

PREVENTION OF ENDEMIC GOITRE WITH IODIZED SALT*

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The paper describes a study, carried out over 16 years, of the use of iodized salt for the control of endemic goitre in a valley of the Himalayan foothills. From 1956, salt was fortified with either potassium iodide or potassium iodate to provide an estimated daily intake of 200 µg per head. There was a progressive and significant decline in goitre prevalence, together with a return of the pattern of iodine metabolism to within normal limits. It is concluded that endemic goitre can be successfully controlled by iodization of domestic salt.

Endemic goitre is a worldwide disease and the number of persons afflicted with it has been estimated at 200 000 000 (Clements et al., 1960). Although the essential role of iodine deficiency in the etiology of goitre is well established, the possible role of other goitrogenic factors of dietary origin is raised from time to time (Delange & Ermans, 1971). Much progress has been achieved in its control in different parts of the world through iodine prophylaxis, and injectable iodized oil has been used with success in recent years (Hetzl, 1970). However, there are still large parts of Asia, Latin America, and Africa where goitre persists in a highly endemic form, and the relationship of the disease to other coexisting public health problems is not clear (PAHO Scientific Group on Research in Endemic Goitre, 1969; Ramalingaswami, 1973). The experience obtained in this study of continuous prophylaxis with iodized salt in a Himalayan valley may be applicable in other parts of the world. This disease is widespread and endemic in the Himalayas (Ramalingaswami, 1953). The Indian goitre belt extends over a distance of 2 400 km along the southern slopes of the Himalayas and the adjoining plains. McCarrison's pioneer work on the etiology of goitre in the early part of this century indicated that it was of complex derivation and related to infection with intestinal organisms and to faulty and unbalanced diets (McCarrison & Madhava, 1932). Later, the possibility that fluoride and an excessive intake of calcium salts through drinking hard water might be implicated in the genesis of endemic goitre in the Himalayan foothills was investigated (Stott et al., 1931; Wilson, 1941). Recent studies by our group, with radioactive iodine and more refined methods of assay of stable iodine and of its organic compounds in tissue fluids, revealed that the pattern of iodine metabolism observed in persons with endemic goitre in the Himalayas was consistent with the hypothesis that iodine deficiency was probably the primary etiological factor (Ramalingaswami et al., 1961; Ramalingaswami, 1964). Similar thyroid responses suggesting that iodine deficiency was the primary etiological factor were observed more recently in our studies of endemic goitre in Nepal (Ramalingaswami et al., unpublished report, 1970) which is contiguous with the Indian goitre belt, and

in Sri Lanka (Ramalingaswami, unpublished report, 1970; Deo & Subramanian 1971).

BACKGROUND TO THE STUDY

The Government of India, in collaboration with the State Government of Punjab and the Indian Council of Medical Research, decided in 1954 to set up a prospective study to evaluate the effectiveness for preventing goitre of small physiological doses of iodine added to the common salt habitually consumed in the endemic areas. The study was to include a comparison of the effectiveness of potassium iodide and potassium iodate in amounts supplying equal quantities of iodine.

In 1956 three experimental zones were selected and salt containing 1 part of potassium iodide per 50 000 parts of salt was provided in zone A, and salt containing 1 part of potassium iodate per 40 000 parts of salt was provided in zone C. The population of zone B was provided with salt without added iodine. The criteria used in selecting the zones, the main features of the zones themselves, the plan of the study, and the results up to 1962 have been published previously (Sooch & Ramalingaswami, 1962).

THE PRESENT STUDY

In 1962, when it had become obvious that the prevalence of goitre was dropping rapidly in zones A and C, while that in zone B remained unchanged, it was decided to provide iodized salt (1 part of potassium iodate to 40 000 parts of salt) for the population of zone B also. To facilitate the operations, salt fortified with potassium iodate was, in fact, provided to all three zones from 1962 onwards.

A second survey was made in 1968, and in 1972 a spot-check of goitre prevalence was made by a team of independent physicians who had not been connected with the baseline survey or either of the subsequent surveys. At this time, measurements of thyroid function were also made to correlate the changes in the prevalence rates of goitre with changes in thyroid function. The results of these studies are presented in this report.

METHODS

The survey in 1968 was carried out in two stages: (1) all schoolchildren attending the schools that had been surveyed in 1956 and again in 1962 were re-examined for goitre, and (2) infants aged 0–4 years and children of school age (5–15 years) who were not attending school were surveyed with the general population of the villages that had been surveyed in 1956 and 1962. For reasons of economy, in 1968 only a sample of the general population was surveyed. A systematic sample of house-

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holds (approximately one in three) was selected and all children under 16 years of age who were present when the examiner visited the household were included in the survey. Children in the age group 11–15 years were slightly underrepresented in the sample since some of them were working in the fields at the time of the visit. However, there is no evidence that these children were different from the rest in regard to goitre prevalence, as their households were similar in all respects to the others surveyed, notably in respect of the prevalence of goitre in children under 11 years of age. The number of children under 16 years of age surveyed in schools and in the general population of the three zones in 1956, 1962, and 1968 are presented in Table 1.

The survey technique previously described (Murray et al., 1948) and used in the earlier surveys was followed in the present study. As before, all degrees of enlargement of the thyroid were considered as goitre. The examinations were made by a physician specially trained in the detection and grading of goitre, and his results were checked from time to time in a series of trial cases.

The team of physicians who performed the spot-check of goitre prevalence examined 118 children between the ages of 7 and 12 years in two randomly selected schools in zone A and another 181 children between the ages of 7 and 15 years in two schools in zone B. Some indices of iodine metabolism were measured in these children and the results were compared with those obtained a few months earlier in another group of children of similar age and sex who lived several hundred kilometres to the east of Kangra Valley, in the same goitre belt, but who had not received iodine prophylaxis. The methods of measurement, described below, were identical in both groups.

Neck uptake of radioiodine was determined, 24 h after the oral administration of 25–50 μ Ci of 131 I, by means of a Tracer Lab rate meter and a P-20D scintillation probe. The detector was held 254 mm from the neck. Venous blood samples were collected in iodine-free glass containers and serum or plasma was separated and transported on ice to the All India Institute of Medical Sciences within a few days of collection. Protein-bound iodine (PBI) was estimated in the serum or plasma by the modified method of Barker et al. (1951). Urinary iodide was estimated on casual urine samples by the same method. Creatinine was estimated on the same samples by the alkaline picrate method. Results were expressed as micrograms of iodide per gram of creatinine.

RESULTS

Schoolchildren

The prevalence of goitre in schoolchildren in 1956 and 1962 has been reported previously by Sood & Ramalingaswami (1962). The survey in 1968 showed that the steady decline in prevalence rates had continued in zones A and C. In that year totals of 2 505 and 2 677 children were examined in zones A and C, respectively, and the overall prevalence rates for these zones were 8.5% and

Table 1. Number of children surveyed

	Year of survey	Zone A	Zone B	Zone C
children attending school	1956	2 529	2 027	2 964
	1962	3 495	4 544	3 420
	1968	2 505	2 533	2 677
children in the general population	1956 (all zones)	6036		
	1962	1 576	1 804	1 189
	1968	612	542	516

Table 2. Prevalence of goitre in schoolchildren by sex

Zone	Sex	Prevalence of goitre (%) ^a		
		1956	1962	1968
A	male	34.1 (2 019)	19.3 (2 539)	7.5 (1 683)
	female	51.4 (510)	18.4 (956)	10.4 (822)
B	male	34.2 (1 605)	39.8 (3 262)	17.2 (1 507)
	female	51.7 (422)	41.5 (1 282)	17.0 (1 032)
C	male	36.0 (2 338)	14.5 (2 527)	8.4 (1 821)
	female	47.4 (626)	14.9 (893)	10.6 (856)

^aFigures in parentheses indicate the number examined.

9.1%. The significant difference reported earlier between the prevalence in zone A and zone C in 1962, which was thought to be related to the use of potassium iodide in zone A and potassium iodate in zone C, had disappeared by 1968. In zone B the provision of iodized salt from 1962 onwards resulted in a reduction in overall goitre prevalence from 40.3% in 1962 to 17.1% in 1968. The prevalence of goitre in schoolchildren in 1956, 1962, and 1968 by age group is shown in Fig. 1. The prevalence rates by sex, shown in Table 2, demonstrate the same trends as shown in Fig. 1.

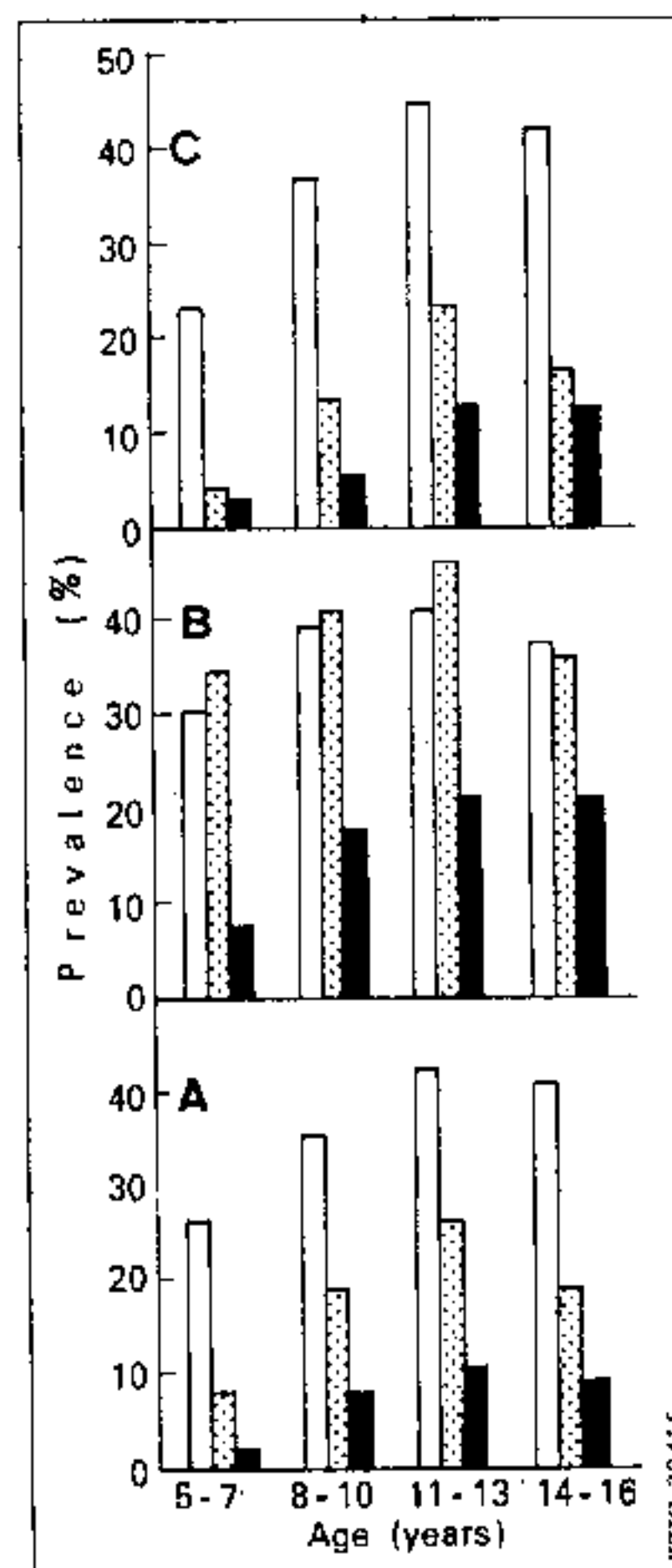


Fig. 1. Prevalence of goitre by age in schoolchildren in zones A, B, and C in 1956, (white columns), 1962 (stippled columns), and 1968 (black columns).

Consideration of the prevalence rates by age group for the different degrees of thyroid enlargement for the period 1962–68 confirmed the earlier conclusions of Sooch & Ramalingaswami (1962) that the reduction in goitre in schoolchildren was brought about mainly by two mechanisms, the prevention of the disease in goitre-free children and reversion of some of the mild goitres to normality.

Children in the general population

Data concerning the prevalence of goitre in these children in 1956 and 1962 were published earlier (Sooch & Ramalingaswami, 1962). The 1968 survey showed that the prevalence continued to decline in zones A and C, reaching levels of 1.8% and 1.2%, respectively. In zone B the prevalence declined from 30.5% in 1962 to 4.8% in 1968, a decrease comparable with that in zones A and C between 1956 and 1962. The change in prevalence from 1956 to 1968 in these children is shown, by age group, in Fig. 2. These data confirm the findings in schoolchildren and show that there were very few cases of goitre in any zone among the children born after the introduction of iodized salt. An analysis of the data by sex (Table 3) shows essentially similar findings.

Of 118 children studied in zone A in the course of the spot-checks by independent physicians, only 2 (1.7%) had mild goitres that were palpable but only just visible after stretching the neck (grade b). Of 181 children studied in zone B, 10 (5.5%) had grade b goitre.

Table 3. Prevalence of goitre in children in the general population by sex^a

Sex	All zones		Zone A		Zone B		Zone C	
	1956	1962	1968	1962	1968	1962	1968	
males	20.4 (2 970)	4.4 (765)	1.9 (312)	26.3 (843)	4.4 (252)	5.6 (556)	0.4 (267)	
females	29.8 (3 066)	5.8 (811)	1.7 (300)	34.7 (961)	5.2 (290)	5.6 (633)	2.0 (249)	

^aThe figures in parentheses indicate the number examined.

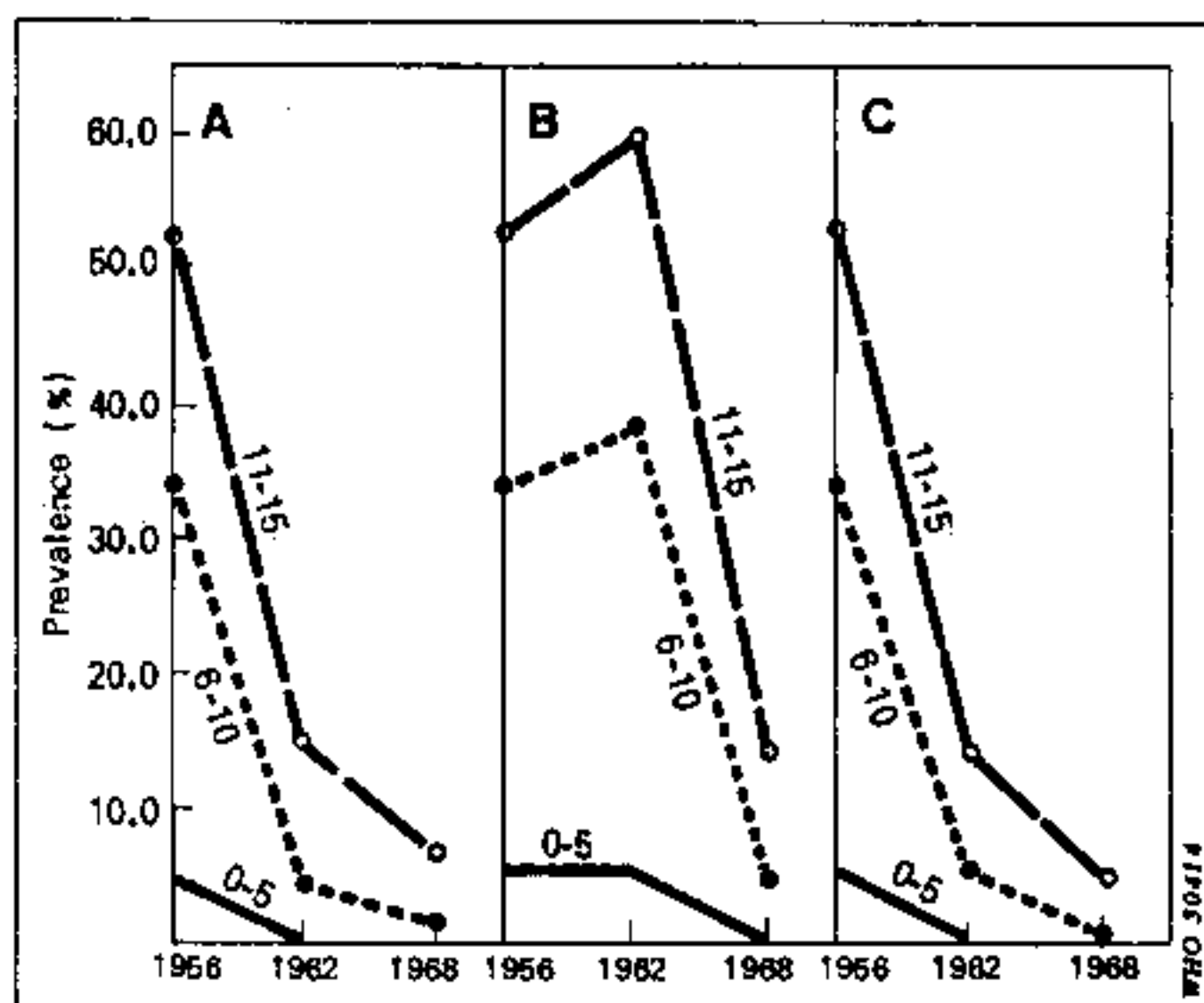


Fig. 2. Prevalence of goitre by age (years) in children in the general population in zones A, B, and C.

Measurements of ¹³¹I in the neck showed that the 24-h uptake was 68.7% of the fed dose in the area east of the Kangra Valley where no iodine was added to the salt, and only 37.8% of the fed dose in zone A. Urinary excretion of iodine was high in zone A (204 µg iodide per g of creatinine) and low in the area where iodine was not added to the salt (30.2 µg iodine per g of creatinine). This pattern of uptake and excretion in the areas where no iodine was added was similar to that found in other endemic areas (Ramalingaswami et al., 1961). The levels of protein-bound serum iodine were higher in zone A (44 µg PBI per litre serum) than in the control area (38 µg PBI per litre serum), but were still not as high as the levels found in nonendemic areas of India (Kochupillai & Ahuja, 1967). These results are summarized in Table 4.

DISCUSSION

This study, carried out over a 12-year period with a spot-check 4 years later, involved in 1956 a population of approximately 100 000 persons in the Kangra valley in the Himalayan goitre belt. The three zones into which the study area was divided were broadly similar in 1956 and the changes that occurred in the socioeconomic status of the populations during the study were similar in all the zones.

The findings are clear. In zones A and C, where iodized salt was provided from 1956, there was a steady and continuous decline in goitre prevalence up to 1968. In Zone B the prevalence of goitre declined between 1962 and 1968 after the provision of iodized salt commenced in 1962. These findings suggest that the fall in goitre prevalence is attributable to the introduction of iodized salt.

It is of interest that there was a steady decline in goitre prevalence throughout the experimental period. A study of the figures by age groups shows that iodized salt provided protection against goitre to those who were born in the area after its introduction. In Zones A and C, where iodized salt has been continually distributed since 1956, there is a negligible amount of goitre in those under 10 years of age and none in the 0–5-year age group. The limited information obtained on goitre prevalence in schoolchildren by means of spot-checks by independent observers suggests that the decline in goitre prevalence is continuing and that the goitres encountered are mild.

The data on iodine metabolism, although limited, also suggest that, with the decline in the goitre rate, the pattern of iodine metabolism has been restored to within normal limits in respect of thyroid uptake of radioiodine and urinary excretion of iodide. The PBI levels have not yet risen to the levels found in nonendemic areas, such as Delhi, where the mean PBI value is about 6.0±0.70 µg per 100 g serum.

Table 4. Comparative data on 24-hour ¹³¹I neck uptake, urinary iodide excretion, and protein-bound iodine in iodized and non-iodized areas of endemic goitre^a

Area	24 hour ¹³¹ I neck uptake (%)	µg urinary iodide/g creatinine	Protein bound iodine (µg/litre serum)
iodized (Kangra valley)	37.8±3.44 (53)	204±8.36 (28)	44.0±2.8 (10)
non-iodized (Eastern U.P.)	68.7±8.30 (70)	30.2±2.87 (46)	38.7±3.1 (24)

^aThe figures in parentheses indicate the number of subjects studied.

RÉSUMÉ

PRÉVENTION DU GOITRE ÉNDÉMIQUE PAR LE SEL IODÉ

La vallée de la Kangra, située dans la ceinture du goitre endémique de l'Himalaya, a été choisie en 1954 pour servir de cadre à une étude prospective de la valeur prophylactique du sel iodé pour la lutte contre la maladie. La région a été divisée en 3 zones: la zone A a été approvisionnée en sel enrichi d'iodure de potassium, la zone C en sel enrichi d'iodate de potassium, tandis que la zone B (zone témoin) recevait du sel ordinaire. On a calculé la teneur en iodure et en iodate du sel de manière l'assurer un apport quotidien d'environ 200 µg par habitant.

L'expérience a débuté en 1956 après une enquête préliminaire montrant une prévalence très semblable du goitre dans les 3 zones. Cinq à six ans plus tard, en 1962, on a enregistré une réduction massive de la prévalence de l'affection dans les zones A et C alors que la prévalence demeurait inchangée dans la zone B. A partir de ce moment, on a cessé de considérer la zone B comme zone témoin et on y a introduit l'usage de sel enrichi d'iodate de potassium. La prophylaxie a été poursuivie dans les zones C et A, cette dernière recevant cependant du sel iodaté comme les zones B et C.

En 1968, on a noté une nouvelle réduction de la prévalence dans les zones A et C, alors que dans la zone B on constatait une diminution notable du nombre des cas, comparable à celle enregistrée dans les deux autres zones de 1956 à 1962.

En 1972, des enquêtes par sondages dans les zones A et B ont montré que la prévalence du goitre endémique continuait à décroître; dans la zone A, soumise à la prophylaxie depuis 1956,

on notait une quasi-absence de la maladie parmi les enfants de moins de 10 ans. Des examens portant sur la captation de l'iode radioactif et l'excrétion urinaire d'iode ont donné des valeurs normales dans les régions bénéficiant de la prophylaxie.

On conclut de ces observations que le goitre endémique peut être efficacement combattu dans la région de l'Himalaya par un enrichissement du sel à usage domestique par l'iodure ou l'iodate de potassium ajoutés à petites doses physiologiques.

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Earlier studies by Robert McCarrison of endemic goitre in the sub-Himalayan region indicated that the cause might be contaminated water. This publication from Ramalingaswami's group demonstrated for the first time that severe environmental iodine deficiency was the cause of endemic goitre in the sub-Himalayan region, based on the results of radioactive iodine uptake and serum protein-bound iodine levels which indicated lowered levels of thyroid hormone. This paved the way for the subsequent large community-based trial in India of the use of iodized salt as prophylaxis.

The second paper describes the well controlled study in the Kangra valley on the effectiveness of long term supplementation of iodine through iodized salt. During 1956-72, the study covered more than 100 000 persons over a period of 16 years. The study successfully demonstrated the feasibility and effectiveness of the use of iodized salt for public health programmes in India. The promising results of the study led the Government of India to set up a National Goitre Control Programme with the objective of supplying iodized salt to endemic goitre areas in India.

These studies provided a model for similar studies in many other countries.

In addition to endemic goitre, iodine deficiency in the mother is an established cause of foetal brain damage. Iodine deficiency disorders (IDDs) are now recognized by the World Health Organization (WHO) as the most common preventable cause of brain damage in the world today and an estimated population of 1.6 billion are at risk.

A recent WHO report indicates that there are some 130 IDD affected countries, of which 105 (81%) have well developed IDD elimination programmes using universal salt iodization (USI) with 68% of households having access to iodized salt.

The results of these two studies in India have been a historic landmark in this great achievement.

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