

An Anniversary to Remember from the Pharmacology: The Nuremberg Trials

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Editorial

Between 1945 and 1949 after World War II, the former leaders of the German Nazi regime were tried as war criminals by an international military tribunal consisting of judges from the four Allied nations: the United States, Britain, France, and the Soviet Union [1] at the famous Nuremberg Trials. Exactly 70 years ago, in December 1946, hearing began in the trial of 23 doctors or collaborators implicated in the crimes of this totalitarian regime (The Doctors' Trial; United States of America vs. Karl Brandt). This trial exposed a terribly abnormal ideology which sanctioned and institutionalized criminal behavior related to public health and human research [2]. Among violations of ethics in medical professionals, transgressions included the use of drugs.

In 1933, Adolf Hitler became Chancellor of Germany and the National Socialist Party (*Nationalsozialistische Deutsche Arbeiterpartei*) gradually established a one-party state. The whole regime had stayed in power only for about 12 years, from 1933 till 1945 after its defeat at the end of WWII by the Allies Forces. But the damage under Nazi regime was tremendous, including the medical ethics. The Nazi government was soon enacting a series of laws referring to racial segregation and protection of the race, collaborating with certain sectors of the German medical community. The use of pharmacological tools in numerous activities, regardless of ethical codes, was a common practice. During this period, drugs were used in persons subjected to enforced sterilization, within the framework of implementation of the *Gesetz zur Verhütung erbkranken Nachwuchses* (Law for the Prevention of Genetically Defective Progeny, better known as the Sterilization Act): subjects with diagnoses of congenital feeble-mindedness, schizophrenia, "circular madness" (manic-depressive psychosis), hereditary epilepsy, hereditary St. Vitus' dance (Huntington's chorea), congenital blindness and deafness, pronounced bodily malformations of a hereditary nature, or severe chronic alcoholism [3,4]. Drugs were also used in the Euthanasia Program (*Gnadentod*, "mercy death"), popularly known as Action T4, a program that allows the mass extermination of patients with "deficiencies" or mental pathologies, and fundamentally in a variant known as "wild euthanasia", where procedures carried out in the "healthcare" institutions themselves [3,5,6]. In some institutions, health personnel hastened the patients' deaths with the long-term use of low doses of barbiturates, leading to terminal pneumonia. Even exterminations were carried out less discreetly, using the lethal injection of drugs, such as opiates and scopolamine [7]. Despite the sterilization and euthanasia programs, there were also drug research projects in physically and mentally disabled in hospitals and universities did not have any informed consent. Another violation of

ethical principles was the use of healthy subjects from concentration camps for human experiments in pharmacology [7,8] where other sectors of the Nazi regime's health system playing a substantial role, such as the chemical-pharmaceutical industry [9]. Thus, sulphonamide, arsenical derivatives, and other preparations - its composition (B-1012, B-1034, 3382 or rutenol, 3582 or acridine) is not precisely known - were tested in different camps, as Auschwitz [9]. Those tests were generally related to the treatment of infectious diseases, such as typhus, erysipelas, scarlet fever or paratyphoid diarrhoea, and death rates of experimental subjects were extremely high. Experiments with psychotropic drugs were also performed [7-9]: effects of combined administration of metamphetamine (Pervitin[®]) and phenobarbital (Luminal[®]) as well as the anesthetic properties of sodium hexobarbital and chloral hydrate in surgery on healthy subjects, and the lethal injections of aconitine and apomorphine [10] (Buchenwald camp); administration of mescaline to assess the hidden schizophrenic behavior of inmates or to induce it (Dachau concentration camp); "brainwashing" studies with pharmacological agents (barbiturates and morphine derivatives) on Polish and Russian prisoners, resulting in high mortality rates [10] (Auschwitz camp). But the most possible ethical violation in human experiment was using pharmacological agents as tools for murdering healthy and innocent people [7]. Examples of such atrocities also existed in the darkest chapters of the medical history of the Third Reich, as the murder of children with hexobarbital (Evipan[®] or Evipal[®]) in Auschwitz, or Soviet prisoners with aconitine in Buchenwald camp.

In response to the atrocities committed by Nazi doctors, scientists in the field of human research released the details in the Nuremberg war crimes trials. Being published in August 1947, The Nuremberg Code, which was designed to prevent any repeated tragedy resulting from barbarous attacks on human rights and human wellbeing, is the first international code for research with human beings. This is based on the Hippocratic precept of *Primum non nocere* ("first, do no harm"). It laid down norms for experiments on human subjects, with special emphasis on the need to obtain the person's informed consent, which has since then been considered the cornerstone of protecting patients' rights [11,12]. The Nuremberg Code combines both Hippocratic ethics and the protection of patients' rights in a single document, requiring that researchers need to protect patients' interests, and that subjects themselves also participate actively in their own protection.

Although the Nuremberg Code has not been formally adopted as a legal norm by any nation or medical association, it has had a profound influence in the area of human rights and bioethics, and has formed the basis of subsequent norms and codes in the field of biomedicine, as the Declaration of Helsinki (1964) or the International Ethical

Guidelines for Biomedical Research Involving Human Subjects (1982) [11], and nowadays, has been adopted as basic principle by most, if not all, ethic committees for human research or the institutional review boards, to protect the rights of human subjects participating in medical experiments. In relation specifically to the field of pharmacology, various international guidelines were subsequently developed on this ethical model, including the CIOMS (Council for International Organizations of Medical Sciences) and ICH (International Conference of Harmonization) Ethical Guides to Good Clinical Practice (GCP) [9], and in whose drawing-up the pharmaceutical industry played a relevant role. Furthermore, the development of new medicines and the setting up of drug-monitoring programmes on those already on the market were to take place within the framework of strict guidelines, subject not only to control by the relevant national and international health authorities, but also to a series of internal controls, developed by the industry itself to ensure that the benefit and safety of the patient always takes priority over any other objective.

During the last 70 years, it has advanced substantially in the restoration of ethical codes and norms to protect patients. To avoid continued governmental abuse in those fields, a range of strategies is needed, including update and publicize international pacts, agreements, and treaties, as well as do continuing education for health professionals at both undergraduate and postgraduate levels. To be closely vigilant on the part of authorities and human rights organizations is also important. However, the question is whether we can learn, and pharmacology is not an exception, the lessons that, for example, were tried in Nuremberg Trials.

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