(1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practice[s] such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Philosophical Reflections on Experimenting with Human Subjects

Hans Jonas

Hans Jonas argues that if we justify experiments by considering them a right of society, then we are exposing individuals to dangers for the general good. This, for Jonas, is inherently wrong, and no individual should be forced to surrender himself or herself to a social goal.

Any risk that is taken must be voluntary; but obtaining informed consent: Jonas claims, is not sufficient to justify the experimental use of human beings. Two other conditions must be met first, subjects must be recruited from those who are most knowledgeable about the circumstances of research and who are intellectually most capable of grasping its purposes and procedures; second, the experiment must be undertaken for an adequate cause. Jonas cautions us that the progress which may come from research is not necessarily worth our efforts or approval, and he reminds us that there are moral values which we ought not to lose in the pursuit of science.

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Experimenting with human subjects is going on in many fields of scientific and technological progress. It is designed to replace the overall instruction by natural, occasional experience with the selective information from artificial, systematic experiment which physical science has found so effective in dealing with inanimate nature. Of the new experimentation with man, medical is surely the most legitimate; psychological, the most dubious; biological (still to come), the most dangerous. I have chosen here to deal with the first only, where the case *for* it is strongest and the task of adjudicating conflicting claims hardest. . . .

The Melioristic Goal, Medical Research, and Individual Duty

Nowhere is the melioristic goal [of working toward improvement] more inherent than in medicine. To the physician, it is not gratuitous. He is committed to curing and thus to improving the power to cure. Gratuitous we called it (outside disaster conditions) as a *social* goal, but noble at the same time. Both the nobility and the gratuitousness must influence the manner in which self-sacrifice for it is elicited, and even its free offer accepted. Freedom is certainly the first condition to be observed here. The surrender of one's body to medical experimentation is entirely outside the enforceable "social contract."

Or can it be construed to fall within its terms—namely, as repayment for benefits from past experimentation that I have enjoyed myself? But I am indebted for these benefits not to society, but to the past "martyrs" to whom society is indebted itself, and society has no right to call in my personal debt by way of adding new to its own. Moreover, gratitude is not an enforceable social obligation; it anyway does not mean that I must emulate the deed. Most of all, if it was wrong to exact such sacrifice in the first place, it does not become right to exact it again with the plea of the profit it has brought me. If, however, it was not exacted, but entirely free, as it ought to have been, then it should remain so, and its precedence must not be used as a social pressure on others for doing the same under the sign of duty. . . .

The "Conscription" of Consent

The mere issuing of the appeal, the calling for volunteers, with the moral and social pressures it inevitably generates, amounts even under the most meticulous rules of consent to a sort of *conscripting*. And some so liciting is necessarily involved. . . .And this is why "consent," surely a nonnegotiable minimum requirement, is not the full answer to the problem. Granting then that soliciting and therefore some degree of conscripting are part of the situation, who may conscript and who may be conscripted? Or less harshly expressed: Who should issue appeals and to whom?

The naturally qualified issuer of the appeal is the research scientist himself, collectively the main carrier of the impulse and the only one with the technical competence to judge. But his being very much an interested party (with vested interests, indeed, not purely in the public good, but in the scientific enterprise as such, in "his" project, and even in his career) makes him also suspect. The ineradicable dialectic of this situation—a delicate incompatibility problem—calls for particular controls by the research community and by public authority that we need not discuss. They can mitigate, but not eliminate the problem. We have to live with the ambiguity, the treacherous impurity of everything human.

Self-Recruitment of the Community

To whom should the appeal be addressed? The natural issuer of the call is also the first natural addressee: the physician-researcher himself and the scientific confraternity at large. With such a coincidence—indeed, the noble tradition with which the whole business of human experimentation started—almost all of the associated legal, ethical, and metaphysical problems vanish. If it is full, autonomous identification of the subject with the purpose that is required for the dignifying of his serving as a subject—here it is; if strongest motivation—here it is; if fullest understanding—here it is; if freest decision—here it is; if greatest integration with the person's total, chosen pursuit—here it is. With the fact of self-solicitation the issue of consent in all its insoluble equivocality is bypassed per se. Not even the condition that the particular purpose be truly important and the project reasonably promising, which must hold in any solicitation of others, need be satisfied here. By himself, the scientist is free to obey his obsession, to play his hunch, to wager on chance, to follow the lure of ambition. It is all part of the "divine madness" that somehow animates the ceaseless pressing against frontiers. For the rest of society, which has a deep-seated disposition to look with reverence and awe upon the guardians of the mysteries of life, the profession assumes with this proof of its devotion the role of a self-chosen, consecrated fraternity, not unlike the monastic orders of the past, and this would come nearest to the actual, religious origins of the art of healing. . . .

"Identification" as the Principle of Recruitment in General

If the properties we adduced as the particular qualifications of the members of the scientific fraternity itself are taken as general criteria of selection, then one should look for additional subjects where a maximum of identification, understanding, and spontaneity can be expected—that is, among the most highly motivated, the most highly educated, and the least "captive" members of the community. From this naturally scarce resource, a descending order of permissibility leads to greater abundance and ease of supply, whose use should become proportionately more hesitant as the exculpating criteria are relaxed. An inversion of normal "market" behavior is demanded here—namely, to accept the lowest quotation last (and excused only by the greatest pressure of need); to pay the highest price first.

The ruling principle in our considerations is that the "wrong" of reification can only be made "right" by such authentic identification with the cause that it is the subject's as well as the researcher's cause—whereby his role in its service is not just permitted by him, but *willed*. That sovereign will of his which embraces the end as his own restores his personhood to the otherwise depersonalizing context. To be valid it must be autonomous and informed. The latter condition can, outside the research community, only be fulfilled by degrees; but the higher the degree of understanding regarding the purpose and the technique, the more valid becomes the endorsement of the will. A margin of mere trust inevitably remains. Ultimately, the appeal for volunteers should seek this free and generous endorsement, the appropriation of the research purpose into the person's own scheme of ends. Thus, the appeal is in truth addressed to the one, mysterious, and sacred source of any such, generosity of the will—"devotion," whose forms and objects of commitment are various and may invest different motivations in different individuals. The following, for instance, may be responsive to the "call" we are discussing: compassion with human sufferings, zeal for humanity, reverence for the Golden Rule, enthusiasm for progress, homage to the cause of knowledge, even longing for sacrificial justification (do not call that "masochism," please). On all these, I say, it is defensible and right to draw when the research objective is worthy enough; and it is a prime duty of the research community (especially in view of what we called the "margin of trust") to see that this sacred source is never abused for frivolous ends. For a less than adequate cause, not even the freest, unsolicited offer should be accepted.

The Rule of the "Descending Order" and Its Counterutility Sense

We have laid down what must seem to be a forbidding rule to the number-hungry research industry. Having faith in the transcendent potential of man, I do not fear that the "source" will ever foil a society that does not destroy it—and only such a one is worthy of the blessings of progress. But "elitistic" the rule is (as is the enterprise of progress itself), and elites are by nature small. The combined attribute of motivation and information, plus the absence of external pressures, tends to be socially so circumscribed that strict adherence to the rule might numerically starve the research process. This is why I spoke of a descending order of permissibility which is itself permissive, but where the realization that it is a *descending* order is not without pragmatic import. Departing from the august norm, the appeal must needs shift from idealism to docility, from high-mindedness to compliance, from judgment to trust. Consent spreads over the whole spectrum. I will not go into the casuistics of this penumbral area. I merely indicate the principle of the order of preference: The poorer in knowledge, motivation, and freedom of decision (and that alas, means the more readily available in terms of numbers and possible manipulation), the more sparingly and indeed reluctantly should the reservoir be used, and the more compelling must therefore become the countervailing justification.

Let us note that this is the opposite of a social utility standard, the reverse of the order by "availability and expandability": The most valuable and scarcest, the least expendable dements of the social organism, are to be the first candidates for risk and sacrifice. It is the standard of *noblesse oblige*, and with all its counterutility and seeming "wastefulness," we feel a rightness about it and perhaps even a higher "utility," for the soul of the community lives by this spirit. It is also the opposite of what the day-to-day interests of research clamor for, and for the scientific community to honor it will mean that it will have to fight a strong temptation to go by routine to the readiest sources of supply—the suggestible, the ignorant, the dependent, the "captive" in various senses. I do not believe that heightened resistance here must

cripple research, which cannot be permitted; but it may indeed slow it, down by the smaller numbers fed into experimentation in consequence. This price—a possibly slower rate of progress—may have to be paid for the preservation of the most precious capital of higher communal life.

Experimentation on Patients

So far we have been speaking on the tacit assumption that the subjects of experimentation are recruited from among the healthy. To the question "Who is conscriptable?" the spontaneous answer is: Least and last of all the sick—the most available of all as they are under treatment and observation anyway. That the afflicted should not be called upon to bear additional burden and risk, that they are society's special trust and the physician's trust in particular—these are elementary responses of our moral sense. Yet the very destination of medical research, the conquest of disease, requires at the crucial stage trial and verification on precisely the sufferers from the disease, and their total exemption would defeat the purpose itself. In acknowledging this inescapable necessity, we enter the most sensitive area of the whole complex, the one most keenly felt and most searchingly discussed by the practitioners themselves. No wonder, it touches the heart of the doctor–patient relation, putting its most solemn obligations to the test. There is nothing new in what I have to say about the ethics of the doctor–patient relation, but for the purpose of confronting it with the issue of experimentation some of the oldest verities must be recalled.

The Fundamental Privilege of the Sick

In the course of treatment, the physician is obligated to the patient and to no one else. He is not the agent of society, nor of the interests of medical science, nor of the patient's family, nor of his co-sufferers, nor of future sufferers from the same disease. The patient alone counts when he is under the physician's care. By the simple law of bilateral contract (analogous, for example, to the relation of lawyer to client and its "conflict of interest" rule), the physician is bound not to let any other interest interfere with that of the patient in being cured. But manifestly more sublime norms than contractual ones are involved. We may speak of a sacred trust; strictly by its terms, the doctor is, as it were, alone with his patient and God.

There is one normal exception to this—that is, to the doctor's not being the agent of society vis-à-vis the patient, but the trustee of his interests alone: the quarantining of the contagious sick. This is plainly not for the patient's interest, but for that of others threatened by him. (In vaccination, we have a combination of both: protection of the individual and others.) But preventing the patient from causing harm to others is not the same as exploiting him for the advantage of others. And there is, of course, the abnormal exception of collective catastrophe, the analogue to a state of war. The physician who desperately battles a raging epidemic is under a unique dispensation that suspends in a nonspecifiable way some of the structures of normal practice, including possibly those against experimental liberties with his patients. No rules can be devised for the waiving of rules in extremities. And as with the famous shipwreck examples of ethical theory, the less said about it the better. But what is allowable there and may later be passed over in forgiving silence cannot serve as a precedent. We are concerned with non-extreme, non-emergency conditions where the voice of principle can be heard and claims can be adjudicated free from duress. We have conceded that there are such claims, and that if there is to be medical advance at all, not even the superlative privilege of the suffering and the sick can be kept wholly intact from the intrusion of its needs. About this least palatable, most disquieting part of our subject I have to offer only groping, inconclusive remarks.

The Principle of "Identification" Applied to Patients

On the whole, the same principles would seem to hold here as are found to hold with "normal subjects": motivation, identification, understanding on the part of the subject. But it is dear that these conditions are peculiarly difficult to satisfy with regard to a patient. His physical state, psychic preoccupation, dependent relation to the doctor, the submissive attitude induced by treatment—everything connected with his condition and situation makes the sick person inherently less of a sovereign person than the healthy one. Spontaneity of self-offering was almost to be ruled out; consent is marred by lower resistance or captive circumstance, and so on. In fact, all the factors that make the patient, as a category, particularly accessible and welcome for experimentation at the same time compromise the quality of the

responding affirmation that must morally redeem the making use of them. This, in addition to the primacy of the physician's duty, puts a heightened onus on the physician researcher to limit his undue power to the most important and defensible research objectives and, of course, to keep persuasion at a minimum.

Still, with all the disabilities noted, there is scope among patients for observing the rule of the "descending order of permissibility" that we have laid down for normal subjects, in vexing inversion of the utility order of quantitative abundance and qualitative "expendability." By the principle of this order, those patients who most identify with and are cognizant of the cause of research—members of the medical profession (who after all are sometimes patients themselves)—come first; the highly motivated and educated, also least dependent, among the lay patients come next; and so on down the line. An added consideration here is seriousness of condition, which again operates in inverse proportion. Here the profession must fight the tempting sophistry that the hopeless case is expendable (because in prospect already expended) and therefore especially usable; and generally the attitude that the poorer the chances of the patient the more justifiable his recruitment for experimentation (other than for his 1 own benefit). The opposite is true.

Nondisclosure as a Borderline Case

Then there is the case where ignorance of the subject, sometimes even of the experimenter, is of the essence of the experiment (the "double-blind"–control group–placebo syndrome). It is said to be a necessary element of the scientific process. Whatever may be said about its ethics in regard to normal subjects, especially volunteers, it is an outright betrayal of trust in regard to the patient who believes that he is receiving treatment Only supreme importance of the objective can exonerate it, without making it less of a transgression. The patient is definitely wronged even when not harmed. And ethics apart, the practice of such deception holds the danger of undermining the faith in the *bona fides* of treatment, the beneficial intent of the physician—the very basis of the doctor–patient relationship. In every respect it follows that concealed experiment on patients—that is, experiment under the guise of treatment—should be the rarest exception, at best, if it cannot be wholly avoided.

This has still the merit of a borderline problem, The same is not true of the other case of necessary ignorance of the subject—that of the unconscious patient. Drafting him or nontherapeutic experiments is simply and unqualifiedly impermissible; progress or not be must never be used, on the inflexible principle that utter helplessness demands utter protection.

When preparing this paper, I filled pages with a casuistics of this harrowing field, but then scrapped most of it, realizing my dilettante status. The shadings are endless, and only the physician-researcher can discern them properly as the cases arise. Into his lap the decision is thrown. The philosophical rule, once it has admitted into itself the idea of a sliding scale, cannot really specify its own application. It can only impress on the practitioner a general maxim or attitude for the exercise of his judgment and conscience in the concrete occasions of his work. In our case, I am afraid, it means making life more difficult for him.

It will also be noted that, somewhat at variance with the emphasis in the literature, I have not dwelt on the element of "risk" and very little on that of "consent." Discussion of the first is beyond the layman's competence; the emphasis on the second has been lessened because of its equivocal character. It is a truism to say that one should strive to minimize the risk and to maximize the consent. The more demanding concept of "identification," which I have used, includes "consent" in its maximal or authentic form, and the assumption of risk is its privilege.

No Experiments on Patients Unrelated to Their Own Disease

Although my ponderings have, on the whole, yielded points of view rather than definite prescriptions, premises rather than conclusions, they have led me to a few unequivocal yeses and nos. The first is the emphatic rule that patients should be experimented upon, if at all, *only* with reference to *their disease*. Never should there be added to the gratuitousness of the experiment as such the gratuitousness of service to an unrelated cause. This follows simply from what we have found to be the only excuse for infracting the special exemption of the sick at all—namely, that the scientific war on disease cannot accomplish its goal without drawing the sufferers from disease into the investigative process. If under this excuse they become subjects of experiment, they do so *because*, and only because, of *their* disease.

This is the fundamental and self-sufficient consideration. That the patient cannot possibly benefit from the unrelated experiment therapeutically, while he might from experiment related to his condition, is also true, but lies beyond the problem area of pure experiment. I am in any case discussing nontherapeutic experimentation only, where *ex hypothesi* the patient does not benefit. Experiment as part of therapy—that is, directed toward helping the subject himself—is a different matter altogether and raises its own problems but hardly philosophical ones. As long as a doctor can say, even if only in his own thought "There is no known cure for your condition (or: You have responded to none); but there is promise in a new treatment still under investigation, not quite tested yet as to effectiveness and safety; you will be taking a chance, but all things considered, I judge it in your best interest to let me try it on you"—as long as he can speak thus, he speaks as the patient's physician and may err, but does not transform the patient into a subject of experimentation. Introduction of an untried therapy into the treatment where the tried ones have failed is not "experimentation on the patient."

Generally, and almost needless to say, with all the rules of the book, there is something "experimental" (because tentative) about every individual treatment, beginning with the diagnosis itself and he would be a poor doctor who would not learn from every case for the benefit of future cases, and a poor member of the profession who would not make any new insights gained from his treatments available to the profession at large. Thus, knowledge may be advanced in the treatment of any patient, and the interest of the medical art and all sufferers from the same affliction as well as the patient himself may be served if something happens to be learned from his case. But his gain to knowledge and future therapy is incidental to the *bona fide* service to the present patient He has the right to expect that the doctor does nothing to him just in order to learn.

In that case, the doctor's imaginary speech would run, for instance, like this: "There is nothing more I can do for you. But you can do something for me. Speaking no longer as your physician but on behalf of medical science, we could learn a great deal about future cases of this kind if you would permit me to perform certain experiments on you. It is understood that you yourself would not benefit from any knowledge we might gain; but future patients would." This statement would express the purely experimental situation, assumedly here with the subject's concurrence and with all cards on the table. In Alexander Bicker's words: "It is a different situation when the doctor is no longer trying to make [the patient] well, but is trying to find out how to make others well in the future."

But even in the second case, that of the nontherapeutic experiment where the patient does not benefit, at least the patient's own disease is enlisted in the cause of fighting that disease, even if only in others. It is yet another thing to say or think: "Since you are here—in the hospital with its facilities—anyway, under our care and observation anyway, away from your job (or, perhaps, doomed) anyway, we wish to profit from your being available for some other research of great interest we are presently engaged in." From the standpoint of merely medical ethics, which has only to consider risk, consent, and the worth of the objective, there may be no cardinal difference between this case and the last one. I hope that the medical reader will not think I am making too fine a point when I say that from the standpoint of the subject and his dignity there is a cardinal difference that crosses the line between the permissible and the impermissible, and this by the same principle of "Identification" I have been invoking all along. Whatever the rights and wrongs of any experimentation on any patient—in the one case, at least that residue of identification is left him that it is his own affliction by which he can contribute to the conquest of that affliction, his own kind of suffering which he helps to alleviate in others; and so in a sense it is his own cause. It is totally indefensible to rob the unfortunate of this intimacy with the purpose and make his misfortune a convenience for the furtherance of alien concerns.

Conclusion

. . . I wish only to say in conclusion that if some of the practical implications of my reasonings are felt to work out toward a slower rate of progress, this should not cause too great dismay. Let us not forget that progress is an optional goal, not an unconditional commitment and that its tempo in particular, compulsive as it may become, has nothing sacred about it. Let us also remember, that a slower progress in the conquest of disease would not threaten society, grievous as it is to those who have to deplore that their particular disease be not yet conquered, but that society would indeed be threatened by the erosion of those moral values whose loss, possibly caused by too ruthless a pursuit of scientific progress, would make

its most dazzling triumphs not worth having. Let us finally remember that it cannot be the aim of progress to abolish the lot of mortality. Of some ill or other, each of us will die. Our mortal condition is upon us with its harshness but also its wisdom—because without it there would not be the eternally renewed promise of the freshness, immediacy, and eagerness of youth; nor would there be for any of us the incentive to number our days and make them count. With all our striving to wrest from our mortality what we can, we should bear its burden with patience and dignity.

Section 2: The Ethics of Randomized Clinical Trials

How to Resolve an Ethical Dilemma Concerning Randomized Clinical Trials

Don Marquis

Don Marquis addresses the dilemma a physician faces when she believes that one of the two treatments in a clinical trial is better for her patient Should she advise the patient to choose the treatment she thinks best or let him enter the trial and have to accept the randomly assigned treatment? If she keeps quiet she won't be giving the patient the benefit of her judgment but if she doesn't advise him, she will hinder the clinical trial.

Marquis rejects two attempts at resolving the dilemma. The equipoise notion holds that she doesn't really know which treatment is better, because; she's lacking the best evidence, but it wrongly assumes that only such evidence can support a view. The second approach holds that because; the professional community has not decided which treatment is best she need not express her view about the matter; Marquis finds this unpersuasive: we expect the best advice from our physician, just as we do our attorney.

Resolving the dilemma requires that we take informed consent seriously. The physician explains her views to the patient, informs the patient of the alternatives (explaining also that in the clinical trial the patient may not get the experimental treatment), then allows the patient to make the decision.

An apparent ethical dilemma arises when physicians consider enrolling their patients in randomized clinical trials. Suppose that a randomized clinical trial comparing two treatments is in progress, and a physician has an opinion about which treatment is better. The physician has a duty to promote the patient's best medical interests and therefore seems to be obliged to advise the patient to receive the treatment that the physician prefers. This duty creates a barrier to the enrollment of patients in randomized clinical trials. 1–10 two strategies are often used to resolve the dilemma in favor of enrolling patients in clinical trials.

The "Either You Know Which Is Better or You Don't" Strategy

According to one strategy, physicians should not recommend the treatment over another if they do not really know which one is better, and they do not