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Iodine requirements during pregnancy, lactation and the neonatal period and indicators of optimal iodine nutrition

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Abstract

Objective: This paper re-evaluates the requirements for iodine during pregnancy, lactation and the neonatal period, and formulates original proposals for the median concentrations of urinary iodine (UI) that indicate optimal iodine nutrition during these three critical periods of life. This paper also discusses the measurements that are used to explore thyroid functions during the same periods.
Design: An extensive and critical review of the literature on thyroid physiopathology during the perinatal period.
Setting: Human studies conducted in various regions throughout the world.
Subjects: Pregnant women, lactating women, and newborns.
Results: The following proposals are made after extensive review of the literature: the requirement for iodine by the mother during pregnancy is 250-300 μg day^{-1}; during lactation the requirement is 225-350 μg day^{-1}; and during the neonatal period the requirement of the infant is 90 μg day^{-1}. The median UI that indicates an optimal iodine nutrition during these three periods should be in the range of 150-230 μg day^{-1}. These figures are higher than recommended to date by the international agencies.
Conclusions: Pregnant women and young infants, but especially the second group, are more sensitive to the effects of an iodine deficiency (ID) than the general population because their serum thyroid-stimulating hormone (TSH) and thyroxine are increased and decreased, respectively, for degrees of ID that do not seem to affect thyroid function in the general population. Systematic neonatal thyroid screening using primary TSH could be the most sensitive indicator to monitor the process of ID control.

Keywords
Iodine requirements
Pregnancy
Lactation
Neonates
Urinary iodine
Thyroid-stimulating hormone

Introduction

Iodine deficiency (ID) used to be a major public health problem. As recently as 1990, 28.9% of the world's population was at risk of a deficiency, 12.0% of the population exhibited goitre, 11.2 million individuals were affected by cretinism and another 43 million people had some degree of mental impairment due to ID[1]. Therefore, ID is the leading cause of preventable mental retardation during childhood. Concerted international action taken since 1990 has aimed at the sustainable elimination of ID disorders using salt iodisation as the main strategy[1,2]. Spectacular results have been achieved as the consumption of iodised salt has increased from some 5–10% of households in 1990 to 68% in 1999[3]. In countries where systematic and periodic monitoring has been used, these changes have resulted in a clear-cut improvement in iodine nutrition and thyroid function in the general population[4–6]. However, in their latest evaluation of the control of ID in the world, the World Health Organization (WHO) reported that in 126 out of the 192 members states that have data on urinary iodine (UI), only 67 had an optimal status of iodine nutrition (a median UI concentration of between 100 and 200 μg l^{-1}); 54 countries were still iodine deficient (median UI concentration <100 μg l^{-1}); and 4 countries had an excessive iodine intake (median UI concentration >200 μg l^{-1})[7]. Therefore, it appears that major additional efforts are still required in order to reach the goal of the sustained elimination of ID in the world.

However, even in countries that have achieved iodine sufficiency, the status of iodine nutrition in pregnant and lactating women may still be inadequate. For example, in the United States of America, where the status of iodine nutrition is adequate in the general population, with a median UI concentration of 145 μg l^{-1}, 6.7% of pregnant women are nevertheless affected by moderate to severe ID and have a UI concentration below 50 μg per l[8]. This is probably largely due to the fact that women are recommended to limit their intake of salt during pregnancy, which includes iodised salt, but also because of the metabolic changes that occur during pregnancy and

*deceased

lactation that result in an increased requirement for iodine[9–12]. Yet pregnant women are the most sensitive group in the population to the effects of ID, Maternal hypothyroxinaemia due to ID occurring early during gestation, even before the onset of foetal thyroid function, is the cause of irreversible brain damage in the foetus resulting in mental deficiency in the offspring[13–18]. Therefore, the question arises of how to ensure and assess adequate iodine nutrition during pregnancy.

The objectives of this paper are:

1. To review critically, the scientific literature on iodine requirements during pregnancy, lactation and the neonatal period.
2. To offer practical recommendations regarding the value of the indicators of optimal iodine nutrition during these critical periods of life, with particular emphasis on normative values of UI concentration.

Requirements for iodine during pregnancy, lactation and the neonatal period

Pregnancy

The requirement of a mother for iodine is increased during pregnancy as a result of at least three factors: (1) an increased requirement for thyroxine (T_4) in order to maintain normal metabolism in the mother; (2) a transfer of T_4 and iodide from the mother to the foetus; and (3) a supposed greater than normal loss of iodide through the kidneys due to an increase in the renal clearance of iodide[11].

Because of these three factors, the recommended dietary intake of iodine during pregnancy is higher than the value of 150 $\mu g\,day^{-1}$ recommended for non-pregnant adults and adolescents[19,20]. When the intake is below the critical threshold of 150 $\mu g\,day^{-1}$, the iodine balance during pregnancy becomes negative[21]. The WHO, the UNICEF and the ICCIDD[19] recommend a daily iodine intake of 200 $\mu g\,day^{-1}$ by pregnant women, a 33% increase. The Institute of Medicine (IOM) of the US Academy of Sciences recommends a higher intake of 220 μg per day[20], while other organisations recommend between 175 and 230 μg per day[22,23].

During pregnancy, the daily production of T_4 in order to maintain the euthyroidism in hypothyroid women increases by 10–150%, with a median increase of 40–50%[24–26]. This represents an additional 75–150 μg of T_4 day^{-1}, which requires and estimated 50–100 μg of iodine to make.

The amount of T_4 transferred from mother to foetus, including the period before the foetal thyroid gland starts to function, has not been quantified, but it has been estimated that up to 40% of the T_4 measured in cord blood at birth is of maternal origin (reviewed in reference 15).

The transfer of iodide from mother to foetus is also difficult to quantify, but three things need to be taken into consideration: that the iodine content of the foetal thyroid gland increases from $< 2\,\mu g$ at 17 weeks of gestation[27] to 300 μg at full term[28–31]; that the amount of iodine in foetal T_4 at term probably averages 500 μg[32]; and that the substitutive dose of T_4 in hypothyroid neonates is 50–75 μg per day[33,34]. From this, it can be estimated that the transfer of iodide from mother to foetus represents some 50 $\mu g\,day^{-1}$. The estimate made by the IOM is 75 μg per day[20].

It is often stated that the increase in the iodine requirement of mothers during pregnancy is largely due to a greater loss of iodide through the kidney caused by an increase in renal clearance[11,35–38]. This should serve to decrease the concentration of plasma inorganic iodide (PII) in serum. However, on the contrary, Liberman *et al.*[39] showed that there is no significant decline in the concentration of PII during pregnancy. In addition, as shown by the data summarised in Table 1 and reported by Dworkin *et al.*[21], almost all studies of UI concentrations during pregnancy have shown that, in a given environment, the excretion of iodide is almost the same in pregnant women, non-pregnant women and the general population, irrespective of the status of iodine nutrition in each population. Only the studies conducted in Ireland, the United Kingdom and Sri Lanka[40,41], in Hong Kong[42], and perhaps in Switzerland[43] have shown a clear-cut increase in UI excretion during pregnancy. The results reported in another Swiss study[44] are difficult to interpret because of the surprisingly low concentration of UI in a population known to be iodine sufficient[45]. On the other hand, some studies have shown that the UI concentration decreases during gestation[46–48]. Therefore, it appears that the concept of an increased urinary loss of iodine during pregnancy is not firmly established and certainly cannot be quantified.

Finally, it has to be emphasised that there are no data available on the possible storage or loss of iodide from the placenta itself.

Taking all these factors into consideration, it can be estimated that the additional requirement for iodine during pregnancy is at least 100–150 $\mu g\,day^{-1}$, or 250–300 $\mu g\,day^{-1}$ in total. The upper estimate is 100% greater than the 150 $\mu g\,day^{-1}$ recommended for non-pregnant women, and 33% greater than the 200 $\mu g\,day^{-1}$ suggested by the WHO, the UNICEF and the ICCIDD[19]. Consequently, the minimum requirement for iodine during pregnancy is at least 250 $\mu g\,day^{-1}$, and is probably in the range of 250–300 $\mu g\,day^{-1}$. This figure is higher than 220 $\mu g\,day^{-1}$ proposed by the IOM[20], which did not take into account the increased production of T_4 during pregnancy.

Lactation

Considering that the iodine content of breast milk in conditions of iodine sufficiency is in the range of

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Table 1 (a) Comparison of the median or mean (in boldface) urinary iodine (UI) concentration of pregnant women with the general population or with non-pregnant controls using data from countries with no iodine deficiency, (b) Comparison of the median UI concentration of pregnant women with the general population or with non-pregnant controls using data from iodine deficient (ID) countries, 1990–2003. The countries are listed in roughly descending order of the UI concentration of the general population.

Country	UI ($\mu g\,l^{-1}$) in general population or controls	No. of subjects	Study type[a]	Pregnant women		Reference
				Timing[b]	UI conc. ($\mu g\,l^{-1}$)	
Chile	None	19	S	T1	594[c]	39
				T2	469	39
				T3	786	39
				3 months PP	459	39
Iran	193–312	403	C	T1-3	186–338	55
Sweden		51	S	T1	180[c]	89
			S	T2	170	89
			S	T3	145	89
Sri Lanka	147		C	T1	181	41
			C	T2	136	41
			C	T3	154	41
USA	145	348	C	T1-3	141	8
USA	130	290	C	T1-3	148	90
USA		100	C	T1-2	149	92
Switzerland (2000)	115	511	C	T2 and T3	138	43
Switzerland (1992)	91[d]	153	C	T1-3	**205**[c]	44
		31	C	T1	**267**	44
		56	C	T2	**206**	44
		66	C	T3	**172**	44
		15	S	T1	**325**	44
		15	S	T2	**166**	44
		15	S	T3	**183**	44
Scotland	**138**	433	C	T1	**137**	91
Singapore	98	253	C	T3	124	93
Singapore		230	S	T1	107	42
				T2	116	42
				T3	124	42
				6 weeks PP	105	42
				3 months PP	104	42
Italy	46[c]	10	S	T1, T2 and T3	33[c]	66,94
Turkey	85[c]	80	S	T1-3	91[c]	95
Ireland	70	38	S	T1	135	40,41
		38	S	T2	125	40,41
		38	S	T3	122	40,41
		108	C	6 weeks PP	70	40,41
UK	73		C	T1	125	41
			C	T2	170	41
			C	T3	147	41
France	50–80[c]	306	S	T1	50	48
		224	S	T3	54	48
Belgium	50–75[c]	334	C	T1-2	50	46
		334	C	T2-3	45	46
		136	C	T1	56	46
		133	C	T2	50	46
		49	C	T3	50	46
Denmark	50[c]	26	S	T2	51	96
		26	S	T3	40	96
		26	S	1 week PP	30	96
		26	S	26 weeks PP	50	96
		26	S	52 weeks PP	58	96
			C	5 days PP	40	97
Sudan	76	47	S	T3	38	67
		47	S	3 months PP	51	67
		47	S	6 months PP	30	67
		47	S	9 months PP	63	67
New Zealand	24–47[c]	35	S	Monthly	24–52[c]	61
Italy	Marginal ID	67	C	T1 and T2	74	98
Italy	Moderate ID	18	C	T3	50[c]	99
Germany	Mild ID?	70	S	T1	55[d]	100
		70	S	11 days PP	50	100
Hungary	Mild ID	119	C	T1, T2 and T3	57[d]	101

[a] S, sequential, C, cross-sectional.
[b] T1, T2, T3, T1-2 or T1-3, trimesters of pregnancy; PP, *post partum*.
[c] $\mu g\,day^{-1}$.
[d] $\mu g\,g^{-1}$ creatinine.

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150–180 μg per l[49,50] (Table 2), and that some 0.5–1.1 l of milk is produced per day for the first 6 months of lactation, the daily excretion of iodine in human milk is estimated to be 75–200 $\mu g\,day^{-1}$. Consequently, the iodine required by a lactating woman is estimated to be 225–350 $\mu g\,day^{-1}$. The slight difference, if any, compared with the figure of 290 $\mu g\,day^{-1}$ recommended by the IOM[20], results from the use of recent data on the iodine content of breast milk[49,50].

Neonatal period

The iodine requirements of neonates and infants were first estimated to be equal to the mean iodine intake of exclusively breastfed neonates and young infants in iodine replete areas. Up to the late 1960s, the iodine content of breast milk of women in such areas was usually around 50 $\mu g\,l^{-1}$ (reviewed in references 49–51). Considering a daily intake of breast milk of 0.6–1.1 l by neonates and young infants, the assumption was made that an infant gets 30–50 μg iodine per day in milk from an adequately fed mother[52]. However, the iodine content of breast milk is critically influenced by the dietary intake of the pregnant and lactating mother, and of the general population, and recently much higher figures have been recorded[49,50]. For this reason, the iodine requirement of neonates has been evaluated from metabolic studies by determining the value that results in a situation of positive iodine balance, a state that is required in order to ensure a progressively increasing iodine pool in the thyroid gland of the growing infant. Such iodine balance studies were conducted in healthy preterm and fullterm infants aged approximately 1 month in Belgium, a country with a mildly iodine-deficient population[53]. These studies, reported extensively elsewhere[52], indicate that the iodine intake required to achieve a positive iodine balance is at least 15 $\mu g\,kg^{-1}\,day^{-1}$ in fullterm infants and 30 $\mu g\,kg^{-1}\,day^{-1}$ in preterm infants. This corresponds approximately to 90 $\mu g\,day^{-1}$ and is consequently twice as high as the 1989 US recommendations of 40–50 μg per day[54], but is still a bit lower than the present recommendation by the IOM of 110 μg per day[20].

Table 2 Selected examples of the iodine content of breast milk compiled from Semba & Delange[49] and Dorea[50].

Countries with no iodine deficiency	Mean or median concentration of iodine ($\mu g\,l^{-1}$)
Korea	892
Japan	661
	33–385
USA	146
	168
	124
	145
	145
Countries with mild to moderate iodine deficiency	
Germany	93
	15–150
Belgium	95
France	82
	77
	74
	70
Spain	108
	77
United Kingdom	70
Hungary	64
Guatemala	60
Philippines	57
Thailand	50
Italy	43
Countries with severe iodine deficiency	
Morocco	27
Ethiopia	5–16
Congo	15
	13

Indicators of iodine nutrition during pregnancy, lactation and the neonatal period

UI

Since more than 90% of the iodine absorbed by the body eventually appears in the urine, UI excretion is a good marker of recent dietary iodine intake[18]. This means that a median UI concentration ranging from 100 to 199 $\mu g\,l^{-1}$ in the general population is considered to indicate an adequate iodine intake and optimal iodine nutrition[19]. Since the requirement for iodine is increased during pregnancy, the median UI concentration during pregnancy that indicates optimal iodine nutrition needs to be higher than 100 $\mu g\,l^{-1}$. Table 1 shows data from published studies in several countries that compares the UI concentration of pregnant women with the same in the general population. In Table 1, the countries are arbitrarily listed according to a roughly decreasing iodine intake of the general population, starting with Chile[39], whose population is exposed to an excessive iodine intake based on criteria given by the WHO, the UNICEF and the ICCIDD[19], down to countries in which different degrees of mild to moderate ID have been documented. As indicated earlier, there is a striking similarity between the UI concentration of pregnant women and of the rest of the population in the same country, except in reports from Ireland and the UK[40,41] where values during pregnancy are markedly and systematically higher than in non-pregnant controls. For this reason, it appears difficult to derive a reference value for a UI concentration during pregnancy and lactation from the data collected in countries with no ID, because this value varies from 800 $\mu g\,l^{-1}$ in Chile[39] to 138 $\mu g\,l^{-1}$ in Switzerland[43], where the median UI in the general population is barely above the lower limit of normal. In Iran, where ID has been successfully eliminated[55], the median UI concentration of pregnant women in four cities was found to vary from 186 to 403 $\mu g\,l^{-1}$ (see paper by Azizi, this issue) and was roughly the same as values found in the general population in the same cities[56]. The values recorded in Iran during pregnancy are of the same order of magnitude

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as the 250–300 $\mu g\,day^{-1}$ recommended as a daily intake based on metabolic studies. And yet, in spite of these relatively high concentrations, Azizi *et al.*[56] point out that, even with such medians, some 8% of the values are still below the critical threshold of 100 $\mu g\,l^{-1}$ for non-pregnant adults. Azizi *et al.* suggest that the recommended dietary intake of iodine during pregnancy should be still higher[56]. However, it has to be recognised that this figure of 8% corresponds almost exactly to the percentage of values (7.2%) below the threshold of 50 $\mu g\,l^{-1}$, indicating at least a moderate ID in a general population when the median is between 100 and 200 μg per l[57]. This percentage is considered to be acceptable[57] considering the well-documented day-to-day variation in UI concentration, including during pregnancy[58–61].

Taking these facts and factors into consideration, it can be concluded that the recommended median value for UI concentration during pregnancy and lactation has to be based on theoretical grounds. If, as in non-pregnant adults, the recommended median UI concentration of 100–200 $\mu g\,l^{-1}$ corresponds to the recommended intake of 150 $\mu g\,day^{-1}$, the median UI concentration during pregnancy and lactation should be in the range of 225–350 $\mu g\,l^{-1}$. If, on the other hand, this recommended median was based on a recommended intake of 225–350 $\mu g\,day^{-1}$ and a mean daily urinary volume of 1.5 $l\,day^{-1}$, the UI concentration should be in the range of 150–230 $\mu g\,l^{-1}$, only slightly higher than the value recommended for non-pregnant adults.

It should be noted that the thyroid function and the thyroid volume remained normal during pregnancy in Iran[56] as well as in Chile[39] for the values of UI concentration twice as high as in Iran, which strongly suggests that these values are not excessive and not a potential source of side effects[62,63]. On the contrary, in all countries whose populations experience some degree of ID, where the issue has been investigated, thyroid function is critically impaired during pregnancy and in the neonate, even when it remains normal in the general population[64–68]. The anomalies are described in the next sub-section.

In summary, it appears that the recommended dietary intake of iodine during pregnancy of 250–300 $\mu g\,day^{-1}$ and during lactation of 225–350 $\mu g\,day^{-1}$, should be higher than proposed, especially by the WHO, the UNICEF and the ICCIDD[19], and that a median UI concentration in the range of 150–230 $\mu g\,l^{-1}$ would indicate optimal iodine nutrition during pregnancy and lactation.

Table 3 summarises data from papers published on the median UI concentration of neonates in countries or areas where the population is iodine sufficient and from countries with different degrees of ID. There is a large variation in values, even in iodine-sufficient countries, where concentrations range from 736 $\mu g\,l^{-1}$ in Hokkaido, Japan[69] where people have an extremely high iodine intake[70], to 96 $\mu g\,l^{-1}$ in Stockholm[71].

Again these data do not help substantially to identify the optimal UI concentration, therefore, it also has to be defined on the basis of theoretical considerations. Based on the iodine requirement of 90 $\mu g\,day^{-1}$ and a urine volume passed by neonates of about 0.4–0.5 l per day[72], the median UI concentration that indicates optimal iodine nutrition in neonates can be estimated to be about 180–225 $\mu g\,l^{-1}$, but ignoring the fact that the iodine balance of the neonate should also be positive in order to develop an iodine store in the thyroid gland. This concentration, which is higher than recommended for schoolchildren and adults, has been observed when healthy young infants are supplemented with a daily physiological dose of 90 $\mu g\,day^{-1}$ of iodine[73]. It is also the value reported in some parts of the United States in which the population is supposed to be iodine sufficient[74,75]. On the other hand, published studies in which the UI concentration has been determined simultaneously in mothers at delivery and in neonates during the first days of life[47,76,77] indicate that these concentrations are almost similar in mothers and neonates. Therefore, based on the assumption of an optimal UI in pregnant mothers, it can be estimated by extrapolation that the concentration of iodine in the urine of neonates should be around 150–230 $\mu g\,l^{-1}$, which is similar to the figure derived from the iodine requirements of the neonates.

The data reported from neonates in conditions of mild, moderate and severe ID are indeed much lower than ideal, such as $< 20\ \mu g\,l^{-1}$ in German neonates[78] before the partly successful implementation of a programme of voluntary salt iodisation[79]. It is particularly interesting to observe that this concentration progressively increased with time in both Germany and Belgium, for example, following the implementation of programs of iodine supplementation[79,80] or silent iodine prophylaxis respectively[81].

In summary, the recommended dietary intake of iodine in neonates is 90 $\mu g\,day^{-1}$ and the median UI concentration to be expected when this requirement is met is 180–225 $\mu g\,l^{-1}$, a value similar to the one recommended for pregnant women.

Measurements exploring thyroid function

The final objective of campaigns to correct an ID is not only to normalise the iodine intake and UI concentration, but also to correct or prevent abnormalities of thyroid function and the development of goitre[1,4,19]. The measurements used to test thyroid function and assess iodine nutrition are the concentration in serum of thyrotropin (TSH), total T_4 and/or free T_4, thyroglobulin (Tg) and triiodothyronine (T_3). To determine these variables requires blood, which is more invasive to collect than urine, especially for pregnant women and neonates.

The alterations of thyroid function during pregnancy that occur in conditions of ID are described and commented upon in detail elsewhere[82], and within this supplement to *Public Health Nutrition*. They are

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Table 3 Median or mean (in boldface) urinary iodine concentration in neonates in countries in three groups: A. Iodine sufficient; B. Mild to moderate iodine deficiency; and C. Severe iodine deficiency.

Country	Location (year)	*n*	Gestational age[a]	Urinary iodine ($\mu g\,l^{-1}$)	Range	Reference
A. Iodine sufficient						
Japan	Hokkaido	118	FT breastfed	736		69
	Hokkaido	182	FT bottle fed	521		69
Unites States	Boston	N/A	PT ≤ 36 weeks	148	16–510	102
	Torrance	50	FT	921		103
Canada	Toronto	81	FT	148		78
Netherlands	Rotterdam	64	FT	162		78
	Amsterdam	36	FT	**150**		104
Sweden	Stockholm	39	FT	112		78
	Stockholm	61	FT	96		71
B. Mild to moderate iodine deficiency						
Germany	Nine towns (1983)	461	FT	12–29		71
	West Berlin (1985)	87	FT	28		78
	Kiel (1992)	50	FT	33		105
	Frankfurt (1992)	21	FT	37		106
	West Berlin (1994)	177	FT	31		107
	East Berlin (1994)	213	FT	44		107
	Göttingen	22	FT	50		108
	Heidelburg	32	FT	**95**		109
Belgium	Brussels (1983)	103	PT & FT	35	10–150	103
	Brussels (1985)	196	FT	48		78
	Brussels (2000)	90	FT	86		110
Italy	Rome (1985)	114	FT	47		78
	Catania (1985)	14	FT	71		78
	Unknown (1995)	195	FT	56	10–950	111
	Milan (1995)	18	PT 30 weeks	**123**		112
	Turin (1995)	9	FT	67	10–162	113
France	Lille (1985)	82	FT	58		78
	Toulouse (1985)	37	FT	29		78
UK	Belfast (1993)	N/A	FT	**100**		114
Israel	Tel Aviv (1996)	55	PT 30–31 weeks		55–100	115
Czech Republic	Prague (1998)	50	FT	79		76
	Prisbam (1998)	50	PT	78		76
Hungary	Budapest (2002)	55	FT	35		116
	Gyor (2002)	65	FT	57		116
	Miskole (2002)	54	FT	59		116
	Nyiregyhaza	35	FT	75		116
C. Severe iodine deficiency						
Germany	Göttingen (1985)	81	FT	15		78
	Heidelburg (1985)	39	FT	13		78
	Freiburg (1985)	39	FT	11		78
	Iena (1985)	54	FT	8		78

[a] FT, fullterm; PT, preterm.
N/A, data not available.

characterised by a progressively decreasing concentration of free T_4 in serum and increasing concentrations of TSH and Tg during pregnancy, together with the development of thyroid hyperplasia. These abnormalities occur even in conditions of mild ID when they are not present in the general population in the same area, indicating the hypersensitivity of pregnant women to the effects of an ID[11,48]. They are corrected by giving physiological doses of iodine (reviewed in reference 83) and can be prevented even in conditions of severe ID when injections of iodised oil are given before, or even during, gestation. However, the neurological defects of endemic cretinism are prevented only when the oil is administered before pregnancy begins[4]. The value of systematically determining the serum TSH concentration of pregnant women may not be justified in a country in which the population is generally iodine sufficient[84].

In contrast to the situation in mothers, the alterations of thyroid function that occur in neonates experiencing ID are qualitatively similar but quantitatively much more marked, including particularly high serum TSH and Tg concentrations. The reason for this particular hypersensitivity to ID by the neonate is due to the small iodine stores in the neonatal thyroid, which has a very fast turnover (reviewed in reference 85). For this reason, the proposal was made to use neonatal thyroid screening programs which measure primary TSH as the principal monitoring tool in the evaluation of the degree of ID in communities, and of the effectiveness of programs of iodine supplementation[1,85]. The neonatal TSH concentration assesses the saturation of receptors of brain cells with thyroid hormones and constitutes the single best indicator of the risk of brain damage and mental retardation[16]. In normal conditions, the proportion of neonates with a TSH

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concentration above 5 mU l^{-1} in whole blood (or 10 mU l^{-1} serum) is $<3\%$[1]. However, this threshold has to be used cautiously since this percentage can be markedly influenced both by the methods used to collect samples and by the method used to do TSH assays. Another approach with the same concept is to use the recall rate of suspected congenital hypothyroidism in programs of systematic screening. Indeed, in this case, the threshold applied is much higher, usually about 15–25 mU l^{-1} whole blood, or 30–50 mU l^{-1} serum. By using this threshold, it has been reported in Europe that the recall rate started to increase only when the median UI concentration of newborn populations was below 100 μg per l[85], a value clearly lower than the recommended UI concentration both for adults and neonates[1].

Neonatal thyroid screening has been used as a monitoring tool in an increasing number of countries and regions (reviewed in references 85–87) with occasional organisational difficulties[88].

Conclusion

Pregnant and lactating women and neonates are the main victims of the effects of ID because of the impact of maternal, foetal and neonatal hypothyroxinaemia on brain development[13–18]. Therefore, any program to correct ID in a population should pay special attention to these particular groups. However, as yet, there are no firm recommendations presently available on the concentration of UI that indicates optimal iodine nutrition in these groups. This paper constitutes an attempt to propose such normative values. It appears that an extensive review of the literature based, in particular, on the evaluation of UI concentrations recorded in these groups in iodine replete populations does not offer clear answers to the question because of the variability of individual results even in iodine sufficient populations. A first conclusion of this paper is that accurate data should be collected in iodine sufficient countries to compare systematically and at the same time, the UI concentration of the general population, non-pregnant adults, schoolchildren, pregnant and lactating women, and neonates.

However, based on published data, and taking into account the metabolic considerations, it is proposed that the recommended dietary intake of iodine should be 250–300 μg day^{-1} for pregnant women, 225–350 μg day^{-1} for lactating women and 90 μg day^{-1} for neonates and young infants. It is proposed that the median UI concentration that indicates optimal iodine nutrition during pregnancy and lactation should be in the range 150–230 μg l^{-1}. Recommendations for neonates are more difficult still, not only because of the lack of accurate data, but also because the neonate is not in a steady state of iodine metabolism and the UI concentration probably represents a relatively imprecise estimation of the iodine intake. However, based on data from the literature and taking into account the theoretical considerations, it can be concluded that the median UI concentration that indicates optimal iodine nutrition in the neonate should be in the range of 180–225 μg l^{-1}, which is almost the same as the value recommended for mothers.

It has to be emphasised again that these concentrations are higher than those recommended for the general population[19], and may be linked with side effects in adolescents and non-pregnant adults. For this reason, special attention should be paid to giving iodine supplements, while monitoring the UI concentration during pregnancy and possibly during the neonatal period, in addition to programmes of universal salt iodisation in countries in which there is ID.

Monitoring should include a biochemical evaluation of thyroid function by measuring the serum concentration of TSH, Tg, T_4, free T_4 and T_3. Both mothers and infants, but especially infants, are particularly sensitive to ID as their serum TSH is increased and the T_4 concentration decreased, in degrees of ID that do not affect thyroid function in the general population. Systematic neonatal thyroid screening using the concentration of primary TSH is a particularly sensitive index of the degree and impact of ID. After a phase, in which the methods of sampling and doing TSH assays are standardised, it could be the most efficient—if not the single best indicator—used in the process of monitoring the control of ID disorders.

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