

Tröhler U (2010). Towards endocrinology: Theodor Kocher's 1883 account of the unexpected effects of total ablation of the thyroid.



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From the 1830s onwards, surgeons and physiologists in many countries removed the thyroid gland from various species of animal to see what happened. The results were ambiguous: since neither antisepsis nor the existence of the parathyroid glands were known, it was not possible to know whether the post-operative observations reflected infection or an organic failure. As Claude Bernard observed in 1879:

"We know absolutely nothing about the function of these organs [thyroid, thymus], we do not even have an idea of their utility and of the importance they may have, for their removal has not told us anything about this, and anatomy alone remains absolutely silent." (Bernard 1879, p 294).

Theodor Kocher's 1883 lecture to the German Society of Surgery

One consequence of this general ignorance was that, on 4 April 1883, in a lecture to the German Society of Surgery in Berlin, the professor of surgery in Bern, Switzerland, Theodor Kocher ([Tröhler 2010](#)), explained both why surgeons operated on the thyroid and why he had changed his mind about this ([Kocher 1883a](#)):

"Unfortunately the physiologists know next to nothing about the physiological significance of the thyroid gland, and this may have been the main reason for surgeons tacitly assuming that the thyroid gland had no function at all. Once one had achieved certainty that total removal could be happily performed from a technical point of view, one did not hesitate, in cases of disease of both halves of the thyroid gland, to take out the whole organ." ([Kocher 1883a, p 273](#)).

"I shared this opinion for a long time. It was [the influence of] just one case, on whom I had operated in 1874 ... and about whom the doctor had occasionally mentioned that the girl in question had since undergone a complete and substantial change in the nature of her character. Indeed, he had recently informed me that she had become entirely *cretinoid*. This was so important to me, that I now took all pains to see the girl with my own eyes. This was not easy, because the doctor [Dr Fetscherin, a general practitioner in Zäziwil, 18 kilometres east of Bern] had died soon after his verbal message. We insisted all the more because [our] colleague *Reverdin*, in Geneva [see below], mentioned to us that he had seen two cases in whom decreased mental capacity had followed excision of goitre. I was astonished to a great extent by the conspicuous looks of the individual in question [his patient]. In order to fix your views right away, I will pass around among you photographs of the girl with her younger sister before and after the operation ([photographs](#)). According to the mother, the two sisters were said to have resembled each other so much at the time of the operation that they were frequently confused for each other. Whilst the younger sister has now grown up to a blossoming young woman of very pretty looks, the sister operated on has remained small and exhibits the ugly looks of a semi-idiot. This having been ascertained ... I immediately sent invitations to all my

[patients on whom I had] operated for goitre [asking them] to present themselves for examination." ([Kocher 1883a, p 273-4](#)).

In early February 1883, Kocher sent invitations to 77 of his 102 former patients. He did not invite thirteen whom he knew had died or the twelve on whom he had operated within the previous two months. By the time of his lecture in Berlin (4 April), there were no responses from 17 patients; but Kocher had been able to re-examine 34 patients and had received written reports on a further 26 - a total of 60. From the latter he learned that 5 had had cancers and that 2 with benign disease had died during the interim.

Of the 53 living patients whom he knew to have had benign disease, 28 had had only partial removal of the gland. They were deemed to "enjoy the best of health and are [...] very happy with and grateful for the success of the operation." (Kocher 1883a, p 275). The results in patients who had had total removal of the gland were entirely different:

"Of the 34 total excisions ... 3 patients died as a consequence of the operation, 2 died from unclear causes after good [post-operative] recoveries, and one had a cancerous goitre. Of the remaining 28 we were not able to receive information from 4 cases only; however, 18 patients presented themselves in person, and 6 sent in written reports." ([Kocher 1883a, p 275](#)). The key statement in this section of Kocher's lecture was that "Of the 18 patients who presented themselves for examination, only 2 showed unchanged or improved general status compared with earlier." ([Kocher 1883a, p 277](#)).

Such was the basis on which Kocher then continued to describe in great detail the results of his clinical and laboratory examinations of those of his patients who had had total removal of the thyroid. He had used the most up-to-date technologies for evaluation, and his faculty colleagues in internal medicine and ophthalmology had assisted him with blood counts and ophthalmoscopy. There had been slow physical and mental decay following the total removal of the gland. Puffiness of the face, hands and body, and decreased growth in height could be seen in the [photographs](#) of the two sisters, and noticeable pallor was explained by anaemia diagnosed in blood counts. He designated the concurrence of these and other physical signs as a new disease specific to the removal of the gland. Because he concluded that its relation to "idiotism and cretinism" was unmistakable, he had no difficulty in decide to name the condition "*cachexia strumipriva*" (decay resulting from lack of goitre). (Kocher 1883a, p 285).

Kocher's historic lecture ended with a long sequence of theoretical speculations about hypothetical thyroid function, which covered 15 pages in the printed account, referring to the international experimental and clinical literature. He covered explanations about the role of the gland in blood formation, and in regulating blood flow to and from the brain and other organs to prevent the accumulation of carbon dioxide. Kocher put forward his own hypothesis however. He thought that, by ligaturing the thyroid arteries when removing the gland, the vascularisation of the trachea became severely impaired, a view confirmed by his anatomist Faculty colleague. This, Kocher suggested, explained the softening of the trachea, which in turn explained "the high degree of progressive anaemia" and the relative bad after-effects he had observed in children compared with adults. Thus he held as "at least equally justified [as other hypotheses]" that the thyroid regulated circulation of the blood in organs in the neck and therefore also of respiration. For him, the anaemia caused by the lack of this regulation dominated the picture of the newly discovered condition. In conclusion he said that the thyroid's task was "to paralyse the influences which produce stupidity." ([Kocher 1883a, p 298](#)). In support of his hypothesis he used examples from the complete list of all 102 cases on whom he had operated between May 1872 (when he had taken over as head of the Bern surgical clinic) and March 29 1883 (5 days before his lecture in Berlin). A list summarizing the features of these 102 patients was included in the printed version of his lecture, as were another 134 cases collected from 15 colleagues of German and French speaking Switzerland and southern Germany, including those by Reverdin. It was an early example of a complete surgical audit, which included frank reporting of mishaps.

Reactions to the lecture

Kocher had initiated this masterly lecture with a long, critical review of operative techniques in thyroid surgery (covering 16 pages in the printed version). The reactions to his talk embittered him, however. His colleagues smirked, and he felt mocked. The large number of thyroid cases (his was by then the largest reported series operated on by one surgeon) was interpreted as reflecting solely his lust for operating, and was therefore dismissed (Tröhler 1984). Kocher sharply rejected these reactions in the ensuing discussion: "...of course we do not operate on an extraordinarily great

number of cases. I would not have a hundred but several thousand operations if I operated for my private pleasure." (Kocher 1883b, p 38).

With his main point – identification of a new disease entity - Kocher may have excited the curiosity of some. As he wrote to his wife from Berlin on 9 April 1883: "My lecture has prompted very different reactions. A very discerning colleague, Küster, who has invited me to dinner tomorrow evening, has told me: 'This time you have shot the bird from the perch. Your presentation is the most important and the most original.'" (Bonjour 1991, p 17). But most participants at the congress were unreceptive to the new information. They thought that Kocher's *cachexia strumipriva* was nothing really new. For them, referring to Virchow, the early stages of cretinism were characterised by an increase of thyroid volume. So-called *cachexia strumipriva*, they believed, was simply a late stage of cretinism which had developed despite the removal of the thyroid. Such a view meant that there was no specific function of the gland that would have been abolished once the gland had been removed. Kocher insisted that it had a specific function, yet he did not at this time conceptualise the gland as having a remote function. Instead, he explained it mechanistically by its local action. His hypothesis was thus just one among many others. It would have been better if he had acknowledged, as Claude Bernard had done four years earlier, that "nothing was known about the function of these organs" (Bernard 1879). This might have given his main point more weight.

Later developments

Kocher went too far with one of his claims in Berlin, however. He claimed that: "...for the first time – as far as is known to us - a relation of dependence between the thyroid gland and cretinism has been demonstrated with certainty" (Kocher 1883a, p 298). This was an overstatement. Well known clinical and anatomical observations – not least in cretins – had led to such thoughts during previous decades, yet proof had been lacking. Kocher was wrong to believe that he had supplied it.

In fact, as we know from hindsight, Kocher was doubly wrong. First, he overlooked a number of earlier works by British authors - Thomas Curling, Charles Fagge, Sir William Gull and William Ord - as well as one by the Frenchman Jean-Martin Charcot. They had described puffiness in adults with inflammation of the thyroid, or its absence, as confirmed at autopsy. The diagnosis of 'myxoedema' was quite current in England at this time (Slater, in preparation), yet without a causal link having been established. It is no coincidence therefore that Kocher's Berlin lecture was particularly noted in Britain. For instance, Ord wrote promptly to Kocher. In his reply, which Ord read out at the Clinical Society of London meeting on November 23, 1883, Kocher asserted in no uncertain terms that "there cannot be the slightest doubt of the analogy of myxoedema and *cachexia strumipriva*. I was not aware of it before, having never seen a case of the affection [i.e. myxoedema]. I think you will agree with me that, by my observations, the atrophy of the thyroid body, which you have found in your cases, gets much greater importance" (Ord 1883 p 1073; Tröhler 1984, p 134 ff).

Second, Kocher failed to acknowledge his contemporary and colleague in Geneva, Jaques-Louis Reverdin (1842-1929), who, through an offhand remark, prompted Kocher to examine the girl about whom the Zäziwil general practitioner had earlier spoken to him. Aware of the British literature, Reverdin had coined the term *myxoedeme opératoire* in one of a series of articles in the *Revue Médicale de la Suisse Romande*, beginning 11 days after Kocher's lecture in Berlin. The context of the publication of Kocher's and Reverdin's findings led to a priority contest between the two Swiss surgeons. It was led on Kocher's side aggressively and with perseverance right up to his Nobel lecture in 1909, and indeed until the end of his life in 1917. That said, Kocher continued his research on the function of the thyroid until he died, and he is rightly considered as a "founder of endocrinology" (Tröhler 1984).

Both to his contemporaries and to historians, Reverdin was responsible for the discovery that lack of the thyroid gland causes severe physical and mental damage. After 1883, he published only six further communications on the thyroid, and these were reviews and discussions of technical issues. In 1886, he received the *Légion d'Honneur*, and went on to receive its Officer's Cross in 1910, the highest distinction to be conferred on a foreign citizen by the French government. Reverdin's name remains linked with his earlier discovery of skin transplantation, and in later years he was as well known as an entomologist as he was as a surgeon (Bornhauser 1951, pp 74–113; Michler and Benedum 1970; Reverdin 1971).

In conclusion

Both Reverdin and Kocher contributed to the discovery that lack of the thyroid gland causes severe physical and mental damage, thus laying the basis for what we now call endocrinology. That said, Kocher's prompt and detailed description of his investigation of a possible adverse effect of his

therapeutic intervention is real milestone. The paper is a classic example both of surgical audit and of the investigation of unanticipated effects of a treatment which had been deemed to be safe.

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