Use of Max Cloetta's Narcotic Solution for Prolonged Sleep Therapy in Latvia in the 1930s

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Introduction. In 1936, professor Hermanis Buduls (1882–1954), Head of the Department of Psychiatry at the University of Latvia and Director of Rotenberg (Sarkankalna) Hospital for mentally ill in Riga, ordered a narcotic solution developed by Professor Max Cloetta (1868–1940). Cloettal or "Cloetta Mixture" was produced in cooperation with pharmaceutical company Hoffmann-La Roche (Roche) from Basel and used for the so-called prolonged sleep therapy ("Dauersshlaf", "Dauernarkose") for schizophrenic patients. Also Professor Pauls Stradiņš, Medical Director of 2nd Riga City Hospital and Head of General Surgery Department at the University of Latvia purchased the same medicine for undiscovered yet reason. The related documents are found in the archives of the Latvian State Historical archive in Riga and in the Roche Historical archive in Basel.

The aim. The aims of the research are to identify benefits of Cloetta's narcotic solution, to describe the procedure of sleep therapy, and to point out Roche`s role in the production of the solution.

Materials and methods. Sources used were documents from the archives, a publication by Prof. Max Cloetta, Director of the Pharmacological Institute of Zürich University and Prof. Hans W. Maier, Director of the Psychiatric Clinic Burghölzli of Zürich University, describing benefits of Cloetta's narcotic solution (1934). Non-direct sources were different articles about the history of barbiturates after their clinical introduction in the beginning of 20th century.

Results. Official pioneer of sleep-therapy was the Swiss psychiatrist Jakob Klaesi, who used Roche's barbiturate compound Somnifen and described his experience in 1922. In an article published in 1934, Cloetta and Maier pointed out the disadvantages of Somnifen, like severe hyperaemia and impaired circulation in parts of the body, resulting in fever, pneumonia and decrease of diuresis. After the cure, patients were subjected to agitation. Cloetta, convinced of the benefits of sleep-therapy, but aware of the problems with Somnifen, succeeded in developing a mixture of substances that guaranteed stable sleep over a period of 8–12 days with a reduced risk of side effects. He reduced the amount of barbiturates and added other sedatives. The combination was a clear solution containing Isopropylallylbarbiturate, the sedatives and hypnotics Paraldehyde, Amylenhydrate and Chloralhydrate, alcohol. To assist blood circulation in case of minor dysfunctions, the digitalis preparation Digalen and the adrenergic substance Ephedrinehydrochloride were added. The mixture was applied rectally and induced sleep within 15–20 minutes. To maintain sleep, the solution was given 2 to 4 times a day. To avoid aspiration, patients were not fed orally, but received Glucose and saline solutions via rectal infusion. Effects of sleep therapy were, according to Maier, surprisingly satisfying, with several chronically agitated schizophrenics improving for months after the cure. With Cloetta's solution there were no more deaths, though some of the therapies had to be terminated due to side effects. In the course of his clinical trials, Cloetta had to deal with side effects caused by insufficient purity of the solution. To avoid this, Cloetta and Maier entrusted Hoffmann-La Roche with the production of the compound to guarantee impeccable quality. At the time of Cloetta's and Maier's article, the mixture was not on the market and could only be ordered as samples from Roche. Thus, the use outside a clinical setting could be avoided.

Conclusions. In the absence of therapeutic alternatives, sleep therapy seemed a promising approach in the treatment of schizophrenic patients in the 1920s and 30s. Cloetta's solution improved tolerance by reducing the content of barbiturates. To guarantee stable quality the production was delegated to pharma company Hoffmann-La -Roche. Professors H. Budulis and P. Stradins were customers for samples of Cloetta's solution (Cloettal) from Roche. So far this is the only documented indirect evidence found, that the prolonged sleep therapy was used in Latvian mental institutions as well. The decline of sleep therapy can be attributed to safety problems and the availability of new more promising methods like insulin coma therapy and cardiazol convulsive therapy, both introduced in Latvian mental hospitals in the end of year 1936.