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trying to determine whether a question is real or rhetorical, even an utterance like "Eh, what's the difference?" can open onto a hall of mirrors. Boyd never stops to consider that maybe, just maybe, the clever human minds responsible for literature are the same clever human minds responsible for literary theory; if he had, he might have been able to say, more plausibly, that theory started (as do all our endeavors) in the impulse to play and create, and only became routine and stultifying after many weary iterations. At which point, after the 350th New Historicist reading of *The Tempest*, neurons in the substantia nigra and ventral tegmental areas of the brain stopped secreting dopamine.

More important, Boyd is sometimes reluctant to give culture and history their due. He scoffs, for example, at the idea that romantic love was invented at some point in the 12th century, because "cross-cultural, neurological, and cross-species studies have demonstrated the workings of romantic love across societies and even species." This just won't wash. Other species might court and mate for life, but they do not engage in romantic love in the sense that humanists employ the term, save perhaps for the cartoon skunk Pepé Le Pew. "Romantic love" does not mean "mammals doing it like mammals"; it refers to the conventions of courtly love, which were indeed invented in the European middle ages and cannot be found in ancient literatures or cultures. Those conventions are culturally and historically specific variations on our underlying (and polymorphous) biological imperatives, just as the institution of the Bridezilla and the $25,000 wedding is specific to our own addled time and place. Nothing about the evolutionary record, from amoebas to *Homo sapiens sapiens*, is denied or contravened in acknowledging this.

On the Origin of Stories is a fascinating book, even a necessary book. At its best, evocriticism can help to reorient the arts and humanities, renewing (or, in some benighted quarters, sparking) our appreciation for the creative works of human minds and hands, and leading humanists to take a fresh look at the rich evolutionary record. But it will accomplish this, I suspect, only if it is complementary to, and not sweepingly dismissive of, the intellectual traditions humans have devised for the study of human cultures.

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CLINICAL RESEARCH

Help, Harm and Human Subjects

Sheldon Krimsky

WHEN EXPERIMENTS TRAVEL: Clinical Trials and the Global Search for Human Subjects. Adriana Petryna. xii + 258 pp. Princeton University Press, 2009. $65 cloth, $24.95 paper.

EXPLOITATION AND DEVELOPING COUNTRIES: The Ethics of Clinical Research. Edited by Jennifer S. Hawkins and Ezekiel J. Emanuel. viii + 327 pp. Princeton University Press, 2008. $65 cloth, $24.95 paper.

CHASING MEDICAL MIRACLES: The Promise and Perils of Clinical Trials. Alex O'Meara. viii + 263 pp. Walker and Company, 2009. $25.

Those of you who browse bulletin boards or ride in buses or subway cars have undoubtedly come across posters bearing messages like this: "If you are between the ages of 18 and 35 and have difficulty sleeping, you may qualify to participate in a new study that could help your condition." Such solicitations are now nearly ubiquitous. That's because the clinical trial business has grown significantly over the past several decades, largely in response to the growth of drug development and of global markets in pharmaceuticals. To get new drugs into the marketplace, companies must deliver safety and efficacy data from clinical trials to the U.S. Food and Drug Administration (FDA). It is estimated that every year about 2.3 million people take part in clinical trials held in the United States; in 2008, more than 65,000 such trials, sponsored by federal agencies and private industry, were listed in a National Institutes of Health (NIH) database for those trying to locate clinical trials.

Investment in drug development has grown steadily since the 1980s as a result of biomedical advances relating to stem cell research, pharmacogenetics, proteomics and the mapping of the human genome. Recently the drug industry has been spending the money it budgets for research and development on a new generation of cancer drugs. As Big Pharma has investigated these oncologic agents, more volunteers have been needed in clinical trials to evaluate the prospects of various compounds.

Many trials have had difficulty recruiting subjects. According to a 2006 article by Judith M. Watson and David J. Torgerson, "Increasing Recruitment to Randomized Trials" (*BMC Medical Research Methodology* 6:34), a survey of the corresponding authors of articles published in 2000 or 2001 reporting the results of randomized trials revealed that nearly 60 percent of the trials had either proceeded with fewer subjects than initially planned or found it necessary to extend the recruitment period.

And more recently Sarah Kliff, in an article published online in *Newsweek* on March 10, 2009, has reported that 80 percent of clinical trials are delayed at least a month because of low enrollment.

When people cannot be recruited for trials in the United States, the world marketplace becomes the stage for medical outsourcing. Eastern Europe, Africa, Asia and South America have helped fill the demand for human trial subjects, usually with indigent people who have little or no access to health care. According to a report from Visiongain (a company that provides business information to the pharmaceutical industry), in 2008 the global clinical trial business was worth about $50 billion and was growing at a rate of 10 percent a year.

Three recently published books address the subject of clinical trials from different vantage points. *When Experiments Travel*, by Adriana Petryna, is an ethnographic analysis of leaders in the new growth industry of Contract Research Organizations (CROs), which provide clinical-trial services to drug developers. *Exploitation and Developing*

Countries, edited by Jennifer S. Hawkins and Ezekiel J. Emanuel, is a volume of essays by bioethicists focusing on issues of global equity and justice in clinical trials that enroll impoverished groups in developing nations. And *Chasing Medical Miracles* is journalist Alex O'Meara's memoir of his experiences jumping through hoops to gain access to a clinical trial that gave hope of a cure for his diabetes.

In *When Experiments Travel*, Petryna, an anthropologist at the University of Pennsylvania, explores this question: Why are so many of the clinical trials sponsored by companies in the United States being held in developing nations? To explain the phenomenon known as "offshoring of trials," Petryna analyzes information gleaned from government sources, the Web sites of nonprofit organizations, and interviews with leading scientists and entrepreneurs who have founded CROs. She learns that, as is true of many trends in globalization, government policies play a central role. "In the early 1990s," she notes, "the FDA began to actively promote the globalization of clinical trials, declaring that the search for sites and sources of data is part of its mandate."

After examining the global marketplace for human subjects, Petryna concludes that the norms of protection vary significantly among countries. The book is built primarily on her scholarly, detached presentation of qualitative interview data and an analysis of published statistics. However, she periodically expresses moral judgments such as the following: "The benefits deriving from globalized research are arguably uncertain, and its risks are unevenly distributed and its costs, unjust."

Petryna condemns First World companies and complicit governments for exploiting vulnerable, impoverished patients as experimental subjects. However, many of the complex ethical issues of transnational human trials are left unexplored in her book. Among those are whether desperate people can be both exploited and helped, and what set of humane principles should guide outsourced clinical trials. These are the subjects of the volume edited by Hawkins and Emanuel, *Exploitation and Developing Countries*.

The essays in this collection are organized primarily around two cases, which serve as the grist for ethical analysis. In the Havrix case, 40,000 school children in Thailand received either an inactivated hepatitis A vaccine or a hepatitis B vaccine in a randomized controlled trial sponsored by the U.S. Army in conjunction with SmithKline Beecham Biologicals and Thailand's Ministry of Public Health. In the Surfaxin case, 650 premature infants in Bolivia who had respiratory distress syndrome (RDS), for which the standard treatment was lung surfactant replacement therapy with one of four approved surfactant drugs, were subjects in a placebo-controlled trial of a new surfactant made by Discovery Labs. In addition, in the introduction to *Exploitation and Developing Countries*, there is a discussion of trials in sub-Saharan Africa in which women were treated with antiviral agents to reduce maternal-fetal transmission of HIV.

Is it ethical to use placebo controls against a new drug in clinical trials when some form of effective therapy exists for a medical condition and is the standard of care?

The essayists reflect on a series of moral dilemmas. Can there be informed voluntary consent when the clinical trials are conducted in countries in which people face extreme poverty, illness and desperation? Is it ethical to use placebo controls against a new drug in clinical trials when some form of effective therapy exists for a medical condition and is the standard of care? When is a clinical trial protocol exploitative of desperate human subjects? Should U.S. companies engaged in overseas trials be required to follow ethical and medical standards that are no less stringent than those they would be required to follow in the United States? Or should the moral acceptability of a trial be based on whether the company's actions will improve the lives of the population of the country where the trial will be conducted?

A number of the essays address the complex issue of placebos. Thomas Pogge ("Testing Our Drugs on the Poor Abroad") explores the question of whether it is "wrong to test a new medicine (Surfaxin) for some life-threatening medical condition (RDS) with a placebo-control design when there already exists an effective medicine for this condition against which the new drug could be tested." Pogge points out that if the Surfaxin trial had had an active control design, the lives of more than 280 infants might have been saved; nevertheless, with the placebo-control design, the trial saved the lives of 140 infants who probably would have died if the trial had not been conducted in Bolivia.

The book's contributors examine responses to ethical questions through the lens of a variety of ethical theories: utilitarianism (greatest good for the greatest number), deontology (respect for persons), virtue ethics (accepted standards and norms), Rawlsian justice (the most vulnerable must not be made worse off), situation ethics (contextualized to local conditions) and intuitionism (what feels fundamentally fair and just). The meaning of *exploitation* in the circumstances discussed remains elusive; nevertheless, the volume's artful philosophical analyses illuminate the issues. Andrew Siegel, in "Kantian Ethics, Exploitation and Multinational Clinical Trials," expresses the paradoxical dialectic:

> We must also exercise caution when legislating against exploitation, for the perverse reality is that the best prospect some persons currently have for improving their lives is to submit to exploitative exchanges.

In "Exploitation and Placebo Controls," Jennifer Hawkins proffers a set of conditions that she believes are jointly sufficient to morally justify the use of placebo controls even when participants fail to receive the best care available.

The last chapter consists of a consensus statement obtained from participants at an international conference on research in developing countries. It addresses the question of whether it is unethical to recruit persons in a poor country to be clinical-trial subjects when neither they nor their country will benefit from the medical advance being investigated.

Overall, these are essays of high quality. However, the anthology is limited in one obvious respect: It has no contributions (with the exception of the consensus statement) from ethicists in those parts of the world most adversely affected by clinical-trial outsourcing.

The two books already discussed, which are soberly academic in tone, were written by scholars pursuing broad explanatory themes and universal ethical principles. Alex O'Meara's *Chasing Medical Miracles*, the first-person account of a clinical-trial subject, is almost breezy in comparison—the book is a page-turner.

O'Meara, a journalist, has type I diabetes complicated by hypoglycemic unawareness that has repeatedly landed him in emergency rooms. He describes the lengths to which he goes to be included in a somatic gene therapy trial that would afford him some hope that his body would begin producing its own insulin. What makes his memoir unique and captivating is that he steeped himself in the culture of clinical trials, entering not as a naive and ill-informed subject but as a fully informed and tenacious advocate of the trial, which he hoped would liberate him from having to wear an insulin pump. His personal story is so compelling that the intervening background chapters feel like an unwelcome intrusion.

The trial involved transplanting pancreatic islet cells from matched donors into the livers of patients with diabetes. To be cleared for participation, O'Meara had to overcome a number of obstacles. To take just one example, an x-ray of his lung revealed a nodule. He volunteered to undergo surgical removal of the nodule, hoping that it would turn out to be fungal, since in that case he would still be eligible for the trial. The surgeon needed 98 titanium staples to close his lung after the surgery. "I saw the little rivets on my x-ray," O'Meara writes. "They were looking great, the surgeon said. And no, he told me, the staples wouldn't set off metal detectors at airports."

If the book has a weakness, it is that the author makes it appear that, to qualify for a trial, a candidate must be in tip-top physical shape (O'Meara was a marathon runner). His case is hardly representative of the way people actually get recruited for trials or of the type of medical screening that usually takes place to ensure that the trial candidate meets the letter of the protocol.

O'Meara's trial was fraught with risks, and things did not go smoothly for him: He experienced multiple complications and got mixed results. Thus his experience left him well qualified to write the book's useful afterword, in which he presents a set of soul-searching questions that anyone who is considering enrolling in a clinical trial would do well to consider.

Chasing Medical Miracles provides a useful counterpoint to the detached, scholarly approach of social scientists and ethicists featured in the other two books. It reminds us that people in desperation over their illnesses seek hope, and that many of them grasp that hope in a clinical trial that offers them an experimental treatment. Taken together, these three books reveal the profound complexity of the task of meeting the needs of vulnerable populations while advancing medical science for the benefit of future generations.

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BIOLOGY

Development in the Real World

Marvalee H. Wake

ECOLOGICAL DEVELOPMENTAL BIOLOGY: Integrating Epigenetics, Medicine, and Evolution. Scott F. Gilbert and David Epel. xvi + 480 pp. Sinauer Associates, Inc., 2009. $49.95 paper.

What constitutes a new field in science? Must it be the consequence of a new synthesis? Does it need to take research in a new direction based on new ideas or new techniques? Or is it something that we recognize after the fact as a paradigm change? If we take these to be the criteria, then ecological developmental biology certainly qualifies as a new field, for it fulfills them all.

Anyone wanting to learn more about "eco devo" would do well to read Scott F. Gilbert and David Epel's recent magnum opus, *Ecological Developmental Biology: Integrating Epigenetics, Medicine, and Evolution*. The same applies for those who may have been wondering what the currently emphasized "new biology" is all about. The new paradigm for biology in the 21st century is integration—of the various subfields of biology, and of biology with other fields, including physics, chemistry, geology, the social sciences and the humanities—and the goal is to understand the complexity of living systems and their dynamic nature. Several scientists interested in integration have been writing discourses on why it is important and how it can be facilitated. But Gilbert and Epel have chosen to leapfrog that discursive step to produce a compelling portrait of the new biology in action.

The authors have two goals for the book: to offer a "fresh and challenging way of looking at biology," so that a different set of questions can be asked, and to show how ecological developmental biology is needed to diagnose and potentially help cure many of the problems of our planet. They emphasize four "revolutions" that are currently under way in biology: Inheritance has been shown to involve the transmission of gene expression patterns as well as gene nucleotide sequences; developmental and ecological explanations for human diseases are being found; phenotypic plasticity is being recognized as a "driving force" in the development and organization of biodiversity; and there is a new focus on analyzing relationships within networks of interaction. The book demonstrates that ecological developmental biology is significant in all four of these trends. Gilbert and Epel hope that by showing how to use the many facets of development to integrate disparate disciplines, the book will stimulate new research.

Of course, development in nature can differ in important ways from development in a controlled laboratory environment. Research on development in *Drosophila* and in mouse models, despite having been enormously productive, has not lent itself to a synthetic approach, because it takes place in laboratories, where the environment is considered constant and consequently unimportant.