Commentary: From iodine deficiency in Papua New Guinea to a global programme of prevention

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Our research work in New Guinea [at this time, I was Professor and Head of the University of Adelaide, Department of Medicine at the Queen Elizabeth Hospital (QEH), Woodville SA.] carried out in collaboration with the Papua New Guinea (PNG) Public Health Department of what was then a Territory under Australian colonial administration, eventually led to a global UN programme for the elimination of brain damage due to iodine deficiency.

It began in 1963, when I was asked by the Editor of the Medical Journal of Australia to review a paper by Dr Terry McCullagh on the use of injections of iodized oil (Lipiodol®) in PNG.1 This was a new technology proposed to assist the control of the severe goitre problem in remote villages in the Highlands where iodized salt (the usual technology) could not be easily introduced. An initial controlled trial carried out by McCullagh, at the request of the then Director of Public Health Department (PHD), Dr John Gunther, showed that one injection of iodized oil would prevent goitre for up to 3 years.1 No laboratory work had been done to determine whether iodine deficiency was present nor just how effective the injection was in correcting the deficiency.

I visited PNG (Huon Peninsula) in October 1964 as a consultant to the PHD. I was impressed with the...
severity of the problem of goitre in the area. Laboratory studies were initiated in collaboration with the PHD.

These revealed very low urine iodine levels indicating severe iodine deficiency and correction of this deficiency for up to 5 years by a single dose of Lipiodol.²

Apart from the very large and frequent goitres to be seen in the villagers, there were many severely brain-damaged individuals who were also deaf-mute and often had a squint and a spastic weakness of the limbs. These were the ‘cretins’ being reported at the time from similar remote mountainous situations in South America (Andes), Africa (Zaire), China as well as earlier in Europe.³

There was at that time considerable dispute as to whether or not this condition was related to iodine deficiency—it had apparently spontaneously disappeared in various parts of Central and Southern Europe without any known correction of the iodine deficiency.

After the successful demonstration of the long duration of the effect of the single injection, I realized that with iodized oil, we had the means to carry out a controlled trial (which would not have been possible with iodized salt) to see whether correction of the severe iodine deficiency would prevent cretinism.

After approval by the PNG Research Advisory Committee, the trial was set up by Ian Buttfield from my department, with PHD staff in the Western Highlands north of Mount Hagen in August, September 1966. Alternate families were given injections of iodized oil and saline. As Dr Roy Scragg (Director of the Public Health Department) pointed out, it was not possible to inject the large-at-risk population all at once. So, it was reasonable to segregate some to the control group.

Follow-up of the trial was carried out by Dr Peter Pharoah,⁴ an experienced PNG medical officer who was seconded for this work by Dr Scragg at my request. As described in his paper, Pharoah made an assessment of brain development in the newly born infants without knowledge of which injections the mother had received (i.e. double blind). Particular attention was paid to the motor milestones, age of sitting up and walking, with evidence of squint and deafness reported by the mother and confirmed by a simple tuning fork test.

More than 3 years of careful and laborious work included Pharoah’s extensive climbing to reach the mountain villages for the repeated visits that were required for the assessment of new born infants. When the code was broken, there was no doubt that motor retardation (evident in the control group) had been prevented by injection of the iodized oil before pregnancy. Six of the seven retarded infants born to iodized oil-treated mothers were already obviously pregnant when injected and this may have been the case with the other one as the date was uncertain.⁴

After completion of the study, injections of iodized oil were then given to 120,000 people in the Highlands followed by an iodized salt programme.

The report of this work was published in The Lancet⁴ and was duly accepted as definitive.⁵ The spontaneous decline in Europe has since been attributed to diversification of the diet associated with economic and social development and the use of iodine supplements.

The finding clearly demonstrated for the first time the aetiology of the cretinism as fetal iodine deficiency in the first half of the pregnancy. The trial also showed the effectiveness of prevention by correction of the deficiency before pregnancy.

Animal models

During the 1970s, it became apparent to me that there was a great gap between our knowledge of the effects of iodine deficiency on brain development and its application in the developing world. More evidence was needed.

One of the factors leading me to become Chief of the Division of Human Nutrition (1976–85) at the Commonwealth Scientific and Industrial Research Organization (CSIRO) was the opportunity of developing an animal model in the sheep to confirm the effect of iodine deficiency on fetal brain development. This was duly done (for the first time) both in the sheep and then in a primate model (the marmoset monkey) over the period 1976–85 by an excellent CSIRO team with past experience of trace element (copper and cobalt) deficiencies in sheep.⁶

These animal studies indicated the significant effects of iodine deficiency on growth and development. The effects on the brain (cerebral cortex and cerebellum) were part of a spectrum of effects, including abortion and stillbirths as well as goitre, brain damage and growth retardation of the fetus.⁷

Clearly, the concept of iodine deficiency as ‘goitre’ was outmoded.

A new concept—the iodine deficiency disorders

A new concept, beyond that of ‘goitre and cretinism’, was needed which would better reflect the increase in knowledge that had occurred over the preceding 25 years particularly in relation to brain development. After much pondering, including two stimulating visits to China and with the sympathetic encouragement of colleagues, I proposed an epidemiological concept ‘iodine deficiency disorders’ (IDD) to denote all the effects of iodine deficiency on the growth and especially brain development of a population, which could be totally prevented by the correction of the iodine deficiency (Table 1). This concept was supported in a Lancet editorial.⁸ It was rapidly adopted
INTERNATIONALLY INCLUDING ADOPTION IN CHINA WITHOUT TRANSLATION. MY CHINESE COLLEAGUE POINTED OUT THAT CONFUCIUS WOULD HAVE APPROVED THE TERM AS IT REFERRED TO THE PRIMARY CAUSE AND WOULD THEREFORE LEAD TO APPROPRIATE MEASURES FOR CONTROL.

INTERNATIONAL ACTION

The announcement by the World Health Organization (WHO) of the global eradication of smallpox in 1980 encouraged me to point out the possibility of the elimination of IDDs with available technology using iodized salt or iodized oil.7 In Indonesia (1976–81) and China (1981–84), I became aware of the massive nature of the problem with the large populations at risk—subsequently estimated by WHO worldwide to be a total in excess of 2 billion at risk in 130 countries.7,8

Effective preventive measures were suitable for mass application (iodized salt or iodized oil). There were available methods for epidemiological monitoring and surveillance of the programme (salt iodine and urine iodine measurements) so that it could be shown whether the programme was effective.

In a report which I was asked to make to the United Nations Nutrition Sub-Committee, I noted the great delay in the application of existing knowledge on IDD and its prevention, to the detriment of the many millions in developing countries who were suffering irreversible damage to brain development. To help bridge this gap, I proposed that an expert consultative group of scientists and other public health professionals be established to assist in the development of IDD control programmes at the national levels in collaboration with WHO and United Nations International Children’s Emergency Fund (UNICEF).9

THE INTERNATIONAL COUNCIL FOR CONTROL OF IODINE DEFICIENCY DISORDERS

The decision to establish such a group, the International Council for Control of Iodine Deficiency Disorders (ICCIDD), was made in Delhi in March 1985, when I put the proposal to a group of 10 consultants and advisers with WHO and UNICEF representatives who were attending a WHO/UNICEF inter-country workshop on the control of IDD in South East Asia. This was followed by the inaugural meeting with official WHO and UNICEF support in 1986 in Kathmandu.10 A logo was adopted which emphasized the importance of the brain. I was appointed Executive Director of the ICCIDD (1986–95) and then Chairman (1995–2001).

The ICCIDD now consists of a multidisciplinary international expert network of 700 endocrinologists, epidemiologists, nutritionists, public health administrators, technologists, communicators, economists and other experts from 100 countries, with a majority from developing countries, who are committed to assisting national governments and international agencies in the development of national programmes for the elimination of IDD as a public health problem.11

I adapted my previously proposed social process ‘wheel’ model for the national IDD elimination programme.9 Particular importance was given to political will, which has been obviously lacking in the past, but has now been mobilized through the UN system, particularly through the World Summit for Children, held at the UN in 1990 with a Declaration signed by 71 heads of state and eventually by 88 other governments. This Declaration accepted a series of goals for the better health and education of children throughout the world, including the virtual elimination of IDD by the year 2000.12

Since 1986, the ICCIDD has held a series of regional meetings with WHO and UNICEF designed to foster the development of these National Control Programmes. These meetings have been attended by Ministry of Health representatives from countries of the region.

A later report (1999) indicated that of the 130 countries that had a significant IDD public health problem, two-thirds had universal salt iodization programmes in place. From 1990 to 1998, the number of countries

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<th>Table 1 The IDDs</th>
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<tr>
<td><strong>Fetus</strong></td>
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<td>- Abortions</td>
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<td>- Stillbirths</td>
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<tr>
<td>- Congenital anomalies</td>
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<tr>
<td>- Increased perinatal mortality</td>
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<tr>
<td>- Neurological cretinism: (mental deficiency, deaf-mutism, spastic diplegia, squint)</td>
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<tr>
<td>- Hypothyroid cretinism (dwarfism, mental deficiency)</td>
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<td>- Psychomotor defects</td>
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<tr>
<td><strong>Neonate</strong></td>
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<td>- Goitre</td>
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<tr>
<td>- Hypothyroidism</td>
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<td><strong>Child and adolescent</strong></td>
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<td>- Goitre</td>
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<td>- Hypothyroidism</td>
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<td>- Impaired mental function</td>
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<td>- Retarded physical development</td>
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<tr>
<td><strong>Adult</strong></td>
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<tr>
<td>- Goitre</td>
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<tr>
<td>- Hypothyroidism</td>
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<tr>
<td>- Impaired mental function</td>
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<tr>
<td>- Iodine-induced hyperthyroidism</td>
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<tr>
<td><strong>All ages</strong></td>
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<td>- Increased susceptibility to nuclear radiation</td>
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with salt iodization programmes had increased from 46 to 95. By 1998, household coverage of iodized salt was estimated to be 68%. This compares with <20% before 1990.

This result reflects the political impact of the World Summit for Children and the work of the ICCIDD at regional and country levels in association with WHO and UNICEF. This is an achievement that relates to the World Summit Goal of the virtual elimination of IDD by the year 2000.

However, there is a need to ensure the sustainability of this achievement—this depends on epidemiological surveillance with urine iodine measurements to establish the absence of iodine deficiency. Sustainable elimination of IDD is only possible if this continues—recurrence can and has readily occurred.

At the 2005 World Health Assembly (WHA), a resolution proposed by Canada and Australia was adopted requiring countries to report to the WHA for the monitoring of their programmes for the elimination of iodine deficiency in 2007 and every 3 years thereafter. This resolution provides the necessary political support for future sustainability of the programmes. Furthermore, WHA resolutions on sustaining the elimination of IDD were passed in 2007 and 2010.

Conclusion
It has been a great experience to assist in the development of a UN programme for the elimination of iodine deficiency as the most common preventable cause of brain damage. This programme has been made possible by targeted research which established the relationship between iodine deficiency and brain damage. This research included the controlled trial in the field (PNG) followed by studies in animal models. Rapid development of the elimination programme has been made possible by the effectiveness of iodized salt as a population measure and the availability of a simple laboratory method for the determination of urine iodine as a marker for iodine deficiency and its correction in populations. A dedicated group of multidisciplinary professionals in the ICCIDD has provided the scientific leadership in collaboration with national governments, WHO and UNICEF assisted especially by the aid programmes of Australia, Canada, Holland and the World Bank.

I believe the non-governmental organization (NGO) model of the ICCIDD is relevant to many other international health problems. In the ICCIDD, a multidisciplinary group of concerned scientists and public health professionals have come together to define the problem and then develop a programme designed to solve the problem in collaboration with the UN agencies—in the case of IDD it has been WHO and UNICEF.

As pointed out at the 1999 World Health Assembly by the Director General of WHO (Dr Gro Brundtland), the elimination of brain damage due to iodine deficiency will be a global health triumph comparable with the eradication of smallpox and the elimination of polio.

Conflict of interest: None declared

References