# I Thought We Were in This Together?

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# *I Thought We Were in This Together?*

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Despite all of the unprecedented events occurring around the globe today, it is still very difficult to open up a newspaper without finding an account of another "disaster" in the world of clinical research. There is a steady drum beat of horror stories in which patients were allegedly misinformed or mistreated by doctors acting in ignorance or in violation of widely held ethical standards to the detriment of their patients. These include the tragic death of a young woman in a pulmonary physiology study at Johns Hopkins and the intervention by the Maryland State Court to halt a clinical study evaluating different methods for environmental lead abatement and to assert its legal authority over the assessment of risks involved in all clinical research in children.

One of the key issues around which much of the criticism of clinical research has revolved is the use of placebos. This discussion has become even more heated following the performance of a number of placebo-controlled trials in HIV-infected patients that were conducted in Third World countries but that did not incorporate the latest findings from ACTG investigations in the United States (Angell 1997; Lurie and Wolfe 1997; Varmus and Satcher 1997). This has culminated in the recent publication by the World Health Organization of a directive against the use of placebo-controlled trials for any disease in which there is a proven effective therapy. Miller and Brody (2002) succinctly summarizes the history of these developments, and the authors make a compelling argument in favor of judicious use of placebo-controlled trials. They demonstrate that clinical research is not synonymous with clinical care and that the same rules of conduct are not always valid in both domains. Moreover, they repeat the persuasive arguments of Temple and Ellenberg (2000a; 2000b) that validity may require a placebo-controlled study design. Miller and Brody conclude that valid science is congruent with the most ethical approach to the problem.

While the essay by Miller and Brody is an admirable defense of a reasoned research strategy, I think there is an important element that is being overlooked in the discussion of this topic. The underlying assumption when problems arise in clinical research seems to be that the investigator alone is either guilty of willfully neglecting well-accepted ethical standards or is merely ignorant of how to protect the best interest of patients. Whether it is time pressure, inappropriate financial incentives, inattention to psychosocial complexities, or competition to succeed, the clinical researcher is viewed as prey to forces that compromise ethical conduct in research.

I suspect it was not always this way. Many clinical investigators probably began their careers when they realized the limits of their medical knowledge and capacity. Guided by senior mentors, they were motivated to figure out improvements in treatment that might help their patients. Clinical research was considered a worthy enterprise, an integral part of medical care, and not an afterthought. Some physicians may have made a legitimate profit, and others may have abused the system for personal gain. But these were usually egregious exceptions among the large group of clinical researchers. Most important, the investigators viewed themselves as allies of their patients working as a team to gain a deeper understanding and, hopefully, better therapy for disease.

It is hard to determine if this is a nostalgic look back at something that never actually existed. However, my vision of clinical research is based on a virtue that seems to be in short supply: a sense of duty. I speculate that a decade of economic plenty and nearly a generation of Pax Americana have worn down people's sense of a shared stake in handling medical problems. This is manifest in a persistent

resistance to real change in the structure of the healthcare delivery system to insure equitable and affordable medical treatment to every person in this country. I think it underlies the perceived conflict of interest between patients and clinical researchers.

There are several consequences of this decline in duty. First, unlike the therapeutic encounter, in which the doctor and patient are partners, clinical research is not seen as a covenantal relationship in which the investigator and the patient are equally responsible for insuring the success of the interaction. Second, rigid codification of rules for conducting clinical research hinders open dialogue between doctors and patients about how to manage clinical care and research. Although clinical research by design utilizes well-defined protocols, a one-size-fits-all approach underestimates the complexity of the process and rarely improves the outcome (Mueller and Furedy 2001a; 2001b; Burman et al. 2001.). The extensive literature on all aspects of clinical research from informed consent, to subject selection, to the use of placebos implies that there are no moral absolutes in virtually any aspect of this work (Truog et al. 1999; Freedman 2001.). Finally, no intervention, in either the therapeutic or research setting, is guaranteed to succeed. Just as there is risk involved in participating in a clinical trial of a new therapy, administration of established treatments may result in unexpected bad outcomes. Increased regulations and formalized study designs will never eliminate human errors, failures, and adverse events. If patients and doctors were to conduct clinical research with mutual respect and a sense of shared duty to find the best therapy for disease, then both parties would not need to rely on inflexible rules and would accept the outcome knowing that an honest effort had been made to study and treat disease.

There is a need for thoughtful oversight of the research process, constant review of the goals and methods that are being utilized, and an ongoing effort to do things better. However, I suggest that the tempest over placebo-controlled trials represents a not-so-subtle questioning of the fundamental integrity of clinical investigators and an abdication of the responsibility of the lay community to do all it can to alleviate disease. Recreating a shared sense of duty on the part of all concerned—patients and doctors alike—would go a long way to restoring health and vigor to a very important aspect of medical care, namely clinical research.

The terrifying attacks on the Twin Towers and the Pentagon have reawakened Americans to the realization that defense of liberty and freedom are an ever-present communal responsibility, one that is ignored at our peril. These events have also fostered renewed respect for institutions that may have been taken for granted just a few short months ago. It is sobering to think that it requires tragedy to inspire people to face up to their responsibilities. I acknowledge that it would be cruel to view sick patient as conscripts in an "army" against disease. However, I am advocating the position that clinical research is a commitment to combat illness that is shared by both patients and trained physicians. It is a vital and integral part of our society, like national defense and education, to which we should all be expected to contribute and from which we are all entitled to benefit. Unfortunately, as patients, many of us may be asked to make good on this obligation at some time in our lives. Because of circumstances and differences in individual temperament, it is inconceivable that everyone will fulfill this duty equally. But the benefits of clinical research are all too real to the person who can take a pill or undergo a procedure that restores them to health and a productive, meaningful life. That will probably be each and every one of us. ■

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