinical trial . . . one must defend the claim that the knowledge to be gained is worth the risk of permitting . . . major complications," it is worth noting that by "worth the risk" he means worthwhile from the point of view of society's interest in the knowledge to be gained. Clinical trials that are worthwhile from this point of view will not always be worthwhile from the point of view of the health and well-being of the patient-subject. This raises the moral dilemma of which point of view (benefit to society or benefit to patient) should prevail in cases of conflict.

How concerned ought we to be about the danger that scientific research may suffer a serious (perhaps even a devastating) setback, if a policy of disclosure is stringently implemented?

### Disclosure of Preliminary Data

There is an additional problem, one which is likely to aggravate the adverse effects on subject recruitment for randomized clinical trials. Problems of informed consent do not vanish once investigators have obtained informed consent from their patients to participate in a trial. Many trials last for an extended period of time—perhaps months or even years. As new information becomes available (based on early trends from preliminary data), are physicians then obliged morally to withdraw their patients from the trial if the therapy to which their patients have been randomized appears less than optimal for that patient? If the physician does not go this far, is he or she obliged to convey this information about early trends to the patient so that the patient can make an informed choice as to continued participation or withdrawal?

Levine's position, at least with respect to some randomized clinical trials, is: "To the extent that preliminary evidence indicates efficacy of the active agent, there should be an increasing presumption of the requirement to inform prospective subjects of the preliminary evidence and its implications." Some will want to go further and insist that physicians have an obligation to share *all* information about preliminary data with their patients.

The problem is, however, that the feasibility of undertaking *any* randomized clinical trial (posing more than minimal risks) would be seriously undermined by an insistence upon such disclosure. If full disclosure of physician treatment preference (either at the beginning or developed during the course of the trial) were to result in a very high level of refusals to participate or to premature subject withdrawals, this could have potentially disastrous effects on the advancement of medical knowledge. In many cases, proper scientific validation of medical hypotheses might become unattainable. Of course, one must concede to Levine that if a trial is scientifically unnecessary (because, e.g., the knowledge sought is already available from clinical trials or medical practice in other countries), then it would be unethical to expose research subjects to more-than-minimal risks. On the other hand, it is important to emphasize that it is often scientifically inappropriate to rush to judgment on the basis of early or incomplete data. The history of medicine teaches the lesson that clinical experience unchecked by properly controlled scientific experiments is a highly unreliable compass.

Few medical scientists would dispute the important role played by randomized clinical trials in promoting medical knowledge. Such trials have a crucially high value in assessing treatments, sorting the efficacious from the inefficacious, distinguishing the dangerous from the safe, and guiding us in the allocation of scarce medical resources. It is at least arguable that potential benefits to society and to future generations of patients require the subordination or sacrifice of some patient rights. Perhaps traditional physician ethics, with its highly individualistic commitment to patient welfare, needs to be modified. A more socially oriented ethic might permit randomized clinical trials to proceed with a statistically adequate sample of patient-subjects.

Would a less individualistic, more socially oriented, approach necessarily involve a betrayal of patient trust? As Levine points out, placebo-controlled randomized clinical trials will not be deceptive so long as prospective subjects are informed that they might receive a placebo and they voluntarily accept their ignorance. Analogously, I would argue that so long as physicians inform their patients that certain information may be withheld from them, information about preliminary trends and as yet scientifically unvalidated treatment preferences (together with an explanation as to what is meant by "scientific validation"), then they would not be guilty of a betrayal of patient trust. If the traditional ethical rules governing physician-patient interaction are to be changed, then all parties should be made aware of this fact.

A final concern needs to be flagged. Would a sufficient number of patients agree to participate as subjects in randomized clinical trials under these conditions? That is, would a sufficient number of patients agree to be research subjects if it were disclosed to them that, as research subjects, they would forfeit their right to full disclosure of some materially relevant information? It is not easy to answer this question with any high degree of confidence. Much will depend upon the advantages that patients anticipate that they might receive from participation (for example, treatment by leading specialists, possible access to otherwise unavailable experimental therapies, enhanced hospital care). Nor should one dismiss patient altruism as a potentially powerful motivating factor.

I draw the following conclusions. A policy of full and complete disclosure to patients of all materially relevant in-

formation is likely to have disastrous consequences for medical research. A policy of concealment, which deceptively permits (or, worse, encourages) patients to believe that their interests are primary, when in fact they are partially subordinate to the interests of medical research, is seriously unethical. The most reasonable compromise would appear to be the adoption of a policy of honest disclosure to patients

of the conflict, and of the extent to which there will be nondisclosure. Such a policy would represent a shift from a totally patient-centered ethic to a blend of patient-centered and public-good-centered ethic. But there would be no deception or betrayal, and the ultimate choice of whether to give informed consent to participation in research as a subject would properly remain with the individual patient.

## CALENDAR

**APRIL 15:** A symposium entitled "Religious Ethics and Medical Experimentation" will be held from 9:00 am to 4:00 pm at Bellarmine College, 2001 Newburg Road, Louisville, Kentucky. The Kentuckiana Interfaith Community will sponsor this symposium to allow the religious community to begin to address the sensitive issues raised in the field of medical experimentation, particularly in the area of heart surgery. Several nationally prominent religious ethicists and physicians will take part: Fr. Richard McCormick, S.J., Dr. Isaac Franck, Dr. J. Robert Nelson, Dr. Laman A. Gray, Jr., M.D., and Dr. Allan M. Lansing, M.D. The moderator for all panel discussions will be Dr. Richard Barber of the University of Louisville. Among the issues to be addressed are: mechanical transplants and the human image; advise and consent issues; quality of life; and justice. For further information, contact the Kentuckiana Interfaith Community at 502-458-4076.

**APRIL 21-22:** Loma Linda University will sponsor a conference on "Biomedical Ethics Today: Old Models and New." An introduction to the conference will be given by Daniel Callahan, Director of The Hastings Center; other sessions will cover topics such as "Ethical Issues in Neonatology," "Ethical Challenges of New Technologies," "Justice and Health Care in the United States," and "Moral and Immoral Uses of Living Beings in Biomedical Research." For more information, contact David Larson, Associate Director, Department of Bioethics, Loma Linda University, Loma Linda, CA 92350.

**APRIL 24-25:** PRIM&R will sponsor a meeting on "AIDS—Ethical, Legal and Social Considerations." The meeting will be held at the Park Plaza Hotel in Boston, and precedes an NIH/NIAD meeting on AIDS which will highlight the major medical and epidemiological issues in the treatment of AIDS. The PRIM&R meeting will explore the impact of AIDS on affected individuals, the public health problem presented by the disease, and policies dealing with patient concerns. For a complete program and further information, contact Joan Rachlin, Executive Director, or Valwyn Hooper, Assistant to the Director, PRIM&R, 132 Boylston Street, Boston, MA 02116, or call 617-423-4112 or 423-1099.

**MAY 23-24:** The Scientists Center for Animal Welfare and leading universities are sponsoring a workshop titled "Animals and the Scientist: Institutional Responsibilities—How to Run an Effective Animal Care and Use Committee" at the Aspen Institute in Aspen, Colorado. This workshop is part of a series of regional programs to assist those doing research with animals in biomedical research and testing to establish and run effective Animal Care and Use Committees. For information on course content and registration contact Barbara Orlans, Ph.D., Executive Director, Scientists Center for Animal Welfare, P.O. Box 9581, Washington, DC 20016, or call (301) 229-8045.

**JULY 21-27:** The Hastings Center and the Department for External Studies at the University of Oxford, England, plan to cosponsor a one-week workshop on ethical issues in health care, to be held at Oxford. Among those serving as faculty will be Daniel Callahan, Willard Gaylin, Carol Levine, and Arthur Caplan of the Center's staff. For further information, contact Arthur Caplan, Box O, The Hastings Center, 360 Broadway, Hastings-on-Hudson, NY 10706.