The Prevention and Control of Iodine Deficiency Disorders – Nutrition policy discussion paper No. 3

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UNITED NATIONS **NATIONS UNIES**

ADMINISTRATIVE COMMITTEE ON COORDINATION/SUBCOMMITTEE ON NUTRITION

ACC/SCN STATE–OF–THE–ART SERIES
NUTRITION POLICY DISCUSSION PAPER NO. 3

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and an introduction by M. Lotfi and J. B. Mason

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UNITED NATIONS

ADMINISTRATIVE COMMITTEE ON COORDINATION –– SUBCOMMITTEE ON NUTRITION (ACC/SCN)

The ACC/SCN is the focal point for harmonizing the policies and activities in nutrition of the United Nations system. The Administrative Committee on Coordination (ACC), which is comprised of the heads of the UN Agencies, recommended the establishment of the Sub–Committee on Nutrition in 1977, following the World Food Conference (with particular reference to Resolution V on food and nutrition). This was approved by the Economic and Social Council of the UN (ECOSOC). The role of the SCN is to serve as a coordinating mechanism, for exchange of information and technical guidance, and to act dynamically to help the UN respond to nutritional problems.

The UN members of the SCN are FAO, IAEA, IFAD, ILO, UN, UNDP, UNEP, UNESCO, UNFPA, UNHCR, UNICEF, UNRISD, UNU, WFC, WFP, WHO and the World Bank. From the outset, representatives of bilateral donor agencies have participated actively in SCN activities. The SCN is assisted by the Advisory Group on Nutrition (AGN), with six to eight experienced individuals drawn from relevant disciplines and with wide geographical representation. The Secretariat is hosted by WHO in Geneva.

The SCN undertakes a range of activities to meet its mandate. Annual meetings have representation from the concerned UN agencies, from 10 to 20 donor agencies, the AGN, as well as invitees on specific topics; these meetings begin with symposia on subjects of current importance for policy. The SCN brings certain such matters to the attention of the ACC. The SCN sponsors working groups on inter−sectoral and sector−specific topics.

The SCN compiles and disseminates information on nutrition, reflecting the shared views of the agencies concerned. Regular reports on the world nutrition situation are issued, and flows of external resources to address nutrition problems are assessed. State−of−the−Art papers are produced to summarize current knowledge on selected topics. SCN News is normally published twice per year. As decided by the Sub−Committee, initiatives are taken to promote coordinated activities − inter−agency programmes, meetings, publications − aimed at reducing malnutrition, primarily in developing countries.

ACKNOWLEDGEMENTS

A brief presentation of part of this report was included in an overview chapter of the author in the monograph "The Prevention and Control of Iodine Deficiency Disorders", Eds. B. S. Hetzel, J. T. Dunn and J. B. Stanbury, Elsevier Press, Amsterdam 1987. This monograph includes chapters by other authors which review more detailed aspects of programme implementation and evaluation. The papers were presented at the Inaugural Meeting of the International Council for Control of Iodine Deficiency Disorders (ICCIDD) held in Kathmandu, Nepal, 24−28 March 1986.

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FOREWORD

This paper is the third in the ACC/SCN's State−of−the−Art series. Like the two previous papers, on nutrition education and control of vitamin A deficiency, it provides information to assist decisions on policies and programmes to prevent widespread nutritional problems. Iodine deficiency is one of these, affecting some 200 million people. Yet science and technology have provided most of the answers needed for effective programmes, especially for dealing with severe deficiency. The control methods are safe, low−cost, rely on locally available human and material resources, and are readily replicable. This document describes the problem and its prevention in terms that should help establish and expand control programmes.

The paper and following discussions are contributions of leading scientists in the field. Introductory remarks on the subject set the context. The wide spectrum of disorders resulting from severe and even mild iodine deficiency affecting very large numbers of people in the world, now known as 'iodine deficiency disorders' (IDD), are described. The social and economical benefits of IDD eradication and the contribution their prevention makes to global improvement in nutrition are stressed. Dr. Hetzel has given the necessary information on the prevention of IDD by distribution of iodized salt and iodized oil, summarizing steps to take to design and implement appropriate programmes.

Prevention of IDD is the objective of a Ten–Year UN programme –implemented by UN agencies, bilateral organizations and national governments concerned. This programme benefits greatly from scientific support and initiatives taken by the International Council for Control of Iodine Deficiency Disorders (ICCIDD), of which Dr. Hetzel is the Executive Director, and Dr. Stanbury (whose discussion of the paper is included) the Chairman of the Executive Committee. The ACC/SCN, through its Working Group on IDD, helps to coordinate the sustained action needed to prevent IDD's. This publication is intended to be useful to all those engaged in the campaign against iodine deficiency, thus improving health and productivity in many of the poorest regions of the world.

A. Horwitz
Chairman, ACC/SCN

INTRODUCTION AND POLICY IMPLICATIONS

Mahshid Lotfi and John B. Mason[1]

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Effects of iodine deficiency – goitre and cretinism – have been observed since ancient times. Dietary treatment has been known nearly as long, making iodine deficiency perhaps the earliest nutritional disease to be recognized (quoted from Gillie, 1978). Control programmes through fortification of salt with iodine compounds have been implemented, usually following legislation, in more than 50 countries since the 1940's (DeMaeyer et al, 1979); Switzerland was the earliest, in the 1920's, to legislate salt iodization. In most cases iodine deficiency has been largely controlled, although pockets remain. But at least 40 countries have significant iodine deficiency without effective control programmes. Up to *20%* of the world's population live in iodine deficient areas, the majority of these in countries where iodine distribution has not yet been undertaken.

Enlargement of the thyroid gland (whose production of hormones requires iodine) is the best–known sign of iodine deficiency, called goitre. Unless massive, goitre is not itself particularly harmful. It is the deficiency of the thyroid hormones that has very serious consequences: the worst effect is cretinism – severe mental retardation. However, there is increasing evidence that mild iodine deficiency causes lesser degrees of mental retardation, also preventable by iodine, with extensive consequences for education, productivity, and well–being.

Effects of iodine deficiency begin before birth, and have various results throughout the life cycle. Dr. Hetzel begins by documenting the range of these effects in his Table 1 on page 35. They include still–births, increased infant and child mortality, developmental abnormalities, but above all effects on brain development. Whilst iodine deficiency is most commonly assessed by goitre, this is as much an indicator as the primary disorder. Thus the term "Iodine Deficiency Disorders (IDD)" introduced by Dr. Hetzel (Hetzel, 1983) has now become accepted.

The disorders affect not only the individual but entire communities. Iodine deficiency often occurs in clusters, frequently in remote areas, so that communities may have even a majority of members with goitre, a significant proportion of cretins, and most probably lowered intellectual development among others. Whole societies, usually the poorest and most inaccessible, suffer. But because of this clustering, the beneficial effects of iodine distribution on societies can be rapid (for examples, see Section 6 of Dr. Hetzel's paper).

Surveys of the global occurrence of IDD have been compiled by WHO over the years. In 1960, WHO (Kelly and Snedden, 1960) estimated that some 200 million people had goitre taking available national statistics as a guide; by 1979, although a number of control programmes had been implemented, the number was thought to be about the same because of population growth. Moreover, with improving availability of information and assessment techniques, additional affected populations are still being identified. For example, in 1971 WHO listed only 5 African countries as having information on iodine status (DeMaeyer et al, 1979, p.51); by 1987, data had been compiled from some 30 countries from this region (WHO/UNICEF/ICCIDD, 1987).

Causes of Iodine Deficiency Disorders

Dr. Hetzel's focus is on the prevention and control of iodine deficiency disorders (IDD) through iodine supplementation. To set the context, here we give a brief introduction to the causes of IDD, and to the biological mechanisms involved.

By far the commonest cause of iodine deficiency is a low content of iodine in the local environment. This interacts with poverty and remoteness, when there is little contribution of food from outside an iodine–deficient area to the diet, as is the case with much subsistence agriculture. Poverty, with poor sanitation and general malnutrition, may worsen the effects of iodine deficiency. Goitre can improve with socio–economic development. However, there is evidence from all over the world that iodine distribution programmes have a dramatic effect as single interventions, even without a rapid improvement of other aspects of poverty. The many examples of effective programmes, cited by Dr. Hetzel (Section 6) and in the ACC/SCN's global strategy to combat IDD (ACC/SCN, 1987), virtually all succeed because they deal directly with this single primary cause, by replacing missing iodine for the individual. The two main methods are by fortification, usually of salt; and by injection (every 3–5 years) of iodized oil as an emergency measure. Administration of iodized oil by mouth may become a more widely used method in the future.

The principle factor related to the occurrence of IDD, therefore, is inadequacy of iodine intake due to environmental deficiency of this essential element. This occurs where iodine is leached out and washed away from soil by glaciers and heavy rains in hilly and mountainous areas like the Andes, the Himalayas, the Alps and the Pyrenees. However, it is now clear that IDD are significantly prevalent also in plains, flooded riverine and even coastal areas – almost wherever they are looked for in the developing countries (Stanbury, 1985). Surveys outside the known goitre areas in states of India, in other countries of Southeast Asia (Bangladesh, Burma, Nepal), and elsewhere have shown the presence of IDD in most regions irrespective of their geographical conditions.

Inadequacy of iodine intake, although the major cause, is not the only factor responsible for all cases of IDD. For instance, the degree of iodine deficiency is not always related to severity of goitre in communities with low iodine intake (Delange et al, 1968; Thilly et al, 1972; Ermans et al, 1983). Some degrees of goitre persist in regions where iodine intake is apparently adequate (Gaitan et al, 1978;Ziporyn, 1985), and not all affected people benefit to the same extent from iodine supplementation (Ingenbleek and De Visscher, 1979).

The importance of many other factors in causing iodine deficiency has been revealed by nutritional and epidemiological surveys (Gaitan, 1980; Benmiloud et al, 1983). The role of cassava which contains linamarin, converted to thiocyanate in the body, has received a lot of attention. Such compounds are known as goitrogens. Contribution of cassava to the etiology of IDD in man is confirmed, especially in North Zaire (Delange and Ahluwalia, 1983, p.17). Although a number of other staple foods contain potential goitrogens (e.g. maize, lima beans, sweet potatoes), in contrast to cassava the goitrogens are in the inedible portions of the plants and do not contribute importantly to IDD. Moreover, effects of most (but not all) goitrogens can be countered by iodine supplementation. Other naturally occurring agents with goitrogenic and/or antithyroid effects listed by Gaitan et al (1978) include sulfur–bearing organic compounds, industrial pollutants, artificial and bacterial contaminants of water.

Other forms of malnutrition, notably protein–energy malnutrition (PEM) and vitamin A deficiency, may have secondary effects on iodine nutritional status. Surveys in Lebanon (Najjar and Woodruff, 1963), Brazil (Lobo et al, 1969), Ecuador (Fierro–Benitez et al, 1969) and other parts of the world have demonstrated that endemic goitre preferentially affects rural populations and low income groups living under poor sanitary conditions. A common observation is that with improvement of socioeconomic standards even without iodine supplementation, goitres may spontaneously regress (Ingenbleek and De Visscher, 1979). Many studies show that severe PEM affects thyroid function and the metabolism of thyroid hormones (e.g. Ingenbleek and Beckers, 1975; Becker, 1983). Iodine malabsorption may be associated with PEM and thus contribute to endemic goitre (Ingenbleek and Beckers, 1973), particularly where iodine intake is limited. PEM may also interfere with iodide uptake by the thyroid (Gaitan et al, 1983), and with thyroglobulin formation (Ingenbleek and De Visscher, 1979). On the other hand, very severe PEM in some areas with extremely low iodine intakes may impair the ability to develop goitre with a resultant mild prevalence rate for this condition (Delange, 1986 p.44); this point should be remembered in any IDD prevalence survey in developing countries.

Low blood retinol levels, an indicator of vitamin A status, are correlated with higher goitre incidence (Ingenbleek and De Visscher, 1979). As cited by Ingenbleek and De Visscher (1979), dietary shortage of vitamin A as a causative factor in the development of goitre in rats was first suggested by McCarrison (1930), and similar findings were subsequently reported in man (Borjas and Scrimshaw, 1954; Horvat and Maver, 1958). Studies in Senegal have shown that concomitant vitamin A deficiency increases the severity of iodine deficiency (Ingenbleek and De Visscher, 1979; Ingenbleek et al, 1986). (The mechanism suggested for this is that decreased retinol could reduce thyroid hormone synthesis by defective glycosylation of thyroglobulin and its subsequent inefficient iodation. This is in line with vitamin A's known function in controlling production of some specific glycoproteins in other tissues (Jackson and Fell, 1963; De Luca et al, 1970; Kim and Wolf, 1974)). Out of the 34 countries with vitamin A deficiency as a significant public health problem (ACC/SCN,

1985; Vest and Sommer 1987, p.7), a great majority are reported to also have considerable iodine deficiency, although this may affect different population within the country.

Thus iodine availability for the thyroid gland can be altered by dietary or other factors especially when iodine intake is marginal, dietary patterns are less varied, and when individuals are exposed heavily and continuously to their effects.

These considerations explain something of the etiology of IDD and their continuing discovery in diverse parts of the world. But, in contrast to protein–energy malnutrition for example, there is one primary or contributory cause common to all occurrences of IDD that can almost always be corrected: a low dietary intake of iodine. Thus, although there are interactive factors, iodine supplementation can cut through these and prevent the debilitating effects of IDD.

Iodine Metabolism and Consequences of Deficiency

About half of the iodine in the diet, absorbed from the intestine as inorganic iodide, is normally taken up by the thyroid gland (the rest is excreted in urine) and there incorporated into protein (thyroglobulin) to form precursors of two related types of hormone, triiodothyronine (T–3) and thyroxine (T–4). The hormones are released into the blood, often over quite long periods, in response to various stimuli controlled by thyroid stimulating hormone (TSH). The synthesis and availability of the thyroid hormones is reduced in iodine deficiency. Hence blood levels of T–3 and T–4, as well as TSH, are used for assessment of thyroid status; in iodine–deficient areas this may be interpreted as reflecting iodine status. This much of the physiology is well–understood. Effects of deficiency of thyroid hormones are also well–described, although the mechanisms of action of the hormones, and hence the pathological effects of deficiency, remain to be fully worked out. One result of deficient hormone synthesis, in this context due to iodine deficiency, is enlargement of the thyroid gland itself – as it were in an attempt to compensate – hence the presence of an enlarged thyroid, known as goitre, is the main clinical sign of iodine deficiency.

The thyroid hormones have extensive effects throughout the body. They influence metabolic rate, protein synthesis, enzyme function, cellular transport, and other physiological processes. They have specific effects on growth in children: low levels retard growth, causing stunting and poor development. The thyroid hormones have at least two effects on brain function. Throughout life, a normal range of thyroid hormones is needed for active intellectual function; hypothyroidism is associated with apathy. This effect is probably reversible at least in the adult, in that when normal thyroid function is restored mental processes return to normal. But low thyroid activity at crucial developmental stages (including vulnerability of the foetus to maternal hypothyroidism starting soon after conception) causes irreversible brain damage, at its extreme expressed as cretinism and deaf–mutism. Lesser degrees of brain damage manifest as deafness, mental retardation, and lowered intelligence quotient.

Goitre is defined as endemic when its prevalence rate exceeds 10% in a given region; iodine intakes in such areas are generally below 50 mcg/day (ACC/SCN, 1987) compared to the recommended intake of between 150 to 300 mcg/day (Matovinovic et al, 1974). When goitre prevalences are higher than 30%, 5–10% of the population can have severe and irreversible mental retardation associated with anomalies of physical development, known as endemic cretinism. However, even higher prevalences have been reported, for example in Bhutan, parts of Indonesia (Clugston and Bagchi, 1985, p.16; 49) and Bolivia (Pretell and Dunn, 1987). Two extreme types of cretinism have been described, although mixed types also exist, namely a more common neurologic type with impaired voluntary motor activity, spasticity, deafmutism and subnormal thyroid function; and a myxoedematous endemic cretinism with clinical signs of long standing hypothyroidism, dwarfism, myxoedema, sexual underdevelopment and severely deficient thyroid function. These are described by Dr. Hetzel in section 2.

Increased foetal and prenatal mortality is frequently found in iodine deficiency (McMichael et al, 1980), lessening with iodine supplementation (Gillie, 1978; Hetzel, 1986). Iodine deficiency is reported to increase child mortality rates in many countries, e.g. in Tasmania (Potter et al, 1979), in Zaire (Thilly et al, 1980) and Papua New Guinea (Pharoah et al, 1971). Its correction is reported to increase child survival (Stanbury, 1987). Surviving infants often show low birth weight and congenital abnormalities, as well as results of intra–uterine brain damage.

Deaf–mutism has been suggested as an indicator of the severity of IDD (Goslings et al, 1975). Nearly 80% of all deafness globally occurs in developing countries, with disabling hearing impairment involving perhaps between 40 to 70 million people in the world (Wilson, 1987). The major causes are infections, but IDD accounts for hearing impairment in at least 50,000 neonates annually (Wilson, 1985). This figure may be a

considerable underestimate. First, it does not include cases where hearing impairment is not recognized. Secondly, most IDD manifestations are not, even now, ascribed to iodine deficiency (Clugston and Bagchi 1985, p.2; WHO, 1986); thus much deafness in iodine–deficient areas, even when diagnosed, may not be recognized as IDD–related.

As with vitamin A deficiency (Vest and Sommer, 1987, p.3), there are reports of an association between iodine deficiency and decreased Immunity which is reversed by administration of iodine. In iodine deficient hypothyroid subjects phagocyte dysfunction has been documented, reversed on administration of triiodothyronine and correction of the hypothyroid state (Chandra, 1981). Similarly, the necessity of iodine for normal delayed immune response in school children has been reported (Marani et al, 1985).

Not only the consequences of severe iodine deficiency but also the damage done by lesser degrees of iodine inadequacy are being increasingly recognized. All the residents of a community affected by endemic goitre are potentially exposed to suboptimal levels of thyroid hormones during their development. This may become evident only after an increase in physiological needs (DeMaeyer et al, 1979). Thus there may be serious but subtle effects on the quality of the society at large. Motivation, spontaneity, creativity and intelligence may be diminished (Gillie, 1978). As quoted by Berg (1987) and by Dr. Hetzel here the apathy described among adults in northern India has been ascribed by some investigators to chronic mild deficiency of iodine. Economical and social burdens are imposed on any community by the existence of mentally retarded cretins; but a profound implication of iodine deficiency is that large sections of the population in these areas could be intellectually impaired yet appear normal. Environmental iodine deficiency is probably causing much more brain damage than is evident as overt cretinism in the millions of people living in endemic areas (Kochupillai et al, 1985).

Endemic cretinism is not an all–or–none effect, rather iodine deficiency may lead to a spectrum of subclinical deficits which place the children born to mothers on an iodine deficient diet at a developmental disadvantage (Connolly et al, 1979), which undermines children's physical and mental growth, sapping their energy and slowing the progress of both individual and community (UNICEF, 1986).

The Extent of the Problem

Areas of iodine deficiency throughout the world are shown in Fig. 1. Many of these are mountainous, but other areas exist where iodine has been leached from the soil. Important patches of the deficiency are still being identified, particularly in Africa. Estimates of the numbers of people affected in developing countries, compiled by WHO, are shown in Table 1. The estimated population at risk of 800 million refers to those living in iodine–deficient areas amounting to nearly 30% of the population of 2.8 billion in the regions assessed. Nearly a quarter of this at–risk population has goitre, some 190 million; and over 3 million are estimated to show overt cretinism.

Although trends have not been assessed directly, reports since the 1960's have consistently indicated a figure of around 200 million people worldwide with goitre, showing the persistence of the problem.

The data on goitre may underestimate the full extent of iodine deficiency disorders. A number of the surveys are local rather than national, and may select the age groups examined. For example, many were carried out on school children. These exclude both those children too severely affected to attend school, and often also the poorest in the community. Nonetheless, they are of the same order of magnitude as other estimates of IDD. For example, some 43 million people in South East Asia were estimated recently to be suffering from different degrees of mental and physical impairment due to iodine deficiency (Clugston and Bagchi, 1986).

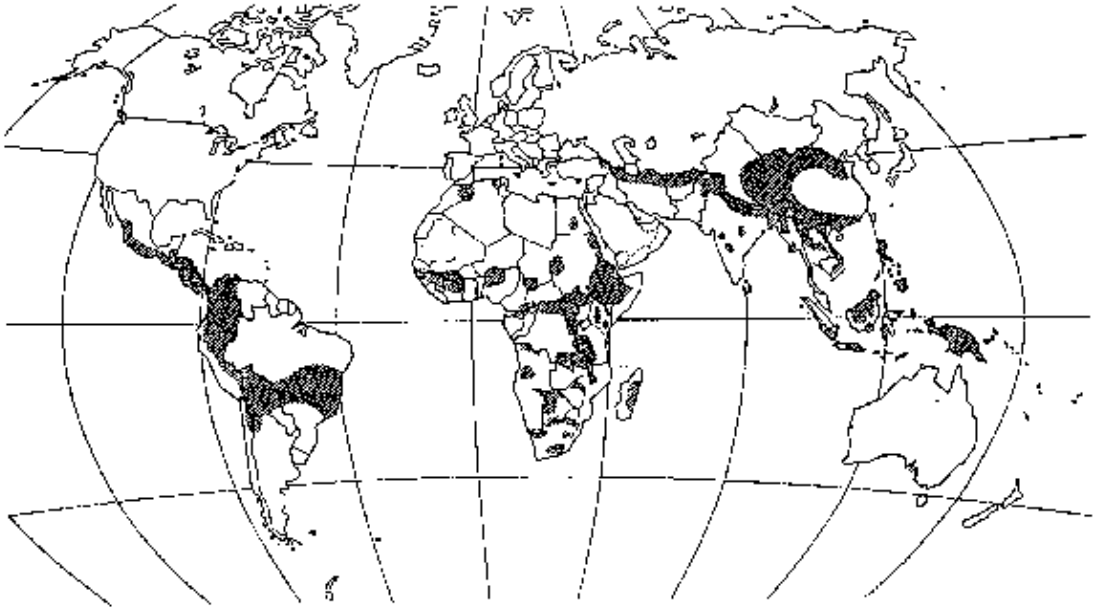

Figure 1 Distribution of Iodine Deficency in Developing Countries

WHO86819
Source: ACC/SCN, 1987

More and more new areas are being identified with iodine deficiency in Africa, Latin America and Asia (Kavishe, 1985; Martin, 1986; Pandav et al, 1986; WHO/UNICEF/ICCIDD, 1987; Ekpechi, 1987 a,b). A number of factors may account for this continuing uncovering of the problem. First, surveys have hitherto tended to be local, concentrating on known areas of deficiency. Second, diagnostic methods are improving: systematic criteria for defining goitre (given by Dr. Hetzel in Section 7 below) are more widely used, and tests such as urinary iodine ft excretion are more common. Moreover, as the damaging effects of IDD become better realized, mis−diagnosis decreases; nonetheless Clugston and Bagchi (1986) consider that much IDD remains unrecorded. Third, and of particular concern, new cases of iodine deficiency may be occurring due to environmental changes, as has been suggested with drinking water supplies in Nigeria (Van Amelsvoort, 1969, 1971).

A characteristic of iodine deficiency is that prevalences of IDD can be very high in the endemic areas. These concentrations tend to be obscured by averaged data, such as those in Table 1 below. Goitre rates of 50% or higher are commonly reported in populations where iodine intakes are less than 20 mcg/caput/day, or where there are significant contributory factors, notably goitrogens in the diet. Endemic cretinism itself, although relatively rare, has an alarming prevalence of 13% to 35% in several parts of South East Asia (Clugston and Bagchi, 1985, p.l67). Screening for neonatal hypothyroidism, which if not treated can lead to severe cretinism, has shown an incidence of 15% in parts of the state of Uttar Pradesh in India, compared with only 0.04% in non−endemic areas (Clugston and Bagchi, 1985, p.17). Some surveys have reported prevalences of IDD of 60% in parts of Bolivia (Pretell and Dunn, 1987), and a national prevalence of endemic goitre of 11% in Bangladesh, occurring in almost all regions of the country (Clugston and Bagchi, 1985). Extensive pockets of IDD are still being identified in Africa (WHO/UNICEF/ICCIDD, 1987).

TABLE 1

IODINE DEFICIENCY DISORDERS IN DEVELOPING COUNTRIES BY WHO REGION

Regions	Total Population (millions)	Number at Risk(millions)	Number with Goitre(millions)	Goitre Prevalence	Number with overt cretinism (millions)
Africa	360	60	30	8%	0.5
South East Asia	1050	280	100	10%	1.5

Asia (other countries)	1070	400	30	3%	0.9
Latin America	360	60	30	8%	0.25
Total	2840	800	190		3.15

Source: ACC/SCN, 1987

While Table 1 refers only to developing countries, even in developed parts of the world recent reports show that goitre remains a significant problem in some countries. The prevalence appears not to have decreased in at least 12 European countries, where IDD continues to be a major problem, occasionally involving cretinism (European Thyroid Association, 1985; Gutekunst and Scriba, 1987).

More details from surveys in many other countries are available, for example in DeMaeyer et al (1979); Dunn et al (1986); ACC/SCN (1987) and Hetzel et al (1987).

Overcoming Iodine Deficiency Disorders

Undisputed evidence shows that IDD can be successfully and inexpensively prevented and controlled (ACC/SCN, 1987).

The major methods that have been used are:

- Fortification of salt with iodine compounds;
- Periodic injection of iodized oil.

These two methods are described in detail in this paper by Dr. Hetzel. They form the basis for the United Nations Ten-Year Programme for Prevention and Control of Iodine Deficiency Disorders (ACC/SCN, 1987), which draws scientific support from the International Council for Control of Iodine Deficiency Disorders (ICCIDD). Further technical details and results of experience are given in a number of publications from the UN agencies (e.g. WHO, DeMaeyer et al (1979); PAHO/WHO, Dunn et al (1986); ICCIDD, Hetzel et al (1987) and others.

Briefly, iodization of salt has the long-term advantage of high cost effectiveness, assuring regular intakes when salt supplies come from a centralized source. Disadvantages are related precisely to some of the problems of communities affected by the deficiency. Fortified salt must penetrate isolated communities, often accustomed to (and preferring) local supplies. Expansion and sustained maintenance of salt fortification requires organization and management; problems have recently been experienced in India, for example, in this aspect. But there is little doubt that initiating and steadily improving salt iodization and distribution programmes is feasible and constitutes a major way of preventing IDD in many needy areas.

Dr. Hetzel's paper gives the essential details of ongoing salt iodization programmes in the world.

Programmes to inject iodized oil are indicated under two main circumstances. First, where IDD is severe, there will be continuing irreversible damage to infants and growing children which demands preventive action faster than can be expected from iodized salt distribution. Second, isolated communities may simply not be rapidly accessible to iodized salt. While marketing systems, infrastructure and trade develop for such communities, there may be no alternative to direct individual intervention. Iodized oil injections have been convincingly demonstrated as effective on a large-scale – for example in Papua New Guinea. These programmes are reviewed by Dr. Hetzel. In his commentary, Dr. Viteri elaborates his views on the relative merits of injection versus salt fortification, emphasizing that urgency for rapid results should not obscure the long-term need for fortification.

The balance of intervention types must be decided on a case-by-case basis. But, again to set the context and round out the subject, we first introduce the other possible measures, some of which may be considered as complements to the major policy options of salt iodization and iodized oil injection.

Other possible approaches to IDD prophylaxis include:

1. Diversification and modification of the habitual diet consumed in the endemic areas, with e.g. imported foods from outside.

2. Iodine supplementation of foods and water for human consumption.

3. Iodine medications (notably oral administration of iodized oil) to directly supplement the inhabitants at risk of IDD in endemic areas.

4. Active prophylaxis of domestic animals; use of iodine materials for plants or iodine deficient soils.

Generally, overall socioeconomic development of the community can result in diversification of dietary pattern, with imports from non−endemic areas. An interesting example is in China, where large quantities of seaweeds have been distributed in highland areas (Michanek, 1981). Here public awareness of the ways in which the new variety of foods, like seaweeds, can be prepared and the benefits in their consumption are important for their intake. Some local foods may be available with relatively higher iodine contents, but iodine deficient populations may be unaware of their presence/value or not consume them for different reasons, e.g. relatively high cost of seaweeds in Malaysia (Ma and Lu, 1987). More often, perhaps, the process of development has, as a by−product, led to increased consumption of foods with adequate iodine.

Modifying food habits is another possible means of increasing iodine intake. Conserving iodine in the process of meal preparation; eliminating goitrogens, e.g. by adequate soaking in the case of cassava (Ekpechi, 1987 a); and knowing the benefits of iodine for health are all important if the dietary iodine consumption is to be improved without iodine supplementation. However, in severely deficient areas this approach alone would not be enough to control IDD.

Apart from salt, many food items such as condiments, sauces, oil, sweets, chocolates, cereal, flours (bread), baby foods and dry skimmed milk, etc. have been used for iodization. iodization of weaning foods has been proposed in endemic areas for controlling IDD in babies. With supplementary food aid programmes an appreciable segment of vulnerable populations can be iodine−supplemented (as in the case of vitamin A fortification of dried skimmed milk powder). This issue has been emphasized recently for Africa (ICCIDD, 1987 a). In countries with major food aid programmes, the possibility of iodine fortification of donated items has been recommended for serious consideration (ACC/SCN, 1987, p.11).

Water iodization has been tried successfully in Thailand, Sicily and Malaysia, and small low cost equipment is available for this purpose (ACC/SCN, 1987, p.11). Further research is under way for using water as a vehicle for iodine (Vigneri et al, 1982; Filetti et al, 1985). Such methods are only feasible for areas with a centralized water supply. In rural areas, a few drops of Lugol's iodine solution can be added to drinking water containers for providing iodine and sterilizing water at the same time. Continuous application of such methods is required (Bailey, 1987).

Iodine medications to supplement directly the inhabitants of endemic areas have been used in various forms other than intra−muscular (IM) iodized oil injection, like oral iodized oil, drops and tablets. Administration of oral iodized oil is an effective means of controlling IDD. It should be simpler, cheaper and safer than iodized oil injection, requiring less technical training, fewer instruments and less time (Dunn, 1986). While experience with this route of iodine supplementation is not extensive, it offers an attractive alternative to injection of iodized oil and is being used increasingly for iodine supplementation in many endemic areas (Li, 1987). The duration of IDD protection offered by oral iodized oil may be half that of injection judging from urinary iodine levels after oral and intra−muscular iodized oil administrations. Since effectiveness of oral iodized oil obviously depends on the fraction of orally administered iodine absorbed from the intestine and its storage is largely limited to the thyroid and adipose tissue (Dunn, 1986), when iodine is supplied orally, its absorption and utilization in subjects with PEM must be carefully monitored. (See page 4).

Iodine prophylaxis of domestic animals has been only briefly explored. Domestic animals are likely to be iodine deficient in endemic goitre areas, adversely affecting their growth, reproduction and productivity (ACC/SCN, 1987 p.5). According to Gillie, (1978). 'goitrous sheep produce less wool, horses do less work, hens with decreased thyroid activity produce eggs with insufficient calcium in the shells leading to egg breakage and higher chick mortality. Goitre in cattle causes sterility or sickly calves and poor milk production'. (In fact, such effects are also probable in humans: as early as 1947, Robinson (1947) reported improvement in lactation and increases in breast milk output in lactating women treated with iodine). In Finland, iodized feed for cows is used extensively because it had been shown to increase their milk production (Lamberg, 1986). As a result of active iodine prophylaxis in animals, in Finland, milk and dairy products contribute more to total iodine intake than iodized salt (although this is also partly due to a gradual decrease in salt consumption). Highly effective prophylactic programmes involving iodization of animal as veil as human foods in Finland, Norway and Sweden have made these three countries goitre free in spite of having the problem in the past

(European Thyroid Association, 1985; Gutekunst and Scriba, 1987). Different means of soil enrichment, e.g. use of iodine rich sea algae practiced in USSR (ACC/SCN, 1987 p.13), iodine fertilizers and iodine recycling through excreta of iodine supplemented animals (Koutras, 1986) can increase iodine in both animal and plants. Developing seaweed mariculture and utilization of the product for areas with iodine deficiency could also be emphasized (Michanek, 1981).

Global Status of Salt and Oil Iodization Programmes

Dr. Hetzel's paper reviews country–by–country the position of IDD control programmes (section 6). Here are some highlights on a regional basis, by way of introduction. According to data available from WHO (DeMaeyer et al, 1979, p.51) out of 50 countries with salt iodization programmes worldwide only 22 countries – mainly in Europe, South and North America – have large scale salt iodization programmes. Elsewhere, programmes are operating at limited level or not at all. Salt iodization in many countries in Europe and the Americas has been a major factor in significantly controlling IDD. However, even in some European countries more effective programmes are required: for example, Italy, Spain and Portugal with the highest reported goitre prevalences in Europe have control programmes functioning at voluntary/limited basis (DeMaeyer et al, 1979, p.51; European Thyroid Association, 1985).

In Latin America most countries with known severe IDD have implemented IDD control measures. Unfortunately the effective programmes in Guatemala (Sigui, 1986) and El Salvador (Molina, 1986) have recently lapsed. In Guatemala 93% of salt produced was iodized by 1969 but in 1976 this decreased to only 15% and in El Salvador from 56% in 1977 to 17% in 1981, thus there are indications of an increase in previously reduced goitre rates (Pretell and Dunn, 1987). Maldistribution of available iodized salt in Peru resulted in distribution in endemic areas of only 30% of the 86% of salt iodized for human consumption by 1976 (Pretell, 1986). On the other hand, pilot programmes using iodized oil injections have been successfully performed in some Latin American countries like Ecuador and Bolivia (Pretell and Dunn, 1987).

Of at least 32 African countries with severe IDD only 7 have instituted any significant control measures with varying degrees of success. In some countries, use of iodized salt has not been successfully maintained (Ekpechi, 1987 a).

Some of the 8 South East Asian countries with known severe IDD have already implemented control measures while others have yet to start (Clugston and Bagchi, 1985). Some pilot programmes have begun but require wider implementation, e.g. in Burma, Thailand and Bangladesh (Venkatesh Mannar, 1987). Operational problems have resulted in ineffectiveness of such programmes in parts of India (Clugston and Bagchi, 1985, p.18); in certain areas goitre prevalence rates were reported as actually higher after ten years of salt iodization (Pandav et al, 1986). China, Papua New Guinea and Pakistan have implemented continuing control measures: salt iodization has remained at a pilot stage in Pakistan, in China much progress has been made (Venkatesh Mannar, 1987).

To summarize, about half of the countries in the world with severe/moderate IDD have taken measures, including pilot studies, to control these. Comparing goitre prevalences after prophylaxis with the level of iodine in salt, for 25 countries with such data. available, generally a higher prevalence was found to correspond with lower salt iodization levels (Lamberg, 1985). On the other hand, the level of iodine is often lower than intended due to faulty iodization or loss of iodine from salt during handling and storage.

What proportion of vulnerable population is covered in those countries with some IDD control measures? Such data are not available in systematic and comprehensive manner, but are needed to evaluate progress. In India, iodized salt produced covers only 16% of the total projected needs of the known goitrous regions (Pandav et al, 1986). In Uttar Pradesh – one of the most severely IDD affected states of India–only 9 of the 16 districts have goitre control programmes (Agarwal and Agarwal, 1983). In two severely affected areas of Pakistan, the coverage of iodized salt ranges from about 10% to 80% (Mahmud, 1986). However, in China with 330 million people at risk of IDD, iodized salt now covers 87% of the iodine deficient population (Ma and Lu, 1987) compared to less than 50% in 1982 (Ma et al, 1982). Even in Germany, with reported 40% goitre prevalence in school children in some parts, iodized salt used on voluntary basis covers less than one third of the population (Gutekunst and Scriba, 1987).

Iodized oil has successfully been given in Papua New Guinea, where in a mass campaign 100,000 inhabitants were injected (McCullagh, 1963). Indonesia, with probably the most developed IDD control programme in S. E. Asia, has been able to give 4.9 million injections of iodized oil during the period 1979–1984 (Clugston et al, 1987). In Nepal 28 remote northern districts are now covered with iodized oil injections, with more than 2 million people being injected (Acharya, 1987). Similarly on the average, 85% of the vulnerable population in

one district in Zaire is reported to be covered by iodized oil injection (Ermans et al, 1983).

Policy decisions: Benefits, costs and approaches

In countries with iodine deficiency, it is clear that severe and widespread disadvantages occur, in terms of human welfare and the thriving of society. These can be prevented within existing technology, at modest cost whether measured in absolute terms against alternative programmes, or by economic benefit. In global terms, there is the promise of achieving a significant betterment of the human condition through applying these results of modern science, moreover aimed at the poorest of the poor. For both national policy–makers and international agencies, decisions remain to be made to fully commit the necessary resources, organizational as much as financial. A brief review of the costs, benefits, related to the available interventions, may help to facilitate this commitment.

The benefits of preventing iodine deficiency have been introduced here, and are given in detail in Dr. Hetzel's paper: simply, they would make cretinism a matter of history; depression of communities' abilities from mild IDD – intellectual and productive – a thing of the past; and help lift societies to a better realization of their potentials. Unfortunately, these individuals and societies are usually remote, and the benefits would only slowly be perceived in national capitals and donors headquarters; but far–sighted policies should aim to achieve just this.

The costs of preventing iodine deficiency are not extensive, and methods are well known. The cost of salt iodization from experience in S.E. Asia is 5 cents/person/year. Intra–muscular oil injection was estimated to cost 10 cents/person/year, from such programmes in Zaire and Nepal (ACC/SCN, 1987, p.40). Since iodized salt covers the entire population of affected areas, whereas injection programmes are more targetted, the difference in cost of these measures might be less (Levin, 1987). Oral compared to intra–muscular iodized oil will, in most instances, cost somewhat less, but there are no good data available on this yet. Cost of iodized water is less or similar to that of iodized salt. Costs should also be separated into (a) cost of supplies and equipment and (b) costs of delivery (ACC/SCN, 1987, p.37). In Peru (Hetzel et al, 1980, p.528) and Bolivia (ICCIDD, 1987 b), of total costs of iodized oil injections, the costs of oil, syringes and needles were 83% and 68% respectively, while in Central Africa (Hetzel et al. 1980, p.529) only 41% of the total cost was needed for these.

At present using the estimate of population at risk of IDD in developing countries, cited in Table 1 on page 9, and assuming that of 800 million at risk population, 95% (760 million) are to be covered by iodized salt and 5% (40 million) by intra–muscular iodized oil injection (ACC/SCN, 1987, p.40) the annual total cost of supplies would be around US$ 42 million to supplement all estimated at risk populations in developing countries. Within individual countries, cost can be estimated from figures such as those given here. They would always work out a fairly minor proportion of, for example, the health budget– and much less of the national government expenditure. Furthermore, donor assistance should become available.

Projected regional and global costs of support programmes in affected areas (ACC/SCN, 1987, p.43–52), is about US$ 2.2 million per year. Actual costs depend on the size and severity of IDD in different regions. Supplementation and support programmes together thus have an estimated annual cost of around US$ 44 million.

Costs of iodine supplementation may be further decreased. Simultaneous fortification with both iodine and iron, already tried at field level in India (Rao, 1987) seems promising. Iodized oil cost less with mass packaging and if cheaper oil bases are used (WHO, 1987). Iodized oil for oral use can be made at lower cost than for injection because of less stringent quality controls. Use of primary health care systems can reduce the cost of delivery. Combining iodine prophylaxis and delivery of vitamin A with immunization as suggested by WHO (1986, p.10) allows cost sharing. The feasibility of linking iodine supplementation with EPI has already been shown in Nepal and Papua New Guinea (ICCIDD, 1987 c).

With the lifetime disabilities caused by IDD, the economic benefits of their correction naturally outweighs the costs incurred. One study in Federal Republic of Germany, as Dr. Hetzel has stated, showed the annual costs of diagnosis and treatment of goitre in 1979 as US$ 200 million (Pfannenstiel, 1985)– over 4 times what is required for controlling IDD. Controlling mild IDD in Ecuadorean children, showed that benefits in terms of improvements in lifetime earnings exceeded costs of intervention considerably (Correa, 1980): the overall effect of a 20% reduction in cretinism was estimated to give a 4.7% increase in per capita income (Hershman et al, 1986). This translates into about a $50 million increase in national income for a country of 1 million population and $1000 annual per capita income, if cretinism prevalence can be decreased by 20% (e.g. from 5% to 4%). Screening and treatment of congenital hypothyroidism in USA showed benefits equal to 3 times

costs (Barden and Kessel, 1985). Cost–benefits have been calculated for different levels of endimicity (Dulberg et al, 1986).

IDD control has been shown to present returns on investment better than any health interventions in some endemic areas. With high goitre prevalences in rural central Java, for example, controlling IDD was found to result in a larger improvement in the health status (measured as mortality and morbidity reductions) than did equal investments in EPI or the development of medical care. Even with low IDD endimicity (goitre prevalence of 10%–20%), IDD control is cost–effective unless the total health budget is extremely limited (Clugston et al, 1987). Results also depend on general health conditions. With moderate IDD and low infant mortality, either salt iodization or intra–muscular/oral iodized oil were cost–effective. In contrast, when infant mortality and infections are high, it has been estimated that salt iodization alone is most cost–effective for controlling moderate IDD and manpower can be more effectively used in immunizing against infectious disease than for iodized oil injection (Dulberg et al, 1986).

Addressing the benefits of raising the iodine content of livestock is somewhat easier since improvement in their production is largely reflected in products with market values, such as meat, wool, etc. (Hetzel and Maberly, 1986, pp.164–173). Iodine supplementation of farm animals also merits consideration to prevent human deficiency.

The first national policy decision is to address iodine deficiency: this may require assessment of the extent and severity of the problem and the potential benefits, related to costs, of preventing it. A related decision involves methods to be used, and organization to apply them. Guidance is given in Dr. Hetzel's paper and the discussions that follow it. And assistance is available from international agencies, and from the International Council for Control of Iodine Deficiency Disorders (ICCIDD).

The UN system has proposed a ten–year international programme of support to countries (ACC/SCN, 1987). Firm commitment and close cooperation of national governments, UN agencies, government sponsored bilaterals and NGO's for technical and financial support are essential for success. National governments and consumers have in some countries already accepted part of the costs incurred. UNICEF has borne the cost of supplies and equipments in some places and WHO with UNICEF cooperation has offered technical assistance in a number of countries.

Accelerating implementation is now required. Identifying countries and areas where IDDs are prevalent with no control measures available (especially in Africa), and publicizing of such information are urgently needed. National prevention and control programmes involving a number of government sectors in countries with IDD need to be established. In such programmes the problem and potential solutions, availability of resources, national capabilities and possibilities of external assistance, technical and financial, need to be assessed to achieve complete coverage in the shortest time and at the lowest cost. External assistance may be needed to enhance national capacity for developing proposals, programme planning for funding, organization, administration, monitoring and both technical and managerial aspects of the measure taken.

The values and problems associated with the two classical methods of iodine prophylaxis i.e. iodized salt and oil, have been discussed in this State–of–the–Art Review Paper by one of the leading scientists in the field, Dr. Basil Hetzel, who is best known for his extensive work on IDD prevention and control especially in Central Java, Papua New Guinea and some province of China. The importance of the processes necessary for large scale intervention programmes, using iodized salt or intra–muscular iodized oil injection for affected populations is stressed. Practical guidance based on the scientific background provided by Dr. Hetzel and others given in this paper should be valuable to many and especially to those involved in IDD control in developing countries, The contributions made by Drs. Delange, Stanbury and Viteri in the discussion part of this volume provide some of their experiences in this same topic and are useful views of experts.

IDD prevention and control is indeed as called by ICCIDD "a major opportunity for success in the field of international nutrition and health". Undoubtedly not only the economic benefits accompanying IDD correction, but the social dimensions and values of improved quality of life for millions of people in the world, are important reasons for eradication of iodine deficiency.

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SUMMARY

Recent evidence indicates a vide spectrum of disorders resulting from severe iodine deficiency which puts at risk more than 400 million people in Asia as well as millions in Africa and South America. These iodine deficiency disorders (IDD) include goitre at all ages, with associated impairment of mental function; endemic cretinism characterized most commonly by mental deficiency, deaf−mutism and spastic diplegia and lesser degrees of neurological defect related to foetal iodine deficiency; increased stillbirths, perinatal and infant mortality.

Evidence is now available from both controlled trials and successful iodization programmes that these disorders can be successfully prevented by correction of iodine deficiency.

The social impact of IDD is great. Prevention will result in improved quality of life, productivity, and educability of children and adults. It is now clear that iodine deficiency is a major impediment to human development.

Iodized salt and iodized oil (by injection or by mouth) are suitable for correction of the condition on a mass scale. Alternative vehicles for iodine supplementation need to be sought.

A single injection of iodized oil can correct or prevent IDD for three to five years. Such injections offer a satisfactory immediate measure using primary health care services for the millions living in regions where iodized salt cannot be used, until a salt programme can be effectively implemented. Iodized oil could also be administered orally through the primary health care system.

In general, IDD can be categorized at three levels of severity:

(a) Mild IDD with goitre prevalence in the range 5–20% (school–children) and with median urinary iodine levels in excess of 50 mcg/g of creatinine. Mild IDD can be controlled with iodized salt at a concentration of 10–25 mg/kg (or ppm). It may disappear with economic development;

(b) Moderate IDD with goitre prevalence up to 30%, some hypothyroidism with median urinary iodine levels in the range 25–50 mcg/g of creatinine. Moderate IDD can be controlled with iodized salt (25–40 mg/kg). Otherwise, iodized oil either orally or by injection should be used through the primary health care system;

(c) Severe IDD indicated by a high prevalence of goitre (30% or more), endemic cretinism (prevalence 1–10%), median urinary iodine below 25 mcg/g creatinine. Severe IDD requires iodine as iodized oil administered either orally or by injection – the fastest and most effective method–for complete prevention of central nervous system defects.

[1]See footnote in Section 4.8

The main hazard of iodization is transient thyrotoxicosis seen mainly in adults over the age of 40. It is caused by autonomous thyroid function resulting from long–standing iodine deficiency. It can be minimized by lessening iodization for those over the age of 40.

The availability of suitable technology, while the basic requirement for a national iodization programme, is only one element of an IDD control programme. The reasons for success or non–success in various programmes have been investigated, and political, social and economic factors have all been found to be relevant. Experience indicates that there is a social process involving six elements or steps which comprise the programme.

They are as follows:

(a) Situation analysis: epidemiological data on IDD, including goitre surveys, with data on water iodine and urinary iodine levels and if possible thyroxine (T–4) levels.

(b) Communication of: operational data to health the findings professionals and the public with the assistance of the media using a social marketing approach.

(c) Plan of action: to be developed by the Ministry of Health with a national inter–sectoral IDD control commission, based on situation analysis with options dependent on cost considerations, including consultation and assistance from international agencies and bilateral support.

(d) Political support: to be developed following (a), (b) and (c). Concept of IDD expressed in social terms is essential. Authority to be given to the national IDD control commission with full political and legislative powers to carry out the programme.

(e) Implementation: organization of staff and resources, training, and establishment of cooperation with region.

(f) Monitoring and: measurement of effects on urinary evaluation iodine (salt iodine) and blood T–4. Evaluation by surveys of IDD incidence and prevalence.

There is a need for better coordination of research and iodization programmes focussed on the eradication of IDD. This has led to the establishment of an international consultative group similar to that already established for Vitamin A (IVACG) and nutritional anaemia (INACG). This is the International Council for Control of Iodine Deficiency Disorders (ICCIDD) which provides an expert resource for international agencies and national governments on all aspects of IDD and IDD control programmes.

Priority attention should be given to the prevention and control of severe IDD. This means that resources and technology can be focussed with particular reference to the use of iodized oil. A plan involving population targets and only can be drawn up with reference to previous experience with the EPI programme in many countries. With a moderate allocation of resources major progress could be achieved in a number of countries within the next five to ten years.

A resolution of the 39th World Health Assembly notes that prevention and control of IDD as a public health problem by reduction of goitre rates below 10 percent in schoolchildren is feasible within the next five to ten years. It also noted that such control will lead to improved quality of life and productivity and improved educabillty of children and adults and so make a significant contribution to health for all by the year 2000.

GLOSSARY

IODINE DEFICIENCY DISORDERS

arborization	the branching of the processes of the nerve cells, which enable them transmit impulses
colloid	constituent of the thyroid gland in which thyroid hormone storage takes place
creatinine	a product of metabolism in muscle which is excreted in the urine at about the same level from day to day
diplegia	a state of paralysis affecting the legs
epiphyses	the growing end of bones
Ethiodol	another name for Lipiodol (see below)
extensors	the muscles which extend the hands and feet
glucosides	sugars and salts in foods
hippocampus	part of the brain concerned with emotion
hyperplasia	increased number of cells due to stimulation
hypothyroidism	the result of a lowered level of circulating thyroid hormone
iodate	e.g. potassium iodate (KIO3), an iodine containing salt, more stable than potassium iodide in the moist tropics
iodide	iodine in chemically bound form usually with sodium or potassium as a salt
iodism	sensitivity to iodine, indicated by a skin rash
iodophors	iodine containing antiseptics used in the dairy industry
leucine	an amino acid which is a constituent of proteins
linoleic acid	a polyunsaturated fatty acid with 18 carbon atoms and two double bonds, which is a major constituent of vegetable oils, especially sunflower or safflower oils
Lipiodol	radio−opaque dye used in radiology for many years
lymphocytic	describes blood cells which are part of the immune reaction of the body
myxoedema	the result of severe hypothyroidism, when the skin and subcutaneous tissue thicken because of accumulation of mucin
neuroblast	early form of the nerve cell (neurone)
neuropil	space between the brain cells
plantar response	response to stroking the sole of the foot that indicates disease of the motor tract from the brain to the spinal cord

QRS	the major electrical impulse in the heart that causes the heartbeat and is recorded in an electrocardiogram
radio–opaque	opaque or dense to x–rays – used to show holes in organs
sequelae	longer–term effects
subluxation	partial dislocation of a joint
thiocyanate	substance produced in the liver by metabolism of cyanide from eating cassava
thyroxine	thyroid hormone which contains four atoms of iodine–known chemically as tetraiodothy–ronine
triiodothyronine	thyroid hormone containing three atoms of iodine
TSH	thyroid–stimulating hormone which comes from the pituitary gland at the base of the brain

1. INTRODUCTION

The causes, prevention and cure of goitre and cretinism, now included in the more general term iodine deficiency disorders (IDD), have been known for more than half a century; yet their total eradication remains an elusive goal. They have been discussed at international meetings such as the World Food Conference in 1974 and the International Nutrition Congress (Rio de Janeiro, 1978) for more than a decade, and were the subject of a detailed series of recommendations at the Fourth Asian Congress of Nutrition held in Bangkok in 1983.

Until recently the problem of iodine deficiency has been seen essentially as goitre. This no longer adequately reflects present knowledge on the subject. We now know that iodine deficiency causes a spectrum of effects on growth and development, particularly brain development in the foetus, neonate and child, justifying a much higher priority now for its prevention and control than in the past. Apart from diminishing the toll in human misery, the prevention of IDD would mean improved educability of children, greater productivity, and better quality of life for many millions living in the iodine–deficient regions of the world. It is now clear that iodine deficiency is a major impediment to human development.

1.1 WHAT IODINE DEFICIENCY DISORDERS ARE

The best–known effect of iodine deficiency is endemic goitre, of which it is the chief primary etiological factor. Another major effect is endemic cretinism. In its commonest form this is characterized by mental deficiency, deaf–mutism and spastic diplegia.

Goitre was well known in the ancient world and has continued to be of interest over the centuries. Extensive reviews of its geographical occurrence have been published, notably by Kelly and Snedden (1960) and Stanbury and Hetzel (1980). Endemic cretinism in Alpine Europe was identified by the Sardinian Commission of 1848, and both goitre and cretinism in the northwest frontier region of India were described by McCarrison in 1908 for the first time in modern medical literature.

In the last 20 years endemic cretinism has been rediscovered in remote places such as certain areas of Papua New Guinea (McCullagh, 1963; Choufoer et al., 1965). It had been 'forgotten' because of the isolation of the iodine–deficient populations from modern investigative facilities.

The relation of iodine deficiency to goitre was defined in the first decade of the 20th century in Marine's studies on experimental goitre in rats (Marine and Lenhart, 1909). Marine showed that when the iodine content of the thyroid fell below 0.1 percent, hyperplasia occurred with thyroid enlargement and the production of goitre. Intermittent iodine deficiency produced alternating hyperplasia and involution with production of the familiar 'colloid goitre'. In 1921 the successful prevention of goitre by iodide supplementation was shown by Marine and Kimball (1921) in a controlled study in school–children in Akron, Ohio. Iodized salt was introduced

into Switzerland in 1924 and has since been used in many other countries.

Stanbury et al. (1954) used radio−iodine for the first time in the field in Mendoza, in the Argentinian Andes, to demonstrate iodine deficiency.

Since 1960 the effects of iodine deficiency have been studied in many remote, predominantly mountainous areas around the world, including the Himalayas (India, Nepal, Burma), the Andes (Peru, Ecuador, Bolivia, Chile), and Indonesia, New Guinea and Zaire, as well as the more Isolated parts of some European countries (Bavaria, Sicily, Portugal, Greece).

It is now known that endemic cretinism is associated with high rates of goitre and with severe iodine deficiency; for example, with dietary iodine intakes of about or below 20 mcg (micrograms) per day compared with a normal daily intake of 80−150 mcg; while goitre alone is seen at intake levels below 50 mcg iodine per day. The manifestations of cretinism vary, but they are clearly an important iodine−related public health problem in the community in which they occur because they cause severe disabilities.

It is also now known that endemic cretinism occurs with other problems related to severe iodine deficiency such as high stillbirth rates and high perinatal and infant mortality. In addition, it is associated with hypothyroidism and consequent varying degrees of mental deficiency, with or without goitre, in infancy and childhood. All these conditions can be prevented by correction of the iodine deficiency.

Goitre itself can arise from causes other than primary iodine deficiency, due to a variety of agents (goitrogens). These, however, are in general of secondary importance as etiological factors.

Recent research (Bourdoux et al., 1978, 1980a, 1980b) has shown that staple foods in some developing countries, such as cassava, maize, bamboo shoots, sweet potatoes, lima beans and millets, contain cyanogenic glucosides capable of liberating large quantities of cyanide by hydrolysis. Not only is the cyanide toxic but the metabolite is predominantly thiocyanate, which is a goitrogen. With the exception of cassava, however, these glycosides occur in the inedible portions of the plants, or, if in the edible portions, in such small quantities that they cannot generally produce toxic effects.

The role of cassava in the etiology of endemic goitre and endemic cretinism has now been demonstrated by Delange et al. (1982) from their studies in Zaire, observations confirmed by Maberly et al. (1983) in Sarawak, Malaysia. Cassava is cultivated extensively in some developing countries and represents an essential source of calories for more than 200 million people living in the tropics. (Delange et al, 1982)

Apart from goitre itself, more recent work on iodine deficiency has revealed a great variety of effects on human growth and development. These disorders, which are best described in relation to four different phases of life (see Section 2), are listed in Section 2.4. (Table 1).

1.2 THE MECHANISM OF IODINE DEFICIENCY

Iodine deficiency causes depletion of thyroid iodine stores with reduced daily production of thyroid hormone (T−4). A fall in the blood level of T−4 triggers the secretion of increased amounts of pituitary thyroid−stimulating hormone which increases thyroid activity with hyperplasia of the thyroid. Increased efficiency of the thyroid iodine pump occurs, with faster turnover of thyroid iodine. This can be demonstrated by an increased thyroidal uptake of radioactive isotopes 1(131) and 1(125) (Hetzel and Maberly, 1986; Buttfield et al., 1966).

Iodine deficiency is demonstrated by determining urinary iodine excretion using either 24−hour samples or more conveniently, casual samples, to measure iodine per gram of creatinine (see Section 5). In general iodine intake in endemic goitre areas is well below 100 mcg per day, with the appearance of goitre at intake levels below 50 mcg (Stanbury and Hetzel, 1980; Clements et al., 1960; Pretell et al., 1972). The prevalence of goitre increases as iodine excretion falls, so that goitre may be almost universal at iodine intake levels below 10 mcg per day (Karmarkar et al., 1974).

1.3 NATIONAL AND INTERNATIONAL PROGRAMMES TO CONTROL IODINE DEFICIENCY DISORDERS (IDD)

The recent WHO success in eradicating smallpox raises the possibility of similar approaches to other preventable diseases. Such an objective seems appropriate for both iodine deficiency and vitamin A deficiency (WHO, 1984). Certain requirements must be met for an eradication programme to be feasible. These are:

1. The problem is important and of sufficient size;
2. There are effective preventive measures for mass use;
3. Delivery systems are available;
4. Practical measures exist for monitoring and evaluation.

This report sets out to show that these requirements are indeed met where IDD are concerned. The necessary resources must now be found to prepare, implement and evaluate plans for prevention and control.

Increasing momentum has already been generated by some demonstrable success of major national iodization programmes in the large iodine–deficient populations of Indonesia (Dulberg et al., 1983) and China (Ma et al., 1982). Some successes in smaller countries, e.g., Guatemala and Papua New Guinea, were achieved earlier (Thilly and Hetzel, 1980).

These large national programmes have used both iodized salt and injections of iodized oil. The convenience and effectiveness of the latter in correcting severe iodine deficiency as originally shown in Papua New Guinea has made eradication more feasible because of its suitability for many millions of people, particularly in Asia, who are living by subsistence agriculture, and whose diet cannot be adequately supplemented with iodine through their salt supply.

Public health programmes (including IDD control programmes) should concentrate on areas where economic development is likely to be delayed. IDD are likely to regress in association with economic development due to diversification of the food supply, providing an increased intake of iodine, as has occurred in parts of Europe since 1920. In regions in developing countries where significant development is not likely to occur yet for some time, however, the persistence of IDD can be anticipated and justifies a public health intervention.

Much more than technology is involved in a global IDD–control strategy, however. It requires the spreading of information to the many millions living in iodine–deficient regions who are at risk. Only awareness of the problem will encourage political and financial commitment, and this is particularly important in maintaining the required continuity of effort.

A high proportion of the start–up costs of a large–scale control programme may have to be borne by international agencies and bilateral donors. Effective action depends, however, on governments, which will have to shoulder recurrent costs eventually, and their willingness to do so will depend in turn on an informed electorate. In this way the elimination of IDD as a significant public health problem could come about.

The World Health Assembly in May 1986, noted that total prevention and control of IDD by reducing goitre rates below 10 percent in school children is feasible within the next five to ten years (39th World Health Assembly, Resolution 29). It also noted that such control would lead to improved quality of life and productivity, and improved educability of children and adults, for many millions living in the iodine–deficient areas of the world.

A great opportunity exists to remove or control an ancient scourge of mankind. The necessary knowledge and technology are available; what is needed now is their effective application in national public health programmes.

2. IDD IN HUMANS AT FOUR STAGES OF DEVELOPMENT AND IN ANIMAL MODELS

The spectrum of iodine deficiency disorders which occur at various stages of development is shown in Table 1. Each of the four states is considered in detail here below.

TABLE 1

THE SPECTRUM OF IODINE DEFICIENCY DISORDERS

FOETUS	Abortions	
	Stillbirths	
	Congenital anomalies	
	Increased perinatal mortality	
	Increased infant mortality	
	Neurological cretinism	– mental deficiency
		deaf–mutism
		spastic diplegia
		squint
	Myxoedematous cretinism	– dwarfism
		mental deficiency
		Psychomotor defects
		Foetal hypothyroidism
NEONATE	Neonatal hypothyroidism	
	Neonatal goitre	
CHILD AND ADOLESCENT	Goitre Juvenile	
	Hypothyroidism	
	Impaired mental function	
	Retarded physical development	
ADULT	Goitre with its complications	
	Hypothyroidism	
	Impaired mental function	

Source: Hetzel and Maberly, 1985.

2.1 IODINE DEFICIENCY IN THE FOETUS

Iodine deficiency in the foetus is the result of iodine deficiency in the mother. It is associated with a greater incidence of stillbirths, abortions and congenital abnormalities, which can be reduced by iodization (McMichael et al., 1980).

Another major effect of foetal iodine deficiency is endemic cretinism. This condition is still widely prevalent, affecting for example up to 10 percent of the populations living in severely iodine–deficient areas in India (Pandav and Kochupillai, 1982), Indonesia (Djokomoeljanto et al., 1983) and China (Ma et al., 1982). Its commonest form is referred to as the 'nervous' (neurological) type in contrast with the less common "myxoedematous" type characterized by hypothyroidism with dwarf ism. The differences between the two types are summarized in Table 2. The clinical features in a series of 254 cretin subjects from Papua New Guinea (Buttfield and Hetzel, 1969) are listed in Table 3. Detailed studies of bilateral hearing defects in Central Java suggest that they are a marker of great specificity (Pharoah et al., 1980).

The condition described by McCarrison in 1908 still exists in the same areas of the Karakoram Mountains and the Himalayas (Pandav and Kochupillai, 1982). Neurological, myxoedematous and mixed types are found in

the Hetian District of Sinkiang, China (Fig. 1). In both China and India, the condition occurs most frequently below the mountain slopes in the fertile silt plains that have been leached of iodine by snow waters and glaciation.

In all the areas where cretinism is found, with the exception of Zaire, neurological features predominate (Buttfield and Hetzel, 1969). In Zaire the myxoedematous form is more common, possibly due to the high intake of cassava (Pharoah et al., 1980).

The common form of endemic cretinism is not usually associated with severe clinical hypothyroidism as in so−called sporadic cretinism. When mixed forms do occur, however, the neurological features are not reversed by administering thyroid hormones, unlike hypothyroidism (Fierro−Benitez et al., 1970).

The apparently spontaneous disappearance of endemic cretinism in southern Europe raised doubts about its relation to iodine deficiency. This disappearance without iodization was noted by Konig and Veraguth (1961) in Switzerland and by Costa et al. (1964) in northern Italy.

Under these circumstances it was decided in the nineteen−sixties to set up a controlled trial in the Western Highlands of Papua New Guinea to see whether endemic cretinism could be prevented by iodization. This study, carried out in collaboration with the Public Health Department, was based on the use of iodized oil in a single intramuscular injection of 4 ml of Lipiodol, which provided approximately 2 g. of iodine. This dose had previously been shown (Buttfield and Hetzel, 1967) to provide satisfactory correction of severe iodine deficiency for a period of between four and five years. Iodized oil or saline injections were given to alternate families in the Jimi River District at the time of the first census in 1966. Each child born subsequently was examined for evidence of motor retardation, as assessed by the usual tests of sitting, standing and walking, and for evidence of deafness. Examination was carried out without knowledge of whether the mother had received iodized oil or saline. Infants with the full syndrome of hearing and speech abnormalities together with abnormalities of motor development with or without squint were classified as suffering from endemic cretinism. Later follow−up confirmed the diagnoses of cretinism in these cases.

TABLE 2

COMPARATIVE CLINICAL FEATURES IN NEUROLOGICAL AND HYPOTHYROID CRETINISM

	Neurological cretin	Hypothyroid cretin
Mental retardation	Present, often severe	Present, less severe
Deaf−mutism	Usually present	Absent
Cerebral diplegia	Often present	Absent
Stature	Usually normal	Severe growth retardation usual
General features	No physical signs of hypothyroidism	Coarse dry skin, husky voice
Reflexes	Excessively brisk	Delayed relaxation
ECG	Normal	Small voltage QRS complexes and other abnormalities of hypothyroidism
X−ray limbs	Normal	Epiphyseal dysgenesis
Effect of thyroid hormones	No effect	Improvement

Source: Hetzel and Maberly, 1986

TABLE 3

ENDEMIC CRETINISM IN PAPUA NEW GUINEA – CLINICAL FEATURES

	Number	Percentage
Males	129	(51%)
Females	125	(49%)
Total	254	
Visible goitre rate	165	(26%)
Deaf−mutism (partial and complete)	177	(70%)
Characteristic vacant faces	161	(64%)
Brisk reflexes	156	(61%)
Extensor plantar response	122	(48%)
Mental abnormalities	120	(47%)
Flexural deformities	70	(28%)
Muscular incoordination	65	(26%)
Dvarfism	65	(26%)

Source: Buttfield and Hetzel, 1969

Full details were published (Pharoah et al., 1971) and the results of the follow−up are shown in Table 4 and Fig. 2.

It was concluded that an injection of iodized oil given prior to pregnancy could prevent the neurological syndrome of endemic cretinism in the infant. The presence of the syndrome in women who were pregnant at the time of injection indicated that the damage probably occurred during the first half of the pregnancy.

In the light of recent experimental findings (Obregon et al., 1984) it is most likely that this is because of reduced maternal thyroid hormone availability to the foetus, and not because of iodine deficiency of the foetus itself as originally suggested (Pharoah et al., 1971). It is now known that the foetus in its early stages depends on maternal thyroid hormones which cross the placenta (Obregon et al., 1984 al.,1984; Woods et al., 1984). This possibility is supported by other evidence from Papua New Guinea indicating a relationship betweem maternal thyroxine levels and psychomotor development in the child (Pharoah et al., 1984).

Figure 1. Severe IDD: a dwarfed cretin woman with a barefoot doctor of the same age from the Hetian district in Sinkiang, China (Courtesy of Dr. Ma Tai of Tianjin. Reproduced from Hetzel, 1983, with permission).

Recent studies in Papua New Guinea and Indonesia have demonstrated the existence of a coordination defect in otherwise normal children exposed to severe iodine deficiency in pregnancy (Bleichrodt et al., 1980; Connolly et al., 1979). Lesser degrees of neurological damage are also observed (isolated deaf–mutism and mental deficiency) which probably reflect less severe foetal iodine deficiency. In China, these less severe forms are called 'cretinoids' (Ma et al., 1982).

2.2 IODINE DEFICIENCY IN THE NEONATE

The availability of methods for neonatal screening in developed countries (Burrow, 1980) has led to their application in developing countries such as India and Zaire. In India observations on cord blood in iodine–deficient areas indicate as many as 4 percent of neonates with serum thyroxine levels below 3 mcg percent (Kochupillai et al., 1984). In Zaire up to 10 percent of neonates have been observed with low thyroxine levels (Ermans et al., 1980a). These frequencies should be compared with 0.02 percent in most developed countries with normal iodine nutrition (Burrow, 1980).

In a further study from Zaire, the effect of an injection of iodized oil on birth weight, perinatal and infant mortality, and development quotient was assessed by comparison with an untreated group (Thilly, 1981). The findings are shown in Table 5. They indicate substantial improvements in birth weight of infants, with reductions in perinatal and infant mortality and improvement in the development quotient. These findings indicate the necessity of iodine and normal thyroid function for general foetal development and neonatal health. Longer–term benefits evident in children up to the age of 10 to 12 years have been shown in controlled studies following injections of iodized oil before or during pregnancy (Connolly et al., 1979; Pharoah et al., 1984; Fierro–Benitez et al., 1986). These include improved psychomotor performance and improved school performance.

TABLE 4

CHILDREN BORN IN JIMI RIVER SUBDISTRICT (PAPUA NEW GUINEA) TO TREATED AND UNTREATED MOTHERS FROM 1966

Treatment received by mother	Total no. of new births	No. of children examined	No. of deaths recorded	No. of endemic cretins
Iodized oil	498	412	66	7 (1)
Untreated	534	406	97	25 (2)

Source: Pharoah et al., 1971 See also Fig. 3

(1) Mothers of 6 already were pregnant when injected with oil
(2) Mothers of 5 already were pregnant when injected with saline solution

TABLE 5

EFFECT OF INJECTION OF IODIZED OIL GIVEN DURING PREGNANCY, IN ZAIRE

	Not treated		Treated	
Birth weight (g.±)	2634 ± 552	(98)	2837 ± 542	(112)
Perinatal mortality per 1 000	188	(123)	98	(129)
Infant mortality per 1 000	250	(263)	167	(252)
Developmental quotient	104 ± 24	(66)	115 ± 16	(72)

Modified from Thilly, 1981
Sample size in brackets

All differences were significant (P<0.05).

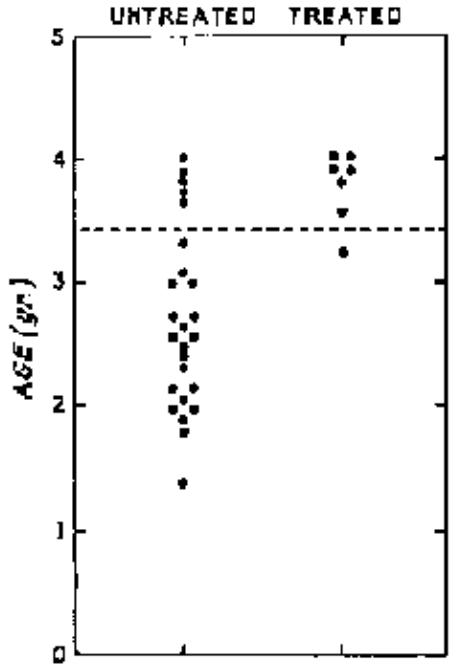

Figure 2. The results of a controlled trial of iodized oil injection in the Jimi River district of the highlands of Papua New Guinea. Alternate mothers were given an injection of iodized oil and saline in September 1966. All newborn children were followed up for the next five years. Each dot represents a cretin child. The figure shows the disappearance of cretin children among births to mothers given iodized oil injections in comparison with their persistence in the untreated group. (Reproduced from Pharoah et al., 1971 with permission)

2.3 IODINE DEFICIENCY IN CHILDREN AND ADOLESCENTS

Iodine deficiency in this period is characteristically associated with endemic goitre. Prevalence increases with age, reaching a maximum after the first decade of life. The condition can be effectively prevented by iodization using various methods following the original demonstration by Marine and Kimball in 1921.

Recent studies of children in China (Wang Dong et al., 1985) indicate a higher general prevalence of lowered intellectual performance (as measured by IQ and other tests modified for use in China) in iodine–deficient areas compared with areas without iodine deficiency.

There is increasing evidence of impaired mental function in apparently normal children living in iodine–deficient areas. Recent observations by Bleichrodt et al. (1987) indicate lower scores in measured mental and perceptual development in children in a severely iodine–deficient area in Spain, compared with a control group carefully matched by socioeconomic status and educational level. Similar data are available from Chile (Muzzo et al., 1986).

A recent study from a mountain village in Bolivia suggests that improved intelligence in school–age children followed the oral administration of iodized oil in a fully controlled study (Bautista et al., 1982). The improvement was related to reduction of goitre and was particularly evident in girls. iodization programmes have been shown to increase the level of circulating thyroid hormones in children in India (Sooch et al., 1973) and in China (Zhu, 1983). These changes occur whether or not the child is goitrous and indicate a mild degree of hypothyroidism without any obvious symptoms.

The major determinant of brain (and pituitary) triiodothyronine (T–3) is serum thyroxine (T–4) and not serum T–3 (Crantz and Larsen, 1980). Low levels of brain T–3 have been demonstrated in iodine–deficient rats in association with reduced levels of serum T–4 and the animals have been restored to normal with correction of the iodine deficiency (de Escobar et al., 1986).

These findings provide a rationale for suboptimal brain function in subjects with goitre and lowered serum T–4 levels and its improvement following correction of iodine deficiency (Bautista et al., 1982; Fierro–Benitez et al., 1974, 1986).

2.4 IODINE DEFICIENCY IN ADULTS

The common result of iodine deficiency in adults is endemic goitre. One of its accompanying effects is a high degree of apathy as noted in populations living in iodine–deficient areas in northern India. This may even affect domestic animals such as dogs. It is apparent that reduced mental function is widely prevalent in iodine–deficient communities with effects on their capacity for initiative and decision–making. Characteristically there is an absence of classical clinical hypothyroidism, but laboratory evidence of hypothyroidism with reduced T–4 levels is common (Fig. 3). This is often accompanied by normal T–3 and raised TSH levels (Maberly et al., 1978; Zhu, 1983; Patel et al., 1973; Goslings et al., 1977).

Iodine administration in the form of iodized salt (Zhu, 1983), iodized bread (Clements, 1960) or iodized oil (Buttfield and Hetzel, 1967) have all been demonstrated as effective in preventing goitre in adults. Iodine supplementation may also reduce existing goitre (Fig.4). This is particularly true of iodized oil injections. The obvious benefit leads to ready acceptance of the measure by people living in iodine–deficient communities.

A rise in circulating thyroxine can be easily demonstrated in adult subjects following iodization (Fig. 3). As already pointed out, this could mean a rise in brain T–3 levels with improvement in brain function.

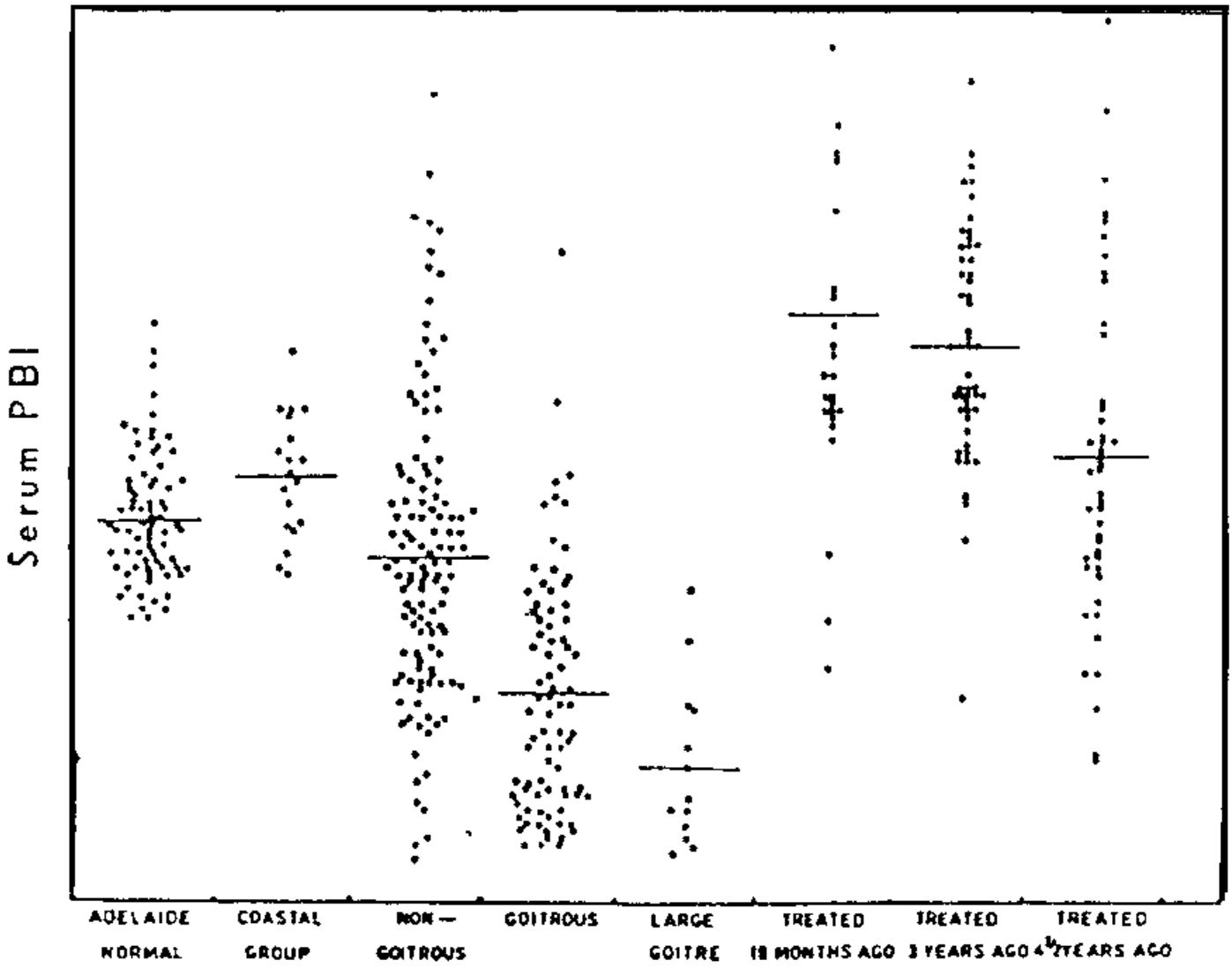

Figure 3. Effect of a single injection of iodized oil on the level of thyroid hormone (serum protein–bound iodine PBI) in subjects in the Papua New Guinea highlands. Each dot represents an individual. The horizontal lines show the mean level for each group. The figure shows that a single injection of iodized oil causes a rise in the level of thyroid hormone for up to four and a half years. (Reproduced from Buttfield and Hetzel, 1967, with permission). WHO 70219

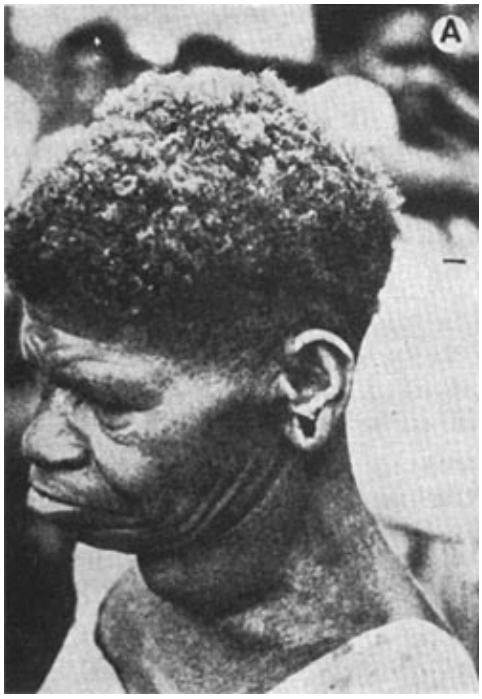

Figure 4. Disappearance of goitre from the neck of a middle–aged woman in Papua New Guinea three months after the injection of iodized oil. (Reproduced from Buttfield and Hetzel, 1967, with permission). – A

Figure 4. Disappearance of goitre from the neck of a middle–aged woman in Papua New Guinea three months after the injection of iodized oil. (Reproduced from Buttfield and Hetzel, 1967, with permission). – B

The general social effects of iodization are demonstrated by the case of the Chinese village of Jixian near Jamusi in Heilongyang Province, northeast China (Li et al., 1985). In 1978 there were 1,313 people in the village with a goitre rate of 65 percent, and 11.4 percent of cretins. The cretins included many severe cases which caused the village to be known locally as "the village of idiots". Its economic development was hindered – for example, no truck driver or teacher was available. Girls from other villages did not want to marry and live there. The intelligence of the student population was known to be low; children aged 10 had a mental development equivalent to others aged 7. Iodized salt was introduced in 1978. The goitre rate had dropped to 4 percent by 1982. No cretins were born after 1978. The attitude of the people changed greatly – they were much more positive in their approach to life, in contrast with their attitude before iodization. The average income had increased from 43 Yuan per head in 1981 to 223 Yuan in 1982 and 414 Yuan in 1984, higher than the average per–caput income in the district. In 1983 cereals were exported for the first time. Before iodization, no family had a radio, but now 55 families had a TV set. Forty–four girls came from other villages to marry boys in Jixian. Seven men joined the People's Liberation Army whereas before they had been rejected

because of goitre. These effects were due mainly to the correction of hypo−thyroidism by iodized salt. The social impact of IDD control programmes needs to be investigated further.

2.5 ANIMAL MODELS

The significant role of iodine deficiency in the etiology of endemic goitre has been confirmed by extensive studies in animals. The major morphological and functional abnormalities can be readily reproduced as originally shown by Marine and co−workers (Marine and Williams, 1908; Marine and Lenhart, 1909).

Experimental iodine−deficient goitre is usually diffuse, but with long−standing deficiency, nodules appear in rats which show an increased number of cells and follicles. As Marine originally demonstrated, when the iodine deficiency subsides the goitre becomes of colloid type and does not return to normal.

In the last decade, systematic experimental studies of the effects of iodine deficiency on development, particularly foetal development, have been carried out. The most extensive studies have been done with sheep but more recently the effects on rats and on marmosets (Callithrix Jacchis Jacchis) have also been studied. These studies have been particularly concerned with foetal brain development because of its relevance to the human problem of endemic cretinism and other forms of brain damage due to foetal iodine deficiency (Hetzel and Hay, 1979) (see Section 2.1). More recently animal models using rats have been established in China with diets closely resembling those consumed in endemic areas.

2.5.1 IODINE DEFICIENCY IN SHEEP

Severe iodine deficiency has been produced in sheep with a low−iodine diet of crushed maize and pelleted pea pollard (8−15 mcg of iodine/kg of diet) which provided 5−8 mcg of iodine per day. After five months, although body weights were maintained, iodine deficiency was evident with the appearance of goitre, low plasma T−4 and T−3 values, elevated TSH levels and low daily urinary excretion of iodine. Control animals received the same diet but were given an injection of iodized oil before pregnancy. The ewes were mated with normal fertile rams, dates of conception established, and foetuses delivered at 56, 70, 98 and 140 days' gestation by hysterotomy (Potter et al., 1982).

Goitre was evident from 70 days in the iodine−deficient foetuses, and thyroid histology revealed evidence of hyperplasia from 56 days' gestation. The increase in thyroid weight was associated with a reduction in foetal thyroid iodine content, reduced plasma T−4 values and increased plasma TSH.

At 140 days the iodine−deficient foetuses were grossly different in physical appearance from the control foetuses. There was reduced weight, absence of wool growth, goitre, varying degrees of subluxation of the foot joints, and deformation of the skull. Delayed bone maturation as indicated by delayed appearance of epiphyses in the limbs was also present (Fig. 5).

There was a lowered brain weight and brain DNA as early as 70 days, indicating a reduction in cell number probably due to slowed neuroblast multiplication which normally occurs from 40−80 days in sheep (Hetzel and Potter, 1983).

Retardation of foetal brain development in severe dietary iodine deficiency was revealed also by histological studies at 140 days gestation (Potter et al., 1982). Delayed maturation of the cerebellum was shown by reduced migration of cells from the external granular layer to the internal granular layer and increased density of Purkinje cells. The greater density of Purkinje cells indicated a reduction in Purkinje cell arborization. In the cerebral hemispheres the cells were more densely packed in the motor and visual areas while the pyramidal neurons in the hippocampus were denser, indicating severe retardation in neuropil growth.

The effect of iodine administration on this retarded foetal brain development caused by iodine deficiency was investigated with a single intramuscular injection of oil containing 500 mg of iodine given at 100 days' gestation. The difference between foetal brain weights in iodine−deficient and control sheep was reduced from 10.8 percent to 6 percent by the iodized oil injection. The difference in body weight was also reduced and maternal and foetal plasma T−4 values were restored to normal (Hetzel et al., 1984).

The effects of severe iodine deficiency on the sheep's foetal brain development were more extensive but similar to those of foetal thyroidectomy carried out at 50–60 days or at 98 days. Maternal thyroidectomy carried out some six weeks before pregnancy had a significant effect on foetal brain development in mid–gestation. The combination of maternal thyroidectomy and foetal thyroidectomy at 98 days produced more severe effects than those of iodine deficiency alone.

The findings following maternal, foetal and combined thyroidectomy suggest that the effect of iodine deficiency on foetal brain development is mediated by the combination of reduced maternal and foetal thyroid secretion and not by a direct effect of iodine. The effect of reduced maternal secretion occurs in the first half of pregnancy and the effect of reduced foetal secretion in the latter half (Hetzel et al., 1984). This conclusion is consistent with recent evidence of the passage of maternal thyroxine in rats across the placental barrier early in pregnancy (Obregon et al., 1984; Woods et al., 1984).

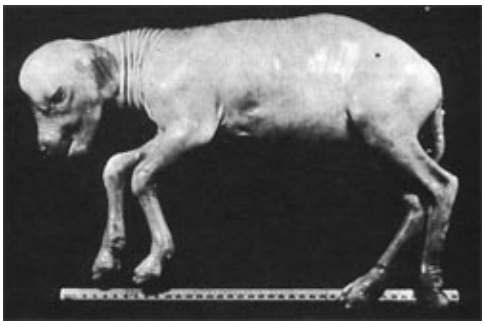

Figure 5. Effects of a severe iodine deficiency on lamb development during pregnancy. (A) A 140–day–old lamb foetus subjected to severe iodine deficiency through feeding the mother an iodine–deficient diet (5–8 mcg per day) for 6 months prior to and during pregnancy (full term: 150 days), compared with (B) a control lamb of the same age fed the same diet with the addition of an iodine–supplement. The iodine–deficient lamb shoved absence of wool coat, subluxation of the leg joints and a dome–like appearance of the head due to delayed skeletal retardation. The brain was smaller and contained a lower number of cells, compared with the control. – A

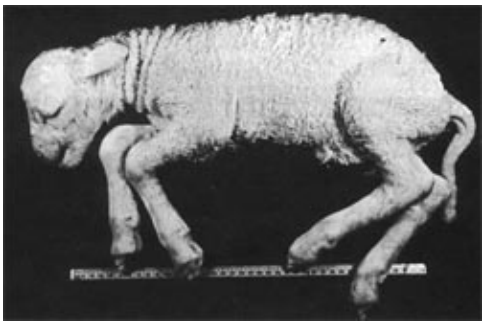

Figure 5. Effects of a severe iodine deficiency on lamb development during pregnancy. (A) A 140–day–old lamb foetus subjected to severe iodine deficiency through feeding the mother an iodine–deficient diet (5–8 mcg per day) for 6 months prior to and during pregnancy (full term: 150 days), compared with (B) a control lamb of the same age fed the same diet with the addition of an iodine–supplement. The iodine–deficient lamb shoved absence of wool coat, subluxation of the leg joints and a dome–like appearance of the head due to delayed skeletal retardation. The brain was smaller and contained a lower number of cells, compared with the control. – B

2.5.2. IODINE DEFICIENCY IN MARMOSETS

Severe iodine deficiency has been produced in marmosets with a mixed diet of maize (60 percent), peas (15 percent), torula yeast (10 percent) and dried iodine–deficient mutton (10 percent) derived from the iodine–deficient sheep produced in the study described in the section above on sheep. There was a gross reduction in maternal T–4 levels with greatly reduced thyroid iodine. After a year on the diet, the animals were allowed to become pregnant and the newborn animals were studied following the first pregnancy and again following the second pregnancy. Significant effects on brain development were apparent in the first pregnancy and more striking ones in the second. There was other evidence of hypothyroidism in the form of impaired hair growth and some skull deformity but there were no striking effects on epiphyseal development. In general the findings in this primate resembled those in sheep (Potter et al., 1984).

2.5.3 IODINE DEFICIENCY IN RATS

Studies on rats using diets consumed in two endemic areas in China were carried out. In both instances foetal hypothyroidism was produced.

The most extensive studies were carried out by Li et al. (1985) using the diet consumed by the people of Jixian village in northern Heilongyang province. This village, as already noted (Section 2.4), was severely iodine–deficient with an endemic cretin rate of 11.4 percent. The diet included available main crops (maize, wheat), vegetables from the area with an iodine content of 4.5 mcg/kg (Li et al., 1985) and water (1.0 mcg of iodine per litre). The rats were housed and fed in a specially constructed animal laboratory in the village. Control animals received the same diet with the addition of iodine providing 54.7 mcg iodine/kg. Special attention was paid to the foetal thyroid and brain during gestation (16–20 days) and birth (1–60 days). After the mother had received the diet for four months, there was obvious neonatal goitre (T–4 3.6 mcg percent compared with controls 10.4 mcg percent), and higher 1(125) uptake, with reduced brain weight. The density of brain cells was increased in the cerebral hemispheres. The cerebellum showed delayed disappearance of the external granular layer with reduced incorporation of tritium labelled leucine in comparison with the control group.

Similar effects have been reported with the iodine–deficient diet (mainly rice) being consumed in south China in Guijou province (Zhong et al., 1983).

Extensive studies have also been carried out with mice, using the iodine–deficient diet consumed in Chemeng, Inner Mongolia. There were definite effects on learning capacity observable in over 10 generations (Ma et al., 1983).

So far, in these Chinese models the effects observed are those of foetal hypothyroidism as in sheep and marmosets. In spite of the predominant occurrence of neurological cretinism in the two endemic areas studied in north–east and south China, this condition has not yet been reproduced in rats. This may yet occur in succeeding generations and with more extended observations into the post–natal period. There may, however, be other environmental factors which together with iodine deficiency produce the condition.

Other studies of iodine–deficient rats by Escobar et al. (1986) have demonstrated a decreased reproductive competence in The adult rats, with a reduced number of viable embryos. These findings are consistent with human data indicating reproductive failure (stillbirths) which can be prevented by correction of iodine deficiency (McMichael et al., 1980). The demonstration of cerebral hypothyroidism in iodine–deficient rats has already been cited.

Implications of Results from Animal Models

These results from animal models provide strong support for the human observations of the major effects of iodine deficiency on growth and development. When taken together they have major policy implications.

The implications of these human and animal observations are that iodine deficiency is responsible for a massive problem of reduced mental function due to the lowered level of thyroid resources in the blood affecting the brain. This condition can be reversed by increasing iodine intake, which means that millions of people living in iodine–deficient regions can benefit from removal of this impediment to the achievement of their genetic potential.

3. PREVALENCE OF IODINE DEFICIENCY DISORDERS (IDD)

In the 1960 WHO monograph, Kelly and Snedden estimated a population of 200 million in the world to be suffering from goitre (Clements et al., 1960 p.28). More recent estimates exceed this figure in spite of extensive iodization programmes. The worldwide distribution of Iodine Deficiency Disorders (IDD) in developing countries is shown in Fig. 1 in "Introduction and Policy Implications" Section.

There is consensus that some 800 million people are at risk of IDD from living in iodine–deficient environments, with 190 million suffering from goitre and more than 3 million with overt cretinism, while millions more suffer from some intellectual deficit (Hetzel, 1987 p.7).

In the Southeast Asia Region eight countries – Bangladesh, Bhutan, Burma, India, Indonesia, Nepal, Sri Lanka and Thailand – all have significant IDD problems. Altogether in these eight countries, it has been estimated in the light of extensive surveys that 277 million are at risk of IDD, some 102 million have goitre, 1.5 million are cretins, and many more suffer from some degree of mental or motor impairment as a result of iodine deficiency (Clugston and Bagchi, 1985).

In the People's Republic of China, it has been estimated that some 300 million are living in iodine–deficient regions and therefore exposed to the risk of IDD. Only one–third of this population was reported as adequately covered by control programmes in 1982 (Ma et al., 1982)[1]. Fever data are available from Africa, but the indications are that the IDD problem is widespread (see Section 3.3). In Latin America the problem persists in Bolivia, Peru, Ecuador and many other countries, in spite of attempts to control IDD with iodized salt (WHO, 1984). IDD persist in many European countries including Germany (both F.R.G. and G.D.R.), Romania, Poland, Spain, Portugal and Italy (European Thyroid Association, 1985).

[1]More recent information (Ma and Li, 1987) indicates coverage expanding to 87% of the deficient population.

Detailed information from the major regions follows. Individual country programmes are considered in Section 6.

3.1 EUROPEAN REGION

The report of the Subcommittee on Goitre and Iodine Deficiency in Europe of the European Thyroid Association (ETA) makes the following comment: "The Scientific Community of the ETA has the obligation to contribute to the eradication of endemic goitre and iodine deficiency in Europe. With the available knowledge it seems an anachronism that endemic goitre in Europe still prevails (European Thyroid Association, 1985). The report goes on to note the lack of information. The available data were confined largely to local areas. The report was nevertheless made because even with these limitations the data were "alarming enough".

The data are summarized in Table 6. Available information is confined to goitre prevalence, urinary iodine excretion surveys and prophylactic measures. The report notes, however, that assay of TSH in neonatal screening programmes is "a sensitive parameter for iodine deficiency".

TABLE 6

COUNTRIES (BY REGION) WHERE IODINE DEFICIENCY DISORDERS ARE SIGNIFICANT HEALTH PROBLEM

REGION	CATEGORY A	CATEGORY B	CATEGORY C
	Situation analysis made, national programme under way	Situation analysis made, or partially made. National programme not under way (pilot studies only)	Situation analysis made, probability based on indirect evidence, no programme
Europe(I)	Austria;+Belgium(V);		
	Bulgaria; *FRG(V);		
	Finland; France; *GDR;		
	+Greece(V); Hungary;		

	Ireland(V); +Italy(V);		
	+Netherlands; Norway(V);		
	*Poland; + Portugal(V);		
	*Romania(?); +Spain(V);	* Goitre – national problem	
	Sweden; Switzerland;	+ Goitre – local problem	
	+Turkey; USSR; Yugoslavia	V Voluntary programme	
Africa(2)	Kenya, Mali,	Burkina Faso,	
	Mozambique,	Cameroon, Cote	
	Tanzania	d'Ivoire, Ethiopia,	
		Lesotho, Nigeria,	
		Senegal, Sierra	
		Leone, Zambia	
		Zimbabwe Iraq,	
Southeast Asia(3)	Bangladesh, Bhutan, Nepal	Burman, India,	
	Indonesia	Sri Lanka	
	Thailand		
Western Pacific(4)	China	Philippines	Kampuchea, Laos,
			Malaysia, Vietnam
Eastern Med.(5)		Iran,	Afghanistan
		Pakistan, Sudan	

(1) From European Thyroid Association, 1985
(2) Goitre Control in the African Region, WHO, 1984
(3) Clugston and Bagchi, 1985
(4) Personal observations by T. Ma and C.H. Thilly
(5) Personal report by M. Benmiloud

Some data on neonatal levels of serum T–4 and TSH in Greece have been reported (Beckers et al., 1981) and are shown in Table 7. The table indicates a lowered level of serum T–4 and raised TSH in the endemic area where there is moderate iodine deficiency without clinical endemic cretinism. Urinary iodine levels are in the range of 13.4 –33.9 mcg/d.

TABLE 7

NEONATAL THYROID FUNCTION IN GREECE

	No.	T–4 (mcg %)	SD	TSH (mcgU/ml)	SD
Endemic area, full term	54	8.8	4.8	15.37	8.20
Non–endemic area, full term	73	10.0	2.9	11.93	4.99
Athens, full term	98	10.3	3.3	10.96	6.33

Source: Beckers et al., 1981

The report notes that "there are some countries where endemic goitre is still prevalent when the country is regarded as a whole". This applies, for instance, to the Federal Republic of Germany and the German Democratic Republic.

In other countries – Spain, Portugal, Prance, Italy, Greece, Romania, Turkey, Poland and Yugoslavia – regional goitrous areas are well documented. This may also apply to Belgium, Denmark, Great Britain, Ireland and the Soviet Union. Further epidemiological studies are strongly recommended for some of these countries.

The report notes the large sums of money spent for the diagnosis and treatment of thyroid diseases in Europe, e.g. DM 308m for outpatient diagnosis and medical treatment of thyroid disorders in the Federal Republic of Germany in 1979. This money is mainly for the surgical expenses because of goitre and its complications. There is therefore a cost benefit to be gained from effective iodization programmes.

Conclusion

The persistence of the IDD problem in Europe, a continent of generally rich countries, is remarkable when control measures are readily available and affordable. There should be no further delay in setting up programmes aimed at eradicating them.

3.2 AMERICAN REGION

A recent report (Noguera et al., 1983, revised in 1984) notes that "Iodine deficiency and endemic goitre are still a problem in many countries in Latin America. In Bolivia, Ecuador and Peru cretinism is a frequent syndrome associated with higher prevalences of endemic goitre". It goes on to note that while there are legal provisions for the iodization of salt, these are not adequately carried out. There is also a need for educational programmes. A tabulation of detailed data on goitre prevalence and urinary iodine levels for all countries in Central and South America is provided in the report and is reproduced in Table 8. Further data are available in the recent PAHO/WHO monograph from the meeting in Lima, Peru (Dunn et al., 1986).

Conclusion

The tabulations indicate persistence of goitre in school children at a prevalence of over 10 percent in all countries with the exception of Costa Rica, Cuba and Uruguay. Urinary iodine levels are in the range 25 – 90 mcg/g of creatinine. A more effective iodization programme is clearly needed in all these countries.

TABLE 8

STUDIES ON ENDEMIC GOITRE PREVALENCE IN LATIN AMERICA (PAHO)

Country (year)	Type of population Studied	Population sampled	Size of sample	Method of goitre classification	Overall prevalence
Argentina					
1967	Sch/children	Departmental	4,431	Perez & Scrimshaw	49.8
					(12.5–61.9)
1967	20 years	Departmental	47,679	Perez & Scrimshaw	15.6

					(4.3–53.6)
Bolivia					
1976	Sch/children	La Paz	4,200	WHO modified	68
1979	Sch/children	Pando	680	WHO modified	77
1981	Sch/children	National	38,500	WHO adapted	60.8
Observation: WHO classification adjusted locally					
Brazil					
1966	Sch/children	45 municips.	45,924		27.2
1967	Sch/children	41 municips.	48,443		21.9
1975	Sch/children	National	266,373	WHO adapted*	14.7
Observation: *Only the inspection criterion was considered					
Chile					
1972	General	Community	8,407	Perez & Scrimshaw	24.8
Colombia					
1945	Sch/children	National	183,243	Old classification	53
Observation: 385 municipalities examined					
1945	Sch/children	Departmental	8,062	Old classification	83.1
Observation: 8 municipalities examined					
1952	Sch/children	Departmental	6,511	Old classification	33.9
1965	Sch/children	Departmental	12,166	Old classification	1.8
Observation: In 1952 and 1965 the same municipal!tes were examined					
Costa Rica					
1966	General	National	4,065	Perez & Scrimshaw	18.0
1979	Sch/children	National	5,061	Perez & Scrimshaw	3.5
Cuba					
1974	6–20 years	Baracoa	2,664	Perez & Scrimshaw	30.0
1976	General	Habana	6,149	Perez & Scrimshaw	3.4
Ecuador					
1969	Sch/children	National	28,639	Perez & Scrimshaw	23.7
1978	Sch/children	National	36,962	Perez & Scrimshaw	12.0
Observation: In 1969 and 1978 the same localities were examined.					
El Salvador					
1966	General	National	3,231	Perez & Scrimshaw	48.0
Guatemala					
1949	General	National	4,113	Old Classification	38.0
1965	General	National	2,995		5.2

				Perez & Scrimshaw (Original)	
1979	Sch/children	National	3,654	Perez & Scrimshaw	10.5
Honduras					
1966	General	National	3,654	Perez & Scrimshaw	17.0
Mexico					
1950	General	8 states	1,000,000		54.6
Nicaragua					
1966	General	National	3,477	Perez & Scrimshaw	32.0
1977	General	National	13,814	Perez & Scrimshaw	33.0
1981	General	National	6,252	Perez & Scrimshaw	20.0
Panama					
1967	General	National	3,071	Perez & Scrimshaw	16.5
1975	General	National	4,084	Perez & Scrimshaw	6.0
Paraguay					
1976	General	National	4,078	Perez & Scrimshaw	18.1
1980	Maternal/ child	3 communities	343	WHO modified	23.6
1982	Sch/children	6 communities	420	WHO modified	16.40
Peru					
1968	Sch/children	National	181,118	Perez & Scrimshaw	22.0
1976	General	National	9,293	WHO modified	15.0*
Observation: *Average prevalence in mountains, jungle and coast					
Uruguay					
1973	Sch/Children	Departmental	2,515	Perez & Scrimshaw	9.0
1980	Sch/Children	Departmental	1,245	Perez & Scrimshaw	2.0
Venezuela					
1966	Sch/Children	National	470,207	Perez & Scrimshaw	13.0
1981	Sch/children				
	& adolescents	National	14,709	WHO modified	21.37

Source: Noguera et al., 1984
Note: Municips. = Municipalities

3.3 AFRICAN REGION

An extensive report (WHO, 1984) provides a valuable survey (see Table 6). The situation is summarized as follows (see also Table 9).

1. Goitre. Practically all countries of the region have significant goitrous areas and in some of them the problem is severe, e.g. 85 percent of female children aged 11–15 years in East

Cameroon had palpable goitres of grades 1 to 3 (see Table 9).

2. Control is relatively easy from the technological viewpoint, by

a) iodized salt;
b) injecting iodized oil (every five years).

The strategy proposed by the WHO Africa Regional Office is to iodate salt where feasible within the country, preferably at national or provincial level, and (simultaneously or afterwards) deal with the remaining pockets by injections of iodized oil.

For most countries what is lacking is the political will, backing, and financial resources for the necessary intersectoral action, since the Implementation of such a programme necessitates at least the cooperation of the Ministries of Health, Trade and Commerce, Finance and sometimes other specialized bodies (laboratories for quality control of iodated salt, etc.).

More detailed data from Algeria, Zaire and Senegal have recently been published (Benmiloud and Ermans, 1986). The roles of retinol deficiency in Senegal and cassava consumption in Zaire have been identified as exacerbating the effects of iodine–deficiency. The fragmentary nature of the data from east, central and southern Africa has been pointed out (Volde–Gebriel, 1986).

Difficulties in Tanzania mentioned by Kavishe et al. (1981) include defining the magnitude of the problem, lack of laboratory facilities, the technology and organization of salt iodization at sector level, manpower and staff training. Recent data are given by Ekpechi (1987).

It seems likely that there is a high prevalence of goitre throughout the extensive southern Africa plateau which includes large areas of Zimbabwe, Zambia, Botswana and Mozambique, all of which have substantial IDD problems. In Zimbabwe, cretinism has been seen only in the more remote eastern highlands, justifying overall classification of the IDD problem as moderate.

TABLE 9

PREVALENCE OF ENDEMIC GOITRE IN SELECTED AREAS OF AFRICA

Country		Palpable goitres grades 1–3 (%)(1)		Visible goitres grades 2–3 (%)(1)
Cameroon				
East Cameroon:				
Adults:		M 48	F 70.7	–
Children:	11–15 yrs.	M 61.5	F 85.1	(grade 3) 1.3–12
	5–17 yrs.	M 51–85	F 59–92	
West Cameroon:				
Children:	5–17 yrs.	M 40–58	F 37–70	
Ethiopia				
ICNND 1959 (2)				
Molineaux –	Gondar	M 10–14	F 30–39	4–12
				47
				90
Hofvander	Ijaji			27

	Bako			53
Ethiopia Nutrition				
Institute (1978)				
	Bora		53	28
	Ankober		71	48
	Ebantu		28	5
	Bure		67	37
Cote d'Ivoire				
9 subprefectures				
	0–7 yrs.	M 66	F 7.1	–
	8–15 yrs.	M 11.9	F 12.9	–
	16–25 yrs.	M 4.2	F 15.9	–
	25	M 9.3(32)	F 32.1	–

(1) See Section 7 for definition of grades
(2) ICNND – Interdepartmental Committee on Nutrition
M = Male
F = Female for National Defence (USA)

Country	Palpable goitres grades 1–3 (%)		Visible goitres grades 2–3 (%)	
Kenya				
Eburu Naivasha				
(Rift Valley)	M 41	F 60	M 18	F 39
Roret (Kericho)	M 40	F 58	M 16	F 32
Lesotho (1957–58)				
	M 30–50			
	(41)			
(1–12 years)			M 7	F 9
(13–18 years)			M 14	F 22
(above 18 years)			M 23	P 15
Mali				
Pales 1948	10.2%			
Hellegouarch 1968:				
Boubouni	F 24–41	M 13.25		
Bandiagara	F 43–69	M 30–63		
Ag Rhaly				
1974 Icati, Dio, Neguela	42–97			
1975 quartier Samakebougou (Kati)	F 53	M 48		

1976 Neguela	F 67	M 53		
1978 Neguela–Koulikoro (Ile Region)	48–72			
Nigeria				
1966 Nwokolo, Ekpeche & Nvokolo Nsukka	F 14–59	M 15–20		
Ogoja	P 10–81	M 26–58		
1965 Nutrition Survey,				
Nigeria				
Lagos (children)	F 11			
Savannah (5–15 yrs.)	F 15			
Plateau (5–15 yrs.)	F 10			
Jos/Pankshin (5–llyrs)	F 16	M 14		
Asaba (5–11 years)	F 42			
Olurin 1970–74				
Oyo	12–32			
Ashoun	15–50			
Ijesha	18–32			
Ekiti	20–37			
Afemai	16–20			
Senegal				
Children				
6–12 years:	M 32	F 41		
13–18 years:	M 26	F 36	Casamance	
			F 11 – 48	
			Eastern Senegal	
			F 23 – 51	
Adults	M 18	F 50		
Sierra Leone				
South–Eastern Province				
Kono	56			
Koinadugu–Koranko	M 43	F 71	–	
Kenema, Kalhun	M 19	F 25	–	
Lowlands	0		–	
Burkina Faso (all ages)	7.7 (0–18% Didougou)		–	
Zambia	M 42	F 59	M 8	F 19

Source: Goitre Control in the African Region. WHO, 1984

Conclusion

In general, only fragmentary data are available for Africa and technical resources are severely limited. More attention to the IDD problem in Africa is urgently required. In southern Africa salt iodization could be an effective solution. In more severe endemias such as Zaire iodized oil has been used and will probably need to be continued. Many other countries fall between these extremes.

3.4 SOUTHEAST ASIAN REGION

This region has a major IDD problem in eight countries (See Table 6). Estimates are given in Table 10 and point to the large numbers of people affected, living in areas of defined environmental iodine deficiency where prevalence of goitre is more than 10 percent of the population. A full report is now available (Clugston and Bagchi, 1985).

TABLE 10

ESTIMATED POPULATIONS AT RISK AND PREVALENCE OF ENDEMIC GOITRE IN EIGHT COUNTRIES OF THE WHO SOUTHEAST ASIAN REGION (numbers in thousands)

Country	Total POP.	Population at risk (TGR > 10%)		Endemic goitre prevalence	
		Number	%	Number	%
Bangladesh	97 438	37 150	38.1	10 225	10.5
Bhutan	1 446	1 466	100.	946	65.4
Burma	39 920	14 545	36.5	5 694	14.3
India	746 010	149 588	20.0	7.3	
Indonesia	161 003	29 773	18.5	9 759	6.1
Nepal	16 386	15 099	92.0	7 555	46.1
Sri Lanka	16 099	10 565	65.6	3 112	19.3
Thailand	52 709	20 439	38.8	7 740	14.7
TOTAL	1 131 011	278 605	24.6	99 349	8.8

Note:

TGR = Total Goitre Rate (prevalence)
Percentages shown are percentages of total population

Source: Clugston and Bagchi (1985, p. 14) and for total population data UN Demographic Yearbook 1981/1982

An important indication of the severity of IDD is given by determinations of blood T–4 and TSH on cord blood samples from neonates in Gonda, Uttar Pradesh, as compared with New Delhi (Table 11). These data indicate a 4 percent rate of neonatal hypothyroidism.

TABLE 11

UMBILICAL CORD BLOOD T–4 AND TSH BY DIRECT ASSAY

Mean Values (± SE)

Area	No. subjects	T–4 mcg/dl	TSH mcU/ml	Hypothyroids detected
Gonda	132	5.75 ± 0.2	15.50 ± 2.8	5
New Delhi	160	8.5 ± 0.2	8.7 ± 0.5	1

mcU – microunit Source: Kochupillai et al., 1984
Source: Kochupillai et la,. 1984

Follow–up is required in order to evaluate the persistence of such rates and to determine whether these infants are likely to develop permanent brain damage. A preventive programme is urgently needed (preferably with iodized oil).

The persistence of goitre in the face of a national iodized salt programme in India has been well documented by the Ministry of Health (Table 12). The findings show the need to monitor the iodization programme and urgently consider remedial measures, including the possible use of alternative technology. (See Section 6).

Conclusion

The largest populations living in iodine–deficient environments and therefore at risk of IDD are to be found in Asia. There is an enormous opportunity to improve quality of life and productivity by correcting iodine deficiency in these countries.

TABLE 12

IMPACT OF IODIZATION PROGRAMMES IN INDIA

District/ state	Baseline survey year	Prevalence percentage rate	Commencement of salt supply	Resurvey year	Prevalence percentage rate
HIMACHAL PRADESH					
Sirmoor	1959	35.8	1963	1980	28.07
Kangra	1956	41.2	1962	1962	32.10
PUNJAB					
Gurdaspur	1961	52.3	1964	1969	42.30
Hoshiarpur	1961	40.3	1964	1969	23.60
Chandigarh	1969	11.2	1968	1977	45.90
BIHAR					
Champaran(East and West)	1960	40.3	1964	1979	64.51(East)
					57.20(West)
WEST BENGAL					
Darjeeling	1965	34.5	1967	1975–76	35.58
UTTAR PRADESH					
Dehra Dun	1965	39.7	1966	1969	16.90
Bijnore	1960	23.2	1960	1969	23.60

Source: Nutrition Foundation of India, 1983

3.5 WESTERN PACIFIC REGION

A report from China indicates a massive problem with about 30 percent of the population at risk of IDD (Table 13). Effective programmes have been operating since 1978. In that time, it was claimed that IDD have been completely controlled in six of 27 provinces (mainly with iodized salt), but in another 11 provinces the programmes, although started, have not yet been adequately established and shown (through monitoring) to be effective. There are about 10 million people in Xinjiang and Tibet who need an iodized oil programme, but transportation in these provinces is very difficult (Ma, 1984). Limited data from Vietnam, Laos and Kampuchea indicate that severe IDD exist. (See Table 6).

TABLE 13

EXTENT AND EFFECT OF IODIZATION PROGRAMMES IN THE PEOPLE'S REPUBLIC OF CHINA

Population at risk of IDD	Methods of IDD Correction	Population covered by Programme	Evaluation Dates	Remarks
1983: 310,000,000 Some south China provinces not included	Chiefly iodized salt programmes, Certain areas use iodized oil injection	1984: 270,000,000 Some 60,000,000 people at risk not covered by iodization programmes	Among the 27 provinces with IDD endemia: 1. IDD controlled in 6 provinces by 1984. 2. Iodization programmes not well established in 11 provinces by 1984.	Although 310,000,000 are at risk of IDD under iodization programmes more than one third are not well quantified. Modern monitoring systems lacking to guarantee the quality of iodization programmes
1984: 330,000,000 Still some China provinces not included	Additional iodized oil injections for young married women in certain areas			

Source: Ma Tai, 1984 Conclusion

China has made remarkable progress with salt iodization since 1978. This indicates the priority of prevention in the country's political philosophy. (See Sections 6 and 8).

3.6 GENERAL CONCLUSIONS

These data indicate a massive global problem. Where IDD have disappeared in Western countries, this has been brought about by an increased dietary intake of iodine either through specific supplementation with iodized salt or by dietary diversification as one of the outcomes of economic development. The problem can be expected to persist in the absence of either of these factors. Therefore the effects of iodine deficiency in the form of IDD on growth and development (Section 2) will continue to be evident. National and international action is indicated. Priority should be given to those areas and regions where the persistence of severe IDD can be anticipated as already pointed out in Section 1.

4. METHODS TO CORRECT IODINE DEFICIENCY

4.1 IODIZED SALT

Many methods of iodization have been used to increase iodine intake. These include the addition of iodine as iodide or iodate to various foods such as bread, water and milk. The addition of iodide to sweets has been used in Mexico. Salt iodization, however, is by far the most widely used and simplest method available. The intake of salt as a condiment tends to be constant from day to day, unlike various foods and water. One problem which remains is its acceptability to people who may not eat salt or to those people (as in Thailand and China) who prefer their own salt which does not contain iodine.

There are yet unsolved problems, however, in ensuring the production and distribution of iodized salt of adequate quality in sufficient amounts for large iodine–deficient populations, as in Indonesia, India and China. Cost is also a problem whether it is met by governments or not, as is true of any other methods to correct IDD.

Recommended levels of iodization vary in different countries and must be monitored. In Finland an increase of 10–25 mg iodine/kg salt (10.25 ppm) was found to be required for effective control of goitre (Lamberg et al., 1981). On the assumption of an intake of 5 g. of salt per day an iodization level of 10 mg/kg (10 ppm) would provide 50 mcg of iodine per day. If the salt intake is lower than this, as it often is in populations in some developing countries, a higher level of iodine supplementation is required. In general an iodine intake level of 100 mcg per day can be regarded as adequate for the prevention of goitre and cretinism. In view of the significance of high salt consumption in the development of hypertension, higher levels of salt iodization would give more iodine with lower salt consumption.

The most popular and simplest technique of salt iodization consists of applying a solution of an iodine compound on salt by a drip or a spray. If the salt is then dried well, is free of impurities (in particular ferric iron) and has a slightly alkaline pH, potassium iodide is well suited and will be quite stable.

On the other hand if the salt retains or acquires moisture, contains impurities, or has a pH below 7.5, iodide may be oxidized to molecular iodine and evaporate (net loss), or it may move in the water film downward or into the fabric of the container (segregation). In such instances potassium iodate is the preferred iodization compound. Iodate has a remarkable stability even in impure salts and under adverse climatic conditions (Burgi and Rutishauser, 1986).

Potassium iodide is used extensively for supplementing refined (table) salt. It is highly soluble but easily oxidized with higher temperature and humidity. This can be reduced by the addition of stabilizers such as 0.1 percent sodium thiosulphate and 0.1 percent calcium hydroxide combined.

There are many problems in the distribution of iodized salt. For example, in remote mountainous areas as in Nepal, supplies must be transported on the backs of sheep; in the Sahel camels have to be used. Salt may not be available in the marketplace, as in remote parts of Bolivia.

Surveillance of an iodization programme should include: monitoring of salt sales; checks on the iodine content of iodized salt at the production site, and in the retail stores; and analysis of urinary iodine excretion (Burgi and Rutishauser, 1986; Hunnikin and Wood, 1980).

In the USA and Japan, iodine is produced mainly from brine wells. China is totally dependent on Japan for its iodine supplies, and the price is rising. Chile is no longer so Important a source of iodine as salt iodization competes with the fertilizer industry (Hunnikin and Wood, 1980). Iodate generally has to be imported, so it requires foreign currency.

Recent experience in China has revealed a major problem with salt iodization plants. In general the units presently available have only one to two years' effective life in this country. This is due to rust, in spite of the plants being carefully cleaned between processing. The cost has also escalated so that one unit (capacity 8–30 tons per hour) now costs US$ 15 000 whereas three years ago it was only US$ 4 000. However, there are solutions to these problems.

In general there are 30–40 plants per province in China. Central factories operate in Guijou, Sechuan, Hebei, Henan and Chinghai – these can iodize salt more effectively than a multiplicity of units and for this reason there is a tendency in China to centralize production of iodized salt production more.

The difficulties in the production and distribution of salt to the millions of people that are iodine–deficient, especially in Asia, are vividly demonstrated in India, where some breakdowns in supply have occurred. The difficulties are discussed in a detailed report prepared by the Nutrition Foundation of India (1983). The gap

between the actual production (106 000 metric tonnes 1978–1979) and the annual requirement (7 000 000 metric tonnes) – see Table 14 – is substantial, and the Indian Government has considered other alternatives such as the use of iodized oil.

In Asia, the cost of iodized salt production and distribution has been calculated as 2–4 cents per person per year (WHO/UNICEF, 1984). This must be considered very cheap in relation to the social benefits described in the previous section.

TABLE 14
PRODUCTION OF IODIZED SALT IN INDIA

Total annual requirement of iodized salt	700.000	MT
Total installed capacity of 12 iodization plants already set up	376.000	MT
Total annual quota fixed for production for use in India	220.000	MT
Production quota in the Sambhar Lake and Khargoda area for supply to Nepal	60.000	MT
Total actual production for both India and Nepal together		
in 1974–75	122.000	MT
in 1978–79	106.000	MT

Source: The National Goitre Control Programme: A blueprint for its intensification. Nutrition Foundation of India, Scientific Report 1, p. 57 (1983)

There is still the problem of getting the iodized salt to the iodine–deficient subject, however. It may be difficult to preserve the iodine content – the salt may be left uncovered or exposed to heat; for instance, iodized salt should be added after cooking to reduce the loss of iodine. The loss of iodine from iodate (which is more stable than iodide) when uncovered and exposed to moisture is substantial. An example is shown in Table 15.

Finally, getting people to consume iodized salt may be difficult. While the addition of iodine makes no difference to the taste, the introduction of a new variety of salt to an area where salt is already available and familiar and much appreciated as a condiment is likely to be resisted. In the Chinese provinces of Sinjiang and Inner Mongolia, the strong preference of the people for desert salt with very low iodine content necessitated a mass iodized–oil injection programme to prevent cretinism (Ma et al., 1982).

TABLE 15
LOSS OF POTASSIUM IODATE (%) OVER TIME IN DIFFERENT STORAGE CONDITIONS IN INDIA

	Open		Covered		Only Top Covered	
Days Storage	Loss(%)	Rain (mm)	Loss (%)	Rain (mm)	Loss(%)	Rain (mm)
9	2.9		3.3		2.9	
17	2.8	–	4.4	–	5.2	–
27	19.1	153	3.8	–	6.3	–
34	24.7	181	5.1	–	6.9	–
44	42.8	241	5.1	–	6.9	–
55	53.9	327	5.7	–	16.4	434
68	–	–	7.8	–	–	–
78	–	–	7.2	–	–	–

Initial iodate content = 27.2 ppm.

Source: The National Goitre Control Programme: a blueprint for its Intensification. Nutrition Foundation of India, Scientific Report 1, p.51 (1983).

4.2 IODIZED OIL BY INJECTION

The value of iodized oil injection to prevent endemic goitre and endemic cretinism was first established in New Guinea with controlled trials involving the use of saline injection as a control (see Section 2.1). These trials established the value of the oil in preventing goitre (McCullagh, 1963) and cretinism (Pharoah et al., 1971). Experience in South America confirmed the value of the measure (Pretell et al., 1972). The quantitative correction of severe iodine deficiency by a single intramuscular injection (2.4 ml) has been demonstrated (Buttfield and Hetzel, 1967) (Table 16) (Fig. 3).

Iodized oil can be injected by local health services where they exist, or by special teams. In New Guinea more than 100 000 people were injected by public health teams who at the same time injected triple antigen (immunization) (Hetzel, 1983).

Iodized oil is singularly appropriate for the isolated village community so characteristic of mountainous areas with endemic goitre. It has been used extensively in the Himalayan region – Pakistan, Burma and Nepal (Hetzel et al., 1980).

In a suitable area, the iodized oil should be administered to all females up to the age of 40 years and all males up to the age of 20 years. A repeat of the injection is required in three to five years, depending on the dose given and the age of the subject. Children's needs are greater than those of adults and the recommended dose should

TABLE 16

THE EFFECT OF IODIZED OIL ON THYROID FUNCTION IN NEW GUINEA SUBJECTS[1]

[1]Statistical analysis shoved highly significant differences between the treated and untreated groups in urinary iodine, 1(131) uptake and serum PBI ($P<0.001$). There was no significant difference in the 1(131) uptake or serum PBI between subjects treated 3 years and 18 months before. The figures given are for the mean + the standard deviation, with the number of subjects tested shown in parentheses. be repeated in three years if severe iodine deficiency persists. The dosage schedule formerly recommended is shown in Table 17. More recently, however, the recommendations have been simplified to 0.5 ml for 0– to 1–year–olds and 1 ml for all later ages, for prevention for three years. (Stanbury et al., 1986).

	Mean ± S.D			
Group	Urinary iodine (mcg/24h)	I(131)uptake (X at 24 h)	Serum PBI (mcg/100 ml)	T–3 resin uptake (% of normal)
Untreated	11.55±12.4 (91)	70±19 (181)	4.1±2.1 (204)	91±12.1 (195)
Treated 18 months and 3 yrs before	67±83 (47)	33±20 (94)	8.0±2.0 (79)	97±14.8 (77)
Treated 3 months before	258±109 (8)	6.±03 (20)	44.7±18.4 (20)	110±15.5 (20)
Treated 18 months before	119±114 (18)	31±20 (51)	8.2±2.6 (27)	97±15.8 (27)
Treated 3 yrs before	35±25 (29)	37±19 (43)	7.8±1.6 (52)	97±14.7 (50)
Treated 4+ yrs before	23±21 (11)	44±18 (67)	6.4±2.4 (43)	99±16.0 (43)
Australian normal range	70–140	16–40	3.6–7.2	70–110

Source: Buttfield and Hetzel, 1967

TABLE 17

RECOMMENDED IM DOSAGES OF ETHIODIZED OIL CONTAINING 37% IODINE

Age	Iodine (mg)	Dose (ml)
0–6 months	95.0 – 180.0	0.2 – 0.4
6–12 months	142.5 – 285.0	0.3 – 0.6
12 months – 6 years	232.5 – 465.0	0.5 – 1.0
6–45 years	475.0 – 950.0	1.0 – 2.0

Source: Stanbury et al., 1974

Note:

1) The dosage should be reduced to 0.2 ml for all persons with nodular goitres or single thyroid nodules without goitre.

2) Recent recommendations are given in Dunn et al., 1986, p. 128.

Iodized walnut oil and iodized soya bean oil are preparations developed in China in the past five years to avoid the need for foreign exchange. They are cheaper than similar Western products, so they could have wider application. Preliminary reports on their use were given to the Second Asia and Oceania Thyroid Association Meeting in Tokyo (Liu, 1983; Ouyang et al., 1983).

Iodized oil has been shown to be suitable for use in a mass programme. In Indonesia 1 036 828 injections of iodized oil were given between 1974 and 1978, together with a massive distribution of iodized salt (Djokomoeljanto et al., 1983). A further 6 000 000 injections of iodized oil were given by specially trained paramedics in the period 1978–83. In Sinjiang, China, 707 000 injections were given by 'barefoot doctors' between 1978 and 1981, and a further 300 000 – 400 000 in 1982.

An advantage in the use of injections is their association in people's minds with the successful campaign to eradicate smallpox. Disadvantages are the immediate discomfort produced, and infrequent development of abscesses at the injection point. Sensitivity phenomena have not been reported. These side effects are not serious.

The major problem of injections, however, is their cost (Stanbury et al., 1974), although this has been reduced with mass packaging. Details are given in Table 18. Again the cost must be considered modest in relation to the benefits obtained. Moreover, it is similar to that of iodized salt, especially if the population to be injected is restricted to women of reproductive age and children, and a primary health care team is available.

TABLE 18

CONTROL OF IODINE DEFICIENCY DISORDERS – COSTS

1. Iodized salt = 2–4 cents/person/year
2. Injection of iodized oil

   Oil 1 ampoule 10 ml = $2.00

   therefore 1 dose 1 ml = 20 cents

   1 dose 2 ml = 40 cents

   Syringe = 3–4 cents

   Needle = 1 cent

Therefore – Total = 25 cents for 1 ml (45 cents for 2 ml)

3. Oral oil – 2 ml (without cost of staff) half coverage period (equiv. to injection)
4. Labour

Staff would usually be available at the primary health care centre – if no primary health care centre system is available, special staff would need to be trained.

5. Summary of relative costs for iodized salt and oil

   (1) For salt

   2 cents/person/year For 10 000 = $200

   4 cents/person/year For 10 000 = $400

   For 3 years coverage: (2cents)= $600, (4cents)$1200

   5 years coverage: (2cents)= $1000, (4cents)$2000

   (2) For iodized oil injection

   For 10 000, 1 ml dose =$2 500; 2 ml dose =$4 500

   (The 2–ml injection would last three years).

   Costs could be reduced by targeting for women and children.

Source: from information provided by WHO/UNICEF (1984)

4.3 IODIZED OIL BY MOUTH

There is evidence of the effectiveness for one to two years of a single oral administration of iodized oil in South America (Watanabe et al., 1974), and in Burma (Kyve–Thein et al., 1978).

More recent unpublished studies in India and China reveal that the effect of iodized oil taken by mouth lasts only half as long as a similar dose given by injection.

Experimental studies on guinea pigs in China indicate that iodized oil taken orally is stored in adipose tissue while the iodized oil injected is stored at the intramuscular site of the injection. Absorption from the muscle is slower than from the adipose tissue. There is also a greater loss of iodine from oral administration route due to de–iodization in the stomach; the iodine is then absorbed but rapidly excreted through the kidneys. In general, there is an 85–percent loss of iodine within 72 hours of iodized oil taken orally, compared with a loss from an intramuscular injection of 30 percent in two weeks, and a loss of 96 percent within 72 hours from iodized salt (Wei Jun and Li Jianqun, 1985).

The production of iodized oil to take orally is clearly a different proposition from that intended for injection. The addition of an antioxidant would be feasible in the case of an oral preparation.

There is an urgent need to increase the production of iodized oil. At present the main, if not– the only, source in the Western world is Laboratoire Guerbet of Paris. This firm is engaged in the production of radio–opaque dyes and not orientated to the large–scale production of one particular preparation.

[1]16–24 Rue Jean–Chaptal, 93601 Aulnay Sous Bois, Cedex Boite Postale No. 15.

Possible chemical methods for iodizing oil have been investigated by Dr. Trevor Morton of the CSIRO Division of Applied Organic Chemistry, Melbourne, Australia (Morton and Guillaume, 1984). A variety of vegetable oils with linoleic acid as a major constituent can be iodized. Studies with safflower oil (76.9–80.5 percent linoleic

acid) indicated that satisfactory and cheap iodization can be achieved with iodide and phosphoric acid. Development of this methodology to an industrial scale is required to demonstrate feasibility. It would seem likely however, that large quantities of iodized oil can be produced, particularly for oral use, at a reasonable cost.

4.4 IODIZED BREAD

Iodized bread has been used in Holland and in Australia. Detailed observations are available from Tasmania, the island state of Australia.

Since 1949 the Tasmanian population has received a number of intended and unintended dietary iodine supplements. These began with the use of weekly tablets of potassium iodide (10 mg) given to infants, children and pregnant women through child health clinics, schools and antenatal clinics whenever possible.

The prevalence of endemic goitre fell progressively over 16 years but goitre was not eliminated. This was traced to lack of cooperation in the distribution of the iodide tablets by a number of schools. The distribution through child health centres to infants and preschool children was also ineffective because of irregular attendance.

For this reason it was decided to change the method of prophylaxis to iodization of bread. The use of potassium iodate up to 20 mg/kg (20 ppm) as a bread improver was authorized by the National Health and Medical Research Council of Australia in May 1963, and the necessary legislation was however, passed by the Tasmanian Parliament in October 1964.

The effect of bread iodization was followed by a series of surveys of palpable goitre rates in school children. A definite effect on visible goitre rate was apparent by 1969 (Clements et al., 1970). Studies of urinary iodide excretion and plasma inorganic iodide in May 1967 revealed no excessive intake of iodide. Correction of iodine deficiency was confirmed by evidence of a fall in 24−hour radio−iodine uptake levels in hospitalized subjects as well as normal plasma inorganic iodine concentration and urinary iodine excretion (Stewart et al., 1971).

It may be concluded that bread iodization was effective in correcting iodine deficiency in the nineteen sixties. A transient increase in thyrotoxicosis was observed (see Section 5).

4.5 WATER IODIZATION

In their original controlled trial in Ohio, 1917−22, Marine and Kimball used a dose of 200 mcg of sodium iodide in water daily for 10 days in spring and repeated this in autumn. They observed satisfactory regression of goitre.

Reduction in goitre rate from 61 percent to 30 percent with 79 percent of goitres shoving visible reduction was demonstrated following water iodization in Sarawak (Maberly et al., 1981). Significant rises in serum T−4 and falls in TSH were also shown. Urinary iodine excretions were variable due to intermittent obstruction of the iodinator but eventually the levels indicated iodine repletion.

Similar results were obtained with preliminary studies in Thailand by Dr. Romsai Suwanik and his group at the Siriraj Hospital, Bangkok, and by Vigneri et al. in Sicily (1982).

In a full report Squatrito et al. (1986) describe the methodology used in the Sicilian town of Troina. The apparatus was a canister filled with coarse crystals, through which water from the main line was diverted. The level of iodization (achieved by regulating the pressure) was 50 mcg/l (50 ppm). School children were studied before and after iodization and compared with those in Catania (iodine sufficient) and Maniaci (iodine deficient). The Troina values of overall goitre prevalence, 24−hour urinary iodine, radio−iodine uptake, and serum T−4, serum T−3 and serum TSH after iodization were similar to those in Catania. At the iodine concentration used, there were no complaints of change in the taste or smell of the water; nor was there evidence of increased incidence of hyperthyroidism associated with iodization. The system was easily maintained and the iodine supply needed to be changed only after several years. iodization also provided effective disinfection of the water supply. The cost was approximately US$ 0.04 per person per year. This

study offers convincing evidence that this method of iodization is safe, effective and economic.

It is suggested that iodized water may be more convenient than iodized salt and the likelihood of iodine–induced thyrotoxicosis may be less. This method is appropriate at village level if a specific source of drinking water can be identified, otherwise there is a heavy cost, as less than 1 percent of a general water supply is used for drinking purposes. This method, which is worthy of more investigation, also offers the benefit of antisepsis.

4.6 OTHER METHODS

In Bangkok, Dr. Romsai Suwanik has developed iodized fish sauce and iodized soy sauce as additional iodized condiments. These sauces are also being used for iron supplementation.

Oral iodide for moderate iodine deficiency should be considered as an option for school children whose compliance can be more readily enforced than that of adults. It cannot, however, be expected to meet the demand of a severe deficiency.

4.7 GENERAL COMMENTS

The various available methods of iodization fall into two categories:

1) measures for the whole population – iodized salt, iodized bread and iodized water;

2) prescriptive measures suitable for a segment of the population at risk – children and women of reproductive age – in the form of iodized oil and iodide tablets.

The great advantage of the prescriptive approach is that it can be carried out through the health care system. It does not require cooperation and enforcement measures involving other government departments and private industry. For this reason, prescriptive measures (mainly iodized oil) should be given more serious consideration than in the past when the tendency was to think of iodized salt as the first choice. The importance of quantitative correction of severe iodine deficiency, particularly in women and children, in order to prevent cretinoids requires a much more critical approach.

Oral administration of iodized oil to children could be carried out through the baby health centres and schools. Periods of 18 months could be covered at present, with 2 ml–doses. This may well be increased in the light of further research investigation. An injection would last longer (2 ml for three years) and is appropriate where it can be carried out by existing primary health–care–centre staff. Cheaper production of iodized oil is readily achievable and should be provided in India and other countries with large populations at risk. The advantages of a single administration of iodized oil against multiple administration of iodide tablets are obvious.

In China an iodized oil injection has been introduced for iodine–deficient young women just before marriage (see Table 13). This covers them for three years to confer protection for the single pregnancy that is now in force as family planning policy.

The complication of iodine–induced thyrotoxicosis is unavoidable for population measures. It is discussed in the next section. Its incidence depends mainly on the proportion of the population over the age of 40 years, a proportion lower in developing countries than in developed ones.

4.8 CONCLUSIONS ON CHOICE OF METHODS

We may summarize present general indications for the use of the two major methods for correction of iodine deficiency in relation to the severity of IDD as follows:

Mild IDD with goitre prevalence in range 5–20% (school children) and with median urinary–iodine levels in excess of 50 mcg/g of creatinine. Mild IDD can be controlled with iodized salt at a concentration of 10–25 mg/kg (10–25 ppm). They may disappear with economic development.

[1]Mild IDD has more recently been defined as urinary iodine excretion between 50 and 100 mcg/g creatinine (Stanbury, 1987 p.37).

Moderate IDD with goitre prevalence up to 30%, some hypothyroidism with median urinary–iodine levels in the range 25–50 mcg/g of creatinine. Moderate IDD can be controlled with salt (25–40 mg/kg (25–40 ppm)). Otherwise, iodized oil either orally or by injection should be used through the primary health care system.

Severe IDD indicated by a high prevalence of goitre (30% or more), endemic cretinism (prevalence 1–10%), median urinary iodine below 25 mcg/g creatinine. Severe IDD require iodine as iodized oil administered either orally or by injection – the fastest and most effective method – for complete prevention of central nervous system defects.

If a primary health care system is available then the cost of iodized oil adminstration is of the same order as that of using iodized salt. The correction of severe IPD is feasible and should have the highest priority with national governments in view of the certainty of great benefit.

5. THE HAZARDS OF IODIZATION

A mild increase in Incidence of thyrotoxicosis has been described following iodized salt programmes in Europe and South America and following the Introduction of Iodized bread in Holland and Tasmania (Watanabe et al., 1974; Stewart et al., 1971; Ramzin et al., 1973). A few cases have been noted following iodized oil administration in South America (Watanabe et al., 1974). No cases have yet been described in New Guinea, India or Zaire. This is probably due to the scattered nature of the population in small villages and limited opportunities for observation (Kavishe et al., 1981). The condition is largely confined to those over 40 years of age.

Detailed observations are available from Tasmania, where in 1966 physicians in Launceston and Hobart first noticed an increase in the number of patients with thyrotoxicosis. Each of these cities had a thyroid clinic serving a population of the order of 180,000, Launceston covering the northern half of the island and Hobart the southern (Vidor et al., 1973).

It was apparent that the rise in incidence of thyrotoxicosis had occurred in association with a rise in iodine intake from below normal to normal levels (Stewart et al., 1971) due to iodized bread consumption which was introduced in April 1966.

Scrutiny of records in northern Tasmania revealed a rise in the incidence of thyrotoxicosis as early as 1964, associated with rise in food imports and the introduction of iodophors to the dairy industry during 1963. There was a much larger rise in thyrotoxicosis incidence from 1966 following the iodization of bread. Analysis of the cases by age revealed the predominance of patients over the age of 40, although a rise had occurred also in those under this age.

A cohort effect was demonstrated because the peak passed – the peak being composed mainly of those over the age of 40 with life–long iodine deficiency and autonomous thyroid glands which continued the rapid turnover of iodine after the increase in iodine intake.

It was clear that the increase in thyrotoxicosis was caused mainly by these patients with toxic autonomous goitre and not Graves' disease. The findings support the old view of two types of thyrotoxicosis – Graves' disease and Plummer's disease (Vidor et al., 1973).

The condition can be readily controlled with antithyroid drugs or radio–iodine. It seems likely that spontaneous remission occurs in many cases. In general iodization should be minimized for those over the age of 40 because of the risk of thyrotoxicosis.

Apart from thyrotoxicosis the risk of iodism or iodide goitre seems to be small. An increase in lymphocytic thyroiditis (Hashimoto's disease) has been claimed following iodization but this is still disputed (Stanbury et al., 1974).

6. RECENT IODIZATION PROGRAMMES

In this section a series of relatively well–documented national iodization programmes are reviewed. They reflect different social and environmental situations in which various methods have been used to correct iodine deficiency. Some have succeeded and some have failed so the implications of experience with these programmes are of interest for future national programme implementation.

The goal of an iodization programme is complete coverage of the iodine–deficient population with iodine supplementation; the problem is similar to that arising with any other preventive measure – although suitable technology is available its successful application is another, and in general more difficult, matter.

These difficulties are described as they occur in countries in various regions. All–important to success is political will and administrative efficiency. These questions are taken up in more detail in Section 8 where a model for a national iodization programme is discussed.

The following programmes have used different methods or different combinations of methods to correct iodine deficiency. They demonstrate the value and limitations of these methods:

Finland	Salt
Papua New Guinea	Oil and salt
Countries of Central & South America	Salt and oil
Zaire	Oil
Indonesia	Salt and oil
China	Salt and oil
India	Salt

6.1 FINLAND (SALT)

Finland provides a good example of a country which has achieved a successful iodization programme. Lamberg et al. (1981) in their assessment of the intensified salt iodization programme in eastern Finland found a reduction in goitre rate to about 1 percent compared with 15–30 percent in the early nineteen fifties. This reduction resulted from salt iodization at a recommended level of 25 mg/kg salt (previously 10 mg/kg or 10 ppm) and greatly increased iodine consumption, so that 75 percent of the total amount of salt sold in 1969 was iodized compared with less than 50 percent in 1959. There was also evidence of increased levels of urinary iodine excretion (less than 45–60 mcg/day in 1959 compared with 200 mcg/day in 1969). It is possible that other dietary changes contributed to the increased iodine intake.

The increased consumption of iodine was promoted actively by the State Commission of Nutrition and the salt iodization programme was combined with a public education campaign.

It may be concluded that where iodine deficiency exists a successful programme requires an adequate dose of iodine as well as a suitable public information and education programme, unless the use of iodized salt is made compulsory, and this can be done only by ensuring that it is the only form of salt available.

An updated and comprehensive review has recently appeared (Lamberg, 1986).

General Comment for Europe

There are many European countries with continuing endemic IDD. They include West Germany, Switzerland, Austria, Spain, Italy and Greece. Although goitre is slowly regressing in some of these countries and iodine intake is increasing without formal iodization programmes, the need for such programmes remains. The European Thyroid Association has gathered the available data (see Section 3). A recent report from the Federal Republic of Germany (Stubbs et al., 1986) presents evidence of the existence of brain retardation in goitrous hypothyroid children. Another report from the German Democratic Republic concerns iodine deficiency in pregnancy and urges the introduction of an iodization programme (Bauch et al., 1986).

The persistence of iodine deficiency in European countries is readily preventable. The low extra costs involved in screening for hypothyroidism (including transient hypothyroidism due to iodine deficiency), and for the investigation of goitre, provide a strong economic incentive in addition to humanitarian considerations.

6.2 PAPUA NEW GUINEA (OIL THEN SALT)

Controlled trials with iodized oil (see Section 4) led to a mass injection programme by the Public Health Department in 1971–1972 involving more than 120 000 people. The injections were given by existing public health teams as part of the Department's prevention programme. No ill effects were observed.

These observations provide a basis for the use of iodized oil in regions and countries where the distribution of iodized salt is not a practical measure (Hetzel, 1974). Iodized oil is particularly appropriate for isolated mountainous communities. In New Guinea the iodized oil programme was regarded as an extension of existing preventive services so legislation was not required, but legislation requiring that all salt used in Papua New Guinea be iodized was passed in 1972. In 1976 there was evidence that food stores in remote highland villages had plentiful supplies of iodized salt. Since that time, however, there has been an economic recession due to falling prices (e.g., of copper), and some evidence of recurrence of goitre in the more remote valleys.

General Comment

The successful iodization programme in New Guinea was made possible by an effective and comprehensive public health service combined with programme–orientated investigations carried out in the field, which demonstrated the value of iodized oil injections in the prevention of goitre and cretinism. The obvious benefit to the people in the regression of existing goitre ensured ready acceptance, and there were no untoward delays caused by political, social or cultural objections. Administration was smooth as the Public Health Department had a strong preventive orientation. Continued monitoring is required to maintain the quality of the programme.

6.3 COUNTRIES OF CENTRAL AND SOUTH AMERICA (SALT THEN OIL)

Schaefer (1974) provided a useful review of salt iodization programmes in Central and South America. By 1973 salt iodization legislation had been enacted in 16 of the 17 Central and South American countries in which iodine deficiency was recognized as a public health problem. He noted, however, the long delay between passage of the legislation and the actual installation of equipment and implementation of the law. Only in Guatemala was legislation followed by immediate implementation of a programme, and in this instance there were commercial factors involved in the possible threat to a national monopoly from suppliers outside Guatemala.

Nicaragua, with an overall goitre prevalence of 32 percent, had not up to 1973 passed legislation. Implementation of laws on salt iodization is still inadequate in Bolivia, Peru and Ecuador where endemic cretinism and a high incidence of endemic goitre are still evident. At the time of Schaefer's survey only a small part of Bolivia's salt supply, 25 percent of Peru's and 75 percent of Ecuador's were iodized.

In response to a questionnaire on the lack of effective implementation, the reasons given were found by Schaefer to be remarkably similar. They included the following.

1. The people, and especially the politicians, were unaware of the severity and magnitude of the IDD problem and their detrimental effects on health, especially in regard to the sequelae of cretinism, deaf–mutism, and other serious neurological defects. There was a failure to inform the public about the seriousness of the problem and its simple solution.

2. The most seriously affected populations usually lived in isolated rural areas where the level of social and economic development was very low. This meant that the problem carried little if any political weight.

3. The traditional system of salt production was not conducive to control, and governments did not provide adequate incentives to the small salt producer.

4. The national salt commissions and government health departments did not enforce the law. Common reasons were the lack of public−health personnel for control activities (although most control procedures do not in fact require technical personnel trained in public health) and heavy work loads.

5. There was a lack of cooperation between the industry and the public health officials or government enforcing agencies.

6. The price of iodized salt had increased by approximately 40−60 percent in some countries (but with simplified enrichment plants, the extra manufacturing cost per kilo of iodized salt was still infinitesimal).

7. The large number of salt−producing plants makes control difficult. This affects mainly Brazil, with nearly 190 plants, and El Salvador, with 37.

The 1973 Guaraja meeting of the Pan American Health Organization (PAHO) was devoted largely to a review of iodization programmes. In the discussion, the problems of cost, of awareness of the medical profession about prevention, and the need for pressure groups were all brought out. The issues raised were the social processes that influence change in health programmes.

The persistence of a high incidence of goitre and cretinism in Peru, Ecuador and Bolivia, caused by problems in implementing salt iodization programmes, led to reappraisal of the strategy. Successful demonstration of the value of iodized oil in the control of iodine deficiency and the prevention of goitre and cretinism in New Guinea (Mc Cullagh, 1963; Hennessy, 1964; Pharoah et al., 1971) suggested an investigation of the use of this alternative measure in a pilot study in several rural communities in Peru and Ecuador.

After two years, the feasibility and effectiveness of these programmes were shown by a sharp reduction in the incidence of goitre and the absence of cretinism among the children of the population injected with iodized oil, although both conditions occurred in the control group. It was concluded that iodized oil was a suitable public−health procedure in South America where salt iodization programmes could not be undertaken; and that the combination of salt iodization and iodized oil injection could provide an effective iodization programme for any region in South or Central America.

There is now an encouraging report (Arraya, 1986) of an iodized oil programme in 174 localities in Bolivia in 1985, when 99 834 people with a goitre prevalence of 69 percent were injected. As a number of communities were remote and difficult to reach, other public health measures including vaccination were administered. The impact of the programme is being evaluated in these communities, and it is planned to continue its activities in the areas not yet reached.

6.4 ZAIRE (OIL)

Thilly et al. (1977) have discussed the problem of iodization programmes in Central Africa. They pointed out the delays in the development of programmes in this region. There are difficulties of geography, economics and administration, as well as the slow passage and implementation of legislation. Thilly et al. (1977) noted that these issues were particularly difficult in Central Africa where they described a number of severe endemias and where iodized salt might be inappropriate. In the light of experience in New Guinea they pursued a strategy based on large−scale iodized oil injection.

Pilot studies with iodized oil in Idjwi Island (eastern Zaire) with a population of 30,000 produced satisfactory results in the prevention of goitre and cretinism. Only one case of cretinism appeared in the treated villages. This child was born to a woman who had been absent from the village when injections were given. In the control village there were three cases of cretinism (Ermans et al., 1980a).

Thilly et al. (1977) found that routine injection of 500−1,000 persons a day could be carried out by a mobile team of three nurses, one clerk and one driver, and that the people readily accepted the injections.

On the basis of this experience, Thilly et al. (1977) employed a strategy to eradicate goitre in the severe endemia of Ubangi Mongala (northwest Zaire) affecting a population of 1,500,000. Preliminary surveys in 12 villages (6 910 people) revealed a goitre prevalence of 27−60 percent in the male population and 48−78 percent in the female. The prevalence of cretinism ranged between 0.7 and 7.6 percent.

In the light of the studies in Idjwi, it was estimated that a mobile team of five workers (as described above) could administer an average of 500 doses of iodized oil per day for 200 days a year, that is, 100 000 doses per year or 500 000 doses in five years. Hence three such teams could inject the whole population of 1,500,000, assuming that an injection is needed every five years for each person at risk. A strong central coordinating unit was set up, directed by an epidemio–logist, to supervise the field work and evaluate the results. The estimated cost of the programme was $500 000 or $0.35 per dose administered. At the time of the report, two of the three teams had been set up (1974 and 1976) and the third was expected to be functional by 1977. By the end of June 1978, 359,565 doses of iodized oil had been systematically administered in villages and communities and by 1984 the number exceeded 1 million.

The programme was gradually merged into the preventive programme of local medical centres, and educational programmes were also introduced to increase public awareness of the problem and gain greater participation by the people.

Comment

The availability of iodized oil injection created the opportunity for an initial programme carried out as an extension of vaccination programmes by public health departments and under their complete control. This contrasts with the lack of control (even with the appropriate legislation) implicit in the process of salt iodization which is dependent on efficient production and distribution to the community as a whole. Salt iodization requires the cooperation of salt producers, who may be large in number, as well as salt distributors. Both of these groups are subject to commercial pressures far removed from considerations of public health. It is in these circumstances that iodized oil can be important in countries where iodization programmes are still needed because of severe endemias characterized by cretinism.

Awareness of the problem of IDD is greatly increased by tangible evidence of benefit from a prophylactic programme. It is in this connection that the dramatic and early effects of iodized oil injection in reducing existing goitre have been so useful in New Guinea and elsewhere. In Zaire the success of the pilot programme in Idjwi led to the political backing necessary for the major programmes in Ubangi Mongala.

The iodized oil injection programme is a stimulus to the development of basic health services which have so far been absent in Ubangi Mongala (Thilly et al., 1977). In New Guinea basic health services were already operating, so the introduction of iodized oil injections was a relatively simple matter. The introduction and execution of the programme in Zaire presents a formidable organizational problem, a situation not by any means unique in developing countries. It seems likely that iodized oil injections will need to be continued for some years. The possibilities of linking such an injection programme to the expanded programme of immunization (EPI) should be fully investigated.

Recent success in EPI programmes in Vest Africa (e.g. Nigeria, Cameroon) have depended on well organized injection teams at local government level. These same teams could be used for the injection of iodized oil in areas and regions with severe IDD.

6.5 INDONESIA (SALT AND OIL)

In Indonesia, IDD control programmes arose from an extensive study of the problem of endemic cretinism in Central Java by Djokomoeljanto (published in 1983). This led to a briefing of politicians and in due course the implementation of a major iodization programme was authorized for 1974–1978.

The plan was similar to that put forward by Stanbury et al. (1974). A detailed "goitre map" of Indonesia was developed and seven hyper–endemic areas designated. Some 1,036,828 injections of iodized oil were given between 1974 and 1978, and up to 20 000 tonnes of iodized salt (iodized at 40 mg/kg or 40 ppm level) per year were produced and distributed. The iodized oil injections were given in the seven hyperendemic areas. In every village with a cretin the whole population under 40 years of age was injected. Appropriate training programmes for the necessary paramedical personnel were undertaken. A total of 1 594 people had been trained for this purpose by 1982.

Evaluation of the programme in one group of villages (pop. 1600) in Central Java has recently been reported by Dulberg et al. (1983). Determination of urinary iodine excretion revealed a normal range compared with the low levels observed in 1972 prior to iodization (Fig. 6). Disappearance of cretinism in children under the age of 7 years (i.e., born since 1974) was demonstrated in contrast to a 7 percent Incidence in children in the age

range 7–16 years. Finally a significant reduction in the age of walking was shown following iodization as reported by mothers interviewed by young Indonesian women in their own language.

A more recent review, however, in which the author took part (November 1985) indicates persistence of goitre in many parts of Java. This is linked to the problem of the many small suppliers of salt, who control 70 percent of the salt market in Java.

In Sumatra there was better control of goitre with more efficient control of salt iodization.

By 1983, the political process had gone further with the passing of legislation prohibiting the consumption of non–iodized salt. The decree was signed by three Ministers directly involved (Health, Welfare and Commerce). The aim is total prevention in the near future. It seems likely that iodized oil will continue to be needed in Java and other areas of severe IDD until effective salt iodization can be achieved.

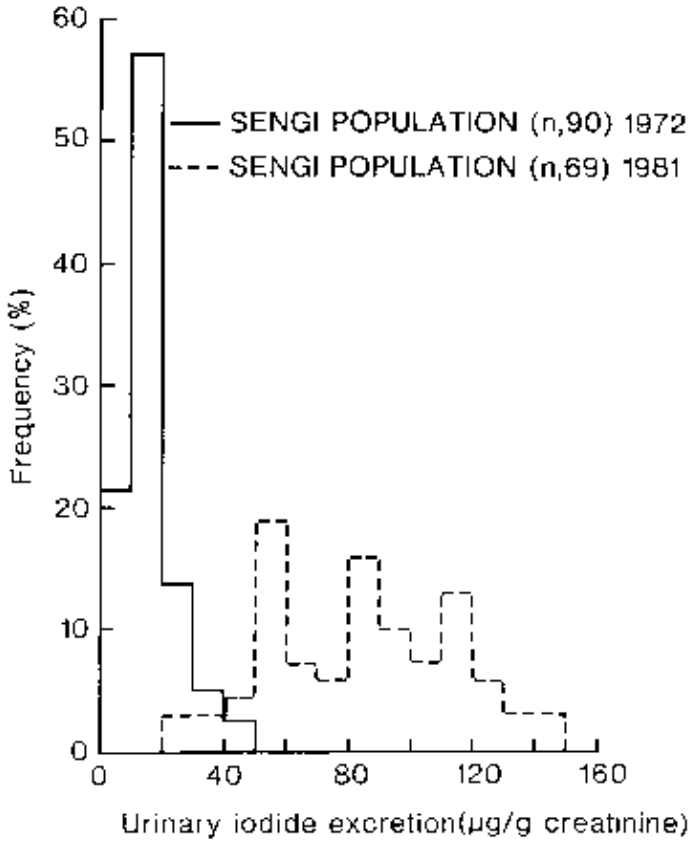

Figure 6. Effect of iodized salt and iodized oil programme in Central Java. Severe iodine deficiency was indicated by low urine iodine excretion in 1972 with 7% rate of cretinism. In 1981 an evaluation indicated normal urine iodine (interrupted line) which was associated with total prevention of cretinism since 1974 when the programme began. (Reproduced from Hetzel, 1985, with permission).

6.6 CHINA (SALT AND OIL)

The massive problem of endemic goitre and cretinism in China has been described by Ma et al (1982). The following quotation is taken from this paper:

"Ever since the establishment of the People's Republic of China in 1949, the Chinese Government and its Ministry of Health have given full attention to the use of iodized salt for goitre prevention. It is a cooperative enterprise under the direction of the Chinese Central Government, with members of the Ministry of Health, Ministry of Chemical Industry, and Ministry of Commerce, and the National Cooperative Head Office as the executive committee. With the help of technical health experts and the close collaboration of the above–mentioned ministries and provincial governments satisfactory results have been achieved.

"It has been reported that up to the end of 1979, in the 16 provinces and autonomous regions in greater North China, including northeastern as well as northwestern provinces, iodized salt has been supplied free of

additional cost to 70 percent of the areas where goitre is known to be endemic. The number of goitre patients decreased from 15 million in 1973 to 7.5 million in 1979. No new cases have been discovered in 20 percent of these areas, and the disease has come under control in several provinces. For example, Shaanxi Province used to be a heavily endemic area, where there were 576 000 goitre patients in 1972. The number decreased to 158 000 in 1979 as a result of persistent use of iodized salt during these years. Also a salt iodization programme has been carried out regularly in Hebei Province, where there were 1 560 000 goitre patients in 1972. By 1979, the number had dropped to 390 000.

"In addition to iodized salt prophylaxis, iodized oil has been used in some areas of China. People living in the Tarim Basin of Xinjiang Autonomous Region and Nei–Monggol (Inner Mongolia) Autonomous Region can get raw rock salt at no cost from the numerous salt deposits in the desert. The ordinary salt iodization programme is not applicable there. Under such circumstances, iodized oil injection is the method of choice. In China, instead of the more expensive ethiodol, iodized walnut oil or iodized soya bean oil has been used for intramuscular injection and has given satisfactory results without significant unfavourable side effects. Oral administration of iodized oil is also under trial.

"However, there are still certain endemic areas, especially in the southeastern and southwestern parts of the country and in Xinjiang Autonomous Region, where iodine prophylaxis has not yet been practised or enforced for various reasons".

Since the 11th Session of the Communist Party Congress in 1978, there has been a major effort to institute massive iodization programmes. In Xinjiang some 707,000 people in the age range of 7 to 45 years have since 1978 been injected with iodized oil. A further 300,000 – 400,000 people have been injected and work begun with orally–taken oil. In this region and in Inner Mongolia the people were unwilling to consume iodized salt because they preferred their traditional desert source. In these circumstances injections are given in order to prevent cretinism. The injections are given by barefoot doctors.

China has an infrastructure appropriate to public–health measures such as mass injections of iodized oil, by contrast with certain other southeast Asian countries with similar IDD problems.

Comment

The Chinese take IDD problems seriously, particularly because of their effects on the brain, so that high priority is given to iodiza–tion programmes. This is especially important in view of the one–child–family policy. The rapid progress made with the prevention and control of IDD since 1978 is remarkable. It reflects a strong political commitment with delegation of administration to provincial and local level to cover the massive population at risk of IDD.

6.7 INDIA (SALT)

A report from the Nutrition Foundation of India (1983) indicates a continuing major iodine deficiency problem. Only 15 percent or less of the known endemic areas have been covered by salt iodization. Endemic goitre and endemic cretinism are widely distributed on the Indian subcontinent with an intense endemia running along the southern slopes, foothills and adjacent plains of the Himalayas extending over 2,400 kilometres from Kashmir in the west to the Naga Hills in the east.

At least 120 million people live in the known endemic goitre regions. Of these about 40 million have been estimated to be suffering from goitre. Other pockets of endemic goitre are constantly being discovered, however, and the total population affected is nearer 300 million with more than 60 million suffering from goitre.

Following the successful Kangra Valley pilot study the Government of India between 1962 and 1955 installed, with the financial assistance of UNICEF, a total of 12 iodization plants in different parts of the country. The concentration of iodate in salt was standardized at 25 parts per million – (25 mg/kg). In 10g of salt, the iodate supplement at this concentration amounts to 250 mcg which is equivalent to 150 mcg of iodine. In India, the average daily consumption of salt per head is between 10 to 15 g (Pandav and Kochupillai, 1982), which would give 225 mcg of iodine per day. This meets the daily requirement of iodine suggested by a WHO seminar on goitre control held in 1967. (WHO, 1967).

The actual availability of iodized salt in India, however, is only 15 percent of the total requirement for the known endemic regions of the country.

In the report of the Nutrition Foundation of India (1983) the following two major reasons are given for inadequacies in the iodized salt programme:

(1) The programme has not been supervised and evaluated at state level due to absence of responsible officers in the state health departments;

(2) There has been no coordination between the state health departments and the supply departments responsible for the production of iodized salt.

The report recommends that much higher priority should be given to this and other public health programmes in India.

In 1985 the Government of India passed legislation making iodization compulsory for all salt used for human consumption. This objective was set to be achieved in the five years to 1990. It involves the stepping–up of production of iodized salt from 0.5 million metric tonnes in 1985–86 to 3 million tonnes by 1989–90 and to 5 million tonnes by 1992.

The need for effective monitoring of the iodization process and distribution of iodized salt is obvious. Evaluation of its effects in reduction of IDD will also require a major effort. But without this effort the enormous investment in salt iodization may be wasted.

Comment

The lack of success of salt iodization in India reflects the limited political awareness of the problem, and insufficient delegation of administration at state and regional levels. This situation is now being remedied, and major media programmes are also being mounted at state level.

7. ASSESSING IODINE DEFICIENCY DISORDERS FOR PUBLIC HEALTH PROGRAMMES

In public–health programmes carrying out iodine supplementation, the problem is to assess a population or group living in an area or region that is suspected of being iodine–deficient. Only a brief outline of the methods can be given here. For additional information, the reader is referred to comprehensive studies elsewhere (e.g., Stanbury and Hetzel, 1980).

The data required include the following:

(1) The total population including the number of children under 15 years of age (in which the effects of iodine deficiency are so important);

(2) The goitre rate, including the prevalences of palpable or visible goitre classified according to accepted criteria;

(3) The rates of cretinism and 'cretinoidism' in the population;

(4) Urinary iodine excretion;

(5) The level of iodine in the drinking water;

(6) The level of serum thyroxine (T–4) in various age groups. Particular attention is now focussed on the levels in the neonate because of the importance of the T–4 level for early brain development.

Basic population data are usually available and make a reference point of obvious importance in developing an iodization programme if it is to be comprehensive. There are difficulties in reaching the whole iodine–deficient population, especially because of the remoteness of many of these communities. Observing school children is one method with advantages of access and convenience, and this has been used extensively in most surveys.

A classification of goitre severity has been adopted by the World Health Organization (Thilly et al., 1980). There are still minor differences in technique among different observers. In general visible goitre is more readily verified than the palpable type. The most recent authoritative review of the classification of goitre and cretinism was carried out at the PAHO/WHO meeting in Lima, November 1983, (Dunn et al., 1986 p.373–4). The following extract is taken from that review.

7.1 DEFINITION OF GOITRE STAGES

Definition of Goitre

A normal thyroid gland should have the minimal size compatible with euthyroidism under conditions of normal iodine intake (100 to 150 mcg/day). This gland would be non–palpable or barely palpable. For practical purposes, the definition of goitre of Perez et al., (1960) is recommended: "A thyroid gland whose lateral lobes have a volume greater than the terminal phalanges of the thumbs of the person examined will be considered goitrous".

Estimation of Thyroid Size

A slight modification of the system of Perez et al. (1960) is recommended.

Stage 0. No goitre.

Stage 1a. Goitre detectable.

Stage 1b. Goitre palpable and visible only when the neck is fully extended. This stage also includes nodular glands, even if not goitrous; see Section C below.

Stage 2. Goitre visible with the neck in normal position; palpation is not needed for diagnosis.

Stage 3. Very large goitre that can be recognized at a considerable distance.

In case of doubt between any two of these stages, the lower should be recorded.

Measurement of thyroid surfaces by the procedure of MacLennan and Gaitan (1974) is particularly recommended for standardization of technique among different examiners and for comparison of surveys in different areas and at different times.

The total goitre rate is the prevalence of stage 1+2+3; the visible goitre rate is the prevalence of stages 2+3.

This classification is appropriate to field surveys for public health purposes. For clinical purposes, more precise information can be obtained by other techniques including scintigraphy and sonography.

Estimation of the Consistency of the Thyroid by Palpation

The diffuse or nodular consistency of the thyroid should be recorded, for nodules usually occur in areas where marked iodine deficiency has been long–standing. This estimation should be independent of that for the size of the thyroid, with the following exception: when one or more nodules are found in a non–goitrous gland, it will be recorded as Stage 1b since nodularity implies marked modifications in the structure of the gland.

7.2 DEFINITION OF ENDEMIC GOITRE AS A PUBLIC HEALTH PROBLEM

An area is arbitrarily defined as endemic with respect to goitre if more than 10 percent of the population or of the children aged six to 12 years are found to be goitrous. The figure 10 percent was chosen because a higher prevalence usually implies an environmental factor, while a prevalence of several percent is common even when all known environmental factors are controlled.

7.3 ENDEMIC CRETINISM AND ADDITIONAL DEVELOPMENTAL ABNORMALITIES

Definition by Three Main Features

1. Epidemiology. It is associated with endemic goitre and severe iodine deficiency.

2. Clinical manifestations. These comprise mental deficiency, together with either:

    a. A predominant neurological syndrome including defects of hearing and speech, squint, and characteristic disorders of stance and gait of varying degree; or

    b. Predominant hypothyroidism and stunted growth.

Although in some regions one of the two types may predominate, in other areas a combination of the two syndromes will occur.

3. Prevention. In areas where adequate correction of iodine deficiency has been achieved, endemic cretinism has been prevented.

Other Developmental Abnormalities

It has now become increasingly clear that endemic cretinism represents only the extreme stage of a broader spectrum of developmental abnormalities including decreased intellectual potential. These abnormalities are also prevented by correction of iodine deficiency."

The prevalence rates of cretinoids and 'cretinoidism' may be difficult to determine. Observations of school children will not detect those most severely affected who are likely not to be attending school. Studies of I.Q. provide additional important evidence justifying programmes.

Urinary iodine excretion can be determined appropriately on 24–hour samples. The difficulties of collection may be insurmountable, however. For this reason, as originally suggested by Follis (1963), determinations may be made on casual samples from a group of approximately 30 subjects (Thilly et al., 1980). The iodine levels are expressed as mcg/g of creatinine excretion and the range plotted out as a histogram. This provides a reference point for the level of iodine excretion which is also a good index of the level of iodine nutrition. Modern automated equipment (autoanalyser) is making the analysis of large numbers of samples quite feasible. Methods have been recently improved so that reliable results can be obtained (Belling, 1983; Garry et al., 1973).

It has been suggested that there are three grades of severity of iodine deficiency in a population that may be determined by urinary iodine excretion (Querido et al., 1974). These are as follows:

Grade 1 Goitre endemias with an average urinary iodine excretion of more than 50 mcg/g of creatinine[1]. At this level, a thyroid hormone supply adequate for normal mental and physical development can be anticipated. This group could be described as suffering from 'mild IDD';

[1]See footnote in Section 4.8

Grade 2 Goitre endemias with an average urinary iodine excretion of between 25 and 50 mcg/g of creatinine. In these circumstances, adequate thyroid hormone formation may be impaired. This group is at risk of hypothyroidism but not of overt cretinism ('moderate IDD');

Grade 3 Goitre endemias with an average urinary iodine excretion below 25 mcg/g of creatinine. Endemic cretinism is a serious risk in such a population ('severe IDD').

The level of iodine in drinking water indicates the level of iodine in the soil which in turn determines the level of iodine in the crops and animals in the area. Iodine levels of water in iodine–deficient areas are usually below 2 mcg/litre (2 ppm).

The level of serum thyroxine (T–4) provides an indirect measure of iodine nutritional status. Radio–immunoassay methods with automated equipment have greatly assisted this approach. Particular attention should be given to levels of T–4 in the neonate; levels below 4 mcg percent must be regarded as

prejudicial to brain development (Burrow, 1980).

In most of the industrialized countries of the world, where iodine deficiency in humans' is rare, all babies born are screened to ensure they have adequate thyroid hormone levels. These screening programmes use blood from heel pricks of neonates, spotted on to filter paper which is dried and sent to a regional laboratory. Blood levels of either T−4 or TSH or both are measured by immuno−assay techniques. The detection rate of neonatal hypothyroidism requiring treatment is about 1 per 3,500 babies screened. This rate varies little among developed countries (Burrow, 1980).

Neonatal hypothyroid screening has been initiated in several less−developed and iodine−deficient regions. As already noted in Section 2, Kochupillai et al. (1984) in India and Ermans et al. (1980a) in Zaire have reported severe biochemical hypothyroidism. T−4 concentrations of less than 3 mcg/dl occurred in 4 percent and 10 percent of neonates respectively. It is evident from these and other reports that within an iodine−deficient population, serum T−4 levels are lowest at birth and lower in children than in the adult population. In addition goitrogens such as cassava seem to be much more potent at reducing serum T−4 levels in neonates and children than in adults (Delange et al., 1982). This may be a critical factor since T−4 levels are lowest at the most crucial time of development, especially brain development. There is thus a strong argument for extending neonatal hypothyroid screening beyond the developed countries to regions where iodine deficiency may be a problem.

To summarize, the most critical evidence is that available from measuring urinary iodine and from measuring T−4, including in the neonate. The results of these two determinations indicate the severity of the problem. They can also be used to assess the effectiveness of remedial measures.

8. ELEMENTS OF NATIONAL IODINE DEFICIENCY DISORDERS CONTROL PROGRAMMES

A global strategy should be based on national and regional iodization programmes. The particular methods to be adopted to correct iodine deficiency will vary by region and by nation. This may depend on the availability of salt, its pattern of consumption, and the acceptability of iodized salt (see Section 6). Iodized oil, both on a small scale in isolated mountainous regions and on a large scale, has provided a major alternative to iodized salt in many countries such as Zaire where using iodized salt is not feasible.

The gradations of severity of IDD provide the indications for an iodization programme. The classifications based on urinary iodine (see Section 7) may be extended to the following general recommendations.

> Mild IDD (Grade I): with urinary iodine (median) more than 50 mcg/g of creatinine[1], requires iodized salt (or possibly economic development alone) for the correction and the prevention of goitre.
>
> [1]See footnote in Section 4.8.
>
> Moderate IDD (Grade 2): with urinary iodine (median) in the range 25−50 mcg/g creatinine, may be prevented by an effective iodized−salt programme; often iodized oil may be necessary in addition, to produce a quantitative correction for the more severely iodine−deficient groups.
>
> Severe IDD (Grade 3): with urinary iodine (median) less than 25 mcg/g of creatinine, requires iodized oil for quantitative correction. Iodized salt might be used as a follow−up measure if economic development permits; but if subsistence agriculture continues, administration of iodized oil needs to be continued.

The availability of suitable technology, while it is the basic requirement, is only one element in an effective iodization programme. The reasons for success and failure in various programmes have been investigated, and political, social and economic factors have all been found to be relevant (Thilly and Hetzel, 1980). A social process is Involved, as demonstrated in Section 6 where individual country programmes are considered.

Figure 7 provides a convenient representation of the relations among these various elements. The steps listed below could be considered as a series of objectives in an iodization programme. A previous form of the model

has been published (Thilly and Hetzel, 1980); it has now been updated following further experience in the southeast Asia Region (Hetzel and Dulberg, 1984; Hetzel, 1987).

The model consists of the following six steps.

1. Assessment (collect data, assess situation).
2. Communication (disseminate findings).
3. Planning (develop or update plan of action).
4. Political decision (achieve political support).
5. Implementation.
6. Monitoring and evaluation.

The process then begins a further cycle with new data, dissemination of the results of the first programme, and development of an improved programme to correct the deficiencies of the first.

It should be emphasized that prevention and eradication of IDD require continual vigilance through regular feedback of epidemiological data Including: estimates of iodine content of salt; iodine content of urine in the vulnerable population (especially school children who are readily accessible through school attendance); goitre prevalence; and levels of T–4 including neonates if possible.

SOCIAL PROCESS MODEL FOR NATIONAL IDD CONTROL

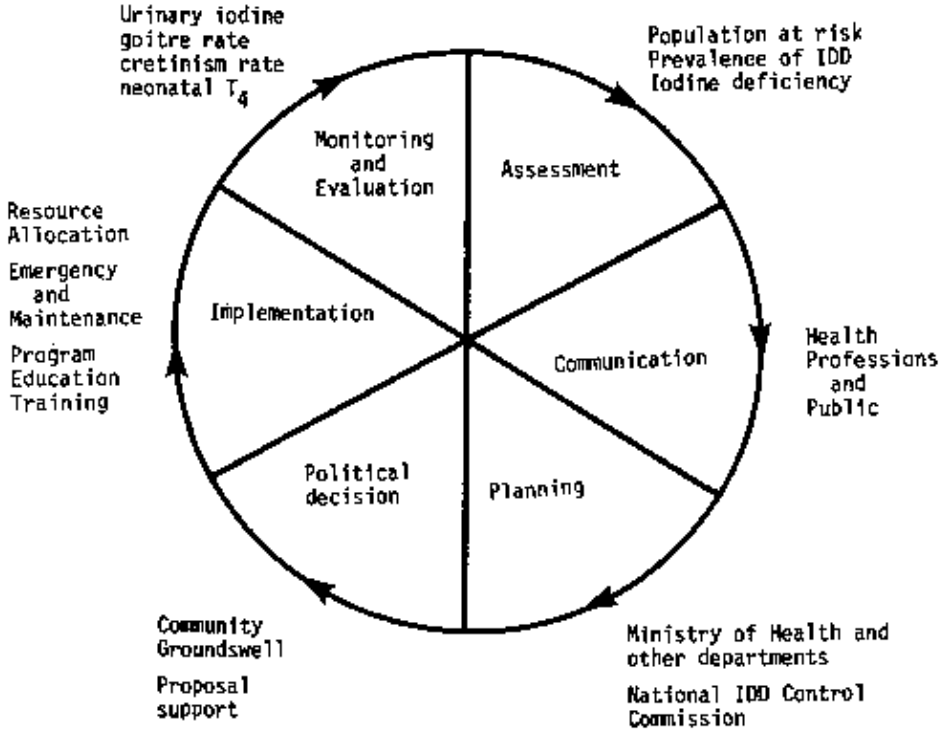

Figure 7. A model shoving the social process involved in a national IDD control programme. The successful achievement of this process requires the establishment of a national IDD Control Commission with full political and legislative authority to carry it out. (Reproduced from Hetzel, 1987, with permission).

8.1 ASSESSMENT

The data required are discussed in Section 6. Multiple regional measurements are usually necessary. Special emphasis should be placed on assessing total populations living in an iodine–deficient area and determining urinary iodine and levels of serum T–4 in neonates if possible. Goitre surveys of selected samples of the population at highest risk are now preferred to time–consuming goitre surveys of the whole population. Laboratories with suitable equipment for determining urinary and water iodine (and salt iodine) are essential. The determination of T–4 can now be conveniently carried out by radio–immunoassay from spots of blood on filter paper. These samples can be sent by post to central laboratories for processing. Automated equipment permits large numbers of samples to be tested cheaply (Hetzel and Maberly, 1985; Burrow, 1980).

8.2 COMMUNICATION

The results of the situation analysis have to be disseminated among administrators, politicians, health professionals and the public.

Recent findings on the impact of iodine deficiency on human growth and development are not well known among health professionals and health administrators in developing countries. There is a need for more education.

The message that requires marketing through all the means available is that the consequences of iodine deficiency are totally preventible, such message must be stated in a way that it is easily understood by the communities at risk.

8.3 PLANNING

Recent experience indicates the need for appropriate national IDD Control Commissions with legislative and political support to be responsible for control programmes. These commissions should have representatives from various government departments (Health, Education, Industry) as well as the salt industry, the pharmaceutical industry, the university system and the media.

The distribution of iodized salt remains the major technology for most programmes but its limitations have now become apparent. In areas of severe iodine deficiency in China, for example, effective iodized salt production or distribution has not always been possible for the huge populations affected. In these circumstances mass administration of iodized oil by injection or by mouth has been shown to be feasible, carried out through the primary health care system.

8.4 POLITICAL DECISION

The resources required for major iodization programmes have to be provided by the decision of politicians. To get their attention, it is important that there is evidence of support by 'ground swell' in the community, and to obtain this, information on the disabilities caused by IDD in terms of loss of productivity and quality of life should be widely published through centres such as schools and clinics and through the media whenever possible. Marketing strategies should be used (Manoff, 1985).

8.5 IMPLEMENTATION

Implementation of an iodization programme can follow once the necessary political support has been obtained and allocation of resources has been made.

Implementation involves discussion, planning and coordination by various government departments such as Nutrition, Family Planning and Mental Health. Training programmes will be required for staff from these sections as well as for the personnel actually carrying out the programme.

8.6 MONITORING AND EVALUATION

The most direct method of assessing success or failure in correcting iodine deficiency is by determining urinary iodine as in the initial situation analysis. This can in due course be supported by evidence of regression of goitre rates and the prevention of cretinism. If laboratory services permit, determining blood thyroxine in adults or neonatal thyroxine in cord blood samples will also indicate whether iodine deficiency has been corrected.

Monitoring and evaluation are essential for iodization programmes, particularly because of the need to ensure quantitative correction of iodine deficiency in order to reduce foetal damage and impaired mental function in children. As already indicated, there should be more use of prescriptive measures for quantitative correction and hence prevention and control of IDD. The availability of iodized oil with a follow−up of iodized salt makes elimination of IDD a feasible goal.

Priority must be given, however, to areas and regions with severe IDD. This means that resources and technology must be focussed. As indicated elsewhere in this report iodized oil is the major technology of proven effectiveness for the prevention and control of severe IDD. Both injection or oral administration of iodized oil are available. The teams and organization already developed in many countries for the Extended Programme Immunization (EPI) programmes could be of great value to an iodized−oil injection programme in a region with severe IDD. Population targets and costs can be specified as in the case of the Extended Programme of Immunization (EPI), using the Primary Health Care system.

Such a transition has taken place in Nepal where some 2 million injections of iodized oil have been given in 28 remote northern districts and where iodized salt could not be distributed. A single injection of the oil (1 ml) provided an adequate supply for prevention of IDD for about four years (Acharya, 1987).

This opportunity is particularly relevant to Africa where recent EPI programmes have had considerable success.

As indicated in Section 6 the details of implementation will inevitably vary by country and by region within a country. Target populations must be specified and sampled before the programme and monitored afterwards. In Section 3, a detailed situation analysis was included, based on data available from the six WHO regions. The population covered by the programmes, by comparison with the total iodine−deficient populations, gives some indication of the gap that still has to be filled to achieve successful control of IDD. Evidence of satisfactory cover is provided by monitoring data.

A national plan will need to specify sequential population targets and costs with particular reference to severe IDD. In this way very significant progress could be made towards of the prevention and control of IDD in the next decade in a number of countries.

9. RECENT DEVELOPMENTS IN CREATING A GLOBAL STRATEGY

Three major steps have recently been taken which give cause for hope of significant international action on the control of IDD:

1. The development of a global strategy by the United Nations Administrative Committee on Coordination through its Subcommittee on Nutrition (ACC/SCN, 1987);

2. The passage of a resolution at the 39th World Health Assembly (Geneva, May 1986) calling for the prevention and control of iodine deficiency disorders;

3. The establishment of the International Council for Control of Iodine Deficiency Disorders (ICCIDD), Kathmandu, March 1986.

These three developments should help to catalyze the global prevention and control of IDD.

A brief review of them concludes this report.

9.1 ACC/SCN's DEVELOPMENT OF A GLOBAL STRATEGY

The planning of a global strategy for the prevention and control of IDD has now been formally taken up for the United Nations by the ACC/SCN.

An initial report prepared for the Australian Government at the request of the ACC/SCN was submitted by the author in February 1985. In October of the same year, the ACC agreed that a definite plan for an international support programme be prepared by the World Health Organization. This plan has now been endorsed by the

ACC/SCN.

9.2 THE WORLD HEALTH ASSEMBLY RESOLUTION

The second major step is the passage of a resolution by the 39th World Health Assembly calling for the prevention and control of iodine deficiency disorders (Geneva, May 1986). This resolution was sponsored by the Australian Government and co−sponsored by 22 countries.

Noting the high prevalence of IDD, affecting more than 400 million people in Asia as well as millions in Africa and South America, and the availability of low−cost, effective technology, the resolution urged all Member Nations to give high priority to the prevention and control of IDD. It requested the Director−General to give all possible support to member states, to prepare suitable materials for use at national level for training health and development workers, and to cooperate with other intergovernmental and nongovernmental agencies in intensive international action to combat IDD, including mobilization of the necessary financial and other resources.

9.3 THE INTERNATIONAL COUNCIL FOR CONTROL OF IODINE DEFICIENCY DISORDERS (ICCIDD)

The recently established ICCIDD (supported initially by UNICEF and the Australian Government) is a source of scientific expertise for international agencies and governments concerned to prevent and control IDD. Its role was made explicit with the development by the ACC/SCN of a 10−year programme aimed at the prevention and control of IDD.

The ICCIDD already has a global, multidisciplinary network of more than 300 members. They include scientists, planners, communicators, salt technologists, clinical chemists and others concerned with IDD control. A registry of members is being compiled and will be published in due course.

The ICCIDD has adopted several strategies to achieve its major aim of bridging the knowledge−application gap. These include:

1. Consultations with international agencies such as WHO and UNICEF, at both global and regional level. Consultation with UNICEF led to important initiatives, including the development of a crash IDD−control programme in southern Peru. In Africa, an ICCIDD regional consultation with WHO and UNICEF has begun the process of developing a strategy for IDD control throughout the continent. In addition, there have been consultations in various countries (e.g Nepal, Indonesia).

2. Publications, including the IDD Newsletter, a quarterly providing a comprehensive review of IDD−related activities, regional reports, and a regular review of the literature. The ICCIDD also has a programme for publication of monographs. The first ICCIDD monograph entitled "The Prevention and Control of Iodine Deficiency Disorders" was published by Elsevier in March 1987. (Hetzel et al., 1987). It provides a systematic and detailed review by a multidisciplinary authorship from papers presented at the Inaugural meeting in Kathmandu, Nepal (22−26 March 1986).

   The ICCIDD subsidized publication of the proceedings of two meetings held before the 9th International Thyroid Conference in Sao Paulo, Brazil (30, 31 August 1985) under the title "Iodine Deficiency Disorders and Congenital Hypothyroidism".

   Other publications such as manuals on special aspects related to IDD and their control (goitre surveys, iodized salt production, and laboratory methods to determine iodine), required for more specific purposes, are planned.

3. Task forces on particular problems that arise in the development of effective IDD control programmes. At this stage there are four designated task forces − on communication, economics, iodized oil, and iodized salt;

4. Regional activities through regional coordinators. These include:

a) the development of regional links with national governments and international agencies, designed to help with effective control programmes;

b) assistance in providing information;

c) assistance in organizing country– or regional–level training programmes and workshops;

d) development of a multidisciplinary team of experts to advise on planning and implementation of programmes;

e) development of regional– and country–level publications on various aspects of IDD control.

10. SUGGESTIONS FOR FURTHER RESEARCH AND INVESTIGATION

These recommendations are for research particularly related to policy issues arising from IDD control programmes.

a) Detailed epidemiological studies of the effects of iodine deficiency on mental performance, on a whole population.

b) An assessment of the social and economic aspects of IDD and the benefits of control.

c) A review of existing salt iodization plants, to find a longer–lasting model.

d) A review of large iodized salt production systems.

e) Further clinical, pharmacological and animal studies with iodized oil for oral administration, including comparisons with injections of the same preparations.

f) Methods to produce iodized oil cheaply and quickly.

g) Systematic studies of mass education methods to improve public understanding of IDD and their prevention.

h) Detailed case studies of successful and unsuccessful iodization programmes.

i) Real incidence of iodine–induced thyrotoxicosis.

j) Immunological aspects of thyroid growth stimulation in endemic goitre.

k) The relationship of IDD to other nutritional deficiencies.

l) New technologies for IDD control.

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PHYSIOPATHALOGICAL ASPECTS OF ENDEMIC GOITRE AND CRETINISM

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I would like to make three short remarks on physiopathological aspects of endemic cretinism and goitre, the two principal manifestations to add to Dr. Hetzel's outstanding review.

Endemic cretinism

There is general agreement that the main public–health impact of a goitrogenic environment is the impairment in brain development and that goitre represents only the tip of the iceberg of the functional consequences of such an environment. The most spectacular consequences in terms of brain damage are endemic cretinism and the endemic mental retardation observed in even non–cretinous individuals.

It should be made clear that there are two types of endemic cretinism and that neither is more "typical" than the other, as frequently stressed in this paper.

It is universally accepted that endemic cretinism is characterized by three major features:

1) Epidemiology. It is associated with endemic goitre and severe iodine deficiency;

2) Clinical manifestations. These comprise mental deficiency, together with either a) a predominant neurological syndrome including defects of hearing and speech, squint, and characteristic disorders of stance and gait of varying degree, or b) predominant hypothyroidism and stunted growth.

Although in some regions one of these two types may predominate, in other areas a combination of the two syndromes might occur;

3) Prevention. In areas where iodine deficiency has been corrected, endemic cretinism is brought under control (Delange et al., 1986a).

The abundant literature, known worldwide, on myxoedoematous cretinism is unfortunately almost ignored in such an extensive review paper.

This myxoedoematous type of endemic cretinism corresponds exactly to the picture found in sporadic congenital hypothyroidism but its frequency (when endemic) can be up to 8–10 percent of the total population Instead of the 0.025 percent for sporadic hypothyroidism in non–endemic areas. The neurological type of endemic cretinism has no specific counterpart in non–endemic areas but its occurrence is critically related to the numerous environmental, socioeconomic and genetic factors involved in the etiopathogenesis of endemic goitre.

Neonatal Thyroid Screening

One of the recently proposed indexes of severity of a goitre endemia is thyroid function in the neonate. At this critical period of brain development the neonate is hypersensitive to the effects of iodine deficiency.

It should be stressed, however, that neonatal TSH is a more sensitive index of impairment of thyroid function and regulation than neonatal T–4. It should therefore replace the latter in thyroid screening procedures in endemic areas, as has been the case in non–endemic areas (Delange et al., 1979; 1986b).

Evaluating the Severity of Endemic Goitre

Another classical index of severity is the urinary I/creatinine ratio: creatinine is used as an index of the volume of urines emitted by unit of time, as would be urinary osmolarity. Urinary creatinine is influenced by other factors as well, however, such as the dietary intake of proteins. In this case, the I/creatinine ratio constitutes a less accurate index of iodine intake than the median or mean concentration of urinary iodine, provided that for the latter a sufficient number of samples have been collected from a representative fraction of the general population (Bourdoux et al., 1986).

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COMMENTARY ON DR. HETZEL'S REVIEW OF THE GLOBAL PROBLEM OF IODINE DEFICIENCY DISORDERS

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Dr. Hetzel has summarized in admirable fashion our present understanding of the iodine deficiency disorders (IDD) and those measures necessary in order to correct them. The control of these disorders no longer requires basic research, but rather lies in the domains of politics, education and economics, even if the process might benefit from some further enquiry. The magnitude and importance of the problem would be appreciated more when it is realized that iodine deficiency is the leading cause of preventable intellectual retardation in the world today.

Much remains to be learned of the distribution of IDD. IDD are not a set of disorders confined to the developing countries: pockets are present to this date in Germany, Italy and Greece. In Africa a huge band of Iodine Deficiency Disorders extends across the centre of the continent from Nigeria in the west to Ethiopia, Tanzania and Kenya in the east, and is found in large areas to the south. Little is known beyond the fact of the existence of IDD in the Central African Republic and Angola. They are found in North Africa in the Atlas Mountains and in Algeria. IDD are well known in the Middle East and across the entire Himalayan chain into northern Thailand and the other countries of southeast Asia, including Indonesia and Papua New Guinea. Much of the People's Republic of China is involved. Indeed one might note that with few exceptions Iodine Deficiency Disorders are found wherever one looks for them: most of the land areas of the world contain an amount of iodine in the soil which is not sufficient for human needs, or only marginally so.

There is need for far more precise epidemiological information than is presently available. An assessment of severity is essential for judging the urgency of the problem. This is especially true of sub−Saharan Africa where IDD are present in many areas and in severe degree, but their magnitude and severity in the region as a whole are still unknown.

The most important aspect of IDD is not endemic goitre. Goitre is largely a disfigurement which is unwanted or perhaps uncomfortable, but in itself generally poses no threat to the life or well−being of the subject. Neither is it the typical cretins who characterize severe endemias of IDD, because these are usually few in number and almost always live in a subsistence economy where they constitute no particular economic drain. It is the large number of persons with psychomotor retardation resulting from iodine deficiency that constitutes an impediment to social and economic development.

The evidence for the existence of this subgroup of iodine−related retardates is now well established, even if further data would be desirable. Investigations as far back as 1969 indicated better IQ scores and neuromotor performance among children who had received iodized oil, or whose mothers had received injections, than those of control subjects. Increasingly sophisticated studies from Peru, Zaire, Ecuador, Indonesia, Spain and the People's Republic of China have conformed. Recently in rural Ecuador, school performance and the results of various tests of children up to age 12 who were judged at age six to be capable of entering school were scrutinized with respect to whether their mothers had received injections of iodized oil prior to or early in pregnancy. School performance, attendance records, dropout rates and several tests of psychomotor and neuromotor function were performed. The children whose mothers had received injections of iodine clearly outperformed the children of mothers who did not.

Pervading the IDD literature is the concept that there are two forms of endemic cretinism, one characterized principally by neurological signs including spastic diplegia, persistence of certain primitive reflexes, and often deafmutism, and the other with myxoedema as the dominant finding, with short stature, chemical hypothyroidism, markedly delayed bone age, and intellectual and auditory impairment which is not as prominent as in the "neurological" cretins.

Examination of the reports which began with that of McCarrison from the northeast frontier in 1908 and include those from Zaire where the myxoedematous form seems to predominate and those from other regions where either the neurological form or mixed forms are found, blurs some of the differences which have been

described in the literature. Myxoedema is often a clinical feature of cretins who have severe neurological damage. Thus neurological deficits are more common than originally reported in myxoedematous cretins. Further, it is reported that cretins with myxoedema and minimal neurological findings may, apart from their intellectual retardation, show a worsening of neuromotor function when the euthyroid state is restored through substitution therapy. Even so, there must be some as yet unidentified factors like excess or lack of some dietary or other environmental elements which accounts for the epidemiological differences that are found among cretins in various endemias of IDD.

As Dr. Hetzel so clearly points out, there are only two effective modalities for IDD prophylaxis: iodization of salt and distribution of iodized oil. Which is used depends on local and regional conditions and the economies involved. While questions have been raised in the past about the safety of administering iodine in any form in an iodine–deficient region because of the production of iodide–induced thyrotoxicosis (or more recently the safety of using iodized oil late in pregnancy) the overwhelming evidence is that these occurrences are rare and easily dealt with, and cause no permanent harm; and that the preventive programmes eliminate cretinism and repair or prevent much of the other damage resulting from iodine deficiency. It has further been shown that preventive programmes, whether with iodized salt or with iodized oil, are cost effective and cost beneficent.

Unfortunately Iodine Deficiency Disorders exist in their most severe forms in those places which are most difficult to reach with preventive programmes. There are areas which depend on local salt production or which use no commercial salt. There are many areas without a health system which might be employed in the distribution of iodized oil. Transport is often difficult, as in much of northern Zaire, the Central African Republic, some of the remoter regions of the Indian Terai, Nepal, Bhutan, the People's Republic of China, Indonesia, Papua New Guinea, and elsewhere. Planning must cope with these logistical problems.

Eliminating IDD is not nearly so easy a task as appears at first glance. Governments must be convinced of its presence and importance. The salt industry must recognize its key position. Iodized salt must be made available at a competitive price. Demand for it must be created through social marketing. Where iodized salt will penetrate the market slowly and where the severity of the endemia requires urgent action, iodized oil must be distributed until such time as iodized salt becomes generally available. It seems unlikely that effective prophylactic programmes will ever be in place where they are needed unless governments establish IDD commissions with appropriate power, autonomy and financing and with dedicated personnel with the requisite skills.

In March 1986 the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) was formally inaugurated in Kathmandu, Nepal, thanks primarily to the efforts of Dr. Hetzel. This organization, supported by UNICEF and the Government of Australia, has a board of approximately 30 persons representing the disciplines of medical science, epidemiology, marketing, communications, and the salt industry. Its membership now numbers more than 200. The purpose of the ICCIDD is to promote prevention of IDD through education at all levels, to furnish consultative help wherever needed and to act as a central information resource. Through its network of regional coordinators it maintains surveillance of regional problems, activities and results, and seeks to promote programmes of prevention. Its quarterly newsletter containing valuable current information on IDD is available on request to Dr. John Dunn, the editor, at the University of Virginia Medical School, Charlottesville, Virginia, USA.

While the technology for elimination of IDD from the endemic foci of the world is well known, there is still much to learn about the disorders and their control which will not only aid in the pursuit of prophylactic programmes, but will also have wider implications. For example, we do not yet know how to organize national programmes better and how to monitor their effectiveness and continuity. We do not know as much about the metabolism of iodized oil as would be desirable, such as the effect of the nutritional state on the rate of the disposal of iodized oil, the frequency of transient thyrotoxicosis following administration, the effects on child survival, on later school and work performance, and so on. What we do know, and is so well documented in Dr. Hetzel's monograph, is that iodine in any form, if given on a regular basis to a population at risk of IDD, will eliminate those disorders from that population, and that this can be done, given the will of governments to do so, the support of governments and international agencies, and the demand of the people at risk of these disorders.

RELATIVE ADVANTAGES AND DISADVANTAGES OF PRESCRIPTIVE VERSUS POPULATION BASED PROPHYLAXIC MEASURES

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Dr. Hetzel's document on global strategy for the eradication of Iodine Deficiency Disorders (IDD) indicates a great variety of effects of iodine deficiency much more extensive than goitre even though this familiar feature is the obvious one. Even mild to moderate iodine deficiency may cause minor but important alterations in mental and sensory functions. Widespread mild to severe disability would not promise a productive life of good quality particularly in the developing world. Iodine supplementation has reduced goitre and cretinism in many parts of the world. Although it also increases survival rate, we should avoid falling into the trap that all that is important is survival per se without further attempts to ensure a productive and full life for those been 'survived'.

The widespread effectiveness of iodized salt (even where iodine deficiency is categorized as severe), if the programme is effectively conducted, is emphasized by Dr. Hetzel in this State–of the–Art–Paper. He has rightly dedicated paragraphs to the effectiveness of salt iodization in the control of IDD in an area of severe deficiency in China. Indeed, in Jixian, salt iodization solved the IDD problem. This proves that even in a population with 11.4% cretins an effective programme can correct very severe IDD. Also, one must not forget the proven efficiency of iodized salt in the control of cretinism in Europe. Yet, in order to control severe to moderate IDD, only iodized oil, orally or intramuscularly has been recommended. I believe that both methods of correcting IDD i.e. iodized salt and iodized oil either orally or intramuscularly, should be promoted and emphasized. Oral oil should be as effective as any other measure in correcting IDD and can be expected to meet the demands of even severe iodine deficiency, if compliance at the population level is good and the programme is not only directed at school children. It should be indicated that with adequate production of oil specifically for oral adminstration the cost would decrease to one tenth of what presented in Table 18 of this document. Also I include in the costs the cost of staff time in all the programmes including staff time for surveillance of the programmes. With regard to dietary diversification, which as Dr. Hetzel clearly indicated, through economic development has been responsible for the disappearance of IDD in Western countries, one should also stress the importance of programmes of iodization and dietary diversification together with other public health programmes. How important a decline in the consumption of goitrogens may be under these circumstances is yet to be defined. While it seems to me that in this document the prescriptive method of IDD correction is emphasized more, i.e. iodized oil, I still think that iodization of salt and other similar measures should be the first method of choice. However, the use of iodized oil by mouth or by injections offers another effective alternative for severe iodine deficiency if the cost of production can be reduced and a system to assure vide coverage can be established and supported. Severe IDD require either an effective and well controlled iodized salt programme or the adminstration of iodized oil either orally or by intramuscular injection to all of the population. Priority groups for initiation of iodized oil by intramuscular injection can be children and women of reproductive age.

The prescriptive approach can have the advantage as well as the limitation that it can be carried out through the health care system and will function only as well as this system can cover the whole population. It may appear that, in contrast to population based measures, i.e. iodized salt, it does not require the cooperation and enforcement of other government departments and private industry. This is not the case. If the population cooperates, if governments and private sectors join efforts in providing universal coverage of prescriptive (mainly iodized oil) methods, these measures are effective. Prescriptive measures are to be given more serious consideration than in the past where the tendency has been to think only of iodized salt and other alternatives have not been heard of. This approach to the eradication of IDD is effective when all of the population can be reached by a team of health workers, therefore it requires excellent population coverage which then becomes extremely expensive because often those in greater need are the hardest to reach and to convince of the benefits of an oil injection. We cannot compare immunization programme coverage to that required to eliminate IDD by iodized oil injection. In the first case 85–90% coverage is more than enough; in the second case it is not adequate. The use of iodized oil by injection to eradicate IDD in large countries, therefore, poses serious logistic and financial problems. Either method of control and prevention demands a concentrated effort for the complete prevention of central nervous system defects. In certain countries more efficient schemes for the production and distribution of iodized salt need to be established, since although guidelines are set, the problem has remained as to how make them appropriate for certain conditions in several countries.

In the section on Central and South America, Dr. Hetzel has provided more up–to–date information on why some of the programmes in Latin America have not been as successful as they should have been, based on the 1983 Lima Conference entitled 'Towards the eradication of endemic goitre, cretinism and iodine

deficiency'. So far in Latin America many iodized salt programmes have shown partial but substantial success. In this region there are no grounds by which iodized oil adminstration (intramuscularly or orally) can be judged at the general population level. One thing is to carry out a pilot study as has been the case of Bolivia, Peru and Ecuador with iodized oil, and another one is to convert this programme into a national one.

Although there are still unsolved problems in ensuring adequate quality of iodized salt in sufficient amounts to be produced and distributed to massive iodine deficient population in many countries, these can be overcome. The reasons for a decline in total actual production of iodized salt in India and Nepal together in 1978–79 compared with 1974–75, as shown in Table 14 of Dr. Hetzel's document should be explored and corrected. Surveillance of an iodization programme should include monitoring of salt sales, checks on the iodine content of salt at the production sites and in the retail stores, monitoring of goitre prevalence in school–aged populations and analysis of the urinary iodine excretions. To get iodine into iodine deficient population, by either of these methods, can prove difficult in remote and isolated areas with IDD problem. In Bolivia llama are often used to transport salt and other goods. In the remote part of this country locally produced salt (extracted from large salars) makes the commercialization of iodized salt very difficult. In Sahel camels are used as usual system to transport goods. However, while salt in these areas is to be transported by camels in the programme of salt iodization, similarly people and equipments need to be transported in this way in the case of iodized oil injection.

Another problem associated with salt iodization is loss of iodine from such salts during storage. This depends on the handling and storage conditions. As it can be seen in Table 15 of Dr. Hetzel's document, keeping salt in covered areas, even when only the top is covered effectively prevents iodine loss. The loss of 16.4% in top covered salt which occurred when there were 434 millimeters of rain in 55 days is still acceptable. Note that this has been really heavy rain compared to other figures. In some countries effective life of salt iodization plants might have only been two to three years. However there are many iodization plants in Central and South America which have been working for over ten years without problems. Moreover, as I indicated there are easy solutions to this problem. There are many systems by which salt can be iodized and there are systems which have overcome technical problems.

In terms of iodine availability to the thyroid and the danger for transient thyrotoxicosis among individuals with nodular goitres or presenting single thyroid nodules without goitre, I do not understand the rationale behind administrating only 0.2 ml. of iodized oil since still 95 milligrams of iodine even with a relatively slow release from the site of injection would amply saturate thyroid needs of overproduction of thyroid hormones. I suggest explaining the rationale and the proof for suggesting this specific dosage. The condition of thyrotoxicosis, as stated by Dr. Hetzel, can be readily controlled with drugs like antithyroid or radioiodine ; experience in Costa Rica showed that during the transient thyrotoxicosis that occurred in that country, Reserpine was extremely effective in controlling the temporary problem.

Spontaneous remission is the norm for this type of thyrotoxicosis. Because of the small risk of transient thyrotoxicosis when compared to the general benefits of iodization programmes to the populations as a whole, it may not be necessary to avoid iodization in those over the age of forty years.

The monitoring of neonatal T–4 is ideal and highly desirable, but not necessary for the monitoring and evaluation of IDD programmes. If iodine excretion in the urine is adequate and there is no goitre, neonatal T–4 determinations may not be necessary for surveillance of the programme. I think that T–4 determinations in neonates should ideally be done in every newborn throughout the world but for other reasons. Since they are not only costly but you need good laboratory facilities to have reliable information. The impossibility of doing reliable T–4 determinations should not impair any actions to diagnose and correct IDD.

The more severe the problem, the greater the insurance needed to have a full and continuous coverage of the population in terms of adequate iodine intake or content in their body. The method is immaterial in my mind; however, I suspect that to achieve the universal coverage needed with iodized oil injections will be extremely difficult and expensive.