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Foundational Justifications for Human Biomedical Experimentation

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Description

A talk given by Dr. Kenneth D. Pimple on ethical justifications for the use of human beings in biomedical research as part of a national Research Community Forum held in Amherst, New York, July 15, 2004 and entitled “What Investigators and Research Staff Need to Know About Human Research Protections.”

Body

Introduction

I am honored to be here and pleased to have the opportunity to open this forum.

The original title for this talk was “Frameworks for Justifying Human Experimentation.” As the paper took shape, that title seemed increasingly inaccurate, so I have changed the title to “Foundational Justifications for Human Biomedical Experimentation.”

As you well know, the dominant guidelines for human experimentation today can be found in the Federal regulations known as the Common Rule. The other three

speakers this morning will talk about regulations; my task is to talk about ethics, the necessary basis for legitimate regulations.

The Common Rule is built upon the 1979 report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research commonly known as the Belmont Report. If you have not read the Belmont Report, you should. I believe it has been included in the materials distributed for this forum.

The Belmont Report starts with a brief discussion of the distinction between practice and research, then describes three basic moral principles that should govern research involving human subjects, along with an application for each of the principles. They are the principle of respect for persons, whose primary application is informed consent; the principle of beneficence, whose primary application is the assessment of risk and benefits; and the principle of justice, which is applied in the manner of subject selection.

The rest of this talk will concern the fundamental considerations and work of earlier ethicists upon which the Belmont Report itself is based. You will be relieved to know that I will not trace this history step-by-step back to Aristotle and Hippocrates, but only to two ethicists whose writings had a clear impact on the Belmont Report. The first is Hans Jonas and his 1969 essay, “Philosophical reflections on experimenting with human subjects.” The second is Paul Ramsey and his 1970 book, The patient as person: Explorations in medical ethics.

Paul Ramsey anticipated the Belmont Report’s focus on principles when he wrote: “Where the ethics of the medical profession no longer speaks of codes, it speaks instead of principles – whose meaning in application is under constant review. The applications are for the doctor or the investigator and their peers to determine, while the principles accord with the ethics of a wider human community” (Ramsey 1970:5, emphases in original). I do not know how Ramsey would have felt about the encoding of the Belmont principles in the Common Rule.

“Justification”

It might be useful to clarify what I mean by “justification.” A typical sentence using the word might be, “How can you justify cheating on your taxes?” In this case, there is a presumption that the action is unacceptable and that it probably cannot be justified, but it opens a rhetorical space for this improbability to be realized.

In many cases, a thorough justification of an identifiable category of human behavior can take the form of a careful delineation of the reasons that the behavior in question is either desirable or necessary along with the moral limitations that must be placed on that behavior. Perhaps a better example than cheating on taxes is war. War has been a part of human experience since before recorded history. It is hard to make a case that war is never necessary, but it is impossible to make a case that war is always good. Over the centuries, a framework known as just war theory has been developed to justify warfare by setting boundaries on the conditions under which a war can be started and how it can be fought.

I would like to suggest that human experimentation has something in common with war: It is always a serious moral undertaking, and at times – probably more often than war – serves a desirable practical and moral purpose. Moreover, war and human experimentation in abstract, general terms are quite different from particular wars and particular human experiments. To say that war can be justified is not to say that any particular war is justified.

I do not want to push this comparison any further. The two main points about human experimentation are straightforward: It must be approached with moral gravity and we must attend to the distinctions between the general and the specific.

In this talk I will spend rather little time defending the good and desirable aspects of human experimentation, and rather more time talking about limits that should be placed on human experimentation.

“Experimentation”

I deliberately avoid the relatively benign and general word “research” and prefer for today’s purpose the word “experimentation” because of its peculiar connotations. “Research” connotes everything from looking up a word in a dictionary to slicing up a person’s brain. My focus today is on the latter end of the spectrum, that is, research requiring physical intervention, typically involving invasion of the body.

“Experimentation” also implies more strongly than “research” the uncertainty of the enterprise – uncertainty as to causes and to effects, risks and benefits. In our ignorance of causes and cures, we experiment without knowing what will result; we may cure, or we may kill.

The tone I mean to strike is not hostile, but rather cautionary. If biomedical research were not uncertain and risky, this meeting would not be taking place. Caution is warranted because human beings can become habituated to just about anything, and it seems likely that sometimes people involved in human experimentation become a bit too comfortable with, and perhaps blinded to, its associated uncertainty and risks.

“Biomedicine”

As my final semantic clarification, I use the word “biomedicine” to refer to the subset of medical practice that has as its focus the treatment of patients, excluding other worthy medical endeavors such as public health and epidemiology. Note that biomedicine is distinct from biomedical science.

The goal of biomedicine is the alleviation of human suffering and, when possible, the prevention and cure of disease. This is an ancient mission and justly honored, even though until quite recently medical practitioners were essentially able to provide nothing more than sympathy in the face of all but a few diseases and injuries.

Biomedicine has also always been an intimate mission, with the health care provider literally touching one patient at a time. Indeed, many of the practices of biomedicine would be indecent and intolerable in any other setting, which is why a fundamental moral tenet of biomedicine requires the consent of the patient for treatment. There are exceptions to the rule of consent, as you well know, and the level of acceptable paternalism in biomedical practice has waxed and waned over the years, but, if it is not absolute, the rule of consent is very strong indeed.

Biomedicine is morally justified by its praiseworthy goals, its generally beneficial results, and its adherence to moral rules, that which requires the patient’s consent for treatment. Here we have a useful, if incomplete, framework for justifying human experimentation: Insofar as human experimentation is like biomedical practice, it is morally justified. But insofar as human experimentation varies from biomedical practice, it requires an independent moral justification.

Science

Part of that independent moral justification – but not very much – comes from the nature of science.

Science is equally ancient, and, like medicine, for most of its history science rarely provided practical benefits. Instead, the key benefit of science was the increase of knowledge and understanding for its own sake. But if mapping the stars and cataloging flora and fauna did little practical good, it also caused little or no harm.

Part of the reason science was harmless for so long was the powerful stigma historically associated with human experimentation. Until relatively recently, even autopsies were illegal and considered immoral; researchers had to steal bodies from graveyards for their studies. Until recently, human experimentation occupied only a small and highly suspect corner of the scientific world.

Medicine and science have together become much more powerful, more useful, and more dangerous in the last two hundred years or so.

Beneficence, practice, and research

Although they have much in common, the two endeavors are also fundamentally different. Where biomedicine is particular and concrete, involved with the individual and singular symptoms and pains of a given patient, science is general and abstract. Science must use the particular, but its interest is in the general. Biomedicine treats patients; science scrutinizes patterns, mechanisms, and causes.

Insofar as these characterizations of biomedicine and science are accurate, it is evident that biomedical science, by its nature, is conflicted. The conflict can be expressed crudely, but, I hope, effectively: A patient is not a symptom, a disease, or a population.

When a biomedical practitioner – call her Dr. Shelley – treats a patient – call him Mr. Victor – she must have a free hand to do her best to cure or otherwise help him, and she must not be compelled to do anything to him that is not in his best interest.[1] As Paul Ramsey put it, “It is axiomatic to medical ethics that a known remedy or protection – even if not perfect or even if the best exact administration of it has not been proved – should not be withheld from individual patients” (Ramsey 1970:53). The physician’s actions must, in other words, be beneficent and non-maleficent.

But when Dr. Shelley is also a biomedical researcher, there will be times when her hands are tied. She will treat her subject, Mr. Victor, according to an experimental protocol that is designed, not with him in mind, but only his symptoms, disease, or population. The protocol may not match Dr. Shelley’s best clinical judgment about

what will be most helpful for Mr. Victor. In short, human experimentation often – perhaps always – departs from the historical moral justification for biomedical practice.

Here we come to the distinction between “research” and “practice.” When Dr. Shelley is treating Mr. Victor and all standard treatments fail, but Dr. Shelley’s best clinical judgment suggests that a non-standard treatment – an innovative treatment – what might be called an “experimental” treatment – is Mr. Victor’s best hope, she is entirely justified, with Mr. Victor’s informed consent, to try the non-standard treatment. As a biomedical practitioner, she can also adjust or modify the treatment as she observes Mr. Victor’s response to it.

As Hans Jonas put it:

> [K]nowledge 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 may be served if something happens to be learned from his case. But this 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. [Jonas 1969:242, italic in original]

The justification for using a non-standard treatment weakens when Dr. Shelley, acting as a researcher, has in mind the well-being of some population of patients. But it is impossible to try a treatment on a population; a treatment can only be tried on individuals. The more closely Mr. Victor fits the profile of the population, and the more freedom Dr. Shelley has to attend to Mr. Victor’s particular needs, the less additional justification is required for using such a non standard treatment.

Obviously, placebo controls, randomization, and masking – perhaps the holy trinity of clinical trials – are all problematic because they limit Dr. Shelley’s freedom to attend to Mr. Victor’s particular needs. Even more problematic are research protocols in which no therapeutic value to the patient is expected at all.

The moral difference between biomedical research and practice does not turn on what the physician does to the patient, nor on the physician’s level of certainty as to the outcome, nor on the degree of risk to the patient. All of these are relevant, but the key factor is whether the physician’s actions are intended to be of benefit to the

patient or to someone else and the degree to which the physician allows her actions to be constrained by considerations other than the wellbeing of the patient.

These moral considerations are rooted in the relationship between the physician and the patient. If the moral constraints proper to the physician-patient relationship were to be strictly applied to the researcher-subject relationship, much biomedical research going on today would have to be suspended and progress in biomedical science would slow considerably.

Respect for persons

My comments this far have centered on the ethical principle of beneficence, or doing good, and its logical counterpart, non-maleficence, or refraining from doing harm. But I have also mentioned the importance of consent in medical treatment, which is the Belmont Report's "application" of the moral principle of respect for persons, which is also sometimes referred to as autonomy.

Respect for persons means refraining from interfering with any person's ability to determine her or his own fate. Of course we only have limited control over our own fates in the best of circumstances, but this makes willful interference with a person's autonomy all the more serious.

The most severe form of interference with autonomy is to force someone into a particular choice through the use of force or deception. This is a serious wrong even if no harm is done because whenever one choice is made, innumerable other choices vanish. When the forced choice also includes an element of risk, along with the offense to autonomy an offense against beneficence is committed.

However, even when it is wrong to force, coerce, or entice someone into taking a risk, it may not be wrong to ask or invite them to do so. Some risks are well worth running, even if they do the risk-taker no practical good. Think of the fire fighters who rushed into the Twin Towers. This is the very stuff of which heroes are made.

When only autonomy is at stake, it is morally acceptable to invite patients who have the full capacity to make decisions for themselves to participate in human biomedical experimentation even when it means they will be taking risks for the sake of others. How the invitation is made, how the patient's capacity to make decisions is ascertained, and how fully informed and free consent can be guaranteed are practical rather than ethical problems.

This, then, is an aspect of biomedical science absent from ordinary biomedical practice that helps to justify human experimentation. When consent is freely given to take part in human experimentation, respect for persons can actually be enhanced even when beneficence is somewhat diminished or compromised.

Proxy consent and its limits

Of course, there are times when consent to medical treatment can be assumed, such as when someone is mortally stricken – perhaps by a heart attack, or in a traffic accident – and is unable expressly to consent to treatment. Especially when no next-of-kin or other capable spokesperson can be located, in cases like this a medical practitioner is morally and legally able – perhaps even obliged – to give aid in the absence of explicit consent.

Parents and guardians are also allowed to give consent to medical treatment on behalf of their children or wards who are not competent to give consent themselves due to mental incapacity, which may be due to youth, mental illness, dementia, and the like. The limits here are theoretically clear, if perhaps at times difficult to discern in practice: When it is a question of medical therapy and the patient is unable to consent, a guardian may do so. Even when the medical therapy is part of an experimental protocol, as long as the experiment has a therapeutic intention, so-called proxy consent is acceptable, given the other kinds of restrictions we have talked about already.

Non-therapeutic experimentation on children and others incompetent to consent is another matter. Paul Ramsey describes the distinction in Anglo-American law and morality between what he calls “harmful invasions of the body” and unwanted touching. The former needs no elaboration: We all know that it is wrong to harm someone else. The latter, however, is sometimes under-appreciated. Touching another person without that person’s consent is, by itself, without any harm being done, a legal battery. It is morally and legally unacceptable because it is degrading and it reduces the person as to the status of an animal or a thing. It is a violation of respect for persons.

As Ramsey puts it: “Since ‘offensive touching’ or ‘unconsented touching’ is ground for legal action for assault and battery even though there has been no damage, it seems clear that no consent rather than no risk or no discernible risk is the decisive point at law. Only the legal fiction of parental or other representative consent keeps

experiment on children from being judged to be battery even where there is no harm. This surely is the morality of the matter: a subject can be wronged without being harmed" (p. 39, emphases in original).

Hans Jonas makes a similar point, though his focus is not on children but on unconscious patients. In his words, that apply equally to children and others who are incapable of consenting to therapy: "Drafting [the unconscious patient] for nontherapeutic experiments is simply and unqualifiedly impermissible; progress or not, he must never be used, on the inflexible principle that utter helplessness demands utter protection" (p. 240).

Ramsey's stance puts rather severe limitations on experiments with children. My imperfect understanding of the Common Rule suggests that it is at variance with Ramsey's conclusions, but I will leave it to the other speakers to take up this point if they wish.

Social benefits

A moment ago I mentioned one moral justification that human experimentation has that is lacking in biomedical practice, namely that giving people the chance to take part in human experimentation can enhance their autonomy. The most obvious moral justification for human biomedical experimentation, however, is the expected social benefits. Even if a clinical trial does not help its subjects, the knowledge gained from it might well be of tremendous benefit to future patients.

Hans Jonas examines the question of the individual versus society with deep wisdom and great eloquence, and I heartily commend his essay to you for reading. I cannot do his entire argument justice here, but I do want to offer for your consideration what I take to be his key point.

The organizing framework of his argument is democratic society, a society in which individual freedom is cherished and preserved. In such a society, the state may not legitimately force particular individuals to risk their bodies and lives except in times of emergency, for example during a military invasion or a raging epidemic. Such emergencies put the very survival of the society at risk.

Our need for better medical care and knowledge do not constitute such an emergency. Simply put: Biomedical progress is a social good, but not a social necessity.

Human experimentation, Jonas argues, is melioristic – that is to say, it aims at biomedical progress, to provide a better future more than to improve the present. Furthermore, progress is not necessary. It is optional.

Quoting Jonas:

> Unless the present state is intolerable, the melioristic goal is in a sense gratuitous, and not only from the vantage point of the present. Our descendants have a right to be left an unplundered planet; they do not have a right to new miracle cures. We have sinned against them if by our doing we have destroyed their inheritance – which we are doing at full blast; we have not sinned against them if by the time they come around arthritis has not yet been conquered. [Jonas 1969:230-231]

Among other things, this suggests that defending biomedical research on the basis of its social utility, or its benefits to future generations, may be harder than some people might like, especially if progress comes at the cost of human rights. Again quoting Jonas:

> 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. [Jonas 1969:245]

I hope I have not made Hans Jonas sound hostile to biomedical research or medical progress. He clearly understands that medical progress is a social good, but a social good that must be weighed against other goods. The first paragraph of his essay ends with this sentence: “Even if the philosophical reflection should in the end achieve no more than the realization that in the dialectics of this area we must sin and fall into guilt, this insight may not be without its own gains” (Jonas 1969:219). It may be, he says, that we must sin and fall into guilt, meaning that to some degree human experimentation might itself be a moral imperative.

Justice

The last Belmont principle, justice, is primarily concerned with the fair distribution of burdens and benefits of research. This principle was probably inspired by the memory of the PHS Syphilis Study at Tuskegee. Although the poor, the racially oppressed, the institutionalized, and other marginalized, “undesirable” groups make convenient subjects for human experimentation, they must not be exploited. If the benefits of research will redound to all of society, then those who sacrifice to make possible those benefits must be drawn from all of society. If only a segment of the population will benefit, then the subjects should be drawn from that segment.

As regards to human experimentation per se, I would say that our country’s record on justice has been steadily improving as, for example, more women and children are being included in research protocols designed to benefit women and children specifically. As regards to biomedical practice, however, our record has been steadily declining. Far too many Americans do not have access to basic, let alone adequate, health care. They do not benefit from much of the medical progress made possible by public funds.

It is a painful and disgraceful irony that the United States, which does the best biomedical research in the world, has a health care system that is also the best in the world except in this one simple and fundamental aspect: It does not deliver health care to many of its neediest members. Although this state of affairs is in the first instance an indictment of American biomedical practice, American biomedical science is also tainted with this shame.

Thank you for your attention.

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- 1Dr. Shelley and Mr. Victor first appear in Pimple and Pedroni 2003.

Notes

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