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IODIZED OIL DURING PREGNANCY

**Safe use of iodized oil to prevent
iodine deficiency in pregnant women**

A statement by the World Health Organization



**World Health Organization
Geneva
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Update/Le point

Safe use of iodized oil to prevent iodine deficiency in pregnant women*

A Statement by the World Health Organization¹

The risks and expected benefits from iodized oil, given orally or by injection, to pregnant women in areas of severe iodine deficiency where iodized salt is not available were evaluated. The conclusions, which were approved by the International Council for Control of Iodine Deficiency Disorders (ICCIDD), showed that for preventing and controlling moderate and severe iodine deficiency, the giving of iodized oil is safe at any time during pregnancy. Maximum protection against endemic cretinism and neonatal hypothyroidism will be achieved when iodized oil is given before conception. The potential benefits greatly outweigh the potential risks in areas of moderate and severe iodine deficiency disorders, where iodized salt is not available and is unlikely to be made available in the short term (1-2 years).

Introduction

Since salt iodization is the optimal way of correcting iodine deficiency, it should continue to be the primary focus, through sustainable programmes, for preventing and controlling iodine deficiency disorders (IDD).^a The level of iodization should be adjusted to provide the recommended dietary intake (RDI) of iodine in the quantity of salt usually consumed. For pregnant and lactating women the RDI for iodine is 200 µg/day (1).

Pending successful establishment of salt iodization in areas of moderate and severe iodine deficiency,^b periodic large doses of iodine are frequently administered to all women of childbearing age, orally or by injection, in the form of slowly resorbable iodized oil. This intervention is an effective short-term public health approach that prevents

goitre and iodine-related brain defects, including endemic cretinism, in children. There are, however, a number of doubts about the safety of using iodized oil, or daily doses of iodine far in excess of normal physiological need, to prevent IDD. For example, maternal iodine overload due to iodized oil during the crucial period of pregnancy could inhibit maternal thyroid function through a Wolff-Chaikoff effect,^c thereby decreasing the availability of thyroxine to the fetus. Iodized oil could also directly affect fetal development. In addition, it has been suggested that iodized oil administered during late gestation could impair fetal and neonatal thyroid function, also through a Wolff-Chaikoff effect (2).

Responding to these concerns, the World Health Organization convened a group of experts to review and evaluate the results of programmes providing iodized oil to pregnant women. A careful review of the literature, and of experiences in several countries where iodized oil has been given at various stages of gestation, indicates that negative results

* A French translation of this article will appear in a later issue of the *Bulletin*.

¹ Based on a WHO Consultation on the Safety of Iodized Oil for Pregnant Women, Geneva, 13-14 September 1994. The participants at this meeting were Dr M. Benmiloud (Chairman), Algiers, Algeria; Dr F. Delange, Brussels, Belgium; Dr C.S. Pittman, Birmingham, AL, USA; Dr S. Yaffe, Bethesda, MD, USA; Dr C. Thilly, Brussels, Belgium; Dr C. Voumard, United Nations Children's Fund (UNICEF), Geneva, Switzerland. *WHO Secretariat*: Dr G. Clugston, Dr B. Underwood, Dr K. Bailey, and Dr J. Zupan. Requests for reprints should be sent to the Nutrition Unit, World Health Organization, 1211 Geneva 27, Switzerland.

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^a *Iodine and health: eliminating iodine deficiency disorders safely through salt iodization*. A statement by the World Health Organization. Unpublished WHO document WHO/NUT/94.4, 1994 (available in English, French and Spanish).

^b Moderate and severe iodine deficiency are defined in: *Indicators for assessing iodine deficiency disorders and their control through salt iodization*. Unpublished WHO document WHO/NUT/94.6, 1994 (available in English, French and Spanish).

^c The Wolff-Chaikoff effect is the inhibitory effect exerted by excess iodine on the iodization of tyrosines in hormone synthesis.

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have not been convincingly demonstrated.⁹ The group concluded that, for purposes of preventing and controlling moderate and severe iodine deficiency, as defined by WHO,⁹ the administration of iodized oil is safe at any time during pregnancy. Maximum protection against endemic cretinism and neonatal hypothyroidism will be achieved when iodized oil is given before conception. During the first trimester of pregnancy the supply of thyroid hormone to the human fetus appears to be critically dependent on maternal thyroid status. This relationship has been conclusively demonstrated in animals (3).

The group concluded that the available evidence conclusively demonstrates that iodized oil administered to women before, or at any time during, gestation has no harmful side-effects. Moreover, iodized oil not only prevents endemic cretinism and mental retardation in infants due to iodine deficiency, but also decreases fetal and perinatal mortality and increases the birth weight.

Prevention schedules and criteria

Dosage levels and frequency of administration, and the duration of protection expected from each are set out in Table 1. The dose selected and frequency of administration should be the lowest that will ensure protection throughout pregnancy, and during lactation for at least the first year postpartum. The

Table 1: Dosage, frequency, and duration of effectiveness of administering iodized oil to fertile women of childbearing age^a

	Intramuscular ^b	Oral ^c	Oral ^c
Frequency, based on duration of effect	>1 year	12 months	6 months
Pregnant women	1 ml	300-480 mg	100-300 mg
Non-pregnant fertile women ^d	1 ml	400-960 mg	200-480 mg

^a Adapted from the International Council for Control of Iodine Deficiency Disorders (ICCIDD).

^b Lipiodol (ultra fluid): 1 ml contains about 480 mg iodine.

^c Oriodol: 1 dose (0.57 ml) contains about 300 mg iodine. Lipiodol (capsule): 1 capsule (0.4 ml) contains about 200 mg iodine.

^d Available data indicate that a dose of 100-200 mg orally protects for 3 months. No such data are available for pregnant women.

dose that is compatible with the circumstances should be selected, and repeated if necessary, to ensure the desired degree of protection.

Criteria for giving iodized oil to pregnant women

Programme planners should carefully review the circumstances calling for the introduction or continuation of iodized oil supplementation programmes. The use of iodized oil for pregnant women and women of childbearing age should be considered only in situations where:

- the prevalence of iodine deficiency disorders is classified as moderate or severe;
- cretinism and neonatal hypothyroidism are present; and
- universal salt iodization programmes will not reach women of reproductive age within 1-2 years (which usually occurs in small areas within countries or regions, thus requiring area-specific interventions).

The reasons why iodized salt will not be available within a year or two should be thoroughly investigated before selecting iodized oil as a public health intervention. Sometimes salt iodization programmes in highly endemic areas cease functioning for unavoidable reasons. Should they be unable to restart soon, iodized oil may serve as a useful temporary measure.

Monitoring

The decision to use iodized oil for women of childbearing age should be made wherever the above criteria are met. Assessment of these criteria these requires baseline information on the distribution and severity of IDD, and on the availability of iodized salt throughout the area, country or region concerned. Assuming that the necessary baseline information is available, a monitoring system is required to evaluate both the programme's efficiency and its biological effectiveness. The system should include sufficient numbers of pregnant women to provide valid data for evaluation purposes and should be established within the context of national IDD control programmes.

Optimal biological and process indicators for effective monitoring of programmes to prevent fetal brain damage using iodized oil are given below.

Biological indicators. These apply to infants and mothers.

^a See article on pages 99-106 of this issue of the *Bulletin* (Delange F. Administration of iodized oil during pregnancy: a summary of the published evidence).

• *Infant*

- birth weight;
- perinatal mortality rate;
- neonatal serum thyroid-stimulating hormone (TSH).

• *Mother*

- urinary iodine concentration;
- breast-milk iodine concentration.

At least one of the indicators should be neonatal TSH or maternal urinary iodine.

Process indicators. These include the following:

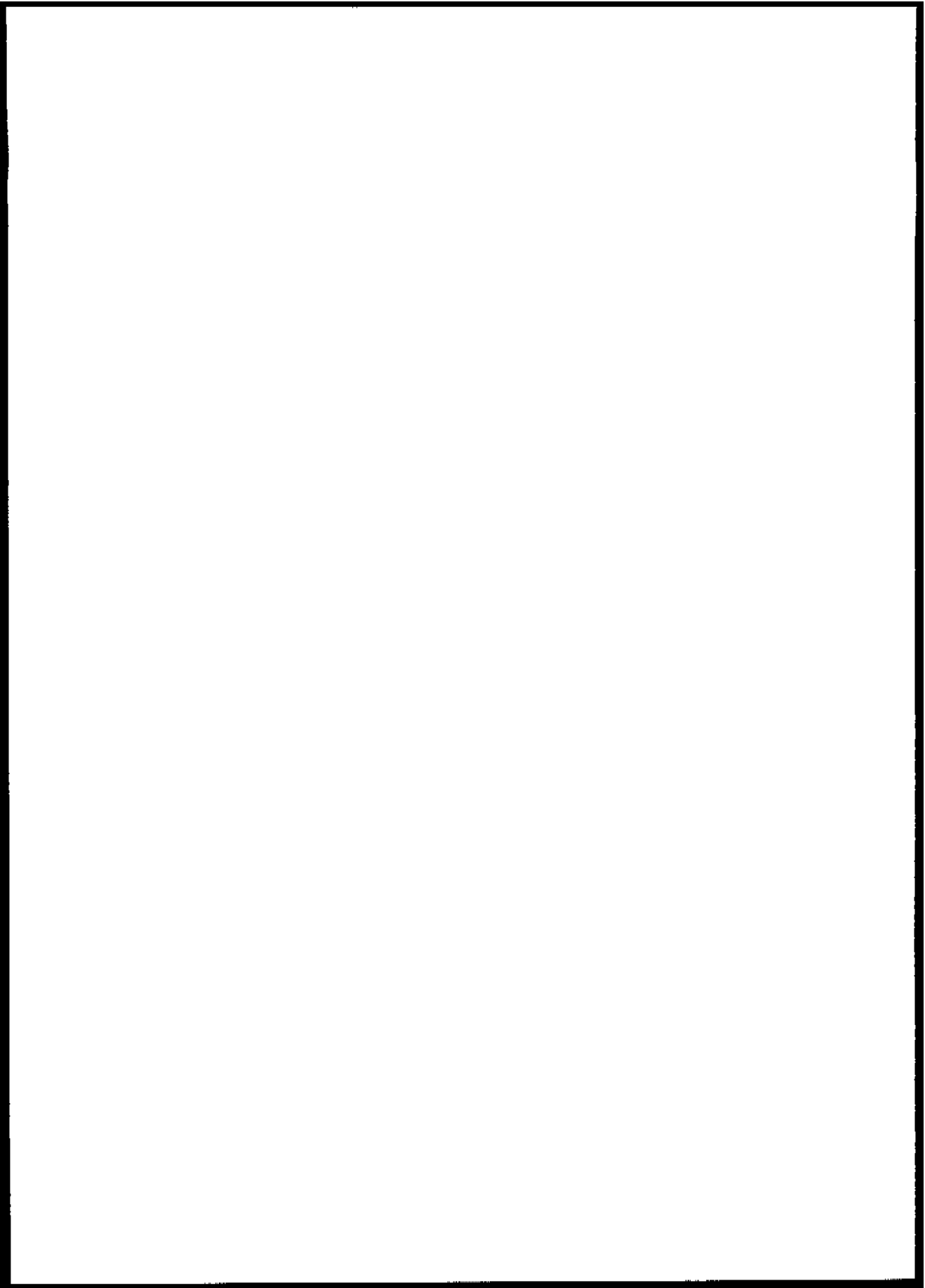
- availability of iodized oil at distribution points;
- system in place for registering and tracking the doses given;
- proportion of a programme's eligible subjects seen antenatally who have received iodized oil;
- system in place to determine pregnancy outcomes.

Conclusion

Based on the available scientific and programmatic evidence, the proposed iodized oil prevention schedule in this statement will lead to no detectable adverse effects on human health. The potential benefits to be derived greatly outweigh the potential risks in areas of moderate and severe IDD prevalence where iodized salt is not available, and is unlikely to be made available in the short term, i.e., within 1–2 years.

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Reviews/Analyses

Administration of iodized oil during pregnancy: a summary of the published evidence*

F. Delange¹

This brief review of the available studies confirms that the administration of iodized oil before or during pregnancy prevents endemic cretinism and brain damage by correcting iodine deficiency and thyroid function in pregnant women, fetuses, neonates, infants and children. The potential benefits derived from using iodized oil immediately before or during pregnancy greatly outweigh the potential risks in areas of moderate and severe prevalence of iodine-deficiency disorders, where iodized salt is not yet available.

The administration of iodized oil to entire populations, and especially to women of childbearing age and during pregnancy, has been proposed as an emergency prophylactic and therapeutic approach in areas with severe iodine deficiency complicated by endemic cretinism where universal salt iodization has not yet been successfully introduced (1). This procedure prevents brain damage due to iodine deficiency in the fetus and the neonate.

Findings

Iodized oil programmes have conclusively been shown to be effective in preventing and treating endemic goitre, and also in preventing endemic cretinism (2-13) and the alterations of neuropsychological development which are frequently encountered in non-cretinous individuals (13-38). However, adverse side-effects have been reported in non-pregnant adults due to the administration of iodine far in excess of physiological need. For example, in a pilot study of 14 subjects in the Solu region of the Nepalese Himalayas, Croxson and colleagues (39, 40) reported a significant fall in serum T₃

(triiodothyronine) and a rise in serum TSH (thyroid-stimulating hormone) concentrations over a period of 4-10 days (mean, 6 days) in 8 subjects with small goitres soon after receiving intramuscular (IM) injections of 400 mg of iodine in oil, which suggests an acute inhibitory Wolff-Chaikoff effect. In addition, three other subjects with large multinodular goitres developed biochemical hyperthyroidism. These findings in pilot studies are compatible with well-documented iodine-induced thyrotoxicosis which occurred in severely iodine-deficient populations following the introduction of iodine prophylaxis by iodized salt (41-46). There are a few reports of iodized oil-induced hyper- or hypothyroidism in public health programmes, sporadic cases of hyperthyroidism having been reported from Ecuador (47), Peru (48) and Argentina (49), but these were not detected in large-scale programmes in New Guinea (2, 50), Zaire (6, 9, 12, 51), Nepal (38, 40, 52), Algeria (53), Indonesia (54, 55) and China (56, 57). Since many of these interventions were conducted under particularly difficult environmental conditions, adverse reactions to therapy could easily have escaped detection (58).

In contrast, detailed studies have been carried out on the effects of iodized oil administered to women just before or during pregnancy, with special attention to the short- and long-term side-effects of iodized oil on thyroid function in the mother, neonate, infant and child (59). In carefully executed studies in New Guinea on the effects of iodized oil administered before or during pregnancy to prevent endemic cretinism (4, 11), biological tests examining thyroid function were rarely available (20, 22) because of particularly difficult environmental condi-

* This article is based on material presented at a WHO Consultation on the Safety of Iodized Oil for Pregnant Women, Geneva, 13-14 September 1994. See also: Safe use of iodized oil to prevent iodine deficiency in pregnant women on pages 1-3 of this issue. Requests for reprints should be sent to Nutrition Unit, World Health Organization, 1211 Geneva 27, Switzerland.

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Table 1: Effects of iodized oil, given just before or during gestation, on the thyroid function of mothers, neonates, infants and children.* The results are given as means \pm SE except where otherwise indicated.

Region and epidemiology	Protocol	Mothers at delivery	Neonates	Follow-up
North-eastern Algeria				
Urinary iodine: 1.6 \pm 0.5 $\mu\text{g/dl}$	Placebo-controlled randomized study (n = 1536)	Urinary iodine: 1.8 $\mu\text{g/dl}$ TSH: 4.1 mU/l	TSH: 12.4 (mU/l); T ₄ : 6.7 $\mu\text{g/dl}$	Mothers: The abortion, prematurity and stillbirth rates were lower in the treated than in the untreated group ($P < 0.001$) None became hyperthyroid At 6 months, urinary iodine remained twice higher and TSH twice lower in the treated lower in the treated group than in the controls respectively
Prevalence of goitre: — global population: 53% — pregnant women (visible goitre rate): 47% Prevalence of cretinism: 1%	Placebo (n = 982) vs iodized oil (n = 554) Iodized oil 0.5 ml (240 mg I) orally: a) 1–3 months before conception (n = 213) b) During the first month of gestation (n = 190) c) During the third month of gestation (n = 151)	Urinary iodine: 9.4 $\mu\text{g/dl}$ ^b TSH: 2.1 mU/l ^b Urinary iodine: 10.1 $\mu\text{g/dl}$ ^c TSH: 2.1 mU/l ^c Urinary iodine: 9.8 $\mu\text{g/dl}$ ^c TSH: 1.9 mU/l ^c	TSH: 4.9 (mU/l); T ₄ : 10.4 $\mu\text{g/dl}$ ^b TSH: 4.6 (mU/l); T ₄ : 11.0 $\mu\text{g/dl}$ ^b TSH: 4.6 (mU/l); T ₄ : 10.8 $\mu\text{g/dl}$ ^c	Infants: The incidence of hypothyroidism was 2/982 in the untreated group and 0/554 in the treated group Hypothyroidism was only transient
Ubangi area, northern Zaïre				
Urinary iodine: 15.5 \pm 1.3 $\mu\text{g/day}$ (n = 243) Prevalence of goitre: — global population: 51% — pregnant women: 75% Prevalence of cretinism: 1–10% Cord serum TSH >50 mU/l: 25% Cord serum TSH >100 mU/l and T ₄ <4 $\mu\text{g/dl}$: 14%	Placebo-controlled, longitudinal, randomized study (n = 983) Placebo (n = 484) vs iodized oil (n = 499), 1 ml IM (480 mg I) during the last two trimesters of gestation (mean: 28th week)	Untreated (n = 246) Urinary iodine ($\mu\text{g/dl}$): 3.63 (3.30–3.99) ^a <5: 63% <2: 25%	Untreated (n = 195)	Infants + children: Untreated Urinary iodine ($\mu\text{g/dl}$): 0–84 months: stable 1.5–3.6 Serum TSH >10 mU/l: 0–36 months: 46–49% 36–84 months: 59% Serum T ₄ ($\mu\text{g/dl}$): 0–84 months: low, stable Overt clinical and severe biochemical hypothyroidism (endemic myxoedematous cretinism): 8.3%

Table 1: *continued*

		<i>Treated</i> (n = 256) Urinary iodine ($\mu\text{g/dl}$) 56.6 (51.3–62.5) ^{a,c} <5: 8% >1000: 5%		<i>Treated</i> (n = 199) Serum TSH (mU/l): 7.19 (6.67–7.76) ^{b,c} T ₄ : 11.2 \pm 0.3 $\mu\text{g/dl}$ ^b T ₃ : 62 \pm 3 ng/dl ^b	<i>Treated</i> Urinary iodine ($\mu\text{g/dl}$): 0–12 months: 15.5 12–24 months: progressive decrease >36 months: as low as in controls Serum TSH >10 mU/l: 0–24 months: 5% 24–36 months: 40% >36 months: as high as in controls Serum T ₄ ($\mu\text{g/dl}$): 0–24 months: normal (except 1) 24–48 months: progressive decrease >48 months: as low as in controls Endemic myxoedematous cretinism: 2.6%
Ntcheu district, Malawi					
Urinary iodine: 3.3 \pm 0.1 $\mu\text{g/dl}$	Placebo-controlled randomized study (n = 627)				
Prevalence of goitre: 59%	Placebo (n = 404) vs iodized oil 0.5 ml (240 mg I) IM or orally during the last trimester				
Prevalence of cretinism: 1%					
		<i>Untreated</i> (n = 404) Urinary iodine: 3.3 $\mu\text{g/dl}$ Serum TSH: 4.7 mU/l T ₄ : 10.5 \pm 3.4 $\mu\text{g/dl}$ T ₃ : 216 \pm 78 ng/dl		<i>Untreated</i> (n = 400) Serum TSH: 11.1 mU/l T ₄ : 8.6 \pm 2.3 $\mu\text{g/dl}$ T ₃ : 85 \pm 54 ng/dl	
		<i>Treated by iodized oil IM</i> (n = 147) Urinary iodine: 28.5 $\mu\text{g/dl}$ ^a Serum TSH: 2.8 mU/l ^b T ₄ : 12.8 \pm 3.1 $\mu\text{g/dl}$ ^b T ₃ : 208 \pm 87 ng/dl		<i>Treated by iodized oil IM</i> (n = 146) Serum TSH: 5.9 mU/l ^b T ₄ : 10.5 \pm 2.7 $\mu\text{g/dl}$ ^b T ₃ : 66 \pm 10 ng/dl	
		<i>Treated by iodized oil orally</i> (n = 76) Urinary iodine: 12.3 $\mu\text{g/dl}$ ^a Serum TSH: 2.6 mU/l ^b T ₄ : 12.5 \pm 2.4 $\mu\text{g/dl}$ ^b T ₃ : 231 \pm 70 ng/dl ^b		<i>Treated by iodized oil orally</i> (n = 73) Serum TSH: 5.6 mU/l ^b T ₄ : 9.7 \pm 2.3 $\mu\text{g/dl}$ ^b T ₃ : 71 \pm 16 ng/dl ^b	

^a Compiled from references 7–9, 12 and 61–68, and from J. Vanderpas & B. Swennen, personal communication.

^b Significant difference compared with the untreated group ($P < 0.001$).

^c These results are geometric means (–SEM, +SEM).

tions, Pharoah (4) reported very low levels of serum protein-bound iodine (PBI) in untreated mothers who delivered cretins, whereas normal values were still found in treated mothers who delivered normal infants 3-4 years after receiving iodized oil injections. Pretell and colleagues (60) reported that in an area of severe iodine deficiency in the Peruvian Andes (daily urinary excretion of iodine, 25 µg; prevalence of visible goitre, 52-59%; and prevalence of cretinism, 1.0-3.6%), umbilical cord serum T_4 (thyroxine) and free T_4 levels were much lower, and TSH levels higher, than in controls from an iodine-replete area. The results for the same variables were normal in neonates born to mothers injected with iodized oil before or during early pregnancy. No adverse side-effects were observed either in mothers or neonates.

The most detailed studies of iodized oil given during pregnancy have been conducted in Zaire (7-9, 12, 61-65), Algeria (66, 67) and Malawi (65, 68) in areas of severe iodine deficiency and endemic goitre, complicated by cretinism (Table 1). The doses of iodized oil were 1 ml IM (480 mg I) in Zaire, and 0.5 ml IM or orally in Algeria and Malawi. Time of administration varied from just before pregnancy in Algeria to the third trimester of gestation in Zaire. The result was a systematic and dramatic increase in maternal iodine supply, with only occasional iodine overload (5% of treated women in Zaire had urinary iodine levels above 1000 µg/dl at the time of delivery). Nevertheless, thyroid function in mothers, which frequently indicates hypothyroidism in the absence of therapy, was normal in all treated mothers at delivery; their serum TSH, T_4 and T_3 levels were similar to those observed in mothers in iodine-replete areas (69, 70). In addition, not a single woman exhibited biochemical evidence of hyperthyroidism and the prevalence of goitre markedly decreased in those who had been treated.

In the absence of therapy for mothers, thyroid function was severely impaired in a large number of neonates (in the Ubangi area of Zaire, 14% of infants had cord serum TSH above 100 µU/ml and T_4 below 4 µg/dl). The extent of deviation from normal values in infants was more severe than in mothers and was directly related to the severity of the iodine deficiency and hypothyroidism present in mothers. Once again, iodized oil administered to mothers entirely normalized the thyroid function in neonates, and the correction occurred regardless of the stage of pregnancy — from the first month to late in the third trimester — at the time of therapy.

In seven years of follow-up after treatment of mothers with iodized oil, no case of hyperthyroidism was reported in either mothers or children. Depending on the dose and the stage of pregnancy at which it was given, the status of iodine nutrition of infants

and children (evaluated by ascertaining urinary iodine concentrations) progressively deteriorated with age, reverting to the degree of iodine deficiency found in untreated individuals from the age of 2 years onwards. Nevertheless, clinical and biochemical hypothyroidism was largely prevented in infants born to treated women, and when they occurred, they were frequently transient in nature. Finally, treating pregnant women with iodized oil resulted in decreased incidence of abortions, prematurity and stillbirths, and an increased birth weight.

These positive results stand out in contrast to the interpretation of the results of a single study, which has frequently been reported in the literature in the last decade (20, 71-74). The study was conducted in parts of Bhutan and India known for severe iodine deficiency (more than 50% of the population with urinary iodine/creatinine ratio below 25 µg/g creatinine and goitre prevalence varying from 60% to 80%). Iodized oil (1 ml IM) was administered to schoolchildren, women of reproductive age, and pregnant women. Cord serum TSH and T_4 were measured in a group of 154 neonates born to mothers who had been injected during the second half of the third trimester of pregnancy (mean of 3.5 weeks before delivery). Selection criteria for neonates and the range of the time interval between injection and delivery were not reported. Sixteen of the 154 infants (10.4%) had cord serum TSH above 50 mU/l and cord T_4 below 3 µg/dl, indicating neonatal biochemical hypothyroidism. The investigators concluded that the iodized oil administered during pregnancy induced thyroid failure in the neonates, and consequently that oil therapy should be rejected as a prophylactic measure during pregnancy.

This interpretation is seriously to be questioned for two reasons. First, in the absence of results for urinary iodine in mothers, there is no evidence that the mothers were indeed injected and were iodine overloaded. Second, and more important, the same incidence of neonatal biochemical hypothyroidism (7.5-13.3%) was reported in the study areas in the absence of an iodized oil programme. Consequently, the study provides no evidence that the iodized oil administered to pregnant women had adverse effects on the neonates.

Conclusion

Detailed studies provide conclusive evidence that the administration of iodized oil prior to, or during, pregnancy prevents endemic cretinism and brain damage by correcting iodine deficiency and thyroid function in pregnant women, fetuses, neonates, in-

fants and children. To prevent neurological damage, it is crucial that iodine deficiency be corrected before or during early gestation. Correction of maternal, fetal and neonatal hypothyroidism can occur at any time during pregnancy, including the last trimester. The duration of postnatal correction of thyroid function depends on the dose of iodized oil administered to the mother, e.g., about two years for 1 ml iodized oil administered orally or IM, but only 6 months for half this dose. Despite the massive doses of iodine administered, no iodine-induced thyroid function abnormalities have ever been conclusively demonstrated at the time of delivery or in the short- or long-term follow-up of pregnant women and their offspring. The potential benefits derived from using iodized oil immediately before or during pregnancy greatly outweigh the potential risks in areas of moderate and severe prevalence of iodine-deficiency disorders, where iodized salt is not available or unlikely to be available within 1-2 years.

Résumé

Administration d'huile iodée pendant la grossesse: résumé des études publiées

Des études détaillées montrent de façon concluante que l'administration d'huile iodée avant ou pendant la grossesse contribue à prévenir le crétinisme endémique et les lésions cérébrales en corrigeant la carence en iode et la fonction thyroïdienne chez la femme enceinte, le fœtus, le nouveau-né, le nourrisson et l'enfant. Pour prévenir les lésions neurologiques, il est essentiel de corriger la carence en iode avant la grossesse ou au début de celle-ci. La correction de l'hypothyroïdisme maternel, fœtal et néonatal peut se faire à n'importe quel moment de la grossesse, même au cours du dernier trimestre. La durée de la correction post-natale de la fonction thyroïdienne dépend de la dose d'huile iodée administrée à la mère; elle est par exemple d'environ deux ans après administration de 1 ml par voie orale ou intramusculaire, mais seulement de six mois pour 0,5 ml. En dépit des doses massives d'iode qui ont été administrées, aucune anomalie de la fonction thyroïdienne induite par cet élément n'a été démontrée de façon concluante au moment de l'accouchement ou ultérieurement chez les femmes enceintes et leurs enfants qui ont fait l'objet d'un suivi à court ou à long terme.

Les avantages potentiels de l'administration d'huile iodée immédiatement avant la grossesse ou au cours de celle-ci compensent largement les risques potentiels dans les régions où la pré-

valence des troubles dus à une carence en iode est modérée à forte et où l'on ne prévoit pas de distribution de sel iodé avant un an ou deux.

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Since salt iodization is the optimal way of correcting iodine deficiency, it should continue to be the primary focus for preventing iodine deficiency disorders. Pending successful establishment of salt iodization in areas of moderate and severe iodine deficiency, administering periodic large doses of iodine as iodized oil to all women of childbearing age is an effective short-term public health approach that prevents goitre and iodine-related brain defects, including endemic cretinism, in children.

Responding to concerns about the safety of using iodized oil, the World Health Organization convened a group of experts to review and evaluate the results of programmes providing iodized oil to pregnant women. The group concluded that the available evidence conclusively demonstrates that iodized oil administered to women before, or at any time during, gestation has no harmful side-effects. The benefits to be gained in areas of moderate and severe iodine deficiency far outweigh risks. This statement and the accompanying review summarize the evidence in this regard.

