Press release

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At least 3000 patients affected by informal drug trials at the Psychiatric Clinic Münsterlingen

From 1946 to 1980, clinical trials involving at least 67 test substances were conducted at the Psychiatric Clinic Münsterlingen, historians at the University of Zurich have shown. Senior psychiatrist and later clinic director Roland Kuhn (1912–2005), known for discovering the first anti-depressant Tofranil, played a key role in the trials. He received around eight million Swiss francs (adjusted for inflation) from pharmaceutical companies. Further involved were the clinic staff, thousands of patients, their relatives, other clinics, private doctors and public authorities.

Dimensions of the trials

The research team led by Marietta Meier, Professor at the University of Zurich, has identified almost 120 experimental substances: 67 substances with clear evidence for clinical trials, and another 50 substances, for which inquiries or deliveries have been documented. The drug trials varied greatly: from short tests with a few patients to large-scale, long-term trials involving over 1000 patients. About 1100 people subjected to tests could be identified by name, while Kuhn himself has mentioned a total of almost 3000 cases. Meier suspects that a lot of cases went unreported – in 34 years of trials, at least 3 million individual doses of test substances reached Münsterlingen – the actual number of individuals affected is likely to be much higher.

Network of actors

In addition to the Psychiatric Clinic Münsterlingen and the pharmaceutical companies, a broad network of institutions and individuals were involved in the trials: inpatients and outpatients, their social environment, doctors in private practice, other clinics and authorities. The trials involved a diverse set of patients. Categories such as gender, social background or guardianship were irrelevant in the selection process. No difference was made between home and foster children and children or adolescents who lived with their parents. The only exceptions were “severe, chronic cases”, which Kuhn regarded as hopeless. He reserved these patients for trialing the effects of substances with which he was not yet familiar.

Testing practice did not comply with standards

Kuhn claimed his method had always been to observe the individuals, never to reduce patients to data only. The Münsterlingen trials were thus exploratory and the conditions of the trials were not fixed from the outset. This open approach contradicted a more systematic, scientific approach that emerged from the 1960s onwards. The pharmaceutical companies, however, hesitated to impose proper restrictions on Kuhn. As a result of the new regulations of drug registering and test methods, Kuhn’s role as an investigator shifted over time: The companies now used him for quick tests at the very beginning of the clinical trial phase of a new substance or gave him a lot of leeway in exploratory long-term trials.

“Kuhn claimed that test patients were always closely observed and monitored,” says Meier. However, the overworked clinic staff lacked the time to supervise test participants closely, to create complete written records or to carry out all the necessary examinations. “Consistent monitoring can therefore not be assumed and there were incidents and deaths,” says Meier. Rarely did patients in Münsterlingen receive comprehensive information on the substances tested, nor did they explicitly consent to clinical trials. Only in some cases, especially with outpatients or psychiatrically trained patients, Kuhn provided more detailed information.

Kuhn's motives

Kuhn always stressed that he had conducted the clinical trials in his spare time. The fact that he had access to the clinic's staff, infrastructure and patients was never acknowledged by him. In his view, the trials and their results were his personal achievement. Therefore, it seemed natural to him that the pharmaceutical companies would pay him for the research work. His research interest and financial motives can hardly be separated. Money was primarily a form of recognition and confirmation of success. At the same time, he was characterized by great pharmacological optimism. Ultimately, the trials ensured access to the latest substances and relieved the clinic's drug budget. This was probably one of the reasons why tests sometimes merged seamlessly into routine medication.

Historical assessment

Around 1962, first regulations on test methods and the approval of new drugs, risks and side effects began to emerge. The tests were now to be gradually standardized and geared to statistical, quantitative measures. Impulses for this change came from the authorities, but also from the pharmaceutical industry. Measured against these standards, Kuhn's testing practice deviated from the norm in three points:

Firstly, some experimental substances arrived at Münsterlingen without having passed all the stages of preliminary testing that were commonplace at the time. A new substance was first to be tested for toxicity in the pre-clinical phase, followed by tolerability tests on voluntary, healthy test persons. Only then did the clinical phase with tests on patients begin. In some cases, however, pharmaceutical companies had not yet completed the toxicological tests when the clinical trial was assigned to Kuhn.

Secondly, Kuhn did not comply with the new methodological requirements. Although these were not legally binding for a long time, they first became necessary for drug registration in the USA and, from the 1970s, also in Switzerland. Thus, his results assumed an important but informal status for pharmaceutical companies. In addition, Kuhn did not adhere to the companies' prescribed starting and end date of a trial. Certain substances were continually used and also passed on to third parties after the pharmaceutical companies had officially stopped the trial.

Thirdly, the Helsinki Declaration of 1964 and the 1970 guidelines of the Swiss Academy of Medical Sciences on experiments with humans introduced new ethical guidelines. In the 1970s at the latest, the medical profession began to develop an awareness of ethical issues in clinical trials on humans and the associated risks and dangers. Kuhn initially took little notice of these and was opposed to patient consent.

Everyday transgressions

In addition, several everyday practices seem problematic from today’s perspective. For example when Kuhn was cautious enough to withdraw a dangerous test substance with one patient, but at the same time included new patients in the same experiment. When drugs with unpredictable effects were first administered to hopeless, so-called “severe cases” in order to gain an initial picture, and then transferred to patients with a more favorable prognosis. When non-registered substances were delivered in disguise or patients were induced to take substances under increasing pressure. When patients were included in trials without information or consent, even though guidelines requiring informed consent already existed. When, not least for financial reasons, a large proportion of patients were treated with test substances instead of approved drugs.

Further research needed

Little is yet known about clinical trials in Switzerland and elsewhere. Münsterlingen is exceptional for its excellent archival situation – for the first time, clinical trials can be investigated closely, and the sources are by no means exhausted. With many questions remaining, such as the number of serious adverse events and deaths for instance, further research is necessary. In order to complete the picture, cases of drug trials in other clinics need to be compared – the sources consulted show a broad spectrum of domestic and foreign testing centers, from clinics to homes and private practices.

Publication

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