100 years ago: The Nobel Prize goes to Swiss surgeon Theodor Kocher for research on goiter and the thyroid

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“Eliminating goiter and cretinism worldwide would amount to more than building the Egyptian pyramids” Theodor Kocher

In 1909, the Swiss surgeon Theodor Kocher was awarded the Nobel Prize in Physiology and Medicine “for his work on the physiology, pathology and surgery of the thyroid gland” [1]. Kocher had no choice but to get involved in the thyroid field: he was born, raised, trained, and appointed professor of surgery at the University of Berne, Switzerland and at that time the region was still ravaged by an incredibly high prevalence of goiter and cretinism. In 1883, in the city of Berne, 55% of schoolchildren had a goiter, often even a large nodular one. In 1923 the Canton of Berne (at that time with a population of about 600,000) housed 700 cretins in special institutions, in addition to those cared for by their family at home [2]. So it is no wonder that of the 143 papers in Kocher’s publication list, 23 papers (16%) deal with the thyroid gland [3].

Kocher was a surgeon, and he assumed his main task was to develop safe methods for removing large goiters causing pressure symptoms. Indeed, he refined the operative technique in a way that let goiter surgery become routine, with a mortality of less than 1%. Kocher used his surgical activity to unravel the function of the thyroid gland which in 1872, the year of Kocher’s appointment to the Chair of Surgery, was still totally unknown. His experience as a surgeon allowed him to define new clinical pictures and pathophysiology, as well and novel surgical and pharmacological treatments for goiter.

In 1883, Kocher reported to a meeting of the German Society of Surgeons on the follow-up of 18 patients after total thyroidectomy [4]. Only two were in good general health. The remaining 16 had developed the following clinical picture: fatigue, weakness and pain in the extremities, cold intolerance, slowing of mental function, movements and speech, swelling of extremities and eyelids, low blood pressure, anemia, growth arrest (if in the growth phase). He coined the term “cachexia strumipriva” for this condition and correctly considered it the same as myxedema, a disorder first described by two English physicians, Ord and Gull. In the following years Kocher elaborated on cachexia strumipriva/myxedema [5], which were improved by oral thyroid extracts or, temporarily, by thyroid tissue transplants.

On December 11, 1909, Kocher gave his Nobel lecture, entitled “Concerning Pathological Manifestations in Low Grade Thyroid Diseases” [6]. By that time, Kocher had further elaborated on the features of cachexia strumipriva; he had correctly concluded that the clinical picture of cachexia strumipriva was the opposite of Graves’-Basedow’s disease. The terms “hypothyroidism” and “internal secretion” appear for the first time in this lecture, which shows that Kocher had advanced in his understanding of thyroid physiology and become familiar with the concept of hormones, though the term had not yet been coined. He had set up a research laboratory where he and his coworkers studied the lymphocyte count and blood coagulation.
in Graves’ disease and on the iodine content of euthyroid and hyperthyroid goiters.

By 1910, Kocher’s group had operated on 469 hyperthyroid goiters [7], an undertaking that before Kocher’s improvements of the operative technique was considered particularly risky. Kocher had meanwhile accepted Mösir’s view that Graves’-Basedow’s disease was due to a hyperactivity of the thyroid gland. He had noticed that there were two forms of hyperthyroidism: Graves’-Basedow’s disease, characterized by exophthalmus and diffuse goitre, and Jod-Basedow (today called iodine-induced hyperthyroidism). The latter occurs in pre-existing nodular goiters, is triggered by iodine intake and lacks exophthalmus [8]. The distinction is clinically relevant, since persons with large nodular goiters should stay away from all forms of iodine.

Thus, over the years, despite his enormous workload as a surgeon, Kocher had made a remarkable number of “non-surgical” discoveries: he had shown that the thyroid gland avidly accumulated iodine, described the clinical picture of hypothyroidism, observed a high lymphocyte count in Graves’-Basedow’s disease, and described a second form of hyperthyroidism: Jod-Basedow.

Kocher’s advances in thyroidology were important, but the most pressing problem in the thyroid field, that is, endemic goitre and cretinism, remained a puzzle. Most researchers thought that factors in food and water were the cause of endemic cretinism and goiter, and there were only few advocates of the iodine deficiency theory.

In 1883/84, Kocher and his team surveyed all 76,000 schoolchildren of the canton of Berne [9]. He plotted the findings on a detailed map, with the intention to correlate goiter with certain geologic formations. The survey showed a highly variable prevalence of goiter, depending on location. The variability of goiter prevalence did not, as claimed by others, correlate with specific geological formations or bacterial contamination of water. All places where cretinism occurred also had endemic goiter, but the reverse did not apply. Some drinking waters appeared to be “goitrogenic”, neighbouring springs not.

In the following years, Kocher focused his interest on the pathogenesis of cretinism. The intriguing question was: which common etiology could explain goitre and cretinism, two radically different disorders affecting the thyroid and the brain? In his review of the available literature, Kocher concluded that all theories were conjectural and unsatisfactory. Frustrated, he agreed with another author that “eliminating goiter and cretinism worldwide would amount to more than building the Egyptian pyramids” [6].

In 1907 a Swiss Goitre Committee was founded. With the help of Kocher, the Committee established a research plan that sounds reasonable and logical to this day. Rats were kept over one year in eight different villages and fed with local food and water. Two pathologists, Langhans and Wegelin, published the results in a monograph in 1919 [10]. In goitrous villages, the rats developed goiters with numerous mitoses. Potassium iodide added to the drinking water prevented these rat goiters. But obsessed by the theory of a goitrogenic agent in water, the researchers failed to consider the obvious explanation for endemic goiter: iodine deficiency!

In 1917, the year of his death, Kocher still favored goitrogenic agents in water as the cause of endemic goitre. David Mariné’s finding of goiters in fish hatched in certain waters supported the water theory, in Kocher’s mind. Nonetheless, he agreed that time was ripe to stop discussions, and that one should cautiously embark on trials of prevention, e.g. by adding small amounts of iodine to water supply systems [11]. Interestingly, the final solution of the problem of goiter and cretinism did not come from the heights of Swiss academic medicine. Rather, the merit goes to two physicians practicing in rural Alpine areas. Bayard, general practitioner in the Valley of Zermatt and Egggenberger, surgeon in the small canton of Appenzell, proved the feasibility of using salt as a carrier for iodine on a large scale.

Kocher did not live to witness the triumph of prophylaxis with iodized salt; he died in 1917, six years before introduction of iodized salt in Appenzell. But his research on goiter and cretinism played a major role in the success of the Swiss iodized salt program, and laid the foundation for future global efforts to control IDD.