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The Emperor's New Scar: The Ethics of Placebo Surgery

Surgical innovation is something of a grey area in medical research. Relative to other doctors, surgeons exercise a high degree of discretion in the trialing of new techniques with their patients. The first patients to undergo a new procedure are, in a real sense, subjects in an experiment. It is always hoped that a new procedure will deliver a clinical benefit but, as often as not, trial means error. The front-line patients bear a higher burden of risk, with lower expectation of success than subsequent patients, who benefit from the experience gained in the early attempts.

While experimentation is as intrinsic to the progress of surgery as any other field of medicine, nowhere is surgical innovation regulated by the kinds of guidelines and oversight required in other human experimentation. One recent study[1] identified 59 papers in US medical journals (1992-2000) which described innovative surgery. A questionnaire was then sent to the authors. Of those surgeons who responded, the majority had not submitted their proposal to an Institutional Review Board and a majority had not mentioned the innovative nature of the procedure on the informed consent form. Two thirds of the respondents stated that government regulation for the protection of human subjects of innovative surgical research would not be appropriate. The authors of this study locate the source of these surgeons' attitudes in a tradition in surgery whereby new techniques, and even new devices, 'are regarded as mere modifications and not as

research'.[2] Thus surgical innovations often bypass processes in place to protect human subjects. Elsewhere, the same authors have noted that:

> The majority of surgical publications involve interventional case reports that consist of a series of patients; outcome measures are usually clinical parameters that are obtained during routine clinical follow-up, without any type of formal written protocol. The implicit assumption in these case reports is that the clinical hypothesis is not formalized until *after* the therapeutic intervention. These types of 'informal research' are viewed as clinical care and are therefore invisible to IRBs.[3]

This kind of informal surgical research is at odds with the increasing trend towards evidence-based medicine. Concerns about the evidential basis for procedures is not limited to novel techniques. Many procedures that were once common have since been abandoned when more rigorous evaluation has disproved their presumed benefits; routine tonsillectomy for instance.[4] Suppose we accept that, in principle, there is a clear need for more rigorous and objective standards for assessing new surgical procedures. In practice this will mean randomized control trials, and this is ethically problematic because unlike placebo sugar pills, surgical placebos are not benign.

Randomized, double-blind, placebo controlled trials are widely recognized as the gold standard for drug trials. Such trials are the most effective way to control for both investigator bias and the placebo effect. A few surgical trials have also been conducted with a placebo control. Patients on the placebo arm of the trial receive 'sham', or

‘imitation’ surgery (as it is sometimes called) such that the patient cannot know whether she received the trial procedure or not. Placebo surgery typically involves anesthesia and an incision equivalent to the incision needed for the actual surgery. To maximize equivalence between the trial and control groups it may also involve the same post-operative drug therapy given to the recipients of the ‘real’ surgery. These trials have proven highly controversial. Placebo surgery obviously involves risks that are not there with placebo pills. Critics of placebo controlled surgical trials (PCST) claim that such trials are straightforwardly unethical because they violate the doctor’s duty to act only in the best interests of the patient.[5] These trials expose patients to some of the normal risks of surgery without any reasonable expectation of benefit. Defenders of PCST point to their considerable scientific value. They argue that without properly designed trials for new procedures we cannot identify false positives and determine their real effectiveness, and in some cases well designed clinical trials require a placebo control.[6]

The use of placebo surgery to control for the placebo effect in the evaluation of surgical procedures was first advocated by Henry Beecher in 1961.[7] There Beecher discussed two PCST, conducted in the late 1950’s, to test the efficacy of ligation of the internal mammary artery for the treatment of angina; a common treatment at the time. Both trials showed that the procedure was no more effective than the placebo, and the operation was subsequently abandoned. These two trials together enrolled 35 subjects and probably prevented thousands of unnecessary operations.[8] We will examine here two more recent trials which have generated some controversy. First a brief description of these trials:

Fetal Cell Transplants for Parkinson's Disease

Parkinson's disease is a motor function disorder characterized by tremors, rigidity, slowness of movement, impaired gait, loss of balance and postural stability. Its main pathological feature is a loss of dopamine producing neurons in a particular area of the brain. The drug 'Levadopa' (a dopamine precursor) is the standard treatment. It is effective at controlling symptoms in the early and middle stages of the disease, but is often ineffective in advanced patients, and the higher doses needed have serious side effects. In animal models it has been shown that 'dopaminergic neurons' harvested from embryos and transplanted to the damaged areas can to some extent regrow the damaged neural structures and reverse the loss of motor control. The transplantation of embryonic cells into the brains of human sufferers has been undertaken in a number of centers around the world. One study reports around 360 transplant procedures at 17 centers to 1999.[9] Results have been mixed, but some centers have claimed to consistently produce significant improvement in patients.

However strong and persistent placebo effects have been reported in the treatment of Parkinson's disease. In one large, double-blind drug trial, patients in the placebo group had a 20-30 percent improvement in motor scores, which persisted throughout the six months of the trial.[10] Because of the wide variations in response to drugs for Parkinson's disease, placebo effects are a major issue in the evaluation of new drugs. Consequently it is possible that the claimed clinical benefits of fetal tissue transplants are actually a placebo effect, or are exaggerated by investigator bias.

One reason why the procedure has always been highly controversial is that the fetal tissue is obtained from aborted fetuses 6.5 to 9 weeks old, but concerns relating to

the moral status of embryos are not at issue here. In the US a ban on federal support for the medical use of fetal tissue was lifted by President Clinton in 1993. The National Institute of Health subsequently agreed to fund two randomized control trials to assess the efficacy of the procedure.

The first trial involved 40 patients with advanced Parkinson's disease, for whom drug therapy had become ineffective. [11] The patients were randomly allocated to receive either the transplant or a placebo operation. Each transplant patient received tissue taken from four fetuses, injected into the damaged areas on both sides of the brain. For the patients given the placebo, risks and discomforts included: a local anesthetic, placing of stereotactic equipment, a scalp incision and the drilling of burr holes (not all the way through the skull). This study reported no significant difference between the transplant and the placebo groups. Unfortunately, in five of the transplant patients the grafts grew too well and these patients suffered uncontrollable involuntary movements and muscle spasms, probably due to an excess of dopamine.

The second Parkinson's trial was designed to address some questions raised by the first trial, which concerned immunological effects and the comparison of different amounts of transplant tissue.[12] This trial had three arms. In one arm patients received tissue from four fetal sources. In the second arm they received a smaller amount of tissue from just one fetus and the third arm was the placebo control. The patients on the placebo arm faced the additional risks of a general anesthetic, low-dose immunosuppresant therapy (cyclosporine), the radio-isotopes used in the brain imaging as well as the other risks present in the earlier trial. The published results of this second trial showed no overall treatment effect. There was early improvement in some of the patients with less

severe symptoms, who received the higher amount of fetal tissue. However thirteen of the transplant patients (more than half) developed dyskenesias (uncontrollable movement) and three needed further surgery to relieve this serious side-effect. Subjects enrolled in the trial were told that if they received the placebo, and the transplants proved safe and effective, they would then be offered the procedure at no cost. In a paper published in advance of the trial, aiming to justify the trial design, the experimenters listed the risks described above, the measures taken to minimize those risks, and described the benefits thus:

> The benefits of participating in the placebo group include contributing to advances in the treatment of a disease of great personal interest to the participants, receiving standard medical treatment at no cost, having the opportunity to obtain a fetal-tissue transplant at no cost if the procedure proves to be safe and effective, and being spared the risks associated with transplantation if it proves to be unsafe or ineffective.[13]

In fact the trials showed a higher than expected mortality rate, a high rate of serious side effects and a significant placebo effect such that there was no statistically significant difference in benefits for the transplant group and the trial group. The results give rise to serious doubts about a procedure which has been undergone by hundreds of patients.

Arthroscopic Surgery for Osteoarthritis of the Knee

Patients with osteoarthritis of the knee, and for whom medical therapy has failed to relieve the pain, often choose to undergo one of two surgical procedures: arthroscopic

lavage or débridement. The lavage procedure involves flushing the joint with at least ten liters of fluid through arthroscopic cannulas, in order to remove debris. The débridement procedure is usually performed after lavaging the joint, and involves shaving away rough cartilage and trimming torn or degenerated meniscal fragments, and then smoothing the remaining meniscus. A study conducted in Texas assessed both surgical procedures against a placebo.[14] In this study a total of 180 patients were randomly assigned to arthroscopic débridement, arthroscopic lavage or placebo surgery. All the procedures were performed by one surgeon. Patients were assessed over a 24 month period after surgery, to assess improvements in pain and function. The surgeons had no role in the follow-up assessment of the patients, and the assessors were blinded to the treatment group assignment. For the placebo surgery, patients did not receive a standard general anesthetic, but instead were given an intravenous tranquilizer and an opioid, which is safer. Three one centimeter incisions were made, and a débridement procedure was simulated, but no arthroscopic instruments were inserted into the knee. Placebo patients spent the night after the procedure in hospital, and their nurses were also unaware of the treatment group assignment. There were two minor postoperative complications in the placebo group: one patient developed a wound infection, which was treated with antibiotics, and another developed calf swelling in the leg that had undergone surgery. Patients in all three groups received the same postoperative care: the same walking aids, the same exercise program and the same analgesics. The study found that the outcomes for both surgical procedures were no better than those after a placebo procedure. The authors concluded that, if their findings are correct, 'the billions of dollars spent on such procedures annually might be put to better use'.[15]

The Dilemma of Placebo Surgery

The moral dilemma presented by PCST is an instructive instance of the kind of dilemma that arises when the imperatives of research are in tension with the imperatives of clinical care. The real source of this dilemma is that the competing normative considerations are grounded in distinct and opposed ethical theories. The claim that doctors have an inviolable obligation to act only in the best interests of their patients appeals to a deontic conception of patients' rights and doctors' duties. However the doctor's duty to do what is 'best' for her patient has an implicit temporal index. The object of the duty is a particular, present patient and the duty of care is a duty to offer that patient treatment in accordance with *current* medical wisdom about best practice. The object of research, however, is not this or that patient but a condition in general. Research on therapies assumes that current best practice is not the best possible practice and aims to provide future patients with more effective therapies than are presently available.

For the most part we cannot say which individuals will benefit from today's research. Research brings benefits to a class of people – future Parkinson's patients, for instance – and for this reason the justification of research typically appeals to utilitarian arguments. From a utilitarian perspective dangers to research subjects can be justified when the potential benefits of new medical knowledge sufficiently outweigh the unavoidable risks of the research needed to gain that knowledge. In the case of surgical research the surgeon is both researcher and treating doctor, and the moral requirements of both roles are not easily reconciled.

In an influential article Ruth Macklin characterizes the dilemma as one 'between the highest standard of research design and the highest standard of ethics'[16]. It is

misleading, I think, to describe the problem as a tension between good science and good ethics, as if the only ethical considerations concern the protection of research subjects. If the benefits of good science did not carry moral weight – if *all* the ethical reasons pulled in one direction – then there would be no moral dilemma. Certainly, historically, the principal concern of research ethics has been the protection of subjects. However, the time frame over which research results are ultimately incorporated into standard practice is such that much medical research does not *directly* benefit the experimental subjects; so if research ethics is *only* about the protection of subjects then most medical research would be unjustifiable. The most effective way to minimize harms caused by research would simply be to do no research. In reality the approval process for research proposals standardly involves judgments about the importance of the research in terms of future benefits. For the most part what justifies risks imposed on research subjects is the utility of the knowledge to be gained, and much of the ambiguity in research ethics arises from the fact that there are no widely accepted methods for ethically evaluating these trade-offs.

Macklin compares PCST to placebo controlled drug trials and finds that the justification for the latter cannot be extended to the former. Experimental drugs are normally trialed against the current standard treatment. It is considered acceptable to use a placebo control only when a drug is being trialed for a condition for which there is no effective drug available.

> The chief reason [why PCST is unethical] is that performing a surgical procedure that has no expected benefit other than the placebo effect violates the ethical and

> regulatory principle that the risk of harm to subjects must be minimized in the conduct of research… It is undeniable that performing surgery in research subjects that has no potential therapeutic benefit fails to minimize the risk of harm. An alternative research design that did not involve sham surgery would pose a lower risk of harm to the subjects in the control group of the study. But herein lies the tension between the scientific and ethical standards: the alternative design would be less rigorous from a methodologic point of view.[17]

This argument is too quick and the problem lies in the ambiguity of the meaning of 'minimizing risk'. If 'minimizing risk *to research subjects*' is construed in an unrestricted sense then risks are minimized by doing no research. Of course that is not the sense in play here. The relevant notion of 'minimizing risk' is relational and only has determinate content relative to a specified objective. The power of a study determines the confidence with which general conclusions may be inferred from the experimental results. Uncontroversially, for any given study, we want the safest possible study design. If two candidate study designs will answer the same question with the same confidence level the design carrying the least risk is to be rationally preferred. Two studies which cannot answer the same question with the same confidence are effectively two different studies. One study may involve less risk than another in an absolute sense, but 'minimizing' does not just mean 'lessening'. One does not minimize the risks of football by deciding to play chequers instead. It is important not to confuse the idea of 'minimizing risk', in the sense of finding the safest design for a study, with the distinct question of whether the best

achievable risk-benefit balance for a proposed study is ultimately acceptable or unacceptable.

Macklin's argument has been criticized by Franklin Miller, in an article defending the claim that PCST (or 'sham surgery' as he calls it) can sometimes be justified.[18] Miller rejects Macklin's understanding of the requirement to minimize risk, along similar lines to the criticism above. But Miller's defense of PCST is flawed. His main charge is that critics of PCST are 'conflating the ethics of clinical research with the ethics of clinical care'. Miller accepts the argument that 'judged by the surgical standard of care' it is wrong to perform placebo surgery on a patient because 'surgeons do not perform surgery unless they judge it to be in the best interests of the patient'. Miller argues, however, that this is not the right perspective from which to evaluate PCST. A randomized clinical trial is 'not a form of personal medical therapy', but is rather 'a scientific tool for evaluating treatments'. Miller notes that not just clinical trials but a wide range of disease studies involve painful or potentially harmful interventions without any prospect of medical benefit to the participants. These risks to participants are generally judged acceptable when the risks are minimized, are not excessive and the research stands to produce valuable knowledge.

> Clinical research, including treatment trials, would be impossible if it were held to the ethical standard of promoting the medical best interests of patients that governs therapeutic medicine. These ethically significant differences between clinical research and medical care – differences in purpose, methods, and justification of risks imply that it is erroneous to hold that clinical research should

> be governed by the same ethical standards as apply to the practice of medicine. Sham surgery is not unethical just because it exposes patients to risks that are not compensated by medical benefits. Sham surgery as a control should be evaluated in terms of the ethical requirements proper to clinical research.[19]

This is a very striking claim – that research participants and patients inhabit two distinct ethical regimes and the exigencies of research demand that the research participants cannot be protected in the same way that ordinary patients are. One important difficulty with this idea is that people enrolled in studies are often both patient and research subject and there is no clear demarcation between research and treatment in many cases. Even if we could always categorize interventions as belonging to either research or clinical care, we may ask how is it that undertaking research confers on the researchers permission to take certain risks with the health of subjects that would be impermissible in the clinical context? The claim here is not that one consistent set of ethical principles has different practical implications in different contexts, but that clinical care and medical research are properly regulated according to different principles. Miller's argument seems to be that because medical research sometimes requires doing things to participants that are not in their best interests, and because research can have valuable outcomes, such risks are therefore justifiable. Yet he accepts that in the context of clinical care it is always wrong to act against a patient's best interest. It may well be true that it is practically impossible to conduct medical research without exposing subjects to risks without any expectation of a health benefit. However, this is not a *moral* argument. Moral requirements are not

proved on grounds of pragmatic necessity. Although it is not explicitly acknowledged Miller's conception of the ethics of clinical research clearly has a utilitarian character.

> The ultimate question of risk-benefit assessment is whether the risks of sham arthroscopic surgery were justified by the anticipated scientific value of the study. We lack any objective tools for measuring research risk-benefit ratios. I contend that the relatively minor risks of the methodologically-indicated sham procedure were justifiable to answer the clinically important question of whether arthroscopic surgery is effective to treat pain associated with arthritis of the knee. This is a matter of judgment about which reasonable people might differ.[20]

Where Macklin opposes the 'standards of research' with the 'standards of ethics', Miller finds that there are two standards of ethics – one for research and one for clinical care. But we are not given any *principled* reason for the division between these domains. Why should the deontic constraints that regulate the doctor-patient relationship suddenly give out at the boundary between treatment and research? Why is the surgeon-qua-researcher entitled to appeal to utilitarian justifications that are forbidden to the surgeon-qua-doctor?

At bottom the reason why PCST is such a difficult and divisive issue is simply that this is a case where utilitarian and deontic principles conflict sharply. The dilemma cannot be resolved by simply ruling one or other of these moral perspectives out of court. The utilitarian focuses on the comparative magnitude of risks and benefits and abstracts away from their distribution. From a utilitarian perspective both the Parkinson's and knee surgery PCST described above were straightforwardly justifiable. In the case of the

Parkinson's trial the researchers, in their paper published before the trial, offered this rationale:

> The inclusion of a placebo group in our study of 36 subjects will permit us to establish whether the benefit observed to date can be attributed to an effect of treatment apart from a placebo effect. If fetal-tissue transplants are found to be safe and effective, thousands of patients with Parkinson's disease stand to benefit, and further research will be encouraged. If the transplants are found to be unsafe or ineffective, or if they offer nothing more than a placebo effect, hundreds or even thousands of patients will be spared the risks and financial burdens of an unproved operation.[21]

Note that the trial is justified here in terms of benefits to future patients. When we consider, in addition, the flow-on effects of reallocating resources away from ineffective procedures, the utility sums clearly weigh in favor of such trials.

The deontic objection to this utilitarian argument concerns not the relative magnitude of risks and benefits but their distribution. Those who bear the risk of placebo surgery are not likely to be the direct beneficiaries of the knowledge obtained; and even where they do later benefit from improvements in treatment, other patients are effectively free-riders on the risks shouldered by the trial participants. There are various ways in which this kind of objection might be phrased. In Kantian terms the subjects are treated as means rather than ends. In Rawlsian terms fairness constraints are violated by making some individuals worse off for the benefit of others. The general form of the deontic

objection to PCST is that such trials involve using patients in a way that is inconsistent with the duty to respect each individual patient's autonomy.

An unrestricted application of utilitarian reasoning would sanction research even where the subjects face substantial and certain harms, provided the research would lead to clearly greater benefits. For instance, imagine that one of the above trials was conducted without informing the subjects that the trial involved a placebo control. Such a trial would be quickly rejected by any ethics committee, although it might in fact be even better from a purely scientific perspective. Because utilitarianism does not give appropriate weight to the protection of individuals and their autonomy, contemporary standards in research ethics surround research subjects with various deontic protections. However, as Miller has observed, an absolute prohibition on harming some for the benefit of others would simply rule out a great part of medical research.

Clearly research on humans is subject to *some* deontic constraints, and the debate around PCST is really about where to draw those limits. In practice, all the stress tends to fall on consent. Consent is the means of reconciling, or at least appearing to reconcile, these conflicting obligations. As long as the subject is informed of the risks and gives a valid consent it appears that autonomy has been respected and researchers can go ahead and impose those risks. The moral acceptability of a PCST will hinge, then, on the quality of consent from its subjects. What does consent to participation in a PCST need to be to do the moral work required of it?

In the case of surgical research this tension is particularly acute. When surgical studies are designed according to good scientific methodology, with a randomized control, then it is uncomfortably clear that human subjects are going under the knife for

research purposes. It is important to recognize here that surgical research has traditionally been conducted informally and this is worse on *both* consequentialist and patient centered grounds. Informal surgical research has less evidential value and the progress of surgical practice goes more slowly and haphazardly than it otherwise might; and when patients undergo procedures unaware that some aspect of the procedure is experimental then the status of their consent is questionable. PCST brings to the surface a moral dilemma that has hitherto been hidden, where surgeons have not been explicit with patients about surgery with a research component. The literature on the ethics of PCST has, for the most part, treated such trials in isolation and focused on the question of whether it is ever acceptable to perform a placebo operation. What has not been noticed is that the main arguments against PCST hold *a fortiori* for informal surgical research, which is the most common mode of surgical research. If it is determined that PCST are ethically unacceptable then this directly raises the question of whether any experimental surgery could be acceptable.

Expected vs. Actual Benefits

To bring this point out I want to draw attention to an important feature of the trials described above, which complicates the comparison with drug trials. Typically a drug trial compares a novel pharmaceutical against the standard therapy (or against placebo if there is none). The PCST conducted so far have aimed to assess procedures that were already in use. Before the Parkinson's PCST were conducted fetal nigral tissue transplants for were being performed by at least 17 centers. For arthroscopic lavage or débridement of the knee, Mosley *et. al.* report that more than 650,000 such procedures

are performed annually in the U.S. What this shows is that surgical procedures can become widespread without the kind of evidence supporting their efficacy that is required for the approval of new drugs. Indeed there is a long history of surgical procedures which were once common and have since been discredited.

As Macklin puts it the 'chief reason' for disallowing PCST is that it is wrong to perform a surgical procedure that 'has no expected benefit'. So what justifies the risks of ordinary surgery is a reasonable expectation of benefit, which raises the question of when such expectations are reasonable? We might think that with common procedures the benefits are well established and the probability of a poor outcome or complications is accurately known. The arthroscopic knee surgery example shows that this is not always true. With more radical procedures, like fetal tissue transplants to repair brain damage, the uncertainty is greater, and centers were reporting a success rate which, it turned out, could not be reproduced in a rigorous, randomized control trial. For patients who received the placebo operation it seems clear that no benefit could be reasonably expected from a 'pretend' operation. But was there a *reasonable* expectation of benefit for the patients who received the transplants, or for the patients who underwent this procedure in other clinics?

Expectations are probabilistic – an operation may offer a high or a low chance of success. It is easy for expectations to be inflated by hope. What differentiates wishful thinking from a reasonable expectation of benefit is that there is an evidence base which supports the judgment that a beneficial outcome is probable. Where the evidence is missing or unreliable, where patients give consent with misleading or no information about the actual probability of benefits and harms, we cannot say that there is a

reasonable expectation of benefit. In the Parkinson's PCST the transplant recipients as a group did not show better than a placebo effect and some experienced serious complications. This means that those who received the placebo operation had roughly the same chance of benefit and a much lower chance of harm than those who received the transplant. It then seems odd to say that it was only the placebo procedures that were wrong because they had no expected benefit. Correct expectations as to the probability of benefit and harm would have offered even less comfort to those subjects who had the trial procedure.

Patients and surgeons may subjectively expect that a procedure will work, but subjective expectations can be sadly mistaken and the mere psychological state of expecting a benefit does not of itself justify running a serious risk. What is required is that benefits are *reasonably* expected, meaning the expectations are supported by good evidence. The very purpose of PCST is to generate good evidence about the efficacy of procedures in cases where it is lacking. Where reliable evidence of safety and efficacy is not available for a surgical procedure then there are no persuasive reasons to expect a benefit from undergoing that procedure. Imagine that you had to participate in a PCST, but you were allowed to choose whether you receive the trial procedure or the placebo operation. If you decide on expected utility alone the rational choice would actually be to join the placebo group. You don't have good reason to expect the experimental procedure to work, but you know that you are far less likely to be harmed in the placebo arm. You could then choose the experimental procedure later, if and when it is proven effective. If surgery is only justified by a sound expectation of net benefit then it is not only placebo surgery that fails to meet that standard. Now we see why PCST presents a deeper

dilemma than its critics have realized. If we accept the principal argument against PCST then, on the same grounds, we should object even more strenuously to speculative procedures and informal surgical research. Yet a ban on PCST means that surgical research remains confined to methods that are morally worse, and ineffective procedures that would be exposed by a PCST may remain in use.

The Consent of the Desperate

When important research unavoidably requires that participants are put at risk, the moral acceptability of that research depends heavily on the quality of consent obtained. The Parkinson's PCST was rightly criticized in this regard because the consent of subjects was likely to be compromised by the 'therapeutic misconception'. The therapeutic misconception is a well-documented problem with patients entering drug trials; particularly Phase 1 trials for cancer and other terminal conditions. Phase 1 drug trials are primarily intended to determine toxicity and dosage limits and they are not designed to yield a therapeutic benefit for the enrolled subjects. Participation in such a trial is really an altruistic act of loaning one's body to medical science. Nevertheless there is considerable evidence that many patients enroll in such trials in hope of getting better. In a paper on the therapeutic misconception in Phase 1 cancer trials, Matthew Miller writes:

> Given that the remission rate is less than 1 percent and that the rate of death due to drug toxicity is comparable, few would claim any aggregate survival advantage for participants. In fact, consent documents state that Phase 1 cancer trials are primarily toxicity studies and that response is neither intended nor expected. Yet

> patients enrolled in these trials overwhelmingly cite hope of physical benefit (rarely altruism) as their primary motivation for enrolling.[22]

How blameworthy researchers are in this regard is a difficult question. Trial subjects who have the therapeutic misconception are being exploited. Yet the psychology of the doctor-patient relationship makes it difficult for doctors to disabuse very sick patients of whatever slim hopes they have. Clearly though, the therapeutic misconception fatally compromises patient consent. Recall that participants in the Parkinson's PCST were told that if they received the placebo, and the procedure proved effective, they would be offered the procedure. Such an offer implicitly invites candidates to believe that enrolling in the trial might offer a route to recovery.

Macklin cites reports of patient anger in the Parkinson's trial when placebo recipients were told that, because of safety considerations, the real procedure would not be offered. She asks if it is overly paternalistic to protect research subjects from risks they seem willing to accept, and suggests that: 'The emphasis today on respect for the autonomy of patients and research subjects creates a reluctance to question whether their choices are fully rational'.[23] Macklin appears to argue that the obstacles to informed consent are too great in this case and patients should not be offered such a choice. Franklin Miller accepts that the therapeutic misconception may have been present in the Parkinson's trial but contends that this result cannot be generalized to all PCST. He contends that the patients in the arthroscopic surgery trial were not 'vulnerable' because although arthritis is painful 'it is not associated with impaired decision-making capacity'.[24]

Perhaps ‘autonomy’ has become a buzz-word often used too carelessly to sanction irrational patient choices. Properly understood, respect for autonomy actually demands that we test the rationality of questionable choices and make greater efforts to help patients understand the salient facts. Irrationality is commonplace and sick people are especially prone to it, but that fact does not warrant a pessimistic retreat to paternalism. Well designed PCST can yield information of great value. The problem with PCST is that participants are asked to submit to risks without a compensating expectation of benefit to their health. It is not irrational for a patient to believe that contributing to medical knowledge or helping future sufferers of his condition is sufficient reason to participate in a surgical trial. PCST are not inherently or necessarily unethical, but we must be sure that participants understand that therapeutic benefit is not the primary goal of the trial and that there is a high chance that they will get no health benefit. Ethics committees reviewing proposed PCST need to be satisfied that there is adequate testing to ensure that participant consent is not motivated by an unfounded hope of improved health. We should expect that this will make it harder to find volunteers and if that is the price of adequate consent then so be it.

I will conclude by pointing out that there is one obvious way to ameliorate the problem of uncompensated harm, and that is to compensate. If participants volunteering for surgical research suffer complications, then they should receive not just treatment but also some monetary compensation for that suffering. Compensating for adverse outcomes is not the same as paying participants and cannot reasonably be construed as an inducement. My proposal is that fair compensatory payouts for various complications are determined in advance, and that this information is part of the informed consent process. I

believe this would help potential volunteers to appreciate the reality and relative seriousness of the risks they are being asked to accept. Such a scheme would require insurance coverage which would increase the cost of trials. If it is objected that this would make surgical trials too costly, that is equivalent to an admission that the funding of such research depends on unfair cost shifting onto trial subjects. The case of PCST offers a stark illustration of how the costs of medical progress are disproportionately borne by research subjects. If we are serious about eliminating exploitation in medical research, then patients who are harmed in such studies must be compensated.

Notes

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[1] Angelique M. Reitsma and Jonathan D. Moreno, "Ethical Regulations for Innovative Surgery: The Last Frontier?" *Journal of the American College of Surgeons* 194, no. 6 (June 2002): 792-801.

[2] Angelique M. Reitsma and Jonathan D. Moreno, "Ethical Regulations for Innovative Surgery," 793.

[3] Angelique M. Reitsma and Jonathan D. Moreno, "Surgical Research, an Elusive Entity," *The American Journal of Bioethics* 3, no. 4 (Fall 2003): 49-50.

[4] Thomas B. Freeman, Dorothy E. Vawter, Paul E. Leaverton, James H. Godbold, Robert A. Hauser, Christopher G. Goetz and C. Warren Olanow, "Use of Placebo Surgery in Controlled Trials of a Cellular-Based Therapy for Parkinson's Disease," *The New England Journal of Medicine* 341, no. 13 (September 1999): 988-992.

The list of inadequately studied invasive or surgical procedures that become part of standard medical practice only to be abandoned after closer scrutiny includes

bloodletting, routine tonsillectomy, routine circumcision, repeated cesarean delivery, internal-thoracic-artery ligation, gastric freezing, jejunoilial bypass for morbid obesity, glomectomy for asthma, prophylactic portacaval shunting, laparotomy for tuberculous peritonitis or pelvic inflamatory disease, adrenalectomy for essential hypertension, and extracranial or intracranial bypass for carotid-artery occlusion. A review of coronary artery bypass procedures showed that 38 percent of indications for the procedures are questionable. (988)

[5] Peter A. Clark, "Placebo Surgery for Parkinson's Disease: Do the Benefits Outweigh the Risks?" *Journal of Law, Medicine and Ethics* 30, no. 1 (Spring 2002): 58-68.

[6] R. L. Albin, "Sham Surgery Controls: Intracerebral Grafting of Fetal Tissue for Parkinson's Disease and Proposed Criteria for use of Sham Surgery Controls," *The Journal of Medical Ethics* 28, no. 5, (October 2002): 322-325.

[7] Henry K. Beecher, "Surgery as Placebo: A Quantitative Study of Bias," *Journal of the American Medical Association* 176, no. 13 (1961): 1102-1107.

[8] R. L. Albin, "Sham surgery controls," 323.

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