FROM IODINE DEFICIENCY TO EXCESS: THE TASMANIAN THYROTOXICOSIS EPIDEMIC OF THE 1960s

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(with three text-figures and one plate)

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Even though iodine deficiency in Tasmania had been known since the 1830s no full account of the thyrotoxicosis epidemic of 1966–67 has ever been recorded. This personal narrative tracks the history of this epidemic in Tasmania during the 1960s, when it first appeared as iodine deficiency, then as iodine excess, how it was formally recognised and the events leading to its eventual treatment. The addition of iodine into the diet of Tasmanians, initially in bread and then unwittingly through use of iodophors in the dairy industry, resulted in a sequence of events that required unravelling by medical practitioners new to the field but aided by experts from elsewhere. The Tasmanian thyrotoxicosis epidemic was, and continues to be, cited in the annals of the scientific literature as an important medical case study.
Key Words: thyrotoxicosis, excess iodine, Tasmanian epidemic, bread fortification, iodophors, dairy industry.

BEGINNING OF THE EPIDEMIC

Launceston over the years has experienced major and minor outbreaks of diseases which have included typhoid, smallpox, measles, diphtheria, the influenza pandemic 1919, polio 1937 and 1950s, HIV and more recently the COVID-19 pandemic of 2020. Iodine deficiency in Tasmania had been known since the 1830s (Parker 1833) and by 1949 the prevalence of iodine-deficient goitre was being considered a serious public health problem (pl. 1). Iodised salt had been used successfully to treat iodine deficiency in several countries but at this time was not considered a practical solution for use in the Tasmanian food distribution system. Nor was it the preferred method of supplementation recommended by the principal researcher at the University of Sydney Dr F.W. Clements, who by 1947 had already successfully reduced the incidence of goitre in Canberra school children using potassium iodide tablets. Tasmanian authorities therefore decided to address the iodine imbalance using the tablet method and in the 1950s, through the Commonwealth Government and the public health system, 10-milligram tablets of potassium iodide were made available to school children for their weekly consumption. While many Tasmanians may still remember being required to take a small white 'goitre tablet', the consensus was that the tablets tasted unpleasant and periodic surveys conducted over 16 years showed that tablet distribution and compliance by children was relatively poor. Nevertheless, there was a gradual fall in the incidence of goitre from the late 1950s onwards, followed by a definite improvement between the years 1960–65, and this was attributable to the tablet supplement.

PLATE 1 — Two Tasmanian women displaying enlarged goitres (from the private collections of Mrs Valerie Crann and the late Dr Marita Bardenhagen).

In April 1966, the Department of Health decided to replace the potassium iodide tablets and instead required iodate to be added to bread made in Tasmania. Potassium iodate, 4 ppm dry weight (designed to produce an intake of 100–150 μg iodine per day), was from then on substituted for potassium bromate as a bread improver used in bread making in the state. The health outcome of adding iodine to bread was immediately obvious and within three years the rate of endemic goitre had been reduced dramatically. By 1967 it was thought that iodised bread had satisfactorily corrected Tasmania's iodine deficiency and this was confirmed through measurement of urinary iodine excretion, plasma inorganic iodide and radioiodine uptake. Tasmania's iodine imbalance had been addressed, or so it was thought.

Within a matter of months, the situation changed. Iodine levels, now regarded as normal, began to rise as more and more people began presenting at thyroid clinics and private medical practices around the state. They were displaying a range of previously unseen symptoms and so it was that Tasmania's iodation epidemic had begun.

Early identification

The Launceston Thyroid Clinic had operated from 1943 and was first established by Dr John Grove Snr with Alan Pryde as surgeon to the clinic until his death in 1959. Dr Grove was joined in 1955–57 by a young resident medical officer, Dr George Vidor, who took over the clinic when Dr Groves retired in 1966. By September 1966, about five months after iodation began, Dr Vidor, reported seeing more thyrotoxic patients than usual and by 1967, at the height of the epidemic, Dr John Stewart was invited to join the clinic to help with the workload. When the flood of thyrotoxic patients threatened to overwhelm the clinic, Dr Vidor recruited me, his partner in general practice at the time, as his Honorary Clinical Assistant thus beginning a partnership in thyroid studies that lasted virtually until his death in 2004. Dr George Vidor became my mentor in diagnosing and treating thyroid disorders but at the beginning of this epidemic we were all novices seeking guidance with this unfolding set of events.

The Launceston Thyroid Clinic had an extremely good record-keeping system, which was linked with the Department of Nuclear Medicine, formerly the Isotope Department of the Peter MacCallum Clinic established in 1950. These records established a sound baseline incidence pattern for comparing 1950–65 with the sudden increase in the number of cases presenting to the clinic in 1966. Good referral patterns, clinical criteria and established evaluation were essential components of what was to be an unprecedented epidemic of iodine induced thyrotoxicosis, with very few cases, if any, bypassing the system. In contrast, the Royal Hobart Clinic had only been supervised for a short period by a specialist endocrinologist — Dr Roger Connolly — and up until 1965 accurate figures were not available on all presenting cases.

Dr Vidor contacted Dr Connolly and several endocrinologists in Victoria for advice. He was soon referred to Basil Hetzel, Professor of Medicine at the University of Adelaide and already eminent in the field of iodine deficiency. When told of the situation in Tasmania, Professor Hetzel immediately understood its significance and took over testing the blood from Launceston thyrotoxic patients in his own laboratory and provided the essential early guidance to medical practitioners.

Iodine-induced thyrotoxicosis had been known since the late nineteenth century but was usually described in individuals who were given large doses of iodine for the treatment of goitre or received large doses of iodine incidentally, such as in radiological contrast media. In epidemic form following correction of iodine deficiency it had been suspected in the USA in the 1920s and in Holland in the 1940s, but the numbers were not large, and the risk not taken seriously. Bread iodation since then in Canberra had had no apparent adverse effect and it was generally agreed that correction of iodine deficiency could do only good. The experience in Tasmania was the first irrefutable evidence of iodine-induced thyrotoxicosis in response to correction of iodine deficiency with modest doses of iodine. It could be described as a first for Tasmania and it was obvious that the epidemic demanded thorough detailed study.

TRACKING THE EPIDEMIC

Whether the dose of iodine was excessive was answered by measurement of urinary iodine in adults and by dietary surveys. This work was carried out by the Tasmanian Department of Public Health and showed no evidence of excessive dietary iodine. The iodine intake of Tasmanians had been increased only to a level that was considered 'normal' and, compared to many naturally non-deficient areas, was quite modest.

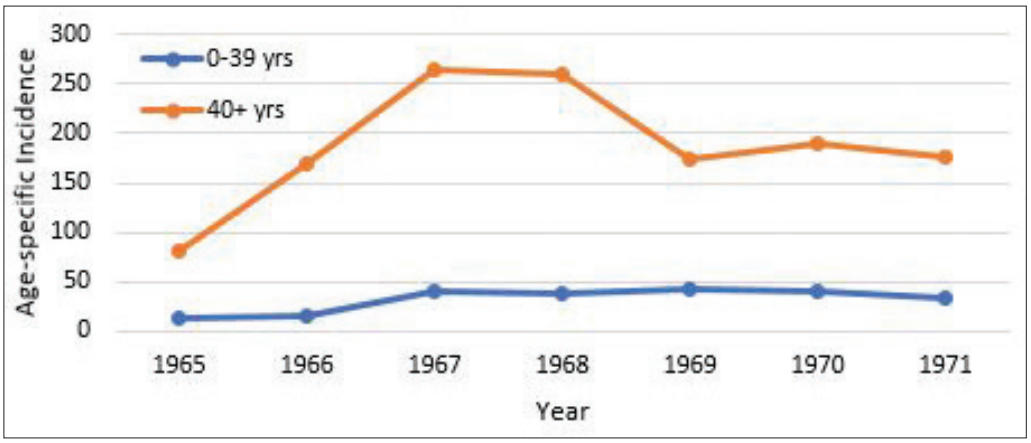
Those most at risk were older people, especially those with pre-existing goitre. Comparing the six years before iodation of bread to the six years after, the factor of increase in those below 40 years of age was x1.6 but in those aged over 50 years was x3.8.

Figure 1 indicates the age-specific incidence of thyrotoxicosis per 100,000 (1965–71) of two separate age groups: 0–39 years and 40+ years. The graph shows that thyrotoxicosis is more common in older people suffering from Graves' disease in a moderately iodine deficient environment when there is an excess of iodine supplementation.

In Figure 2 the sex-specific incidence of those undergoing treatment is shown for northern Tasmania during the period 1960 to 1994, by which time the epidemic had subsided.

It is interesting that prior to the epidemic, the sex-specific incidence of thyrotoxicosis was about 2:1; however, following the iodination of bread and other dietary supplements, this incidence peaked in 1967, almost 9:1 more prevalent in females, confirming a sex bias for this disease which has been well-documented by others.

During this period the incidence of thyrotoxicosis was mirrored by the growing number of patients treated with radioactive iodine.



Age (years)	1965	1966	1967	1968	1969	1970	1971
0–39	12.8	16.4	41.3	37.6	43.3	39.4	33.7
40+	81.4	170.2	265	259	174	190	175

FIG. 1 — Age-specific incidence of thyrotoxicosis per 100,000 (1965–71) of two separate age groups: 0–39 years and 40+ years.

The pathological mechanisms were not so easily determined but it was fortunate that the epidemic occurred at a time when the study of the thyroid was at an exciting stage of discovery. It was only six years earlier that Duncan Adams of Christchurch had published his discovery of the long-acting thyroid stimulator (LATS) in the blood of thyrotoxic subjects. This led ultimately to the recognition that Graves' disease was an autoimmune disorder in which abnormal antibodies stimulated the thyroid into overproduction of thyroid hormone and related antibodies caused the characteristic eye changes. LATS is not found in patients with toxic nodular goitre.

Furthermore, in the 1960s advances in technology were making it possible to study thyroid disorders in greater detail than previously. Techniques for the direct measurement of thyroid hormones and thyroid-stimulating hormone (TSH) in the blood made the diagnosis of thyrotoxicosis easier and more precise and the development of thyroid scanning made it possible to detect autonomous nodules. Thus, for the first time, it was possible to determine with a high degree of certainty which thyrotoxic patients had Graves' disease and those with toxic nodular goitre.

Our studies over several years, involving the cooperation of many researchers from interstate and overseas who applied their new laboratory techniques to blood from Tasmanian patients, led to the conclusion that iodine-induced thyrotoxicosis is not a unique disease. Patients suffering from it can all be shown to have either Graves' disease or toxic nodular goitre; there is no third type of thyrotoxicosis. As previously explained, iodine deficiency causes goitre in children and adolescents. In adult life these goitres become nodular and some of the nodules can, after decades, become autonomous. Autonomous thyroid tissue has lost its dependence on TSH to produce hormone; it secretes thyroid hormone without regard for the need for it. The amount of thyroid hormone produced

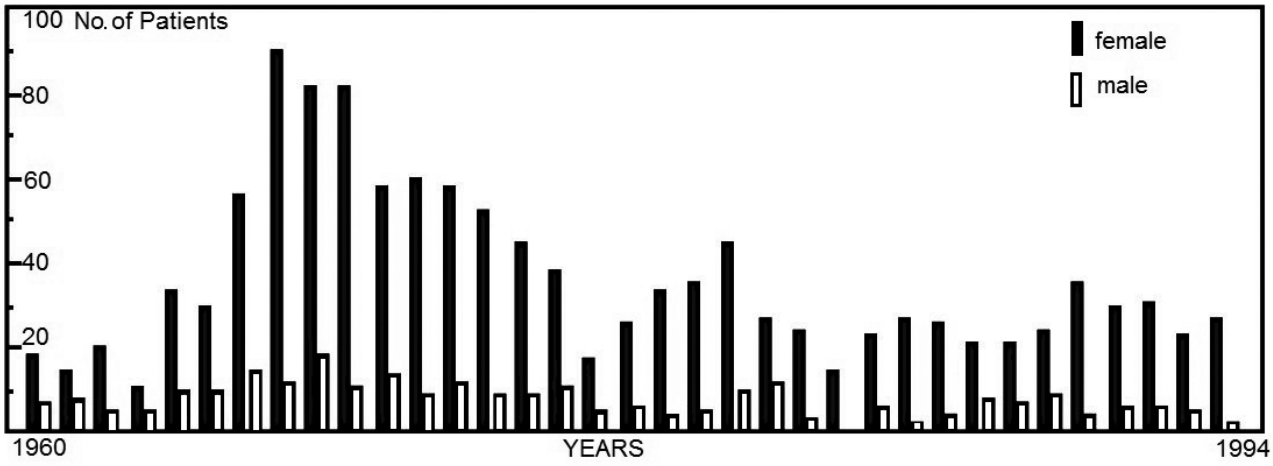


FIG. 2 — Number of patients (males and females) receiving radioactive iodine treatment for thyrotoxicosis in northern Tasmania from 1960 to 1994.

is determined by the amount of autonomous tissue and the availability of iodine.

In a population exposed to iodine deficiency for many years there will be people who, while not unwell, have autonomous thyroid nodules producing hormone in a manner not subject to normal control. There will also be some who have uncontrolled thyroid activity because of Graves' disease but in whom thyroid hormone levels are still normal. If iodine deficiency is relieved the additional iodine allows the uncontrolled thyroid tissue in both groups to produce excess hormone causing thyrotoxicosis. Because nodular goitre is more common in iodine-deficient populations than is subclinical Graves' disease, most iodine-induced thyrotoxicosis is in the form of toxic nodular goitre. This explains the preponderance of older patients in the epidemic.

The duration of the epidemic seemed as if it would be easily determined simply by waiting until it stopped. But, as we eventually discovered, this was not the case.

WHAT WAS THE CAUSE?

The cause of the epidemic was at last revealed in April 1967 when Basil Hetzel met Dr Heather Gibson, the Chief School Medical Officer, to discuss arrangements for a urinary iodine survey which the Health Department had requested and she told him of the bread iodation. Professor Hetzel visited Launceston soon afterwards, studied our figures for thyrotoxicosis to assure himself that the increase was real and then proclaimed to us the condition was known as "Jod Basedow". Jod Basedow Syndrome (iodine-induced thyrotoxicosis) could only be correlated with high levels of iodine intake in the Tasmanian diet (Connolly 1971a, b, 1973) and so the link was made to bread.

While the decision by health authorities to require the iodine supplement in bread was for good health reasons, this was not widely known by the public. When the thyrotoxicosis epidemic eventually unfolded, it led to heightened public suspicion at the authority's motivation especially at a time when the anti-fluoridationists were campaigning against mass medication. As is so often the case when the facts are withheld, speculation concerning the motives for Government secrecy soon led to scurrilous rumours emerging, all of which were proven to be false.

While the link with bread had been made, the cause of the epidemic was in fact not so straightforward. The mean thyroid uptake of radioactive iodine-131 during the period in which the incidence of goitre declined (1960–65) was reflected in the euthyroid patients presenting to the author's department suspected of thyrotoxicosis over the same period. There is no doubt that improvement in the reduction in goitre in the period 1960–65 was attributable to the following range of factors.

In 1960 new shipping services commenced with the Bass Strait ferries bringing foodstuffs into Tasmania including fruit, vegetables, milk and other manufactured goods that had been produced elsewhere. This product expansion corresponded with the rise of large supermarket food chains now stocking a range of frozen products using iodised sanitation methods which unwittingly added even more iodine to the dietary intake of Tasmanians.

In 1963 yet another new group of products entered the Tasmanian food chain. This was the uptake of iodine-based sanitisers in the Australian dairy industry to disinfect milk vats, cow teats and other dairy equipment more effectively. These new products were also being used extensively throughout the Tasmanian dairy industry and introduced yet another concentration of residual iodine into widely consumed products. Iodophors were first marketed in Tasmania in 1963 and their use increased rapidly; by 1970 most dairy farmers used them. It was Dr Roger Connolly who first made the connection between the use of iodophors so that when bread iodation began in 1966 iodine deficiency was already being corrected by the iodophor residues in milk. These revelations led George Vidor and I to reconsider our data on the incidence of thyrotoxicosis. This was not routinely recorded until 1966 and it was only when we were retrospectively gathering such information for the pre-iodation years that it was revealed that the incidence had virtually doubled in 1964 and 1965. We had attempted to explain this by increased imports of food, but it was now apparent that it was due to the increasing use of iodophors from 1963 onwards.

Figure 3 shows that there were three occasions when the incidence of thyrotoxicosis rose: in 1964 following the introduction of iodophors in 1963; in 1966–67 after iodine was added to bread in 1966; and in 1971 after milk processors began using iodophors to clean their road tankers. When each of these practices were stopped, the incidence of thyrotoxicosis began to fall steadily. Before this, all reported iodine-induced thyrotoxicosis had followed the deliberate administration of iodine, either as treatment for individual patients or by dietary supplementation to correct iodine deficiency.

NOT SO STRAIGHTFORWARD

By the beginning of 1970 it seemed that the epidemic was over. The incidence of thyrotoxicosis had peaked in 1967 and in the two years following had declined although the level was still higher than pre-iodation. A goitre survey had shown the virtual eradication of juvenile goitre, so although the epidemic was a high price to pay by one generation it ensured future generations would be free from iodine deficiency. Our thinking was soon to be dispelled by two surprises.

In 1972, the distribution of free milk to schoolchildren was discontinued and a decrease in milk consumption followed this withdrawal (430 ml/day in 1973 to 285 ml/day in 1974). 'Big M' flavoured milk came onto the Tasmanian market in October 1978 with a vigorous marketing campaign resulting in an increase per capita of milk consumption to approximately 300 ml/day (Gibson 1995). Iodine excretion showed a rise, due to the additional milk, and is reflected in the incidence of patients presenting

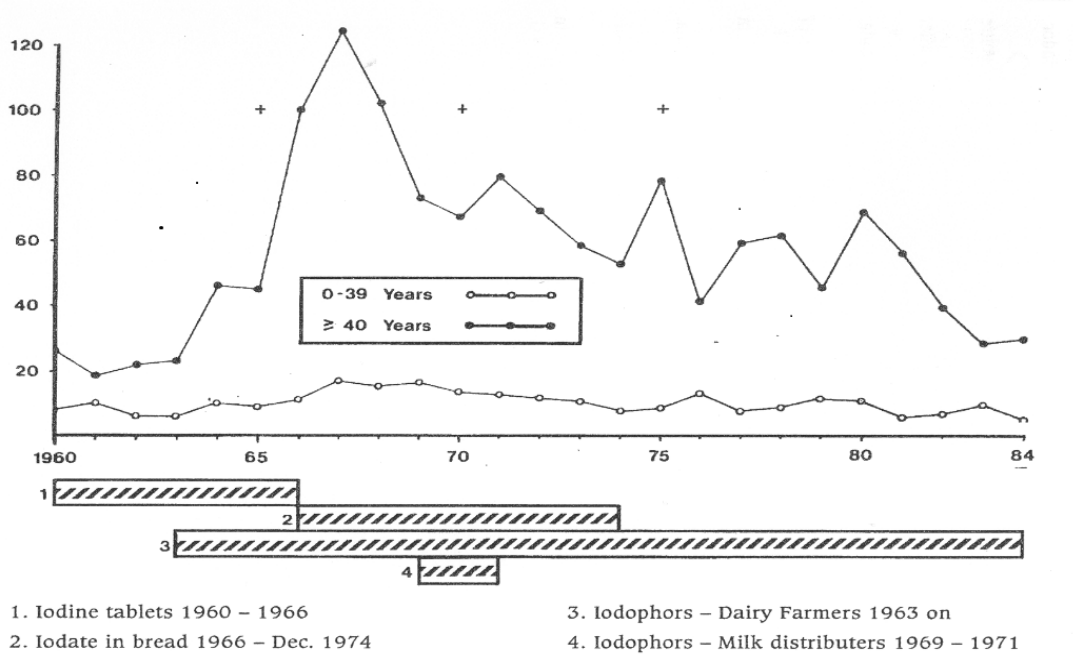


FIG. 3 — Age-specific incidence of thyrotoxicosis cases in the Tasmanian population from 1960 to 1984. (From Gibson 1995)

for treatment of thyrotoxicosis at the Launceston General Hospital. The major rises and falls in such attendances have been consistent with the dietary availability of iodine in the state of Tasmania.

By 1974 bread manufacturers had gradually stopped using the improver containing iodine so from then on bread had ceased to be a source of dietary iodine and without anyone realising it, its place had been taken by milk.

By 1990 the iodophors used as sanitisers in the milk industry were being phased out in favor of chlorine-based sanitisers. At this time the Department of Health stopped monitoring milk as the prevalence of goitre had fallen quite considerably. Dr Heather Gibson, who had been the school medical officer from 1949 to1984, provided a report on iodine-deficient disorders in Tasmania covering the period of her appointment to the Department of Health (Gibson 1995). The situation at the end of 1994 was that after 45 years of iodine supplementation in one form or another (i.e., potassium iodide tablets, iodate added to bread as an improver and iodophor sanitisers introduced to the dairy industry in 1966) we were now only left with iodophors in the dairy industry providing adequate levels of iodine intake in milk for the Tasmanian population.

END OF THE EPIDEMIC

An epidemic can usually be regarded as over when the incidence of the disease returns to the level observed before the epidemic began. This never happened with thyrotoxicosis in Tasmania. Even as late as 1990 the incidence was more than half as much again as that recorded in 1960–63. By 1982, however, the incidence had stabilised at about the level that persisted at least until 1990. The epidemic, therefore, can be said to have lasted from 1964 to 1981. My belief is its long duration is possibly explained by the existence of older people with goitres containing autonomously functioning tissue which, in the 1960s, had not yet grown big enough to cause thyrotoxicosis. Over the ensuing years the autonomous tissue grew and caused them to become thyrotoxic.

The continued raised incidence of thyrotoxicosis after 1982 compared with the years before iodine intake increased is probably an inevitable consequence of the rise in iodine levels. In any population there are a few people in whom thyroid function is no longer under normal control, whether because of Graves' disease or autonomous nodules. An increase in the availability of iodine may lead to increased thyroid hormone production and thyrotoxicosis. Rather than saying that thyrotoxicosis was increased after an increase in iodine intake it could be argued that it was previously depressed by iodine deficiency.

The results of the studies were published in peer-reviewed journals. The first paper, a preliminary communication to the *Lancet*, took some time to complete as it was written in collaboration with Dr Connolly, who by then was serving in Vietnam and drafts had to be exchanged via post. Drs Vidor and Stewart investigated the epidemic assisted by Professor B. Hetzel (Adelaide), Dr C. Eastman (Woden Valley Hospital), Dr D. Adams (Dunedin, NZ) and Dr R. Utiger (Washington, USA) who performed specialist tests to establish the mechanism involved. In 1970 the northern and southern Tasmanian clinics combined their resources which significantly expanded the understanding of thyroid disease and culminated in a number of scientific papers (Vidor *et al.* 1968, Connolly *et al.* 1970, Connolly 1971a, 1971b, 1973, Vidor *et al.* 1973, Adams *et al.* 1975, Stewart *et al.* 1976, Stewart & Vidor 1976). Dr Vidor was an invited speaker at a workshop on iodine-induced thyrotoxicosis held in Boston in 1996 by the International Council for Control of Iodine Deficiency Disorders, and

the proceedings of the workshop were published in the journal *Thyroid* in 1998. In later years these events have continued to be published in books and papers by many research colleagues, and the research continues to this day (Hynes *et al.* 2004, Burgess *et al.* 2007, Richards & Stewart 2007, Seal *et al.* 2007, Richards & colleagues 2020).

WHY TASMANIA AND NOT ELSEWHERE?

There are several theories as to why Tasmania was the site where the first serious epidemic of iodine-induced thyrotoxicosis was described. The combined effect of extra dietary iodine from bread and milk, although not leading to abnormally high intakes, added more iodine to the diet than planned which increased the severity of the epidemic.

In 1966 there were few laboratory tests of thyroid function and most involved radioisotopes. The only isotope laboratories (later to be known as departments of nuclear medicine) were in Hobart and Launceston. This led to a concentration of cases in these two centres making the epidemic more obvious than if the cases had been spread thinly over many practitioners across the state. Iodine-induced thyrotoxicosis must have occurred elsewhere, but the majority of cases were being detected. This is perhaps understandable as much of the work on iodine deficiency in the years after the Second World War was in severely deficient areas such as the Belgian Congo, the Himalayas and the Highlands of New Guinea where medical services were scant and many cases of thyrotoxicosis could go undiagnosed. Furthermore, life expectancy in these countries was such that few people survived beyond the age of 50 years when the risk becomes greater.

CONCLUSION

For the first time the existence of epidemic iodine-induced thyrotoxicosis was irrefutably demonstrated. This caused a global reassessment of the approach to correction of iodine deficiency. It had been made clear that any program of iodine supplementation in an iodine-deficient population carries the risk of causing iodine-induced thyrotoxicosis; and if the population contains many older people, that risk becomes a certainty.

The elimination of iodine deficiency remains as important as ever but is now pursued with greater caution. The dose of iodine is chosen to be as small as is possible while still being adequate to relieve deficiency and medical services are alerted regarding the early detection and treatment of the ensuing thyrotoxicosis.

Tasmania is not assured of environmental iodine stability having discontinued the monitoring of iodine in milk in the mid- to late 1980s. Any rationalisation within the dairy industry (use of iodophor sanitisers) will impact severely on the status of thyroid physiology of Tasmania's population as no other dietary sources would sustain acceptable levels of dietary iodine intake. Potentially the risk of further epidemics of thyrotoxicosis is high especially if unknown sources of iodine supplementation are insidiously introduced to the diet of an ageing Tasmanian population. Despite existing programs of prophylaxis about one billion people worldwide are at risk from iodine deficiency and the prevention of iodine deficiency remains a challenge throughout the developing world.

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