

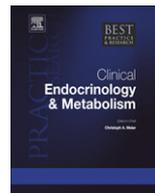


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Cretinism revisited

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Endemic cretinism includes two syndromes: a more common neurological disorder with brain damage, deaf mutism, squint and spastic paresis of the legs and a less common syndrome of severe hypothyroidism, growth retardation and less severe mental defect. Both conditions are due to dietary iodine deficiency and can be prevented by correction of iodine deficiency before pregnancy. Endemic cretinism is now included in the spectrum of the effects of iodine deficiency in a population termed the 'iodine deficiency disorders (IDDs)', which also includes a wide range of lesser degrees of cognitive defect that can be prevented by the correction of iodine deficiency.

Iodine deficiency is now recognised by the World Health Organization (WHO) as the most common preventable cause of brain damage with in excess of 2 billion at risk from 130 countries.

A global United Nations (UN) programme of prevention has achieved 68% household usage of iodised salt by the year 2000 compared with less than 20% prior to 1990.

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History – Europe – Papua New Guinea

The relationship between iodine deficiency and brain damage was originally raised by observations of the association of goitre and mental retardation.

Goitre is most commonly caused by dietary iodine deficiency, and the term 'endemic goitre' refers to this condition as distinct from goitre due to other causes. Records of goitre as seen in mountainous areas date back to 3000 BC.¹

The term 'cretin' was first used in Diderot's *Encyclopedie* in 1754 to refer to an "imbecile who is deaf, dumb with a goitre hanging down to the waist" known at that time to be widely present in Switzerland, Southern France and Northern Italy. The term endemic cretinism is used to refer to its association with endemic goitre.¹

This association was known to the mediaeval world but was finally established by an epidemiological survey ordered by the King of Sardinia, which was published in 1848. At this time the King of Sardinia was also the King of Savoy, which included the European Alpine Region.

In contrast to endemic cretinism, the condition of sporadic cretinism occurs all over the world without any relation to iodine deficiency. It is usually found with evidence of a misplaced or absent thyroid or with goitre due to congenital defect in the biosynthesis of thyroid hormones causing clinical hypothyroidism.¹

After the early descriptions from the 17th to the 19th centuries, the problem of endemic cretinism was mostly forgotten until late in the 20th century because these subjects were often confined to remote areas, which limited access for scientific study.

It was in the 1960s that the problem was rediscovered in various parts of the world – in Latin America (Brazil); Africa (the then Zaire now Republic of the Congo); The People's Republic of China, Indonesia and Papua New Guinea.²

Questions were raised about the relation of iodine deficiency to cretinism in Europe (Switzerland and Northern Italy) because of the apparent spontaneous disappearance of cretinism in the absence of programmes for the correction of iodine deficiency with iodised salt.³

These observations raised the question as to whether iodine deficiency was the cause of cretinism.

Studies in Papua New Guinea

In Papua New Guinea (PNG), studies were carried out in the highlands, in collaboration with the Public Health Department of the Territory (then under Australian administration), where a severe problem of goitre and cretinism had been identified.⁴

Advantage was taken of the availability of iodised oil 'Lipiodol' (a preparation of iodine in poppy seed oil long used in radiology as a contrast medium) for the correction of iodine deficiency in the remote highlands where distribution of iodised salt was difficult to achieve.

A single injection of iodised oil was shown to correct severe iodine deficiency in subjects in the highlands for up to 5 years, depending on the dosage.⁴

Subsequently, prevention of cretinism and stillbirths was demonstrated by the administration of iodised oil before pregnancy in a randomised controlled trial in the Western Highlands of New Guinea (Table 1).⁵ This finding was subsequently accepted as definitive.⁶ A mass injection programme, with iodised oil, was carried out in the highlands from 1971.

Broad experience in all parts of the world indicates that cretinism disappears in a population when iodine deficiency is corrected. The apparent spontaneous disappearance in Europe is now attributed to

Table 1

Children born in Jimi River Subdistrict Papua New Guinea classified according to treatment received by mother.⁵

Treatment received by mother	Total number of new births	Number of children examined	Number of deaths recorded	Number of endemic cretins
Iodized oil	498	412	66	7 ^a
Untreated	534	406	97	26 ^b

^a 6 already pregnant when injected with iodized oil.

^b 5 already pregnant when injected with saline solution.

'silent' correction of iodine deficiency by gradual dietary diversification associated with social and economic development.⁷

The clinical features of endemic cretinism

Definition

An agreed definition of endemic cretinism was adopted by the Pan American Health Organization (PAHO) in 1986⁸, with later confirmation in 1994 WHO/UNICEF/JCCIDD.⁹ The definition consists of 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:
 - (i) A predominant neurological syndrome including defects of hearing and speech and characteristic disorders of stance and gait of varying degree; or
 - (ii) Predominant hypothyroidism and stunted growth.

Although usually the neurological syndrome predominates in some areas a mixture of the two syndromes has been observed.

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

Clinical manifestations

McCarrison reported the two types of endemic cretinism from the Karakoram Mountains (now Pakistan) in 1908.¹⁰ In addition to Europe (Switzerland and Italy), it has been reported from South America (Argentina, Ecuador and Brazil); Africa (Democratic Republic of Congo); Oceania (New Guinea) and Asia (China, India, Nepal, Indonesia, Burma and Pakistan).^{2,11} The association of cretinism with severe iodine deficiency has been uniformly demonstrated.

The different features of the two types are summarised in Table 2.

1. Neurological Cretins: Worldwide, this is the common in areas of severe iodine deficiency^{1,11} (Fig. 1). The obvious clinical features include mental retardation with the following neurological defects:

Table 2
Comparative clinical features in neurological and hypothyroid cretinism.¹

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

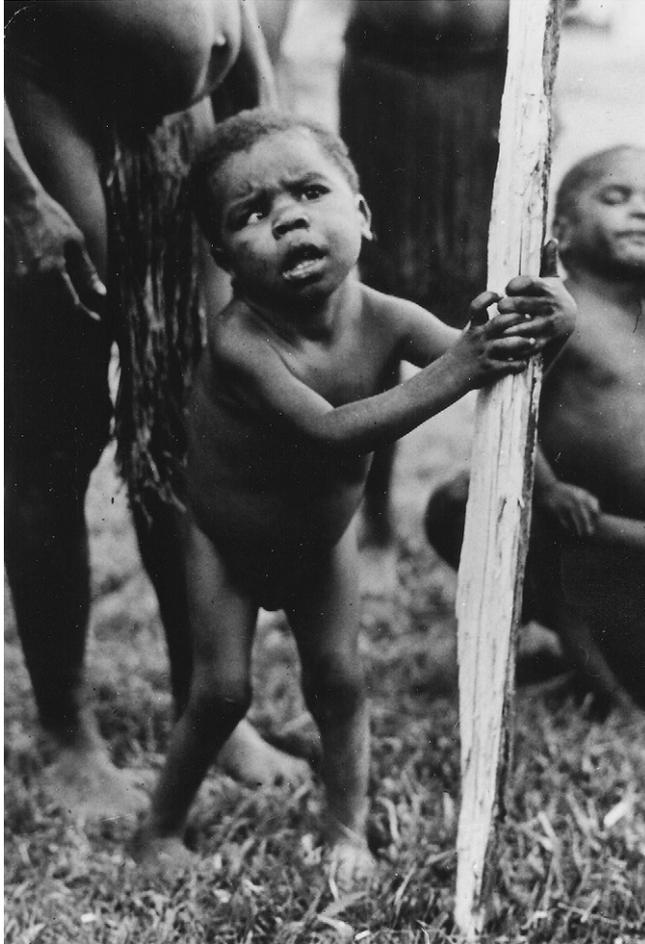


Fig. 1. Child with severe neurological cretinism associated with brain damage, squint, deaf mutism and ataxia, so that he is dependent on the stick he is holding (Papua New Guinea). (Reproduced from Hetzel BS 1989, *The Story of Iodine Deficiency—an International Challenge in Nutrition*, Oxford University Press).

- (i) Defects of hearing and speech – most neurological cretins are deaf-mutes of varying degree.
- (ii) Squint.
- (iii) Predominant neurological signs: Impaired voluntary motor activity involving spastic diplegia or paresis of the lower limbs.
- (iv) Characteristic disorders of stance and gait of varying degree, including spastic gait and ataxia with serious effects on standing and walking.

Neurological cretins are usually euthyroid, but goitre and hypothyroidism can be seen in some cases. Urinary iodine levels are usually less than $20 \mu\text{g l}^{-1}$ compared to normal levels ($100\text{--}150 \mu\text{g l}^{-1}$) with a normal dietary intake.

2. Hypothyroid cretins^{1,10,12} (Fig. 2): Severe or long-standing hypothyroidism is predominant in this type with the following features: dwarfism, myxoedema, dry swollen or thickened skin, sparseness of hair and nails, deep hoarse voice, sexual retardation, retarded maturation of body parts, skeletal retardation, weak abdominal muscles, inactive bowel function and delayed tendon reflexes. A



Fig. 2. Child with hypothyroid cretinism showing thickened features, dry skin and growth retardation (Xinjiang, China). (Personal photograph and property of ZP Chen) (co-author).

typical feature is incomplete maturation of the face: wide-set eyes, saddle-nose deformity with retarded maturation of naso-orbital configurations, mandibular atrophy and thickened lips (Fig. 2).

The mental deficiency in the neurological cretins is more severe than in the hypothyroid type.^{11,12} They demonstrate difficulty in performing simple manual tasks, such as of simple dancing, as observed in southern Xinjiang of China. However, some hypothyroid cretins in the Republic of the Congo (formerly Zaire) exhibit neurologic signs, such as spasticity of the lower limbs, jerky movements, Babinski sign and shifting gait.¹³ The prevalence of goitre in the hypothyroid type is much lower than in neurological cretinism. Usually in the hypothyroid type, lower or undetectable serum T_4 , T_3 and very high levels of TSH are associated with low levels of urinary iodine (less than $20 \mu\text{g l}^{-1}$).^{11,11}

Hypothyroid endemic cretinism is mainly found in the Republic of the Congo (former Zaire); in Pakistan (in the Karakoram Mountains) and the western region of China (Xinjiang, Qinghai, Gansu Provinces and part of Inner Mongolia). The reasons for these geographic differences in the epidemiologic pattern of endemic cretinism are not known but cassava intake is a factor in the Republic of the Congo through the effect of thiocyanate in reducing iodine uptake by the thyroid.¹⁴

Recently, the emergence of neurological cretinism in some remote villages of the southern Xinjiang region of China in 2006 was due to the failure of the local iodised salt programme.¹⁵ No new cretins had been born between 1970 and 1990, following the original iodine intervention.

Subclinical mental retardation

There are a number of individuals who are affected by iodine deficiency but not to the extent as to justify a diagnosis of endemic cretinism. These individuals appear superficially normal; however, they do have mild mental deficiency (IQ 50–69) accompanied with minor psychomotor or neuromotor impairments of varying degree revealed by careful examination.¹⁶ The epidemiological data indicate that mild mental retardation (IQ 50–69) is found in 5–15% of the children in many endemic areas.¹⁷ IQ distribution curves of children show a general tendency to shift to the left, with a mean IQ deficit of 11 points in the population living in IDD areas. This was confirmed by a meta-analysis of 36 studies conducted in China.¹⁷ In China, these individuals with mild mental retardation, together with neuro-motor deficits, have been called 'subcretins' (subclinical cretinism).^{16–18}

Table 3 shows a comparison between the IQ of 8- to 14-year-old students measured by the modified Raven test with those born after iodisation in the same age group from the same population.

The striking feature in these populations is the occurrence of a wide range of defects ranging from individuals with mental deficiency or deaf-mutism with a varying severity of paralysis of the arms and legs. There are also individuals who appear to be normal apart from some coordination defect. This indicates that endemic cretinism is part of a spectrum of defects that occur in the iodine-deficient population now designated by the term 'iodine deficiency disorders (IDDs)' (see below).

Animal models

Experimental studies of the effect of iodine deficiency in animals

Studies on the sheep, the marmoset monkey and the rat have been particularly concerned with foetal brain development because of its relevance to the human problem of endemic cretinism and brain damage resulting from foetal iodine deficiency.

(i) Iodine Deficiency in the Sheep

Severe iodine deficiency has been induced in pregnant sheep²², with a low iodine diet of crushed maize and pelleted pea pollard (8–15 µg iodine kg⁻¹), which provided 5–8 µg iodine per day for sheep

Table 3

Comparison of IQ of 8-14 year old students by modified Raven test in IDD endemics from the same populations born before and after iodization from the same population.

Author	Place	Before iodization			After iodization		
		N	X ± SD	IQ <69 (%)	N	X ± SD	IQ <69 (%)
Chen et al. ¹⁹	Liaoning, Hubei, Shanxi						
	Control	818	104.4 ± 16.7	2.1			
	Mild IDD	240	95.4 ± 15.3	5.0	353	96.8 ± 12.9	1.4
	Moderate IDD	214	90.7 ± 13.6	5.1	241	93.7 ± 12.3	3.3
	Severe IDD	394	89 ± 13.6	7.9	694	94.3 ± 14.8	5.4
Yang, ²⁰	Guizhou						
	Mild IDD	540	90.1	6.0	558	99.4	0.9
	Severe IDD	560	87.4	8.4	580	98.4	1.2
Lin et al. ²¹	Hetian						
	Severe IDD	322	77.1 ± 6.9	25.1	243	95.8 ± 17.5	8.2

N = Number examined

X = IQ

Total Goitre Rate (TGR)

Control TGR 1.2%

Mild iodine deficiency area TGR 5-13.6%

Moderate iodine deficiency area TGR 26%

Severe iodine deficiency area TGR 33%.

weighing 40–50 kg. The iodine-deficient foetuses at 140 days' gestation were grossly different in physical appearance in comparison to the control foetuses fed the same diet with the addition of iodine. There was reduced weight, absence of wool growth, goitre, varying degrees of subluxation of the foot joints and deformation of the skull (Fig. 3). There was also delayed bone maturation as indicated by delayed appearance of epiphyses in the limbs. Goitre was evident from 70 days in the iodine-deficient foetuses, and thyroid histology revealed hyperplasia from 56 days' gestation associated with a great reduction in foetal thyroid iodine content and reduced plasma T_4 values (19 nmol l^{-1} compared with control 137 nmol l^{-1} at 140 days' gestation). Normal sheep gestation period is 150 days.

There was a lowered brain weight and DNA content as early as 70 days, indicating a reduction in cell number probably due to delayed neuroblast multiplication, which normally occurs from 40 to 80 days' gestation in the sheep. Findings in the cerebellum indicated arrested development.²²

Studies of the mechanisms involved in the sheep revealed the significant effect of foetal thyroidectomy in late gestation and a significant effect of maternal thyroidectomy on brain development at mid-gestation. The combination of maternal thyroidectomy (carried out 6 weeks before pregnancy) and foetal thyroidectomy produced more severe effects on the brain than that of iodine deficiency

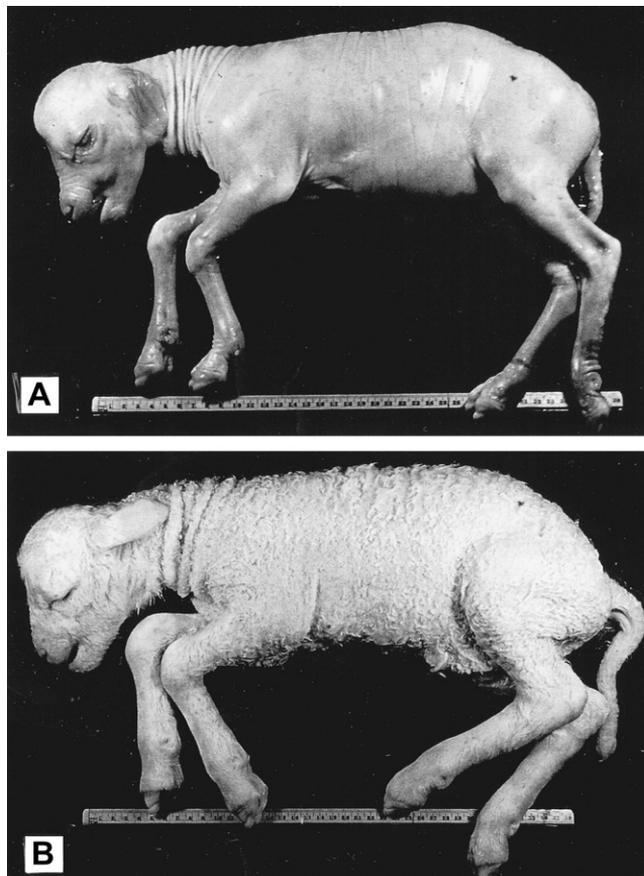


Fig. 3. (A) Lamb (140 days gestation) from iodine deficient mother showing no wool growth and skeletal retardation compared to lamb (B) from control mother with normal iodine intake. The brain is reduced in weight and DNA content compared to the control from seventy days gestation. (Reproduced from Hetzel BS 1989, *The Story of Iodine Deficiency—an International Challenge in Nutrition*, Oxford University Press).

associated with greater reduction in both maternal and foetal thyroid hormone levels.²³ These findings confirmed the importance of both maternal and foetal thyroid hormones in foetal brain development.

(ii) Iodine Deficiency in the Marmoset

Severe iodine deficiency has been induced in the marmoset (*Callithrix jacchus jacchus*) with a mixed diet of maize (60%), peas (15%), torula yeast (10%) and dried iodine-deficient mutton (10%) derived from the iodine-deficient sheep, as already described above. The newborn iodine-deficient marmosets showed some sparsity of hair growth²⁴ with marked reduction in serum T₄ (12 nmol l⁻¹ vs. 142 nmol l⁻¹ in the control animals).

At the end of pregnancy, the brain was smaller and contained a reduced number of cells, compared with that of the control. The effects were greater in the second pregnancy than in the first, suggesting a greater severity of iodine deficiency. There was a significant reduction in brain weight in the newborns from the second pregnancy. The findings were striking in the cerebellum with reduction in weight and cell number evident and with histological changes indicating, as in the sheep, impaired cell maturation and delayed development of the cerebellum. These findings demonstrate the significant effects of iodine deficiency on the primate brain.²⁴

(iii) Iodine Deficiency in the Rat

Studies in rats have been carried out using the diet consumed by the people of Jixian village in China.²⁵ This village was severely iodine deficient with 11% endemic cretinism. The diet included available main crops, maize, wheat, vegetables and water from the endemic area with an iodine content of 4.5 µg kg⁻¹. After the rats had received the diet for 4 months, the newborn showed obvious goitre, foetal serum T₄ was 3.6 µg% compared to that of controls of 10.4 µg%. They had higher radioiodine uptake and reduced brain weight. The density of brain cells was increased in the cerebral hemispheres. The cerebellum showed delayed maturation as in the other species.

These studies establish the significant effects of iodine deficiency in causing retardation of brain development in a variety of animal species, including the primate.²⁶

The spectrum of iodine deficiency disorders (IDDs)

The results of these studies required a re-conceptualisation of the main effect of iodine deficiency from the common lump in the neck (goitre) to a general effect on growth and development, including especially brain development.

The term IDD refers to all the effects of iodine deficiency on the growth and development of a human or animal population, which can be prevented by correction of the iodine deficiency. These include goitre, stillbirths, neonatal and other types of hypothyroidism, but the most significant effect is that of foetal brain damage.²⁷ Effects on brain function occur from hypothyroidism in the foetus, the neonate, child or adult (Table 4).

A meta-analysis of recent research reported a total of 18 studies in which comparison was made between iodine-deficient populations and suitable control populations with a similar social and cultural background.²⁸ These studies revealed that the mean score for the iodine-deficient group was 13.5 IQ points below that of the non-iodine-deficient groups.

Social and economic effects result from iodine deficiency in both human and animal populations. In humans there is reduced school performance in children and reduced productivity in adults. Detailed calculations have been made of the economic costs of medical assessment and the treatment of goitre. In Germany, where there has been much uncontrolled IDD, the costs of diagnosis have been estimated at US\$250 million per year and the costs of treatment have been estimated at US\$300 million per year. The cost of hours lost in working time for this medical care was calculated to be US\$150 million. This makes a total of US\$700 million.²⁹

There are also significant effects on all livestock with impaired reproduction in poultry, sheep, goats and cattle, with reduced wool growth and milk production and reduced rates of survival in offspring.

Table 4
The Spectrum of Iodine Deficiency Disorders (IDD).

Foetus	Abortions Stillbirths Congenital anomalies Neurological cretinism: mental deficiency, deaf mutism, spastic diplegia, squint Hypothyroid cretinism: mental deficiency, dwarfism, hypothyroidism Psychomotor defects
Neonate	Increased perinatal mortality Neonatal hypothyroidism
Child & Adolescent	Retarded mental and physical development Increased infant mortality
Adult	Retarded mental and physical development Goitre with its implications
All ages	Iodine-induced hyperthyroidism (IH) ^a Goitre Hypothyroidism Impaired mental function Increased susceptibility to nuclear radiation

From Hetzel.^{1,27}

^a Transient following iodization minimised by reduced rate of increase in iodine intake.¹

Such effects indicate that correction of iodine deficiency has direct economic benefits. It has been calculated by the World Bank that each dollar dedicated to IDD prevention would yield a productivity gain of \$28.^{30,31}

The IDD iceberg

It is apparent that there is a gradation of the effects of iodine deficiency in an iodine-deficient population, when can be conveniently represented by the concept of an iceberg.

The visible and most serious effect of iodine deficiency is the condition of endemic cretinism, which occurs with a prevalence of 1–10% in a severely iodine-deficient population.

The next gradation is that of less severe brain damage, which may not be apparent until specific psychological testing is carried out. This lesser effect is much more common (up to 30%) than gross cretinism. As already indicated in China, terms such as 'subcretin' or 'cretinoid' are used to describe these subjects.

The most common effect of iodine deficiency apart from goitre is the loss of mental and physical energy due to hypothyroidism. This condition, sometimes called cerebral hypothyroidism, can be reversed by correction of the iodine efficiency seen in village populations, as demonstrated in the observations of Djokomoeljanto in Indonesia.³²

The Village of Sengi, Central Java, Indonesia

Dr. R Djokomoeljanto, Dean of Faculty of Medicine, Diponegoro University, Semarang, Indonesia, tells the following story about the introduction of injections of iodised oil in the village of Sengi in Central Java.³²

"When I came to Sengi for the first time in 1973 the village was so quiet, there were no activities seen or observed by visitors, everyone looked lethargic and gave the impression of being lazy. Not a single child played in front of his or her house.

On 17th April 1973 all villagers received an injection of iodised oil. Dramatic changes were seen within a year. The children were now lovely, playing happily in front of their houses; group activities like badminton, volleyball and chess playing were organised. All were amazed when, at the end of 1974, Sengi received the honour for the best volleyball team and chess player in the sub-district

competition. In subsequent years the school dropout rate fell dramatically. Many students passed primary, and then high school grades and some of them followed with a university education. Public activities increased. Fishing and farming boomed and the community now exports fish and vegetables regularly. The socio economic condition has improved accordingly.”

This condition of cerebral hypothyroidism is associated with a reduction in the level of circulating thyroid hormone, which can be shown in more than half of the goitrous population in an endemic area.^{4,33}

Such a decrease leads to a reduction in thyroid hormone level in the brain, which accounts for the lethargy commonly observed in endemic populations as described in these villages.

The correction of iodine deficiency produces a dramatic reversal of the condition of cerebral hypothyroidism due to restoration of brain thyroid hormone levels. This is a different effect from brain damage during pregnancy, which is not reversible but completely preventable.

The global programme of elimination of brain damage due to IDD

The global elimination programme has been developed through successful application of this knowledge at country level, mainly with the policy of universal salt iodisation (USI), which required all salt for human and animal consumption to be iodised.³⁴

The 1986 World Health Assembly (WHA) passed a resolution calling for the prevention and control of IDD with the use of iodised salt. This was followed by the WHA Resolution in 1990, calling for elimination of IDD by the year 2000 and a later Resolution in 1996, calling for sustainability of the programme through systematic monitoring.³⁵

The International Council for Control of Iodine Deficiency Disorders (ICCIDD) recognised formally by WHO has played an important role in bridging the gap between the research and its application in national programmes. The ICCIDD now comprises more than 700 multidisciplinary professionals from over 100 countries, with a majority from developing countries.³⁶

By 1990, a Global Action Plan for the elimination of IDD by the year 2000 was proposed by the ICCIDD and approved by the UN Subcommittee on Nutrition (SCN), which provided for actions at global, regional and national levels.

The endorsement of the Global Action Plan was followed by the adoption of the goal of elimination of IDD by 2000 by the World Summit for Children on 30 September 1990 at a special meeting at the United Nations, New York.³⁷ This Declaration was signed by 71 heads of state and was subsequently signed by representatives of 88 other national governments. This Resolution provided unprecedented political support for 27 goals for the improvement of the health and education of children.

An informal global partnership following the World Summit developed for the common purpose of the virtual elimination of IDD. This partnership included the people and governments of the IDD-affected countries, the salt industry of the affected countries; the bilateral aid agencies (such as Australia, Canada, the Netherlands, Sweden); the international agencies, such as WHO, UNICEF, the World Bank; the ICCIDD and Kiwanis International.

Subsequently, the Micronutrient Initiative, the Global Network for the Sustained Elimination of Iodine Deficiency, the Global Alliance for Improved Nutrition (GAIN) and the Gates Foundation joined the global partnership with increased impact.^{38,39}

China has demonstrated the virtual elimination of IDD through a policy of USI. This has been achieved by strong political support, together with an effective public health network covering the whole country.⁴⁰ The national data presented clearly show that China had achieved the goal of virtual elimination of IDD by the year 2000 and has succeeded in sustaining these results. This fact is further validated by the results of surveys focussing on the iodine nutritional status of populations groups at risk of IDD, namely women of childbearing age, pregnant and lactating women and their babies.⁴⁰ The effectiveness of the monitoring system was demonstrated by the detection of an outbreak of cretinism in a remote area in association with a failure of supply of iodised salt.¹⁵

The Director General of WHO, Dr Gro Brundtland, has pointed out that the achievement of IDD elimination “will be a major and total public health triumph ranking with small pox and polio.” It will be a major global triumph in the elimination of a non-infectious disease.⁴¹

In summary, endemic cretinism includes two syndromes: a more common neurological disorder with brain damage, deaf-mutism, squint and spastic paresis of the legs and a less common syndrome of severe hypothyroidism, growth retardation and less severe mental defect.

Both conditions are due to dietary iodine deficiency and can be prevented by correction of iodine deficiency before pregnancy.

Experimental studies in animal models (sheep, monkey and rat) have demonstrated the effects of iodine deficiency on foetal brain development with reduced brain weight and DNA. The results of these animal studies have led to a re-conceptualisation of the main effect of iodine deficiency from goitre to a general effect on growth and development, including especially brain development.

Endemic cretinism and goitre are now included in the spectrum of effects of iodine deficiency in a population now denoted by the term 'iodine deficiency disorders (IDDs)', which also include stillbirths and impaired cognition at all ages, which can all be prevented by correction of the iodine deficiency.

Cretinism can recur in areas of severe iodine deficiency if iodised salt programmes fail or are discontinued. This is illustrated in the recent example from western China, where there was an outbreak of cretinism in a remote area with the failure of the supply of iodised salt.¹⁵

Clinical agenda

- Endemic cretinism is due to dietary iodine deficiency in the mother during pregnancy affecting foetal brain development, which produces a multiple neurological defect consisting of mental deficiency, deaf-mutism, squint and a spastic paresis of the legs. A minority of subjects experience severe hypothyroidism with dwarfism.
- WHO now recognises iodine deficiency as the most common preventable cause of brain damage, with in excess of 2 billion at risk from 130 countries.
- Endemic cretinism is one of the spectrums of effects of iodine deficiency in the foetus, neonate, child and adult, now termed the iodine deficiency disorders (IDDs), including lesser degrees of cognitive defect in children as well as goitre and hypothyroidism.

Research agenda

- There is a need for more data on iodine status in pregnancy by measurement of urinary iodine in the light of preliminary evidence of low levels (less than $100 \mu\text{g l}^{-1}$) compared with a recommended dietary intake of $200 \mu\text{g l}^{-1}$ (in Australia).
- There is a need for more data from studies of cognition in children of all ages, including the effects of correction of iodine deficiency.
- There is a need for follow-up studies on the effects of iodine supplementation in pregnancy by various methods – iodised salt, iodine supplements and iodised oil.
- Further studies of the effect of iodine deficiency on brain development in animal models with reference to effects at the cellular and subcellular levels.

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