Iodine content of infant formulas and iodine intake of premature babies: high risk of iodine deficiency

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Abstract

As part of a study of thyroid function in premature babies, the iodine content of their mothers' breast milk, that of 32 formulas from different brands used in Spain, and that of 127 formulas used in other countries was determined. Breast milk contained more iodine - mean (SEM) 10 (1) $\mu\text{g}/\text{dl}$ - than most of the formulas, especially those for premature babies. Iodine intakes were therefore below the recommended daily amount (RDA) for newborns: babies of 27-30 weeks' gestational age took 3.1 (1.1) $\mu\text{g}/\text{day}$ at 5 days of age and 29.8 (2.7) μg by 2 months of age.

This problem is not exclusive to Spanish premature babies as the iodine content of many of the formulas on sale in other countries was also inadequate. It is concluded that preterm infants who are formula fed are at high risk of iodine deficiency.

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The trace element iodine is essential for the synthesis of thyroid hormones. Iodine deficiency leads to a wide variety of disorders (iodine deficiency disorders or IDD). Their severity is related not only to the degree of deficiency, but also to the developmental phase during which it is incurred.^{1,2} Thus severe iodine deficiency in the mother leads to increased rate of abortion, perinatal death, and infant mortality, and to babies born with central nervous system defects. These range from severe mental retardation, deaf-mutism, and spasticity to a milder decrease in intellectual performance.

Iodine deficiency is recognised as a major cause of preventable mental retardation throughout the world. IDD disappear when the deficiency is corrected. The magnitude of the problem, and the ease with which it can be corrected, led the Forty Third World Health Assembly to urge its elimination by the year 2000.³ The United Nations convened a World Summit for Children in 1990; 129 countries have now signed the ensuing declaration, which starts with an initial universal appeal to give every child a better future. It noted that 'enhancement of children's health and nutrition is the first duty, and also a task for which solutions are now within reach'. The Summit

adopted a plan of action, which included virtual elimination of IDD.³

To reach such a goal, the minimum daily dietary iodine allowance should start with an intake of 175 μg a day in pregnant women, rising to 200 μg a day during breast feeding.⁴ The recommended minimum daily intake for pregnant women has recently been increased to 200 μg .⁵ This ought to ensure that the maternal thyroid synthesises enough hormone for her needs and those of the developing fetus, and that there is an adequate supply of iodine for fetal thyroid function, both in utero and during lactation. 'Breast milk is the best source of iodine for the infant and exclusive breast feeding till 4-6 months should be encouraged', according to recommendations on iodine nutrition for mothers and babies in Europe.⁵

Even if the mother's intake is adequate, the infant might be iodine deficient when breast feeding is not possible. The iodine intake of newborns is then entirely dependent on the iodine content of the formulas used to feed them. The risk of iodine deficiency increases further in the case of premature babies: they have been unable to accumulate the amount of iodine found in term newborns, and they are often not able to breast feed. The minimum recommended daily amount (RDA) for iodine was established by the United States National Academy of Sciences as 40 μg for babies aged 0-6 months, 50 μg for those aged from 6 months to one year, 70 μg for children between 1 and 3 years (table 1).⁴ Similar recommendations were made by the American Academy of Pediatrics⁶ and the European Society for Paediatric Gastroenterology and Nutrition (ESPGAN).⁷ To meet these RDAs, the American Academy of Pediatrics recommended that the minimum iodine content of preparations for term newborns should be 5 $\mu\text{g}/100$ kcal, equivalent to 3.5 $\mu\text{g}/\text{dl}$, and considered the same amount to be adequate for premature infants.⁶ ESPGAN considered that term newborn babies would require 45 μg a day and recommended a minimum iodine content for formula of 3.5 $\mu\text{g}/\text{dl}$.^{7,8} The ESPGAN recommendation for formulas for preterm infants is 7 $\mu\text{g}/\text{dl}$.⁹ The European Communities Commission also recommended 3.5 $\mu\text{g}/\text{dl}$ for start and follow up formula preparations,¹⁰ but made no recommendations for premature babies. The RDAs for different age groups have recently been revised⁵ to 90 μg a day, from birth up to 6 years of life

Table 1 Recommendations for minimum daily iodine intake ($\mu\text{g/day}$)

Group	Age	A: before 1992	B: from 1992
Preterm infants		>30 $\mu\text{g/kg/day}$	
	0–5 months	35–40	90
	5–12 months	50	90
	1–3 years	70	90
	4–6 years	90	90
Adults	7–10 years	120	120
		150	150
	Pregnant women	175	200
	Lactating women	200	200

A: RDA from Food and Nutrition Board of the National Academy of Sciences,⁵ American Academy of Pediatrics,⁷ and ESPGAN Committee on Nutrition.^{8,9}

B: Recommendations on iodine nutrition made by ICCIDD.⁶

(table 1). Taking into consideration new information on iodine metabolism in premature and term newborn babies,^{11 12} the iodine content of formulas for premature newborns needs to contain 20 $\mu\text{g/dl}$ and that of follow up preparations 10 $\mu\text{g/dl}$. We will refer here to these new recommendations as those of the ICCIDD (International Committee for the Control of Iodine Deficiency Disorders).

The present study was performed to assess both the iodine content of preparations which are currently used to feed premature babies, and to determine the actual iodine intake of the babies using them. Although most of the information has been obtained for babies from one country (Spain), formula preparations from other countries have also been studied. The main conclusions drawn for Spain also seem to pertain for premature babies from other countries as well.

Methods

As part of a study on the thyroid function of premature babies, performed on 115 infants in the neonatology unit of the La Paz Hospital in Madrid, samples of the different formulas used over a one year period were collected directly from the bottle, when fed to babies of different postnatal ages. Infants exposed to external sources of iodine as a result of radiological examinations were excluded from the study. During the study period iodine-containing topical antiseptics were banned from the neonatology unit. The exact volume taken over a 24 hour period was recorded in each case. The samples had been reconstituted in the hospital kitchen as 14% dilutions in boiled water. All the different types of formula used during this period were also obtained in powdered form and reconstituted in the laboratory as 14% dilutions, using distilled water.

Using Student's paired *t* test there was no difference in iodine concentration between the ready-to-feed samples and those prepared in the laboratory, so results have been evaluated as a whole. Data were obtained for 162 samples of formulas for premature infants, 77 samples of start formulas, and 55 samples of special (medical) formulas. These samples entailed nine different brands, comprising 32 different formulas available in Spain. These were manufactured by Abbott (*n*=1), Alter (*n*=2), Mead-Johnson (*n*=2), Milupa (*n*=7),

Nestlé (*n*=7), Nutricia (*n*=3), Ordesa (*n*=3), Uniasa (*n*=4), Wander-Sandoz (*n*=3).

Formulas from the same and different brands were also obtained from 12 other countries (Czech Republic, Finland, France, Greece, Italy, Japan, Norway, Poland, Switzerland, and the United States of America). There were 103 samples of formulas (65 samples from start formulas, 21 samples from follow up formulas, 19 samples from formulas for premature babies and 35 samples of special formulas). Data on the iodine content of formulas used in Austria, Canada, Denmark and Germany were kindly made available to us for this report.

Seventy one samples of breast milk were collected in sterilised plastic bottles from 34 of the mothers of the premature babies (less than 36 weeks of gestation) included in the study. Thirty four were obtained during the first week after delivery, 15 between the second and fourth weeks, and 14 between the first and second month. Twenty one samples were also obtained from 13 mothers of full term infants – 13 samples at one week and eight samples at one month after delivery.

The iodine concentration was determined using a modification of the method described by Benotti and Benotti¹⁴ for serum, with duplicate 40 μl aliquots of each preparation being digested in 2 ml of chloric acid. This method determines the total iodine content of milk, irrespective of its initial chemical form. The interassay and intra-assay coefficients of variation were 14.7 (SD) (6.7)% and 12.5 (1.8)%, respectively.

Serum thyroid stimulating hormone (TSH) (Dynotest TSH; Henning, Berlin GMBH), thyroxine (T4) and tri-iodothyronine (T3) (radioimmunoassay KIT; Clinical Assays), free thyroxine (FT4) (Two Step Gammacoat Free T4 RIA KIT; Clinical Assays) activities were measured in duplicate by specific radioimmunoassays. Thyroglobulin was measured by IRMA (Dynotest Tg; Henning, Berlin GMBH). When a small blood volume was obtained, only FT4, T3, and thyroglobulin were measured.

Data were subjected to one way analysis of variance. The significance of the difference between the groups was identified using the

Figure 1 Mean (SEM) iodine concentrations in the milk from mothers of premature and term infants, obtained about one, three, and six weeks after delivery.

Newman-Keuls test for multiple comparisons. All calculations were performed as described by Snedecor and Cochran.¹⁵ Multiple regression and partial correlation analysis were performed using the SPSS program; the covariance analysis was done using the SIGMA program.

Results

Figure 1 shows the concentration of iodine in the milk from mothers of premature and term babies at different postnatal ages. No significant differences were found between samples from women after premature and term delivery, or between different times during the breast feeding period. The overall mean (SEM) value ($10.0 (1.0) \mu\text{g/dl}$) will therefore be used for comparisons with the iodine content of the different formulas.

IODINE CONTENT OF PREMATURE AND INFANT FORMULAS AND IODINE INTAKE

Figure 2 shows the iodine content of different formulas for premature infants, start, and follow up formulas, and special (medical)

formulas, used over a one year period compared with the iodine content of their mothers' milk. In most of the preparations the iodine content was significantly lower than that of human milk. Although the iodine content of most start, follow up, and special formulas was similar to that recommended by ESPGAN ($3.5 \mu\text{g/dl}$), it was usually lower than the ESPGAN recommendation for premature babies ($7 \mu\text{g/dl}$). The iodine content of different brands of the same type of formulas (for premature babies, follow up, etc) was, in most cases, very similar. However, different types of formulas from the same brand may have different iodine contents: thus in some cases the iodine content of a start formula is adequate, whereas that of the formulas for premature infants might be very low.

The iodine intake of the premature babies was directly related to the iodine content of the formula and to the volume of milk ingested daily. The latter is related to the postnatal age of the premature baby. We observed that very small premature babies (27–30 weeks' gestational age) ingested about 70 ml/kg six days after birth, 105 ml/kg at 3 weeks of postnatal age, 150 ml/kg by 2 months, and about 175

Figure 2 Mean (SEM) iodine content of different formulas used for premature infants (panel A), start (panel B), follow up (panel C), and special (panel D) formulas, used over a one-year period in Madrid. The numbers in parentheses at the left of the data bars correspond to the number of preparations, followed by the number of different samples for the brand identified by the following initials: A=Alter; AB=Abbott; M-J=Mead-Johnson; M=Milupa; N=Nestlé; Nu=Nutricia; P=Puleva; O=Ordesa; W=Wander-Sandoz. The shaded area corresponds to the 95% confidence interval for the iodine content of maternal milk, as assessed from the data shown in fig 1. The arrow indicates the minimal iodine concentration recommended by ESPGAN.^{7,8}

Figure 3 Panel A shows the mean (SEM) 24 hour iodine intake of premature infants formula fed at different postnatal ages. Panel B shows the corresponding values for premature infants on mixed breast and formula milks at the same postnatal ages. Panel B includes only data from infants receiving more than half their intake as maternal milk. The shaded area indicates the recommendations for iodine intake (35–40 µg a day).^{4,7,8} The 1992 ICCIDD recommendations would be much higher, at 90 µg per day.¹² The data of the premature babies have been grouped according to their gestational age (GA) at birth.

ml/kg by three months. They do not ingest the recommended 150–200 ml/kg until they are more than 1 month old. Less premature babies (31–36 weeks' gestational age) were drinking about 100 ml/kg six days after birth, 150 ml/kg by three weeks of age, and 150–200 ml/kg between 1 and 2 months of age. The volumes of milk ingested were mainly related to their body weight, and these were lower than recommended until the baby weighed about 2 kg. Figure 3 shows the iodine intake of premature babies at different postnatal ages. The actual iodine intake is lower than the RDA in most groups of premature babies taking formulas alone for at least one month after birth, especially in the case of those aged 27–33 weeks' gestation. However, the recommended iodine intake was reached sooner by premature babies on 50% breast milk or more. Again, the 27–30 weeks' gestational age group has the lowest intake, the daily volume ingested is directly proportional to their body weight

($p < 0.01$). The iodine intake of the sick premature babies was even lower than that of weight matched healthy babies. None of the premature babies had an iodine intake approaching the ICCIDD recommendation of 90 µg a day.

Figure 4 shows the mean iodine content for different types of formulas in countries other than Spain. Again, preparations for premature babies and special formulas fail more often to reach the ESPGAN or ICCIDD recommendations for iodine content than the start formulas.

We did not find any significant differences in the iodine content among 12 different brands: the variability around the mean values for each brand was very high. For 32 preparations for one brand, for instance, values ranged from 1.0 to 15.0 µg/dl. We have already commented that the iodine content of different types of preparations from the same brand may be different, and this is also true of those sold in other countries. Another factor increasing vari-

Figure 4 Mean (SEM) iodine content of different types of formulas used in Spain and other countries. AT=Austria; CA=Canada; CH=Switzerland; CK=Czech Republic; DE=Denmark; ES=Spain; FI=Finland; FR=France; GR=Greece; IT=Italy; JP=Japan; NO=Norway; PO=Poland; USA=United States of North America. As formulas from the same brand may have different names in different countries, the data were grouped according to type. The numbers in parentheses at the left of the data bars correspond to the number of preparations, followed by the number of different samples. The arrows indicate the minimal iodine concentration recommended by ESPGAN^{7,8} and ICCIDD.¹² ICCIDD has not formulated a recommendation for special formulas. To convert the iodine concentrations into µmol/l, multiply the tabular values by 0.08.

Table 2 Mean (SEM) iodine content of infant formulas used in different countries

Country	No of participants	Iodine content ($\mu\text{g/dl}$)	Range
Austria	16	6.6 (1.0)	3.3–17.0
Canada	18	9.3 (0.8)	4.0–14.0
Czech Republic	3	8.7 (2.2)	6.0–14.0
Denmark	8	5.5 (1.6)	2.0–13.7
Finland	3	9.0 (1.0)	8.0–10.0
France	17	10.5 (0.8)	4.0–15.0
Germany	5	7.9 (1.0)	5.9–10.4
Greece	3	12.0 (1.8)	9.0–15.0
Italy	16	7.5 (0.8)	2.0–12.0
Japan	5	8.8 (1.6)	4.0–12.0
Norway	2	8.0 (5.7)	4.0–12.0
Poland	2	4.5 (0.7)	
Spain	32	6.5 (0.4)	1.5–11.0
Switzerland	15	9.2 (0.8)	5.0–13.0
United States of America	4	13.5 (1.6)	5.0–13.0

To convert the iodine concentration into $\mu\text{mol/l}$, the tabular values should be multiplied by 0.08. Results of the one way ANOVA: $F_{(13,127)}=4.57$; $p<0.001$.

ability is the country where the formula is sold (table 2). The large variability in the data for the same country is related to the fact that different types of formulas from different brands were included in the calculation of the mean value: although the iodine content of special formulas was not significantly different from that of start formulas sold in the same country, the iodine content of formulas for preterm infants was often lower than the recommended amount. Despite this variability, there were differences between countries, irrespective of brand and type of formula. Thus as a whole, among European countries formulas contain as much iodine in France, Greece, and Switzerland as those used in Canada, Japan, and the United States of America; the iodine content is significantly lower in formulas from Austria, Denmark, Germany, Italy, and Spain whether or not the data of formulas for preterm babies are included. This cannot only be due to the preferential use of formula in each country, because the iodine content of formulas from the same brand may vary between countries.

The iodine content of Mead-Johnson preparations, for instance, is significantly lower in Spain (2.2 (0.3) $\mu\text{g/dl}$) than in Canada (7.2 (1.0) $\mu\text{g/dl}$), France (10.0 (0.5) $\mu\text{g/dl}$) and the United States (12.0 (1.7) $\mu\text{g/dl}$); that of Nestlé preparations is significantly higher in France (14.0 (0.0) $\mu\text{g/dl}$) and Switzerland (10.6 (3.0) $\mu\text{g/dl}$) than in Austria (4.0 (0.5) $\mu\text{g/dl}$), Italy (7.0 (3.5) $\mu\text{g/dl}$) and Spain (6.4 (2.3) $\mu\text{g/dl}$); and that of Milupa preparations is lower in Austria (7.3 (1.6) $\mu\text{g/dl}$), France (6.0 (1.7) $\mu\text{g/dl}$), and Spain (5.1 (2.0) $\mu\text{g/dl}$) compared with Greece (13.5 (2.1) $\mu\text{g/dl}$), Italy (9.0 (3.5) $\mu\text{g/dl}$), Germany (9.9 (2.1) $\mu\text{g/dl}$) and Switzerland (8.7 (3.2) $\mu\text{g/dl}$). The iodine content of start and special formulas from different brands and different countries tends to be similar and more often meets the ESPGAN recommendations than do the preparations for premature babies. For these there is a much greater variability, both between brands and between countries. These differences might be related to different legislation in different countries.

THYROID FUNCTION TESTS

Correlations were found between iodine intake and circulating T3 ($r=0.3$; $p<0.001$), FT4 ($r=0.80$; $p<0.001$), thyroglobulin ($r=-0.3$; $p<0.001$), and thyroid stimulating hormone ($r=-0.3$; $p<0.05$); iodine intake and postmenstrual age ($r=0.58$; $p<0.001$); postmenstrual age and T3 ($r=0.28$; $p<0.01$), T4 (0.17; $p<0.05$), thyroglobulin ($r=-0.30$; $p<0.01$), but not between postmenstrual age and FT4 or thyroid stimulating hormone.

The correlations between iodine intake and postmenstrual age and between postmenstrual age and T3 (or T4, or thyroglobulin) could obviously be influencing the correlation between the several parameters of thyroid function and iodine intake. To assess whether the correlations between iodine and thyroid indicators are merely a consequence of the influence of postmenstrual age on iodine intake and several parameters of thyroid function, or whether there is an effect of the iodine intake on thyroid function independent of the degree of maturation of the premature infant, we analysed the results by multiple regression, partial correlation, and by covariance.

We used only the data from those cases in which all variables had been measured; those cases where one or more variables were missing were omitted from the study. This avoided different variables being assigned greater weight. We also omitted the data from very sick infants to exclude any changes in thyroid function caused by different pathologies. These criteria reduced the study to 90 cases.

Results obtained by multiple regression and partial correlation analysis were quite comparable and showed that iodine intake is highly correlated to postmenstrual age, but that, independently of age, it is also correlated positively with FT4 and T3, and negatively with thyroglobulin.

Covariance analysis was applied to iodine intakes below or above 40 $\mu\text{g/day}$. This iodine intake is the previous RDA. Postmenstrual age was entered as a control variable. Parameters of thyroid function were classified into three groups according to gestational age and corrected by the program for postmenstrual age. The adjusted means (SEM) thus obtained are shown in fig 5, as well as the significant differences obtained between the group of similar gestational age with iodine intakes above the RDA compared with the group with lower intakes. Most babies of the 31–36 weeks in gestational age groups with an iodine intake below 40 $\mu\text{g/day}$ have decreased serum T3 and FT4, and higher serum thyroglobulin and TSH values, than those with intakes above the RDA. Circulating T3 and thyroglobulin were also different in the 27–30 weeks in gestational age premature babies.

Discussion

The iodine intake of newborn babies is entirely dependent on the iodine content of breast milk or of formula preparations. The criteria used initially to define the RDA of term newborns as 30–40 μg a day were based on the amounts

Figure 5 Mean values of circulating FT4, T3, thyroglobulin, and TSH adjusted by covariance analysis to postmenstrual age, for premature babies of different gestational ages with iodine intakes below or above 40 µg/day. *Differences which are significant at $p < 0.05$.

which would be needed for the synthesis of the iodinated hormones metabolised by the term newborn, the likely amount lost via the urine, faeces, and saliva, and the amount needed for the build up of thyroid stores of iodinated compounds. To define the minimum iodine concentration for formula preparations for newborn babies, it was reasoned that their iodine content should be the same as that of breast milk from normal women, a value of 7 µg/dl being taken as the mean value.⁹ This led to a recommendation of 3.5 µg/dl of iodine in reconstituted formula preparations. On this basis, however, term newborns would not reach the recommended intake until they drank 1000 ml or more of formula.

Moreover, mean values for the iodine content of breast milk vary (table 3). Values may vary from 1.2 (0.1) µg/dl in Jena (Germany), known as an iodine deficient area, to 17.8 (1.1) µg/dl in the United States, where the population is considered to receive an adequate iodine intake. The value of 7 µg/dl used by ESPGAN⁹ as a reference for the iodine content of breast milk is lower than the values actually found in women from Madrid and Brussels. The latter have clearly been shown to have moderate iodine deficiency,^{12 23} especially during pregnancy.²⁴ Thus the recommenda-

tion of 3.5 µg/dl for term newborn formulas would lead to an iodine intake equivalent to that of babies born in areas with moderate iodine deficiency.

The recommendation for premature formulas was increased to 7 µg/dl, no explanation being given as to how this value was reached.⁹ On this basis, the 27-30 weeks in gestational age preterm babies would have to ingest more than 500 ml of formula daily to reach the RDA of 40 µg for iodine. The actual volumes, however, which were fed to such babies were lower than expected at least at one month after birth,

Table 3 Mean (SEM) iodine content of breast milk as reported for women from different countries

Country	City	No of samples	Human milk (µg l/dl)	References
Germany	Friburg	41	2.5	16
	Jena*	55	1.2 (0.1)	16 17
Belgium	Brussels	91	9.5 (0.6)	16 17
Spain	Madrid (1988)	69	7.7 (0.9)	18
	Madrid (1991)	52	10.0 (1.0)	
France	Paris	68	8.2 (0.5)	19
Italy	Verona	77	5.4 (0.69)	20
	San Angelo*	59	2.7 (0.3)	16 17
	Sicily			
Sweden	Stockholm	60	9.3	16
USA		61	17.8 (1.1)	21
			15.3 (1.0)	21
Canada			11.0	22

*Areas with endemic goitre.

or longer in the case of the 27–30 weeks in gestational age premature babies. If the formula preparations contained the recommended amount of iodine their iodine intake would be about 5 µg, 9 µg, and 22 µg a day, respectively. Moreover, as many of the preparations for premature babies used in the present study did not contain the recommended iodine content, the actual iodine intake of the 27–30 weeks in gestational age premature babies was 3.1 (1.1) µg/day at 6 days of age, 7.4 (5.5) µg at 3 weeks, and 17.1 (2.9) µg at one month, amounts which are clearly far below the RDA.⁴ The 40 µg RDA had not yet been reached at 2 months of age, when the mean intake was still only 29.8 (2.7) µg. Findings were similar in premature babies of 31–36 weeks' gestational age, who did not reach the above recommended intake until they were 1 month of age, or older.

The previous recommendations for premature babies, apparently derived from those made for term newborns, implied that iodine requirements would be proportional to the weight of the preterm infant, and would thus be lower with increasing prematurity. This, however, has clearly been contested by several subsequent studies,^{11 12 25} which show that iodine metabolism in premature babies presents special features compared with term neonates. For example, Delange *et al*¹² found that the urinary iodine excretion in 29 preterm babies was 1.5 times that of 20 term neonates; the iodine in faeces were very low; and premature babies were frequently in negative iodine balance, attributed to immaturity both of the kidney and the thyroid. As a consequence, and taking into consideration that the growing infant has to build up iodine stores in its thyroid, Delange proposed that to reach a positive iodine balance, the preterm babies would need a minimum of 30 µg/kg iodine per day, which is double the minimum amount (15 µg/kg a day) for term babies.^{11 12} To ensure a positive balance, the minimum RDA would be 90 µm a day (table 1). The recent consensus is that formulas for premature babies should contain at least 20 µg/dl iodine, and start formulas at least 10 µg/dl iodine.¹² Even with this higher iodine content, very small premature babies receiving formula feeds would not reach an intake of 90 µg a day, but they would at least ingest 30–40 µg. These new recommendations are well below the limit (100 µg/kg/day) set by Fisher as the maximum iodine intake compatible with normal thyroid function in premature and term newborns.²⁶

The data presented here show that many preparations presently on the market do not even contain the minimum amount of iodine recommended before 1992. This is especially so for preparations used for preterm infants. Only a few contain the 10 µg/dl now recommended for start formulas, none reaching the 20 µg/dl recommended for premature babies.⁵ Even if the preparations did contain the previously recommended 7 µg/dl, premature babies in the present study did not ingest 40 µg iodine daily until they were more than 2 months old. Like Delange *et al*, we

believe^{11 12 16 17} that the premature babies in our study were iodine deficient, and that this could affect their thyroid function. The results obtained show that iodine intake is highly correlated with postmenstrual age, but that, independent of age, it is also positively correlated with TF4 and T3, and negatively with thyroglobulin. Most babies with an intake below 40 µg/day had lower circulating FT4 and T3, and higher thyroglobulin and TSH than babies with an iodine intake above the RDA. Again, this cannot be entirely attributed to their degree of immaturity. In the present study increased thyroglobulin activities seem to be a clear sign of thyroid stimulation.²⁷

Iodine deficiency in preterm newborns increases the risk of hypothyroidism.²⁵ Alterations in thyroid function in premature babies, leading to low circulating T4 or T3, have been associated with impaired neural maturation, as measured by nerve conduction velocity²⁸ and by lower scores in the Bayley mental and motor scales.²⁹ Iodine deficiency may well contribute to inadequate thyroid hormone activity in premature babies, but could easily be avoided.

In conclusion, in view of more reliable recent information on the thyroid function and physiology of preterm babies, the iodine content of many infant formulas seems to be inadequate. Most premature babies in many countries might not be ingesting the previously recommended amount of 40 µg a day, even fewer the 90 µg recommended in 1992 at a meeting sponsored by the ICCIDD, the World Health Organisation, and the European Community.⁵ Producers of such preparations should be urged to comply with the new recommendations and to specify that their products do so, irrespective of the type of formulas and the country where their products are being used. Premature babies in many countries are now iodine deficient, precisely at a stage of development that is highly sensitive to changes in thyroid function. This may occur in countries where the iodine intake of the rest of the population is adequate.²³

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