Section I

Introduction: The Nature and Magnitude of the Iodine Deficiency Disorders (IDD)

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1. Introduction

Iodine deficiency is the cause of an Ancient Scourge of mankind. This scourge includes goitre and brain damage at all ages beginning with the foetus during pregnancy.

This book describes the development of a global program for the elimination of brain damage due to iodine deficiency mainly by the use of iodized salt.

This global program dates from 1990 when the necessary political support became available through the World Summit for Children with the support of the UN System, through the World Health Organization and UNICEF. This support has led to the development of an informal global partnership of countries, UN and bilateral aid agencies, technical agencies and the salt industry.

Prior to 1990 the necessary scientific basis for the global program had been established by a large group of scientists from many countries of the world over the preceding century.

This scientific work had recently focussed on the role of iodine deficiency in causing brain damage, particularly in the developing foetus during pregnancy. It was then shown that correction of the iodine deficiency before pregnancy would prevent or eliminate this brain damage. This finding provided the basis for a global program for the elimination of brain damage caused by iodine deficiency by the use of iodized salt.

Before 1990 the translation of this knowledge into effective elimination programs had been limited and spasmodic.

The translation had been particularly hampered by inadequate communication with governments, which blocked effective implementation.

This situation was finally remedied by the 1990 World Summit for Children, which included the goal of the virtual elimination of iodine deficiency disorders (IDD) by the year 2000. This unprecedented Declaration included 27 goals for the improved health and education of children–it was signed by 71 Heads of State who attended the meeting at the United Nations, New York. They were followed by signatories from 88 other governments.

Extensive studies throughout the world over the last 20 years have revealed that 130 countries are affected by iodine deficiency, with a total population in excess of 2 billion at risk of the occurrence of varying degrees of brain damage (WHO/UNICEF/ICCIDD 1999).

Since 1990 substantial progress in the elimination of brain damage has been made with two thirds of households having access to iodized salt by 2000. However, there is still another third that does not have access and there is some evidence of 'backsliding' since 2000 by some countries which had already made satisfactory progress. In all countries sustainability has become the challenge.

This book reports in detail the progress of the global elimination program, which aims to cover 130 countries. It reports success and also failure in individual countries and provides an analysis of the lessons learnt from this experience.

The target set by the UN System at the UN General Assembly Special Session for Children (UNGASS) (May 2002) for Elimination of IDD, is now 2005.

The book provides an appraisal of the current situation to help in the achievement of this objective!

We have made substantial progress, we have the necessary knowledge but it is political will that is required by people and by governments to rid the world of this Ancient Scourge! This requires a continued education effort to build awareness of the great opportunity we have. All these issues are explained in detail in this book.

We begin in this Section I with a brief review of the major aspects of the effects of iodine deficiency including some of the research that has led to this great opportunity of eliminating this terrible affliction.

2. Iodine Deficiency and Brain Damage

Iodine deficiency is now considered the most common cause of preventable brain damage in the world today (WHO 1994).

The problem has arisen because people live in an environment where the soil has been leached of iodine due to flooding of river valleys or in hilly and mountainous areas by high rainfall or glaciation.

The deficiency in the soil leads to deficiency in all forms of plant life including all cereals grown in the soil **(fig. 1)**. Hence large populations living in systems of subsistence agriculture particularly in the developing countries, as in the great river valleys of Asia, are locked into iodine deficiency (Hetzel 1989).

Iodine is an essential element for human and animal development because it is a constituent of the thyroid hormones, thyroxine (T_4) and triiodo-thyronine (T_3).

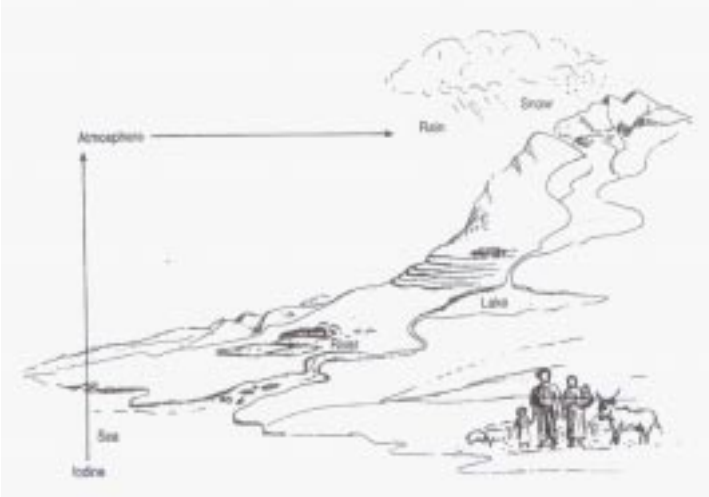

Fig. 1 *Iodine cycle in nature: The atmosphere absorbs iodine from the sea which then returns through the rain and snow to the mountainous regions. It is then carried by rivers to the lower hills and plains, eventually returning to the sea. High rainfall, snow and flooding increase the loss of soil iodine, which has often been already denuded by past glaciation. This causes the low iodine content of food for man and animals (Hetzel 1989).*

Fig. 2 *A mother and child from a New Guinea village who are severely iodine deficient. The mother has a large goitre. The bigger the goitre the more likely it is that she will have a brain damaged child. This can be prevented by eliminating the iodine deficiency before the onset of pregnancy (Hetzel and Pandav 1996).*

Without the thyroid hormones, metamorphosis of the tadpole into the frog will not occur. This indicates their basic significance throughout the animal kingdom.

In iodine deficiency, the thyroid gland enlarges to form a goitre **(fig. 2)** to maintain the level of thyroid hormones in the blood but eventually the level falls with increasing effects on the development of the brain and other organs.

The role of iodine deficiency as a cause of brain damage has been established by a combination of individual clinical studies on subjects suffering from the effects of iodine deficiency, epidemiological investigation of communities and populations and the study of animal models.

We will now briefly consider these studies.

2.1 History

The relation between iodine deficiency and brain damage was originally raised by observations of the association of goitre and mental retardation (endemic cretinism).

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

The term 'cretin' was first used in Diderot's Encyclopedie (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 is Switzerland, Southern France and Northern Italy. The term 'endemic cretin' is used to refer to its association with endemic goitre.

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 King of Savoy, which included the European Alpine Region.

After the early descriptions from the 17th to 19th Centuries the problem of cretinism was lost sight of until later 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 and now Republic of the Congo); The People's Republic of China and Papua New Guinea (Pharaoh et al 1980).

Fig. 3 *A mother with her four sons, three of them (aged 31,29 and 28) are endemic cretins, born before iodized salt was introduced and the fourth is normal (aged 14), born after iodized salt became available in Chengde, China. The three cretin brothers had severe brain damage, were deaf mute with varying degrees of spasticity associated with endemic cretinism. The mother had goitre (Ma and Lu 1996)***.**

There are two types of endemic cretinism as originally recognised by McCarrison in the Himalayan Region–a nervous type and a hypothyroid (myxedematous) type (McCarrison 1908). The condition of neurological endemic cretinism is characterised in its fully developed form by severe brain damage, deaf mutism and a spastic state of the hands and feet **(fig. 3)**. It is the result of iodine deficiency in the first half of pregnancy.

A much less common form is hypothyroid cretinism, which occurs with severe iodine deficiency in late pregnancy. It is characterised by dwarfism, brain damage with severe hypothyroidism **(fig. 4)**. Mixed forms also occur.

Questions were raised about the relation of iodine deficiency to cretinism in Southern Europe (Switzerland, Northern Italy and Yugoslavia) because of the apparent spontaneous disappearance of cretinism in the absence of programs for the correction of iodine deficiency with iodized salt (Costa et al 1964).

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

Fig. 4 *A hypothyroid cretin in Sinjiang, China who is also deaf mute. This condition is completely preventable. Right: The barefoot doctor of her village. Both are about 35 years of age (Photograph courtesy of Dr Ma Tai, China).*

2.2 Studies in Papua New Guinea

This work was carried out in the Highlands of Papua New Guinea, in collaboration with the Public Health Department of the Territory (then under Australian administration) taking advantage of the availability of iodized oil (a preparation of iodine in poppyseed oil long used in radiology as a contrast medium) for the correction of iodine deficiency (McCullagh 1963).

A single injection of iodized oil was shown to correct severe iodine deficiency in subjects in the Highlands for over 4 years depending on the dosage (Buttfield & Hetzel 1967).

Subsequently the prevention of cretinism and stillbirths was demonstrated by the administration of iodized oil before pregnancy in a controlled trial in the Western Highlands of New Guinea (Pharoah et al 1971). This finding was subsequently accepted as definitive (Lancet 1972). A mass injection program with iodized oil was carried out from 1971.

Wide experience in all parts of the world supports the view that cretinism disappears in a population when iodine deficiency is corrected. The apparent spontaneous disappearance in Europe is now attributed to 'silent' correction of iodine deficiency by gradual dietary diversification together with the gradual use of iodine supplements associated with economic and social development (Burgi et al 1990).

2.3 Animal models

To further establish the relation between iodine deficiency and foetal brain development an animal model was developed in the sheep. A major reason for using sheep was the access provided for surgical removal of the maternal and foetal thyroid glands so that the roles of the maternal and foetal thyroid secretions could be defined. Subsequently similar models were developed in the primate marmoset monkey and in the rat (Hetzel & Mano 1989).

Significant effects of iodine deficiency in slowing foetal brain development have been shown in all three species. Further details are given in Section IV.

These studies with animal models confirmed the effect of iodine deficiency on foetal brain development as already indicated by the results of the field trial with iodized oil in Papua New Guinea. The combination of the controlled trial with the results of the studies in animal models clearly established that prevention of brain damage was possible by correction of the iodine deficiency before pregnancy.

Table 1. *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
	Retarded mental and physical development
CHILD & ADOLESCENT	Increased infant mortality
	Retarded mental and physical development
ADULT	Goitre with its complications
	Iodine-induced hyperthyroidism (IIH)
ALL AGES	Goitre
	Hypothyroidism
	Impaired mental function
	Increased susceptibility to nuclear radiation

From Hetzel (1983) WHO/UNICEF/ICCIDD (2001)

A Review of the extensive work on the subject of iodine deficiency and brain damage has been published (Stanbury 1994).

2.4 The Iodine Deficiency Disorders (IDD)

The results of the research required a re-conceptualization 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.

To this end the term iodine deficiency disorders (IDD) was proposed (Hetzel 1983) and has since been generally adopted.

The term IDD refers to all the effects of iodine deficiency on growth and development in a human and 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 important effect is that of foetal brain damage **(Table 1)**. The term IDD

has now been adopted throughout the world, including adoption by the Chinese without translation!

Effects on brain function occur at all stages of life, from foetal damage or hypothyroidism in the neonate, child or adult **(Table 1)**. These features are discussed in more detail in Section IV.

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 (Bleichrodt & Born 1994).

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. These data further indicate-the major population dimension of the effect of iodine deficiency on neuropsychological development.

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 and reduction in goitre.

Detailed calculations have been made of the economic costs of medical assessment and the treatment of goitre. In Germany where there is still 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. (Pfannensteil 1985).

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. Such effects indicate that correction of iodine deficiency has direct economic benefits. **(Table 2)**. It has been calculated by the World Bank that each dollar dedicated to IDD prevention would yield a productivity gain of $28. (Levin et al 1993; Pandav and Rao 1997).

It is important to note that iodine deficiency increases the effect of exposure to nuclear radiation with increased susceptibility to cancer **(Table 1)**.

2.5 The Magnitude of IDD

The at risk population for IDD was estimated in 1990 by WHO to be 1.6 billion including in excess of 20 million with some degree of brain

Table 2. *Effects of Iodine Interventions and Measurements of Economic Benefits*

Human Populations

EFFECTS	BENEFITS
Reductions in:	
1. Mental deficiency	1. Value of higher work output in household and labour market
2. Deaf mutism	2. Reduced costs of medical and custodial care
3. Hypothyroidism	3. Reduced educational costs from reduced absenteeism and grade repetition
4. Goitre	4. Reduced costs of investigation and treatment

From: Levin et al (1993)

Livestock Populations

EFFECTS	BENEFITS
Increases in:	
1. Live births	1. Value of higher output of meat and other animal products
2. Weight	2. Value of higher animal work output
3. Muscle mass	3. Increased meat production
4. Wool coat in sheep	4. Increased wool production

From: Levin et al (1993)

damage due to the effects of iodine deficiency in pregnancy. Iodine is the most common preventable cause of brain damage (WHO 1994).

More recently these estimates have been increased to 2.2 billion at risk of the effects of iodine deficiency **(Table 3)** with the recognition that even mild iodine deficiency in the mother has effects on the foetus.

There are now estimated to be 130 IDD affected countries including the most populous–Bangladesh, Brazil, China, India, Indonesia and, Nigeria (WHO/UNICEF/ICCIDD 1999).

There is therefore a global scourge of great magnitude, which provides one of the major challenges in international health today.

Table 3. *Current Estimates of Population at risk of IDD by WHO Regions**

WHO Region with IDD	Number of Countries Affected	Total population in IDD	At Risk Population**	
		Millions	**Millions**	**% of the Region*** **
Africa	44	610	295	48%
Americas	19	477	196	25%
South East Asia	9	1,435	599	41%
Eastern Mediterranean	17	468	348	74%
Europe	32	670	275	32%
Western Pacific	9	1,436	513	31%
TOTAL	**130**	**5,096**	**2,225**	**38%**

*Based on UN population Division (UN estimates 1997)

**The at risk population is the population living in iodine deficiency areas where total goitre rate (TGR) is more than 5%

***Expressed as a percentage of the total population in the Region

From: WHO/UNICEF/ICCIDD (1999)

3. Anecdotal Reports of the Elimination of IDD at Village Level

The dramatic impact of the elimination of iodine efficiency at the local community level is shown by some anecdotal reports. These include the village of Sengi in Central Java, Indonesia and the village of Jixian in Northern China (Heilongjiang Province) and the village of Padrauna, district (Deoria) in Northern India.

These reports can be replicated from iodine deficient communities from the many countries where people suffer the debilitating effects of iodine deficiency.

3.1 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 iodized oil in the village of Sengi in Central Java.

"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. Nowadays we know that this must be the consequence of hypothyroidism, since 87% of this population had low serum thyroid hormone levels. Many also showed signs of clinical or sub-clinical hypothyroidism and 9% were cretins. Nobody finished the six years of elementary school and the dropout rate was tremendously high. This was due to 'hypothyroidism affecting the brain'-they were anergic.

On April 17th 1973 all villagers received an injection of iodized oil. Dramatic changes were seen within a year. The children were now lively, 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 and chess player in the sub-district competition. In subsequent years the school dropout rate fell dramatically. Many students passed primary, secondary and then high school 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.

Cretins improved physically but not mentally. Mr PA (B) was a hypothyroid cretin but felt himself healthy enough to marry. His wife was a neurological cretin. By that time the iodine deficiency of everyone in the village had been corrected by the injection of iodized oil. This couple had three healthy sons. They grew and developed normally, both physically and mentally. One of the three was well until he died in a vehicle accident. The other two, **(fig. 5)** include Rame (second from right) who ranked first when finishing the high school in Semarang and now (2001) has almost finished his BSc in Chemistry at Diponegoro University. His younger brother, Ramidi (second from left) born in 1983 ranked first of 49 pupils in his high school class. He is now also in Semarang and plans to become a physician. What a difference the iodine in a single injection made to the fate of this family!" (Djokomoeljanto 2001)

3.2 The Village of Jixian, Northern China

This study by Professor JQ Li, (Professor of Medicine Jamusi School of Medicine, Heilongjiang Province, North China) has been reported as follows (Ma and Lu 1996).

Fig. 5 *Iodine gives Cretin Couple Normal Children. (Djokomoeljanto 2001)*

Fig. 6 *A group of lively Indian Children from Padrauna (Deoria), Uttar Pradesh, India who had received iodized oil injections six months before this photograph was taken (Hetzel 1989).*

Table 4. *Effects of iodine deficiency control in Jixian village, China**

	Before (1978)	**After (1986)**
Goitre Prevalence	80%	4.5%
Cretinism Prevalence	11%	Fall
School ranking (of 14 schools in the district)	14th	3rd
School failure rate	>50%	2%
Value of farm production(Yuan)	19,000	180,000
Per capita income(Yuan)	43	550

**From: Ma & Lu (1996).*

Until recently Jixian was known as the 'Village of Idiots'. There were 247 families in the village comprising some 1243 people, of whom 850 (65%) had a goitrous condition. There were 115 cretins, many severe due to brain damage, deaf mutism and spasticity of the legs.

Because of its reputation, no girls wanted to marry young men from Jixian and it was a very depressed community, whose income was appallingly low and with a sense of hopeless inadequacy and glum endurance. On the low hills nearby was a rock shaped like a stone monkey which was thought to be casting an evil eye on the village. The villagers smashed it, but with no effect. The elders also thought that cretinism might be a visitation because ancestors had killed cattle, but no spells or incantations had any effect. Even the dogs and cats showed the effects of iodine deficiency

All the water came from a shallow well. In 1978 the iodized salt program began and in 1979 a deep well was put in by the Central Government at Professor Li's instigation. He believed that the village was built on an ancient river bed-probably an earlier course of the Sung Wha Jiang River-as there was a thick layer of heavy clay, which was preventing the iodine bearing water from permeating to the surface. The deep well has penetrated this thick layer so that all the water now was found to have a much better iodine content. In addition injections of iodized oil were given to all young women of marriageable age and all children.

Since the salt program began and the water was improved, the standard of living has risen, the village has produced enough goods to begin to export and has done best of all the villages in the district. The per capita income has doubled in the last three years and by 1986 many families now had a radio, a watch or even a televison.

Forty-four girls have now come in from neighbouring villages as brides and there is a crop of healthy babies.

It is remarkable to see the improvement and hear about it from enthusiastic people, both from the village and the Medical Centre. **(Table 4)**.

3.3 The Village of Padrauna (district, Deoria), Northern India

In Northern India, a high degree of apathy has been noted in populations living in villages in iodine deficient areas. This may even affect domestic animals such as dogs. The lethargy is so much that dogs continue to sit in the middle of road even when a four-wheel vehicle approaches them. In fact, the deficiency is so severe that enlargement of thyroid gland-goitre was seen even in birds. It is apparent that reduced mental function due to brain hypothyroidism is widely prevalent in iodine deficient communities. It is also an uncommon occurence for children born in this area to reach professional levels-such as physicians or civil servants. This has an effect on their capacity for initiative and decision-making. People who are residents of this area are often referred as "fools". This indicates that iodine deficiency can be a major obstacle to the human and social development of communities living in an iodine deficient environment.

As Dr CS Pandav (All India Institute of Medical Sciences, New Delhi) has found the correction of the iodine deficiency has reversed this situation as is indicated by the lively children from the village of Padrauna in Uttar Pradesh six months following an iodized oil injection **(fig. 6)**. It has been a major contribution to community development as in the case of the village of Jixian.

These accounts describe the remarkable benefits of the elimination of iodine deficiency at village level. These observations can be duplicated in many villages in many countries throughout the world.

Both the human and economic benefits are apparent-the elimination of iodine deficiency is indeed associated with benefits on a remarkable scale. The elimination of iodine deficiency is indeed a major contribution to social and economic development.

This message needs to be much better known to promote the political will of people and governments throughout the world.

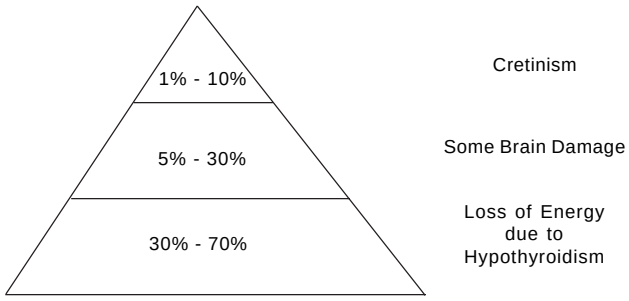

Fig. 7 *The IDD Iceberg (see text) (Hetzel and Pandav 1996)*

3.4 The IDD Iceberg

It is apparent that there is a gradation of the effects of iodine deficiency, which can be conveniently represented by the concept of an iceberg **(fig. 7)**.

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 (as described in Section IV). This lesser effect is much more common (up to 30%) than gross cretinism. 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 deficiency as described in these village populations.

This condition is associated with a reduction in the level of circulating thyroid hormone which can be shown in more than half the goitrous population in an endemic area (Buttfield and Hetzel 1967; Kochupillai et al 1973). Such 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.

4. A Global Program for the Elimination of Brain Damage to Iodine Deficiency

The reasons why the elimination of brain damage due to iodine deficiency was worthy of a global program for major commitment by governments and the major international agencies were the following:

i) The problem was of **sufficient qualitative and quantitative significance** to justify a major allocation of resources. The at risk population for brain damage, due to iodine deficiency, has been recently estimated to be 2.2 billion from 130 countries (WHO/UNICEF/ICCIDD 1999). The economic benefits have been referred to earlier in this Section.

ii) There were effective **preventive measures suitable for mass application** in the form of iodized salt and iodized oil. This had been shown for iodized salt in many developed countries and for iodized oil in a number of developing countries (Hetzel 1989, Hetzel and Pandav 1996, WHO 1994).

iii) There was an **available system for the correction of iodine deficiency through delivery of iodized salt** through the salt industry and for the delivery of iodized oil through the primary health care system. Adequate iodine supplementation can be provided with no increase or even a reduction in salt intake if necessary. Iodized salt is available and sustainable at a minimum cost (US3-5 cents per year). (see further Section V).

iv) There were **practical methods for monitoring the program so that it could be effective and sustainable**. This is achieved by checks on salt iodine at factory, retail or household level and by measurements of urine iodine excretion, which provide a measure of the dietary intake of iodine. Suitable procedures for use with large numbers of samples are available and have been used extensively throughout the world in both developed and developing countries since 1990. (see further Section IV).

These were the major considerations needed to justify a global program and led to the inclusion of the objective of the virtual elimination of IDD as one of the 27 Goals of the World Summit for Children.

An Overview of the global program is provided in the next Section (Section II).

We conclude here that the elimination of brain damage due to iodine deficiency has been established as a feasible objective with great human and economic benefits for in excess of 2 billion people.

It presents the challenge of the elimination of a major non-infectious disease, with great human and economic costs as an Ancient Scourge of mankind.

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Ji Xian Village with its new brick kiln chimney
which dominates the skyline. Unbaked bricks in lines beyond.
The central east road newly repaired, but still many puddles.


Sengi Village
Indonesia
Houses built of woven bamboo screens
and steeply sloping roofs. Small streams -
no doubt frieds of town with small bridges to
each house.