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A story of science and heroism : Rudolph Weigl's Typhus vaccine

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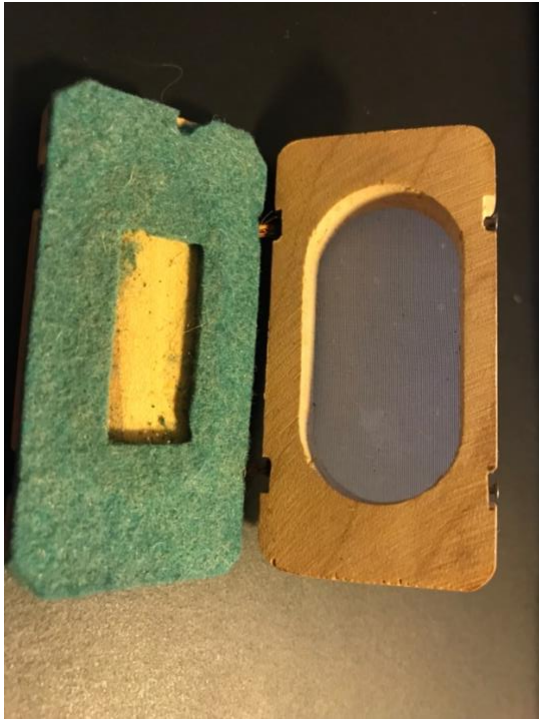
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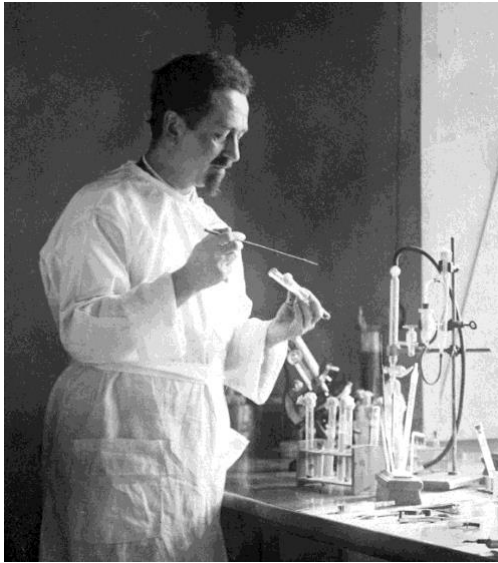
For NPH4 Chapter 1



Figures 1 and 2. The lice cage

The long journey of a life saving lice cage

In April 2023, the Pharmacy Museum in Krakow, Poland received a very special gift – a small cuboid wooden box with a lid attached with delicate wire hinges (Figures 1,2). The major part of the lid was made of strong mill gauze, while the bottom was cut out of felt, possibly from an old military coat. This box was intended to keep the lice that were feeding on human blood sucked out through the mill gauze, as a part of the technology of producing a vaccine against the epidemic louse-borne (exanthematous) typhus. Its inventor was the famous Polish biologist and parasitologist of Austrian origin Professor Rudolph Weigl. In the 1920s, (Figure 3) Weigl described the etiology of this type of typhus and its pathogen - *Rickettsia prowazekii*, discovered in 1916 by Henrique da Rocha Lima and named after two investigators, Ricketts and von Prowazek (Bernardes Filho & Avelleira 2015). Weigl published his description of the anti-typhus vaccine he invented, in 1930. He was nominated for the Nobel Prize, but never received it due to his excessive modesty, politics, and World War 2 (WW2). (Szybalski1999, Gryglewski, 2022). However, he did receive many other awards and distinctions, including recognition as the Righteous Among the Nations from Yad Vashem (Yad Vashem 2023).



Figure

3. Professor Rudolf Weigl

The then Polish city of Lviv where Weigl was working, became a global centre for scientists to research typhus and methods of vaccine manufacture. The first mass-scale use of Weigl's typhus vaccine was the vaccination campaign in the Carpathian Mountains, where typhus remained a very serious threat. Soon after that, mass vaccinations in the Italian, Belgian, and French colonies in Africa took place, and widespread applications in China and Australia. Throughout history, to the mid-20th century, typhus was responsible for major epidemics and millions of deaths. Its first written description comes from the convent near Salerno in Italy in 1083. Severe typhus epidemics were often companions of wars or famines. In the First World War (WW1), major epidemics occurred along the Eastern Front, beginning in Serbia (Tschanz 2023). In World War 2 (WW2), epidemics struck in North Africa and the Mediterranean. (National Library of Medicine,2023) Delousing, sanitary protection and social distancing were the main preventive measures available. At the time of its development, Weigl's vaccine was the first and only clinically effective remedy against this dangerous disease (Szybalski 1999, Gryglewski 2022).

The vector of epidemic typhus is the louse. *Rickettsia prowazekii* grow in the louse intestines and are then excreted with feces, subsequently rubbed into the louse bite wound of a person who is then infected, leading to rapid spread, and causing epidemics. Mortality was up to 60% when untreated, before the antibiotics era (ECDC 2023).

Weigl's method of producing a typhus vaccine included growing healthy lice that were fed with human blood provided by volunteers (human "feeders"). The lice were sucking blood through feeders' skin during sessions lasting for about 30-45 minutes daily, for 12 days, while being kept in small boxes – lice cages – designed especially for that purpose and attached temporarily to volunteers' legs with straps (Figure 4). Then the lice were manually infected under a microscope, with a microcapillary, with typhus so that *Rickettsia prowazekii* could propagate in their midgut cells. The infected lice were grown for 5 more days by sucking the blood of the intensively vaccinated persons, who were injecting the pathogen into their guts. No serious typhus cases occurred among the injectors, confirming the high efficacy of Weigl's vaccine. The lice were then killed by 0.5% phenol, their midgut was dissected, and from this material, the vaccine was manufactured (Szybalski 1999).

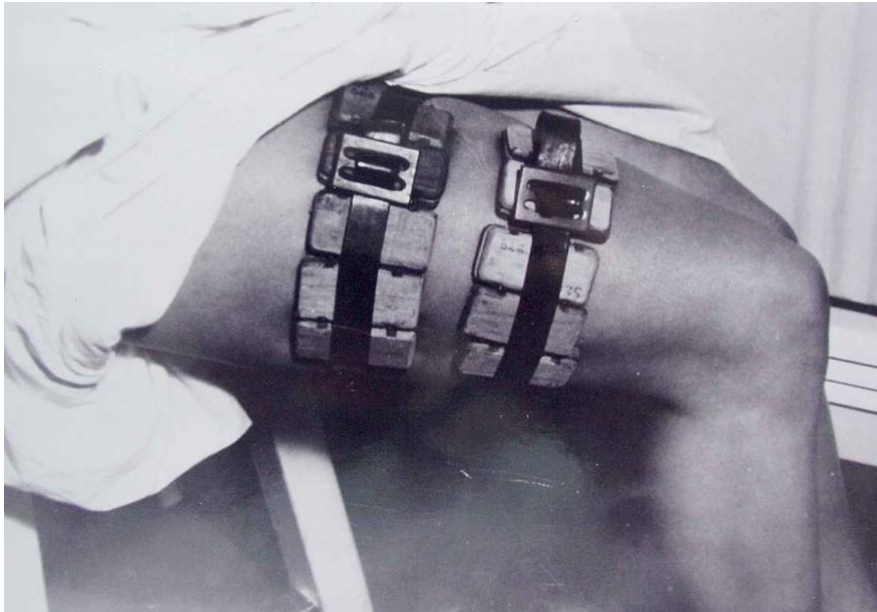


Figure 4. Lice cages on a human 'feeder'

Manufacturing of the vaccine was continued when in 1939 Lviv fell under Soviet occupation, and during the subsequent German occupation in 1941 when the Nazi Third Reich attacked the Soviet Union, its former ally. Weigl stayed the head of the institute where production of the typhus vaccine was taking place, reserving his right to choose co-workers. His work was very much needed by the Germans, but thousands of non-Germans were also benefitting from vaccines smuggled from the laboratories and distributed within the Polish Underground State, as well as the Jewish ghettos of occupied Lviv and Warsaw. Moreover, the lice feeders and other people involved in the production of the vaccine, considered useful for the Nazi state, were receiving from Germans the documents protecting them from repression. 5-6 million individuals were vaccinated in Eastern Europe during the German occupation and thousands of lives were saved through this means.

According to recent research, an important way to contain epidemic typhus in the Warsaw ghetto was the remarkable public health effort, perfectly orchestrated by the Jewish physicians, led by Ludwik Hirszfild. Hundreds of lectures helped to educate the public about the importance of personal hygiene, social distancing, and self-isolating when sick. A *secret university* was set up to train medical students in infection control. Community leaders were mobilized to organize elaborate sanitation programs. Weigl's vaccine smuggled into the ghetto, became the perfect complement to these efforts (Stone et al 2020, Klein 2020, Hirszfild 2011). Sadly, for most of the Warsaw ghetto inhabitants, the successful efforts to save their lives through coordinated science-based public health action were destroyed by the German National Socialism ideology. The Nazis organized the Warsaw Ghetto and then perversely, liquidated it as well. Hypocritically they explained liquidation by the need to combat the typhus epidemic. Jews from Warsaw were exterminated in Treblinka, the German concentration camp in occupied Poland. Nazism shamefully abused public health actions.

Hirszfild participated in combating typhus epidemics and organizing health care already in Serbia, in WW1. He discovered blood types and divided them into O, A, B, and AB groups. As a Polish Jew, he became one of the few Shoah survivors, managing to escape from the ghetto and hide until the end of the war, with the help of the Polish families. In 1950, Hirszfild was nominated for the Nobel Prize for explaining the mystery of the mother-fetus serological conflict (Klein 2020, Hirszfild 2011).

After WW2, Lviv became part of the Ukrainian Socialist Soviet Republic. Prof. Weigl moved to Poland within its new borders, working at the Jagiellonian University, then at the University of Poznan, and continuing vaccine production in new places (Szybalski 1999, Kosiedowski & Basza 2013, Gryglewski 2022).

This small box was made in Lviv or Krakow in the 1940s, where it served as an instrument to produce typhus vaccine. In 2001, the lice cage was presented by Prof. Wiesław Magdzik, the Nestor of the Polish epidemiology, vaccinology, and public health, to his British friend Prof. George Pollock, also a public health specialist. It was later presented to John Middleton, Past-President of ASPHER. In 2023, on the decision of both Britons, the lice cage was brought to Krakow, where it was carefully handed over to Dr. Tomasz Bochenek, the Deputy Director of the Institute of Public Health of Jagiellonian University (Figure 5) This lice cage is a precious relic of public health, epidemiology, and medicine; a relic of pharmacy (a genuine and innovative manufacturing technology of medicinal products) and also a relic of heroic humanitarian support in times of peace and war. It was finally delivered to Dr. Agnieszka Rzepiela, the Director of the Museum of Pharmacy of the Jagiellonian University Medical College (Figure 6).

Let's hope that the museum's visitors, while stopping with curiosity at this small wooden box, think for a moment about those millions of human lives saved in many ways, in many locations of our planet, due to such tiny items.

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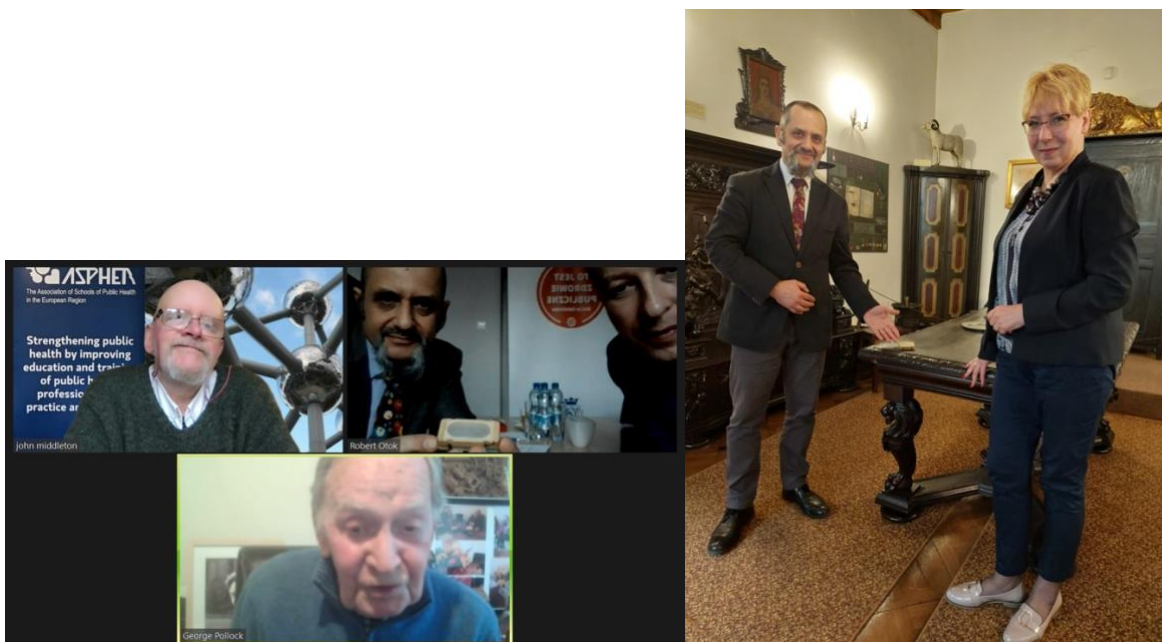


Figure 5. (left) George Pollock, John Middleton, Tomasz Bochenek, Robert Otok ASPHER director receiving the Lice box, virtually, February 21st 2023.

Figure 6. (right) Tomasz Bochenek presenting it to Dr. Agnieszka Rzepiela, Director, Pharmacy Museum of the Jagiellonian University Medical College, April 2023.

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