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MEDICINE AND THE LAW

Exploitation of the vulnerable in research: Responses to lessons learnt in history

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The Nuremberg Trials raised insightful issues on how and why doctors who were trained in the Hippocratic tradition were able to commit such egregious and heinous medical crimes. The vulnerable were considered to be subhuman, of decreased intelligence, of no moral status and lacking human dignity. The reputation of the medical profession had been undermined, professionalism questioned and the doctor-patient relationship damaged as a result of the Nazi medical experiments. The World Medical Association's Declaration of Helsinki has been hailed as one of the most successful efforts in rescuing medical research from the darkness of the scandals and tragedies in health research. The first Research Ethics Committee in South Africa was established in 1966 at the University of the Witwatersrand. From the mid-1970s other institutions followed suit. The promulgation of the National Health Act No. 61 of 2003, in 2004, resulted in strong protectionism for research participants in the country.

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Notwithstanding the examples of Lind, Jenner and self-experimentation, which were discussed in the previous issue,[1] examples of experimental research where people with vulnerabilities have been harmed have surfaced since medieval times. While not typical of experiments of that era, in the thirteenth century, Frederick II of Germany is said to have experimented with neonates so he could obtain knowledge about the development of language in humans.[2] Avicenna, an Arabian physician and philosopher, tested interventions directly on people because he felt that testing these on animals would not have any relevance for their use on humans.[2]

Briggle and Mitcham[3] claim that in the main, the first studies of experimentations on humans took place on slaves and the poor, and that this coincided with the development of the new science of anthropology that Europeans used to study non-European peoples.[3] Generally speaking, human experimentation was initially undertaken on those who were considered to be uncivilised and often less than human, with diminished or no moral status. Even colonial and imperial rule was often justified by anthropological research that described the native peoples of Africa, the Americas and Asia as being of inferior intelligence and ability, and hence in need of paternalistic rule by European powers or immigrants. Their anthropological findings were based on the category of race.[3]

In this article, the Nuremberg Trials and their implications are briefly discussed. The emergence of international norms and standards for protection of participants in research is considered, together with South Africa (SA)'s response to the global scandals and tragedies in health research.

The proceedings of the Nuremberg Trials

Among the greatest tragedies in human research experimentation, the heinous studies conducted during World War II by Nazi doctors on 'racially inferior' Jews and other 'deficient' groups,[4-8] and by Japanese doctors on people, in the main Chinese, that they determined to be less than human[3,9,10] take centre stage as the most notorious.

In the aftermath of World War II, the horrors of experimentations on concentration camp inmates were publicised during the Nuremberg Trials in Germany, which lasted from December 1946 to August 1947.[3,5,7,11] The trial specific to the medical atrocities is the case of the United States of America v Karl Brandt *et al.* – also referred to as the Nuremberg Doctors' Trial.[12] Evidence given at the trial underscored the robust and relentless exploitation and wrongs prevalent in medical studies at that time. The vulnerable were considered to be subhuman, of low intelligence, of no moral status and lacking human dignity. The Nuremberg Doctors' Trial raised insightful issues on how and why doctors who were trained in the Hippocratic tradition were able to commit such egregious and heinous medical crimes. As medicine was supposed to be one of the 'world's most advanced scientific cultures',[11] questions on whether these doctors actually understood that they were committing crimes were raised. The defendants' lawyers during the Nuremberg Doctors' Trial, using a utilitarian approach, highlighted that the Allies had also engaged in medical experiments in servicing the war effort,[5,11] that the type of medical experimentation performed in the concentration camps during the war was commonplace even before the war[11] and that there were no legal restrictions on such experiments.[6] As the prosecution's attempts at demonstrating that there were clear international rules governing medical experimentation wavered, the judges attempted to create their own set of rules, and two medical advisors to the judges, Drs Andrew Ivy and Leo Alexander, were tasked to do this.[4-6] They drafted a ten-point memorandum entitled *Permissible Medical Experimentation*,[7] which then became known as the Nuremberg Code, the aim of which was to obtain a way forward on one of human experimentation's most fundamental conflicts: that of balancing the need for advancing medical science for the benefit of society with the rights of individuals to 'personal inviolability, autonomy and self-determination'.[11]

The trial, however, was based on international law as outlined in the *London Agreement on the Punishment of the Major War Criminals of the European Axis* (London Charter) in 1945.[12,13] Although international law had previously not codified specific war crimes, the crimes specified in the London Charter included those contained in the Hague Regulation of Warfare (1907),[14] which Germany

had signed.[12] Germany had also signed the Kellogg-Briand Pact of 1928,[15] which condemned aggressive wars, and the Geneva Convention[16] in 1929, which specified in its rules how prisoners of war should be protected.[12] Therefore, both the judgment and the Code were *de jure* international in character. The Nuremberg Code is hence undoubtedly the first international medical ethics code.

It is interesting to note that besides Germany being signatory to international instruments for protection of prisoners of war, by the end of the 19th century it had started to develop some of the world's most stringent and clearly defined medical ethics regulations,[2] and in March 1931, the Reich Health Council (*Reichsgesundheitstrat*) issued the *Regulations Concerning New Therapy and Human Experimentation*.[17] The far-reaching directives in these regulations were 'among the most comprehensive research rules by any standard at the time'.[2] Some aspects that involved contentious issues such as voluntary informed consent, therapeutic research, non-therapeutic research and benefits were much more structured and detailed compared with the principles in the Nuremberg Code. It was stressed that the rights and dignity of subjects had to be protected at all times, and on the issue of non-therapeutic research it underscored the prohibition of experimentation in all cases where consent had not been given. Unfortunately, despite the strong protectionism in the regulations, respect for moral status, upholding dignity and according special protections for subjects enrolled in research – fundamental values highlighted in the Reich Health Council's regulations – were ignored.

The international medical community had no option but to reflect on its conduct in the aftermath of World War II and the Nuremberg Doctors' Trial. There were now great uncertainties regarding the role that the medical profession had to play in a post-war society. This was of huge concern to national medical associations as well.[18] The reputation of the medical profession had been undermined, professionalism questioned and the doctor-patient relationship damaged as a result of the Nazi medical experiments. Doctors all over the world were anxious that the profession as a whole could be affected negatively by the sweeping condemnation of the Nazi physicians. Therefore, it is not surprising that the revelations at the Trial were also a major factor leading to the foundation of the World Medical Association (WMA).[19]

The role of the WMA

At the first meeting to discuss an international association of doctors and national medical societies held in London in 1946, there were 32 national medical organisations present. The objective of such an international association would be to promote international medical relations, and the advancement of medicine and its social and cultural aspects. The first meeting of the newly formed WMA in 1947 was held 1 month after judgments had been delivered in the Nuremberg Doctors' Trial.[20] The Declaration of Geneva,[21] a statement on the physician's dedication to the medical profession, was among the first acts of the WMA and was endorsed at the 1948 General Assembly. The importance of this declaration is that when adopted, considerations of nationality, race, party politics and social class would not interfere with the physician's responsibility for the patient's welfare. This applied to both situations of clinical care and research. Already in its very first declaration, the WMA had started the process of protectionism for those patients involved in research.

The Declaration of Helsinki (DoH) of 1964 was among the first international guidelines for human experimentation and it 'reflected the longstanding interest of the WMA in issues of medical ethics and the enduring shadow of the Nazi medical war crimes.'[20] The journey of the first DoH was long and turbulent. It involved more than a decade of active discussion and debate among the WMA members before the final document, which was also strongly influenced by the principles of deontology and virtue ethics, could be presented to the WMA's General Assembly for adoption in Helsinki in 1964.[20] The DoH has been hailed as one of the most successful efforts in rescuing medical research from the darkness of the tragedies resulting from the heinous atrocities in the name of medical research in Nazi Germany.[20] It has undergone several revisions, with the latest being in October 2013.

Protectionism in SA[22]

Henry Knowles Beecher,[23] a professor in research into anaesthesia, published a landmark article in the *New England Journal of Medicine* in 1966, entitled 'Ethics and clinical research'. This article was the catalyst for the establishment of protectionism for research participants in SA. Beecher detailed 22 cases of research conducted by leading researchers at leading research centres that he claimed violated the basic standards of ethical research. These studies had been published in highly acclaimed and reputable reviewed journals. He had submitted 50 cases in his original list but the number had to be reduced due to the space constraints of the journal.[6]

The history of protectionism from a regulatory perspective in SA is quite meagre, and only emerged over the past 2 decades. This is understandable, as prior to 1994, citizens in the country were oppressed and subjected to the repressive apartheid regime in which people who were not white were considered to be subhuman, lacking human dignity and of decreased or no moral status, similar to the European anthropological viewpoint described above. However, the apartheid regime and philosophy were not successful in removing moral agency from the virtuous physician-researcher in the country, and in the late sixties, after Beecher's seminal paper was published,[23] steps were set in motion at the level of individual institutions where research was conducted to introduce protections for all, and in particular the vulnerable, who were involved in research. Cleaton-Jones[24] states that the Beecher paper was considered such a milestone in research ethics that 4 months after its publication, at the suggestion of Prof. John Hansen of the Department of Paediatrics at the then Baragwanath Hospital, which was situated in a racially demarcated township, Soweto, the University of the Witwatersrand formed the Committee for Research on Human Subjects (Medical). Hence, this could be described as the birth of protectionism for research participants in SA. The committee was the first research ethics committee (REC) in the country, and probably one of the first in the world. The committee underwent a name change in 2003 to the Human Research Ethics Committee (Medical)[24] and is still functional today, and is probably one of the leading RECs in the country. From the mid-1970s, other institutions followed suit, and currently there are over 45 RECs registered with the National Health Research Ethics Council in the country.[25]

In the beginning, guidelines for the protection of participants in research were lacking in the country. However, in 1978, Prof. de V Lochner, then vice-president of the SA Medical Research Council (SAMRC), visited the World Health Organization in Geneva, and upon his return, set to work producing a set of guidelines for the SAMRC. In 1979, the first set of guidelines, entitled *Guidelines on Ethics for Medical Research*, was produced by the SAMRC. These guidelines have undergone several revisions since.[24]

The National Department of Health in 2000 produced *Guidelines for Good Clinical Practice in Research*.[24] This was updated in 2006.[26] The promulgation of the National Health Act (NHA) No. 61 of 2003,[27] in 2004, resulted in strong protectionism for research participants in the country. Chapter 9 of the NHA focuses on health research and health

research ethics. As a result of the stipulations of chapter 9, *Ethics in Health Research: Principles, Structures and Processes*[28] was launched in 2004. It was a response to the NHA and, while written as guidelines, had the authority of rules. It has undergone amendment, with the second edition being issued in 2015.[29]

Conclusion[22]

Exploitation in health research of the vulnerable who were considered to be subhuman, lacking in intelligence, moral status and human dignity goes back several centuries. Germany was both signatory to international instruments for protections of prisoners of war and also had a stringent set of guidelines for protection of participants in medical research. Despite this, evidence given during the Nuremberg Trials highlighted the robust and relentless abuse, mistreatment and wrongs prevalent in medical studies at that time. The WMA's DoH provides international norms and standards for protections. In SA, individual institutions responded to the global position by setting up RECs to provide ethical oversight in health research, which have existed since the 1960s. This became a statutory requirement in the early 2000s. In the next issue of the *SAMJ*, I will describe the development of the ethico-regulatory protections in health research in the country.

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