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Experimentation in Humans: Science, History, Politics, Ethics and Ideologies

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Abstracts

(By Author)

Ambiguities in the Ethics of Consent to Research

Shlomo Cohen (Ben-Gurion University of the Negev, Israel)

Much attention has been given to, and much was written on, the ethics of (consent to) research. Accordingly, the basic principles of the ethical treatment of subjects of research are well-known and by now may even seem trivial. In this talk I will focus on some deep conceptual ambiguities that plague the field, specifically with respect to what respecting the autonomy of research subjects is supposed to mean.

A Media-Created Scandal? Clinical Trials of Western Companies in Eastern Germany (GDR)

Rainer Erices (Friedrich-Alexander University of Erlangen-Nürnberg, Germany)

Western pharmaceutical companies conducted clinical trials in the Eastern Bloc during the Cold War. After the collapse of the communist system in 1990, several media reports about alleged human experimentation provoked a wave of indignation. In 2013, a German News Magazine claimed that the GDR had 'sold' its patients as 'guinea pigs' for experiments in exchange for hard currency, for example, for tests on doping effects in premature babies and on treating seriously ill patients with placebos instead of actual drugs. The public debate that followed this revelation was soon taken up by politicians who called for a detailed investigation.

We analyzed the clinical trials performed in the German Democratic Republic based on archival material from the GDR health system and the secret service. We found documents relating to 480 trials involving at least 20,000 patients and more than 70 Western companies including some of the industry's big name firms. Initially, the main goal of the trials was for the GDR authorities to

decide whether to import certain Western drugs into the country. In the 1980s, this intention had changed; the trials now served almost exclusively one purpose, the procurement of foreign currency for the country. The GDR agreed to the trials due to impending bankruptcy and Western pharmaceutical companies capitalized on this situation.

We found no evidence to suggest that the trials systematically and intentionally damaged patients. In 2016, another research group from Berlin came to similar results. The researchers concluded: The studies appeared to have complied with the laws and standards of medical testing at the time, adding that trial practices in West Germany were also more relaxed.

Was the great excitement about the tests therefore just a media-made scandal?

A major problem was that the trials were conducted without the knowledge of the public. We could not discover patient information forms or systematic documentation regarding the provision of patient consent. At least some of the trials were carried out without patients having a comprehensive understanding of what the trial involved. The documents of the secret service are full of clues about illegal pharmaceutical tests. We found only sporadic evidence about a critical debate amongst the doctors involved, considering the high number of tests.

Evidence Based Surgery: Are We Sure We Are Doing the Right Thing?

Mordechai Gutman (Sheba Medical Center, Israel)

Anesthesia and anti-sepsis, developed in the latter half of the 19th century, enabled the development of major surgical procedures that are the basis of the surgical practice of today. All these procedures were developed by bold and knowledgeable physicians who used their research, skill and experience to develop these operations. They were never tested by modern statistical tools to assess their safety and efficacy, e.g. evidence based medicine (EBM). Challenging the old dogma is complicated from both practical and the ethical perspectives.

Although the standard therapy was never proven to be the best option, it is still the common practice. Now any deviation from the common practice requires proof of safety and efficacy; but in order to get this proof, you must conduct an experiment, a randomized controlled trial (RCT), in which you offer your patient a non-standard therapy. Considering the inherent difficulty in obtaining informed consent to surgery, its complexity and irreversibility, it is even harder.

Furthermore, in many fields of surgery RCT is neither feasible nor a realistic option at this time. We need to base our decisions on current data and experience, knowing that in the future we might find that we were wrong. Still, the patient needs a therapeutic plan now. So we must exert

our best judgment, invest our best effort to study the literature, involve ourselves in research, and above all, be totally honest and transparent with our patients.

Israel, Human Research and the Shadow of Nazi Medical Crimes

Etienne Lopicard (and Rakefet Zalashik) (Ashkelon Academic College, Israel)

Since the emergence of bioethics in the early 1970s, the 1946 Nuremberg Medical Trial (NMT) and its related “code of medical ethics” on human experimentation have quite often been referred to by bioethicists and historians of bioethics as the cornerstone of the bioethical discourse. By the same token, the 1964 “Helsinki declaration” of the World Medical Association is said to be a direct legacy of NMT even if historians tend to stress the gap that exists between the two texts, rather than their continuity. In the Israeli context, the first years following the NMT show a relative silence kept by the medical establishment with respect to the trial. Only a small group of physicians who survived the Holocaust were active in promoting a consciousness about Nazi medical crimes and their possible significance for contemporary debate about human experimentation.

To this day, Israel is one of the Western countries where there is a specific law regulating experiments on animals in medicine but not on human beings. Since May 1997, the Israeli Ministry of Health has been preparing such a regulation and even a law draft on the topic passed the first vote in the parliament in 2007; but the law has yet to be enacted. The current legal framework for medical experiments on human beings is based on a 1980 specific additional regulation to the public health order, and on specific policies published from time to time by the Israeli Health Ministry (last one, 2014). This means concretely that Israeli legal policies, while referring explicitly to the 1975 version of the Helsinki declaration, did not refer to the Nuremberg legacy. While Israel may not be alone in this case, it still raises specific questions, since the country welcomed a great number of Holocaust survivors in general and survivors that were victims of these experiments in particular.

In this talk, I examine this relative silence and reconstruct the peculiar Israeli reception of the Nuremberg code up to the 1980 regulation on human experimentation. This relative silence may be explained, on the one hand, by the fact that the few physicians who survived the Holocaust and were active on the topic may have been themselves ill at ease with the Nuremberg medical trial and its conclusions. On the other hand, the medical establishment may have experienced difficulties in recognizing how medicine and medical science were involved in the Nazi medical crimes, beyond the involvement of the perpetrators themselves. Based on extensive research both authors conducted independently on the reception of the Nuremberg medical trial in the Israeli context (archival, IMA bulletin, etc.), the authors proposed to join forces and review the issue

further up to the current day. The issue of the relevance of a reference to Nuremberg or to the critical voice of the victims for future regulation will be examined.

When the impossible comes true: How to deal with promising therapies that are not yet confirmed

Michal Lotem (Hadassah Hebrew University Medical Center, Israel)

In March 2011 the FDA approved a new drug for advanced malignant melanoma, a deadly skin cancer that until then had no curative treatment. The drug, Ipilimumab, is a monoclonal antibody which blocks a negative regulatory mechanism of immune cells. Without any direct harmful effect on the cancer cells, it was demonstrated that the patient's own immune system could be led to induce tumor regression.

Two years later, another class of drugs, PD1 inhibitors, generated a similar clinical effect, benefiting a larger proportion of patients, with an improved safety profile.

The efficacy of these drugs and others are currently being evaluated for an enlarging spectrum of tumor types, all aiming at enhancing immune response against the malignant cells. Benefit, however, varies, with lung and gastric cancers showing a 25% response rate, while ovarian and pancreatic cancers rarely respond.

Aggressive PR campaigns, initiated by pharmaceutical companies, have generated a sense of urgency in patients and care givers to widen criteria of eligibility for the new drugs. Many are willing to pay an enormous amount to be treated even in the absence of proof of effectiveness.

In my talk, clinical data and dilemmas will be presented from the point of view of a clinician-researcher as well as of the patients and their families.

Medical Research in Sub-Saharan Africa: When the Field Became the Laboratory

Maureen Malowany (Hebrew University of Jerusalem, Israel)

While medical experimentation in partnership with observation has a history dating back to at least the 17th century and Robert Talbor's notion of 'tried and tested', it is not until the early 20th century that experimentation was brought to Sub-Saharan Africa by European colonial scientists and medical practitioners. From Robert Koch's quininization trials in the early 20th century in German East Africa through Hilary Koprowski's laboratory-produced lymph for polio immunization campaigns of the 1950s in the Belgian Congo, the laboratory was extended to human subjects in the field driven by a search for medical knowledge through research. Experimentation became a global practice, most often with vulnerable populations. Controls over experimentation following

the Second World War included the development of ethical guidelines and protocols for international application but the fields of Sub-Saharan Africa whose governance was in transition from colonial to post-colonial agendas and administration were not considered part of the regulatory frameworks.

We have moved from colonial pressures to globalized medical research and experimentation within Sub-Saharan Africa in the 21st century. In this presentation, through selected case studies, we will explore the ways in which medical experimentation and research are understood by the non-scientist participants. I suggest that medical experimentation that requires participants at the population level, in the field, is seen by the participants as treatment provision not research. What does it mean to speak of the 'public engagement with science' for the publics involved? We will explore the process of this engagement and the challenges these non-shared understandings pose for medical research.

Human subject research during the Nazi period: Rationalities, Victims, Potential Implications

Volker Roelcke (University of Giessen, Germany)

In contrast to long-existing stereotypes, human subject research during the Nazi period may not simply be understood as the result of outside political pressure, or mere ideology imposed on medical science. Rather, recent historiography has documented that practically all medical research activities in this period, including those in concentration camps or hospitals in the German occupied territories were initiated by physicians themselves. Many of the involved biomedical scientists were members of high-profile university medical schools, or research institutions such as Kaiser-Wilhelm-Institutes, or the Robert Koch-Institute, and at least two Nobel laureates were part of the involved scientific networks. The research questions pursued were perceived as important or even pressing according to the scientific standards of the time and the context of the war (e.g. with the imminent threat of epidemics), and the methods to solve these questions followed the scientific rationalities of the time; in part they even were innovative. These research activities may therefore not be rejected due to their irrational, or "pseudo-scientific" character, but because of their systematic disregard for the physical integrity, the subjectivity, and the wellbeing of the research subjects. Most of the research victims did not have any idea of the research aims or the interventions undertaken, nor did they receive adequate medical care during or after the research activities. Nevertheless, the victims were not anonymous sufferers; rather some of them started documentation of the medical atrocities already while in the camps, and they were important actors in post-war attempts to bring the responsible scientists to trial.