Iodine deficiency diseases in Switzerland one hundred years after Theodor Kocher’s survey: A historical review with some new goitre prevalence data

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Abstract. In certain regions of Switzerland, before prophylaxis, 0.5% of the inhabitants were cretins, almost 100% of schoolchildren had large goitres and up to 30% of young men were unfit for military service owing to a large goitre. Iodization of salt was introduced in 1922 at 3.75 mg I per kg and the iodine content was doubled twice, in 1962 and 1980, to the present 15 mg I per kg. In 1988, 92% of retail salt and 76% of all salt for human consumption (including food industry) was iodized, even though its use is voluntary. Urinary iodine excretion, previously between 18 and 64 µg per day, has now risen to 150 µg per day. No new endemic cretins born after 1930 have been identified. Goitre disappeared rapidly in newborns and schoolchildren, more slowly in army recruits, and incompletely in elderly adults. In some Cantons (by constitution in charge of health matters and the salt monopoly) which allowed iodized salt only in 1952, disappearance of goitre lagged behind accordingly, proof that iodized salt was the cause of regression. The Swiss data provide evidence that isolated deafness, mental deficiency, and short stature, each without the other attributes of cretinism have also decreased. Adverse effects of iodized salt were minimal, possibly because the initial iodine content of salt was chosen very low. Iodization of salt has proved a highly cost-effective preventive measure in Switzerland.

Much of the pertinent literature is only locally known, but we think it might be of use to those countries which are actually considering the introduction of iodized salt.

Early surveys
Over the centuries many travellers to this country have reported on the devastating endemia of goitre and cretinism, and their accounts have been admirably reviewed by Merke (1). Unsatisfied with low yields of the recruitment for the French army, Count de Rambuteau, Prefect of the Département du Simplon (now the Swiss Canton of Valais) conducted a survey at Napoleon’s order which revealed the astonishing number of 4000 cretins among 70 000 inhabitants (1). Rambuteau’s investigation seems to have prompted numerous surveys in virtually all Cantons in the first half of the 19th century (2).

In the years 1886 to 1891, 8 to 11% of 19-year-old men were unfit for service owing to a goitre causing symptoms, smaller goitres not being a reason for exemption (3) (Fig. 1). Bircher, in an exhaustive monograph, compiled tables and maps of goitre prevalence at recruitment from 1875 to 1880 for every single town and village in Switzerland, together with the prevalence of deaf-mutism and cretinism in selected areas (6). He concluded that a. Goitre prevalence varied enormously from one village to another, even in the same county (Fig. 2). Bircher explained this variability with differing soil geology and water supplies which came near to the true cause since the iodine content was
Fig. 1.
Sum of percentages of men aged 19 (age 18 for the years 1914-18 and 1939-45) who were found unfit for army service or fit for auxiliary service only, or whose induction was postponed for a second review because of goitre (O--O) or of mental deficiency (Δ--Δ). The top part also indicates the share of iodized salt as percent of salt sold by retail (□--□). The dips in the rejection rates 1914-18 and 1939-45 are partly explained by more rigorous recruitment during both World Wars, but it should be noted that both for goitre and mental deficiency the rejection rates are much lower for World War II than for World War I. The rejection rates for goitre and deaf-mutism had drastically decreased from 1939 to 1947, whereas it remained constant for other medical reasons. Data for 1884-91 are from Hunziker (3), for 1900-47 from Wespi & Schaub (4), and for 1980 from ourselves (5).

later shown to differ accordingly (7,8). b. The recruitment data for universal military service could be used as an indicator of the goitre endemia since they correlated well with goitre data in schoolchildren. c. Deaf-mutism, well correlated with the prevalence of goitre, could serve as a marker for cretinism which was hard to define and measure (Fig. 2). This highly relevant correlation was confirmed decades later among 11,000 first graders. In three regions of the Canton of Berne large goitres were found in 16, 13.2 and 2.3%; hearing impair-

ment in 3.3, 2.6 and 1.6%, and intellectual impairment in 3.3, 4.4 and 1.8% (9). At the 1870 census, in Switzerland, 24.5 per 10,000 inhabitants were deaf-mute, about three times more than in other European countries where cretinism was less prevalent (6). Bircher (6) published figures of three surveys commissioned by the Canton of Berne. Among its 400,000 inhabitants 0.40, 0.54 and 0.29% were considered cretins in the years 1841, 1846 and 1871, respectively. Of 1799 mentally handicapped persons in the first of these surveys 60% had impairment of speech, 33% were totally deaf-mute, 15% had a goitre, and 2% were of extremely short stature, a symptomatology which closely fits the modern definition of cretinism.

Surveys by Theodor Kocher and others and animal experiments prior to iodine prophylaxis

In 1883/84, Theodor Kocher with 25 of his medical interns and students, examined 76,606 schoolchildren aged 7 to 16 years from all towns and villages of the Canton of Berne (approximately 500,000 inhabitants). He distinguished two grades of goitre: moderate and important enlargement (including nodularity) of the thyroid gland. The results, published in 1889 (10), were plotted on a map and showed a total goitre prevalence of 20 to 100%, with up to 100% nodularity. Kocher refuted Bircher's hypothesis that goitre was associated only with certain marine sediments, but he confirmed the importance of the drinking water, since within certain heavily goitrous villages, groups of families drawing water from separate wells were sometimes entirely free of goitre. Unaware of Chatin's iodine measurements in France (11), Kocher could not explain this phenomenon. Mineral composition (excluding iodine which was not measured) of "goitrogenic" waters did not differ from "non-goitrogenic" wells, but in preliminary experiments bacterial contamination was higher. A Swiss Committee for the study of goitre was founded in 1907, and with the help of Kocher it established a research plan. Rats were given local water or milk over one year in 8 villages. In several locations they developed large goitres with numerous mitoses which were prevented by 75 mg/l iodide in the drinking water. Obsessed by the theory that drinking water must contain a goitrogenic agent, the investigators failed to consider iodine deficiency as the cause of
goitre (12,13). In the light of the works by Marine & Lenhart (14) and Hunziker (15), Kocher later accepted that iodine deficiency might be the cause of endemic goitre, and in 1917, the year of his death, he made a plea for goitre prevention with small doses of iodine (16).

Before iodine prophylaxis, another large survey was carried out by Dieterle et al. (17) in 1912 in a different region of Switzerland, namely in parts of the Cantons of Zürich and Aargau. The latter had already been studied 30 years earlier by Bircher (6). This new survey had several unique features: a. It covered the entire population, not only schoolchildren or military recruits; in fact the authors examined 75% of 7630 inhabitants from 14 villages. b. An exact grading system for goitre was used. c. The same villages were again examined in 1932 and in 1952 (18,19), and iodine data were collected in some of them in 1925 (7,8). The 1913 survey confirmed the high prevalence of grade II (well palpable) or larger goitres: In 9 of the 14 villages it was over 35% and in 2 villages it reached over 65%. As already noted by Bircher (6), two villages were free of goitre. An exact survey of the population by two experienced geologists failed to yield any common denominator of "goitrogenic" waters or geologic formations. Table 1 gives selected data on schoolchildren and of subsequent surveys in this region.

In 1921-22, on the eve of widespread iodine prophylaxis, Stiner again plotted goitre prevalence at army recruitment on maps. Unfitness for military service because of goitre ranged from 0 (some valleys on the south slopes of the Alps) to 20-30% (Cantons Lucerne and Obwalden). In addition, in those men found fit for service up to 30% had goitre and the total goitre prevalence varied from 0 to over 30% (13). After the Surgeon General had issued exact instructions how to grade goitres at military induction centers, the prevalence of clearly palpable (or larger) goitres in 1924/25 was much higher, from 5 to 82%, with 29 of the 136 counties reporting a prevalence of over 50% (21). However, only in 1.4% of the men the goitre was large enough to be a reason for exemption. Before widespread iodine prophylaxis large goitres had thus become rare in young men (see Fig. 1), a fact which we shall try to explain later.

Iodine metabolism in Switzerland prior to prophylaxis

After Kimball & Marine's publications (22,23) and at a time when iodine prophylaxis was already discussed, but before it was widely implemented, Th. Fellenberg, a chemist of the Swiss Federal Office of Public Health, set up an extensive study of iodine metabolism. He carefully reviewed the enormous work of Chatin, the director of the School of Pharmacy in Paris, who between 1850 and 1860 was the first to demonstrate that moderate iodine deficiency in soil, water and food caused goitre, whereas severe deficiency caused cretinism in
Table 1.
Selected data on iodine analyses (7,8) and goitre in schoolchildren (17-19).

<table>
<thead>
<tr>
<th></th>
<th>Iodine (1923)</th>
<th>Well palpable or larger goitres in schoolchildren (%)</th>
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<tbody>
<tr>
<td></td>
<td>in rock (µg per kg)</td>
<td>in soil (µg per kg)</td>
</tr>
<tr>
<td>Effingen, Bözen*</td>
<td>5400-9300</td>
<td>11900</td>
</tr>
<tr>
<td>Kaisten, Asp.,b Schinzach</td>
<td>420-430</td>
<td>820-1970</td>
</tr>
<tr>
<td>Dättlikon, Ellikon, Schindel</td>
<td>47</td>
<td>28</td>
</tr>
<tr>
<td>Marthalen</td>
<td>120-600</td>
<td></td>
</tr>
</tbody>
</table>

* Traditionally goitre-free villages in Canton Aargau, b Goitrous villages in Canton Aargau. Iodized salt since 1952 only (20). c Goitrous villages in Canton Zürich. Iodized salt since 1932 (20). d Ligurian coast in Italy for comparison: Sufficient urinary iodine and goitre-free thanks to sea-food, despite low iodine in rock.

In addition (11). On the basis of Chatin's study, von Fellenberg developed a reliable method for iodine measurement. He measured iodine in soil, rock, well water, rain water, snow, dew, salt, all kinds of vegetables, meat, fish, milk, cereals, and other food and published his data in a large review and in a small summary (7,8). He confirmed Chatin's findings that in goitrous regions soil, rock as well as water, milk and other locally produced food contained little iodine and that the 24-hour urinary iodine excretion was lower than in non-goitrous regions in Switzerland or in the goitre-free Ligurian coast in Italy (Table 1). Measurements of iodine in a typical daily diet in heavily goitrous Signau yielded an intake of 13 µg. The same food and water from less goitrous La Chaux-de-Fonds contained 31 µg iodine per day. He measured intestinal absorption (oral intake minus fecal excretion) of various sources of iodine and found it e.g. 93% for cod-liver oil (7200 µg iodine per kg), and 64% for cress (190 µg per kg), a vegetable which accumulates iodine even on iodine-poor soil. In what was probably the first and most complete iodine balance study ever done, von Fellenberg for

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**Table 2.**

v. Fellenberg's (7) self-experiment on iodine balance during controlled iodine intake over 53 days.

<table>
<thead>
<tr>
<th>Days of study</th>
<th>Diet</th>
<th>Iodine (µg per day, average for each period)</th>
<th>Excretion</th>
<th>Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Intake</td>
<td>Urine</td>
<td>Feces</td>
</tr>
<tr>
<td>21 to 28</td>
<td>Standard</td>
<td>17</td>
<td>7.2</td>
<td>4.0</td>
</tr>
<tr>
<td>29 to 36</td>
<td>Standard plus KI</td>
<td>55.3</td>
<td>23.0</td>
<td>5.5</td>
</tr>
<tr>
<td>37 to 42</td>
<td>Standard plus cod-liver oil</td>
<td>74.6</td>
<td>23.6</td>
<td>6.9</td>
</tr>
<tr>
<td>49 to 50</td>
<td>Standard</td>
<td>17</td>
<td>27.1</td>
<td>5.1</td>
</tr>
</tbody>
</table>

* by iodine measurement in shower effluent and eluate of towels and handkerchiefs.

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53 days consumed a standard diet containing 14 µg iodine (plus 3 µg which he assumed to take in from the breathing of air). Daily he measured iodine in all body excretions including sweat. Table 2 shows that after a 10-day equilibration period his balance was in equilibrium even on the low-iodine standard diet. The balance became positive when iodine was added, and then again temporarily negative when he went back to the standard diet. The changing iodine balance was correctly attributed to uptake and release of iodine from the thyroid. Before the availability of radioiodine, von Fellenberg had solved many problems of iodine mineralogy, physiology and metabolism. He had established beyond any doubt that large areas of Switzerland were grossly iodine-deficient, and he had recognized that 24-hour urinary iodine excretion was a good estimate of iodine intake.

Tablets with iodide and iodinated lipid, and the fight for iodized salt

The Frenchman Boussingault is rightly credited with first suggesting in 1831 that iodine-containing salt should be made available in goitrous regions (24). In short-term trials around 1860 salt containing 100 to 500 mg KI (75 to 400 mg I) per kg was distributed in three French Departments (reviewed in 1 and 25). After Baumann’s demonstration that the thyroid gland accumulates iodine (26) and after Marine & Lenhart’s experiments in fish hatcheries (14) the idea of iodine prophylaxis gained momentum. Marine & Kimball’s idea of prophylaxis in schools (22,23) was avidly taken up in Switzerland.

In a controlled study, Hunziker (27,28) administered 1 mg iodide (as NaI tablets) weekly to 399 schoolchildren near Zürich, leaving 322 of their schoolmates untreated (99 of the latter children had to be excluded because they received iodine supplements from other sources at home, which incidentally testifies to the great popularity of overt-the-counter iodine supplements, a possible explanation for the decrease of goitre prevalence years before universal prophylaxis). After one year, goitre had regressed in 75% of treated and in 19% of untreated children. Three times larger doses given to 30 000 Berne schoolchildren did not produce better results (29). A long-acting form of iodized lipid, dioxidostearic acid (4 mg I as C17H31I2COOH, later supplemented with 1 mg iodide as NaI per tablet) was widely used by Klinger (30,31) and by Silberschmidt (32) and marketed by Hoffman-La Roche since 1912, an interesting precursor of today’s oral iodinated oils. Forty tablets yearly were given and between 1921 and 1926 19 000 schoolchildren had been treated with excellent results (33).

The final important step, the introduction of iodized salt, was made possible largely by the efforts of two general practitioners, Hunziker and Bayard, and a surgeon of a district hospital, Eggengerber. In 1915, Hunziker published a monograph “Goitre, an adaptation to iodine deficient nutrition” (15), which correctly interpreted the thyroidal hyperthyrosis as a physiological response of the body better to utilize scarce iodine. He had found that 100 µg of iodine daily could shrink goitres in his patients and he made the suggestion to add this amount to the average daily salt intake. This dose was orders of magnitude lower than what was usually recommended.

Bayard, a busy general practitioner in the mountain valley of Zermatt, personally provided 5 large families including their baker and their cattle with salt of 5 different iodine contents: 3, 6, 9, 12 and 15 mg I per kg NaCl (34,35). Since goitres shrank, he then supplied two entire villages with salt containing the lowest dose after having established goitre size and prevalence among the 1200 inhabitants; at 6-month intervals the dose was raised in one of the two villages to 7.5 mg and then to 15 mg iodine per kg salt. Bayard found that the lowest dose which supposedly provided an additional 40 µg iodine per day, was capable of shrinking some, but not all goitres. The next higher dose was more effective and even the highest dose (15 mg/kg) was tolerated without adverse reactions (35,36).

Eggenberger, surgeon at the hospital in Herisau, was struck by Bircher’s recruitment data of 1880 (6) that goitre exactly respected the rather erratic boundary between the two adjacent Cantons of Vaud (unusually low prevalence) and Fribourg (high prevalence) (37,38). The difference, which admittedly had narrowed later (13,21), could best be explained by the strictly respected salt monopoly. The Canton of Vaud had its own exclusive salt mine, brine and motherliquor of which in 1894 were rich in iodine. Eggengerber started a campaign of evening lectures in every single community of his small Canton of Appenzell-Ausserrhoden and then collected 3480 signatures for a petition to the government of the Canton, which on February 20, 1922 allowed the distribution of salt.
containing 10 mg KI (7.5 mg iodine) per kg (37-39). Salt was iodized first by Eggenberger himself and his family according to a simple hand- and shovel-method of Bayard, later by a few workers of five local salt shops at little cost (36,39,40). Iodine content and stability being checked in spot specimens by Eggenberger’s rapid semiquantitative method (36-39). Distribution was immediately begun and the effects were spectacular and beyond expectations. Within one year existing goitres had shrunk in 66% of the schoolchildren whose families used iodinated salt on a regular basis, compared with only 28% in those families who did not. Average thyroid gland weight in children entering school had diminished from 21 to 13 g. A palpable thyroid gland formerly present in 50% of newborns had entirely disappeared (39,41,42).

Eggenberger has presented his large experience with iodine deficiency disease in a brilliant handbook article (39). His grading of average daily iodine intakes is still remarkably correct today, after 60 years: I. 80-250 μg; no goitre. II. 50-80 μg: less than 30% goitre in schoolchildren, no cretinism. III. 30-50 μg: 30-50% goitre in schoolchildren, few cretins. IV. 20-30 μg: 50-80% goitre in schoolchildren, many “half-cretins”. V. 10-20 μg: 80-100% goitre in schoolchildren, many full-blown cretins.

The Swiss Goitre Commission and the International Thyroid Conferences in Berne

Meanwhile, in 1922 the Swiss Federal Office of Public Health had appointed most persons engaged in goitre research as members of the Swiss Goitre Commission. After having reviewed Hunziker, Bayard and Eggenberger’s cases (36,43), de Quervain (Kocher’s successor at the University of Berne) and others pleaded for immediate iodization of salt at a dose “which would prevent as many goitres as possible while causing the minimum of iodine-induced thyrotoxicosis” (25). On June 24, 1922 the Commission recommended the 25 Cantons to take up sale of a salt containing 2.5 to 5 mg KI (1.9-3.75 mg I) per kg on a voluntary basis, non-iodized salt remaining available (43,44). It was correctly predicted that this dose would turn out too low to eradicate goitre completely, but it was a compromise to which even opponents of iodized salt could agree. The Commission therefore also recommended distribution of additional weekly iodine tablets to schoolchildren in whom, having fewer nodules than adults, “Jod-Basedow” was considered less likely (43,44).

The Swiss Goitre Commission agreed on a goitre grading system (43) for surveys (see table 5) and it recognized the need for more research and for international cooperation (36). It called for an international goitre conference which was convened in Berne from August 24 to 26, 1927, and which assembled most of the experts from North America and Europe. A second conference was held in 1933 again in Berne. Summaries of the first (39,45) and full proceedings of both conferences (46,47) are available.

The advisory function of the Swiss Goitre Commission was later taken over by the still extant Fluorine-Iodine Commission of the Swiss Academy of the Medical Sciences. Its 11 members represent a wide spectrum of public health officials, dentists, thyroidologists, food chemists, pharmacologists, and salt manufacturers. The Commission makes suggestions to the larger Federal Commission of Nutrition, which in turn can submit new measures to the Conference of Cantonal Health Ministers. This seemingly complex scheme has allowed to pass increases of iodine in salt (see later) or the addition of fluoride for caries prevention with a high degree of public and political acceptance, even within strictly federal structures.

Acceptance of iodized salt, adverse reactions, and influence of further measures on iodine metabolism

Wespi (48) and Nicod (49) have reported exhaustive reviews of the results of prophylaxis until 1940 and 1950, respectively. In November 1922 the United Swiss Rhine Salt Works, the exclusive supplier to 24 of the 25 Cantons, took up production of salt containing 5 mg KI (3.75 mg I) per kg. The wet spray method proved sufficiently reliable, even though complete stability of iodine content was initially not achieved (7,8,49). The United Swiss Rhine Salt Works have retained to this day a great interest in the cause of iodine deficiency and a great expertise in the field (40) and are providing Switzerland with high quality iodized salt at the same price as the non-iodized variety (50,51).

After the breakthrough in Appenzell-Ausserrhoden, the other Cantons complied with the recommendations of the Swiss Goitre Commission
with varying zeal, and by 1930 iodized salt had reached 50% of all salt sales in only 13 of the 25 Cantons (4,49). Ironically, opposition arose from well-known medical experts who could not accept the iodine deficiency theory and who predicted a massive outbreak of iodine-induced hyperthyroidism (52-54). This "Jod-Basedow" had been well described and clinically differentiated from true Graves' disease by Kocher (55) and it received particular attention with the diagnostic means available at the time, but no alleged case could be confirmed in Appenzell after one year of iodized salt (41). At the suggestion of the Swiss Goitre Commission all 3008 physicians practicing in Switzerland were asked by mail to report all cases of hyperthyroidism (iodine-induced and others) seen in the three years 1922-24 (56); 1668 physicians replied and reported 3506 cases (a yearly incidence of 30/100,000 for all types of hyperthyroidism), but a second more detailed questionnaire was returned for only 468 patients. Among these cases, 244 occurred in temporal relationship with iodine administration, but in 225 patients this was with high doses (1 to 750 mg per day). The remaining 19 patients had only received iodized salt. De Quervain examined 15 of these patients personally and the majority turned out to have true Graves' disease with exophthalmos (56). In only 5 was iodized salt considered a possible or probable cause of hyperthyroidism. Even when correcting for the eightfold underreporting mentioned above, this incidence was deemed an acceptable price for eliminating goitre and cretinism.

By 1952 all 25 Cantons had allowed the sale of iodized salt, the iodine content of which was raised to 7.5 mg in 1962 and to 15 mg iodide per kg salt in 1980 (57,58), without causing any protests. The step-up of iodide in salt affected radiiodine uptake and urinary iodine as predicted (Table 3). Excretion of iodine correlates well with that of sodium, suggesting that salt is still an important source of iodine (5). Doubling the salt iodine content in 1980 raised the iodine excretion from 90 to 150 µg per g creatinine (weighted averages from Table 3). Extrapolating these figures backwards yields a daily iodine excretion of 30 µg in the absence of iodized salt, a figure close to what was formerly found (Tables 1 and 3). Milk, which in Scandinavia and the United Kingdom is an important alternate source of iodine, contains only 28±8 µg iodine per kg in summer and 120±36 µg per kg in winter in Switzerland (62).

In 1975, in the so-called Salt Concordate, the Cantons yielded their salt monopoly to the United Swiss Rhine Salt Works, of which they had already been exclusive shareholders since 1909. In 1988 91.7% of retail salt and 75.6% of all salt for human consumption, including salt used in food industry, was iodized (personal communication, United Swiss Rhine Salt Works). The lower use of iodized salt by the food industry is due to foreign food regulations (some countries do not allow added iodine) and to incompatibility of iodized salt for certain meat processing. In 1979 an opinion poll of 908 adults revealed that 90% of them were aware that iodine was added to salt, 46% knew that it

| Table 3. Iodine turnover data in Switzerland from 1923 to 1988 (mean values and sd) |
|----------------------------------|----------------|----------------|----------------|----------------|
| Iodide in salt (mg/kg)          | none | 3.75   | 7.5       | 15            |
| 24-hour radiiodine uptake (%)   | -    | 33±13  | 27±5      | 22±6          |
| Urinary iodine (µg/day for 1923, µg/g creatinine for 1974-88) | 18±8b | -     | 76±44d   | 127±67f      |
| I/Na ratio (µg/mmol)            | 64±27c | -     | 93±44e   | 160±80g      |
|                                 | 0.64f | 0.91f | 1.05f     |

a from ref. 58 b 23 inhabitants of two goitrous villages (7) c 7 inhabitants of a non-goitrous village (7) d 150 hospital patients (59) e 770 healthy adults (60) f 112 ambulatory practice patients (61) g 245 schoolchildren age 7-16 years (5)
Goitre in newborns

Goitres (i.e., palpable lateral thyroid lobes) were previously present in 20% of newborns in the Canton of Appenzell and in 53% in Berne. Within one year of prophylaxis with iodized salt (3.75 mg I per kg) prevalence dropped to 6.4 and 30%, respectively. Not satisfied with this result, Eggengerber enriched the "official" salt to 15 mg I per kg for pregnant women, which had the newborn goitre prevalence drop further to 2.6% (48). In studies involving several thousand newborns Wespi subsequently established that an iodine intake of about 200 μg per day during pregnancy is necessary to avoid goitre in newborns completely (48,64-67).

Table 4 and other autopsy data in newborns (70,71) confirm the disappearance of newborn goitre at a salt iodine content of 3.75 mg per kg, but newborn glands, while of almost normal weight, still showed histological signs of hyperplasia, confirming that this iodine content of salt was not yet optimal (72). In a recent survey Swiss newborns were found to excrete 61 μg iodine per l of urine, an amount considered adequate (51).

Goitre in schoolchildren

The excellent results on goitre in seven-year-olds in the pioneer Canton of Appenzell-Ausserrhoden have already been mentioned (41). In the Canton of Valais (formerly the Departement du Simplon, so heavily afflicted with cretinism) and in Lausanne, iodized salt reached 75% of sales in 1927 and goitre declined rapidly (73) (Table 5). Our own studies in 1988 in Berne and its surroundings have confirmed that goitre prevalence is steadily declining since 1984, even though grade 1a goitres still make up 5-11% (Table 5). In villages of the Canton of Zürich, visible goitre had virtually disappeared by 1952, whereas it persisted, albeit at lower prevalence, in the neighbouring Canton of Aargau, where iodized salt was not yet available (Table 1).

Goitre in army recruits and adults, and goitre operations

Probably because of the popularity of over-the-counter iodine preparations (see preceding section "Tablets with Iodide") goitre in recruits had already declined before universal prophylaxis. Iodized salt made it disappear completely by 1950 (Fig. 1) (49,77), except in 2 of the 25 Cantons which had not introduced it (Fig. 3), hard proof that iodized salt and not any other change in lifestyle or eating habits had eradicated goitre (4). From 1983 to 1987 we had the opportunity of examining 2300 19-year-old military recruits in the Cantons of Valais, Vaud and Geneva: 5.2% had grade 1a, 0.26% grade 1b, and 0.04% grade 2 goitres, not a single one being found unfit because of goitre. In the city of Lausanne 1924/25 23.7% had grade 1b or larger goitres (21), whereas in 1983-87 our figure was only 0.2%.

In 60 major public hospitals, the number of

<table>
<thead>
<tr>
<th>Table 4.</th>
<th>Thyroid weight at autopsy for newborns of both sexes and for males of selected age group (48,68,69).</th>
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<tbody>
<tr>
<td>Iodine, mg per kg in salt</td>
<td>Average thyroid weight (gram) at autopsy</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Year and location</td>
<td>1920-23</td>
</tr>
<tr>
<td>Newborns</td>
<td>Lausanne</td>
</tr>
<tr>
<td>11-20 years</td>
<td>6.8</td>
</tr>
<tr>
<td>21-30 years</td>
<td>34&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>61-70 years</td>
<td>27&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>61-70 years</td>
<td>47&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> mean of two successive 5-year periods <sup>b</sup> In 1949 in Zürich only 77% of salt was iodized which may explain the higher thyroid weights compared to 1936 in Lausanne, where 100% of salt was iodized.

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| Region (with year when iodized salt reached 50%, and other preventive measures) | Reference | Year of survey | Number of children | Percentage of children with goitre grades* |
|---|---|---|---|---|---|---|
| | | | | 0-I | 1a | II | 1b | III + IV |
| Canton of Valais (salt 1925) | (73) | 1920 | 17554 | 28.8 | 54.3 | 16.9 |
| | (73) | 1934 | 18855 | 70.5 | 27.3 | 2.25 |
| City of Lausanne (salt 1924) | (48, 74) | 1923 | 383 | 42.3 | 51.5 | 6.2 |
| | (48, 74) | 1934 | 221 | 97.3 | 2.7 | 0 |
| City of Berne (iodine tablets 1919-35, salt 1936) | (29) | 1919 | ca. 3000 | 16 | 28 | 56 |
| | (29) | 1934 | ca. 3000 | 78 | 10 | 12 |
| Canton of Berne, 5 rural counties or 25 communities therein (salt 1936) | (10) | 1884 | ca. 3000 | 17 | 30 | 53 |
| | (75) | 1933 | ca. 5000 | 31 | | |
| | (75) | 1938 | ca. 5000 | 17 | | |
| | (5) | 1988 | 856 | 87.5 | 11.0 | 1.0 | 0.5 |

* Two gradings were superimposed as fittingly as possible. Swiss Goitre Commission (43): 0 (not palpable), 1 (barely palpable), II (palpable, but neck profile not changed), III (visibly enlarged neck), IV (prominent gland easily identified as goitre), and Delange’s modification of the WHO grading (76): 0 (not or barely palpable, smaller than distal phalange of thumb), 1a (well palpable, not visible even with extended neck), 1b (well palpable, visible with extended neck), 2 (well palpable, visible with neck in normal position), 3 (large goitre, visible at distance). References 10, 29, 75 only used grades normal gland, moderately but clearly enlarged gland, and considerably enlarged gland ("goitre"). Data of reference 10 were calculated by measuring symbols on a map as exactly as possible.

goitre operations had steadily decreased from 3023 in the year 1945 to 2032 in the year 1962, whereas for comparison the number of herniotomies had increased slightly (78). However, in 1967 and 1974, among 1- to 99-year-old hospital patients 30% still had grade 1 and 10% had grade 2 or larger goitres, the prevalence being lower than this average in younger and higher in older patients (61.79). This was blamed on incomplete regression of goitres previously formed under lack of iodine supplementation on one hand, and on ongoing moderate iodine deficiency (Table 3) on the other. Together with data that salt consumption was decreasing and that iodized salt had a share of less than 70% in some Cantons (79,80), this led to the doubling of iodine in salt in 1980. This measure has finally eliminated iodine deficiency (Tables 3-5 and Fig. 1).

Growth, hearing impairment, mental performance, and cretinism

After the introduction of iodized salt in Appenzell in 1922, the average height of 6½-year-old school entrants steadily increased from 111.2 cm in 1922 to 115.7 cm in 1932 and the average height of recruits increased from 161.4 cm in 1920 to 165.8 cm by 1930 (42,81). In the same two periods, the average of men found unfit for service because of stunted growth (height below 154 cm) decreased from 1.85 to 0.72% for the whole of Switzerland (4). It is conceded that this must be seen in the secular trend of acceleration of growth, but this trend was slower, since height of recruits in Appenzell had only increased from 160.5 to 161.4 cm between 1884 and 1920. The findings fit well with Hunziker’s observation that in 1880, i.e. before
Fig. 3.
Goitre as a reason for exemption from military service 1944-46. Basel-Land and Aargau, the only two Cantons which had not yet introduced iodized salt, are conspicuous in the northern part of the map (from 4, with permission). By contrast, in an analogous map prepared in 1921-24 (i.e. before any Canton had introduced iodized salt) the two same Cantons had a goitre prevalence rather below the average (13).
☐: 0 per thousand; ☐: 0.1-1.0 per thousand; ☐: 1.1-2.0 per thousand; ■: more than 2 per thousand.

prophylaxis, the average height of recruits correlated inversely with goitre prevalence (Fig. 4) and that the yearly growth rate of 339 Zürich schoolchildren who received 1 mg NaI weekly was higher than in untreated parallel controls (28).

Admissions to special schools for deaf-mute children in Switzerland averaged 14.3 per 10 000 children between 1915 and 1922. With increasing use of iodized salt it steadily dropped to the rate of goitre-free countries (Fig. 5) (82). These deaf-mute children were capable of schooling and therefore did not fulfil all criteria for cretinism, but the findings are remarkable in view of today's efforts to measure subclinical damage inflicted by iodine de-

Fig. 4.
Mean height versus exemption from service owing to goitre in 19-year-old military recruits 1884-91 in 24 contiguous districts in two north-south sections through western and eastern Switzerland. Recalculated from a figure of Hunziker (28). r=0.8257, p<0.001.
Fig. 5.
Number of pupils per 10,000 children of same age admitted to special schools for deaf-mute children in Switzerland (□-□), and share of iodized salt in percent of total sales (■-■) in Switzerland between 1915 and 1932 (redrawn from 82 with permission).

iciency. Short of overt cretinism, such damage may thus lead to slightly diminished intelligence, stunted growth or increased prevalence of isolated deaf-mutism.

Just before the introduction of iodized salt in the Canton of Berne, de Quervain & Wegelin examined hundreds of cretins in institutions and described the clinical and pathologic-anatomical picture in a classic monograph (83). In 1960, König (84) surveyed the main 6 large institutions for handicapped adults and the 4 homes for mentally retarded children in the Canton of Berne (890,000 inhabitants). He identified 70 cretins, whereas in 1925, according to de Quervain they had housed 700 of them (85). In 1937, Eugster (86) examined all 670 inhabitants born in the severely affected village of Blumenstein and identified 24 (3.5%) full-blown and 10 (1.5%) lesser cretins. In a careful search in 1960, König (84) found only 10 cretins in the same village, all already listed by Eugster. All cretins alive identified by König in the Canton of Berne in 1960 had been born before 1930 (84), the year when iodized salt had reached a 30% share of the market in Switzerland. This fits well with the observation that only small amounts of iodine are necessary to prevent cretinism.

Conclusions and outlook

Iodized salt was the decisive factor in eradicating goitre and cretinism in Switzerland. The Swiss data provide good evidence that iodized salt also prevents in part isolated deaf-mutism, short stature, and mental deficiency without all the other attributes of cretinism, i.e. all aspects encompassed by Hetzel's definition of iodine deficiency disorders (87). Introduction of iodized salt in Switzerland was luckily helped by the constitutionally guaranteed salt monopoly which the Cantons have now secured to the two only salt producers. All surveys show that salt is still the main source of iodine. Among schoolchildren, still about 5-10% have goitres, but only of the clinically irrelevant 1a grade. Iodine supply in Switzerland is now sufficient, but not overly so. If salt intake continues to diminish, the iodide content of salt will have to be raised. The main threat to the iodized salt programme comes from international trade regulations which could eventually break the salt monopoly and cause importation of non-iodized salt.

In summary, iodized salt has without any doubt been the most cost-effective preventive health measure ever applied in Switzerland. At little cost it has prevented a lot of disease and suffering.

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