

Des effets secondaires de l'Iso Bétadine® (PVP-I) chez le fœtus et le nouveau-né via un traitement maternel à l'accouchement

Neonatal side Effects of povidone-iodine disinfection of pregnant or lactating women

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Why talk about iodine in pregnant women NOW?

- Following several belgian publications in the 80's, povidone iodine was not used anymore in pregnant /lactating women as it was shown to induce neonatal thyroid dysfunction
- but things seem to have changed :
 - We observed the frequent use of povidone iodine during parturition or lactation in maternities in and around Brussels and at home after birth
- We observed an increase of the number of cases recalled for positive neonatal screening for congenital hypothyroidism.
 - Mainly eutopic thyroid glands

We thus need to discuss today

- Sources of iodine
- Topical povidone iodine and iodine load
- Iodine and the thyroid
- Congenital hypothyroidism and neonatal screening
- Influence of iodine acute load on neonatal thyroid function

Sources of iodine

- Recommended iodine intake for healthy, non-pregnant adults (150 μg per day). The estimated tolerable upper level of iodine intake in most persons is 1100 μg per day.
- Common sources of excess iodine include
 - iodinated radiographic contrast agents and
 - iodine containing medications (e.g., amiodarone),
 - **topical antiseptics**,
 - dietary supplements (e.g., kelp=seaweed).
- Iodine in food:
 - Dairy products (due to the use of iodophor cleaners for milk cans and teats),
 - some breads (due to the use of iodate bread conditioners),
 - seaweed and other seafood and iodized salt are the most common iodine-containing foods
- A 200-mg tablet of amiodarone contains approximately 75 mg of iodine, and 1 ml of most intravenous radiocontrast mediums contains 320 to 370 mg of iodine.
- Because of its long half-life and high lipid solubility, amiodarone may cause iodine-induced thyrotoxicosis long after its discontinuation.

Sources of iodine : quantities

- **Diet**
- Kelp (per g): 16–8,165 μg
- Milk : 8,8–16,8 $\mu\text{g}/100\text{ml}$
- Infant milk 12 $\mu\text{g}/100\text{ml}$
- Fish fillet (per 100 g, dry weight): 73 μg
- Iodized salt: Variable (20mg/kg. salt consumption 5-10 g/day so 100-200 mcg iodine /day)
- **Other sources**
- Vitamins (prenatal, labelled content per daily serving): 75–200 μg
- Amiodarone (per 200 mg): 75,000 μg
- Iodinated contrast (free iodine content, per CT scan): 13,500 μg
- Topical iodine (povidone iodine): according to body surface, concentration 10% iodine (100mg/ml=100 000 mcg/ml)

Povidone–iodine and iodine load

- Povidone–iodine in the form of a 10% topical solution is one of the most widely used antiseptics.
- Multiple studies have shown **systemic absorption of iodine** from povidone–iodine, both through mucosal surfaces and skin.

- *Safran M, Braverman LE. Obstet Gynecol. 1982; 60:35–40.*

- *Effect of 14 days vaginal douching with polyvinylpyrrolidone-iodine on iodine absorption and thyroid function.*

Iodine and the thyroid

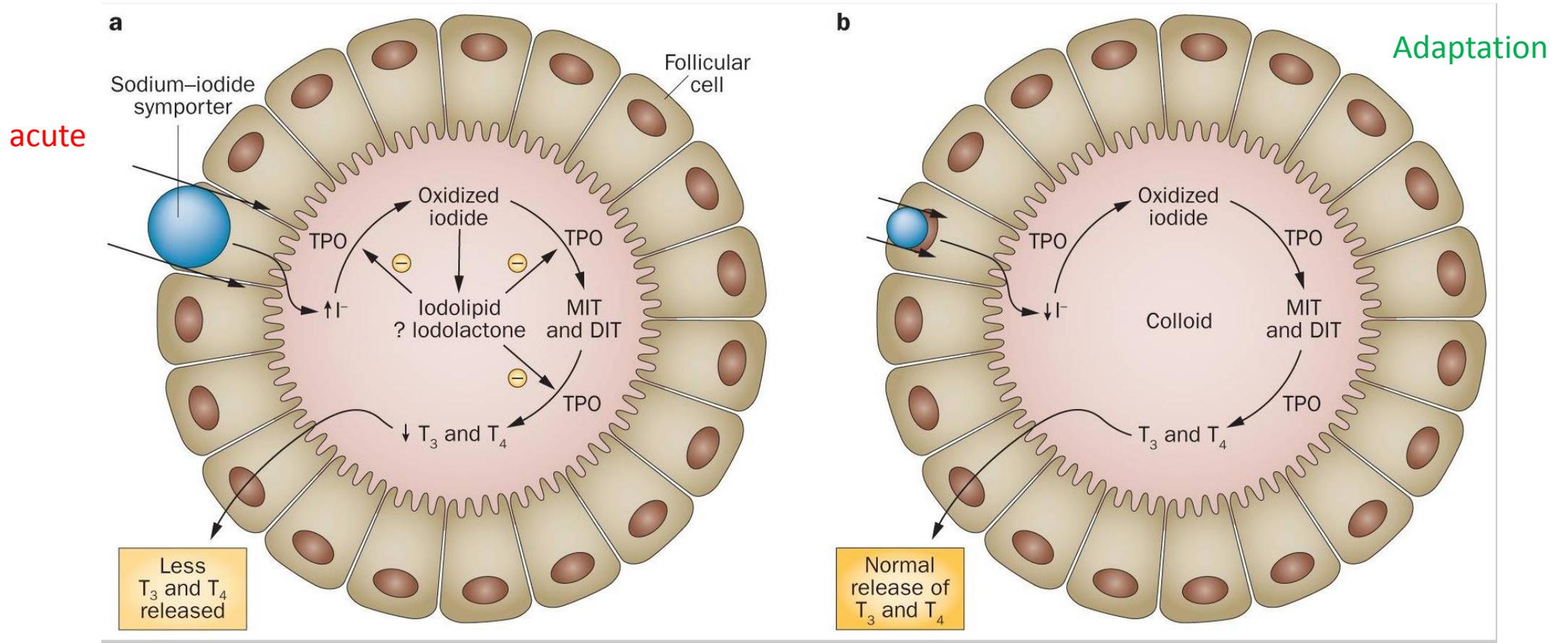
- Iodine is required for the production of thyroid hormones.
- Iodine is primarily taken in through the diet.
- Although excess iodine exposure generally does not result in any apparent clinical consequences, thyroid dysfunction can occur in vulnerable patients with specific risk factors, including those with pre-existing thyroid disease, the elderly, **fetuses and neonates**.

[Nat Rev Endocrinol. 2014 Mar; 10\(3\): 136–142.](#)

Consequences of excess iodine

[Angela M. Leung](#) and [Lewis E. Braverman](#)

Iodine and the thyroid: Wolff and Chaikoff effect



If adaptation, what's the problem?

- Failure to escape from the acute Wolff–Chaikoff effect is more likely during fetal development, in neonates and young children, a period when the hypothalamic–pituitary–thyroid axis is still immature.

[J Endocrinol Invest.](#) 1987 Apr;10(2):183-6. [Robuschi G](#), et al,

Cord blood iodothyronine and thyrotropin concentrations in newborns of mothers exposed to povidone iodine in the last trimester.

Study of thyroid function in neonates at delivery and in their mothers who used vaginal povidone-iodine (PVP-I) during the last trimester of pregnancy:

TSH was normal in mothers but not in cord blood.

Neonates and excess iodine

- Several cases of congenital hypothyroidism caused by ingestion of **excess maternal iodine tablets** during pregnancy have been reported.
- Similarly, hypothyroidism in neonates born to mothers who ingested **excessive amounts of seaweed** or seaweed soup during both pregnancy and lactation have been reported.
- The use of **transdermal iodine** and thyroid dysfunction associated with this practice is often seen **in hospitalized neonates**.

Immediate effect!!

povidone iodine at delivery and cord blood TSH

- [J Endocrinol Invest](#). 1994 Nov;17(10):805-8.

Elevation of cord blood TSH concentration in newborn infants of mothers exposed to acute povidone iodine during delivery.

[Novaes Júnior M¹](#), [Biancalana MM](#), [Garcia SA](#), [Rassi I](#), [Romaldini JH](#)

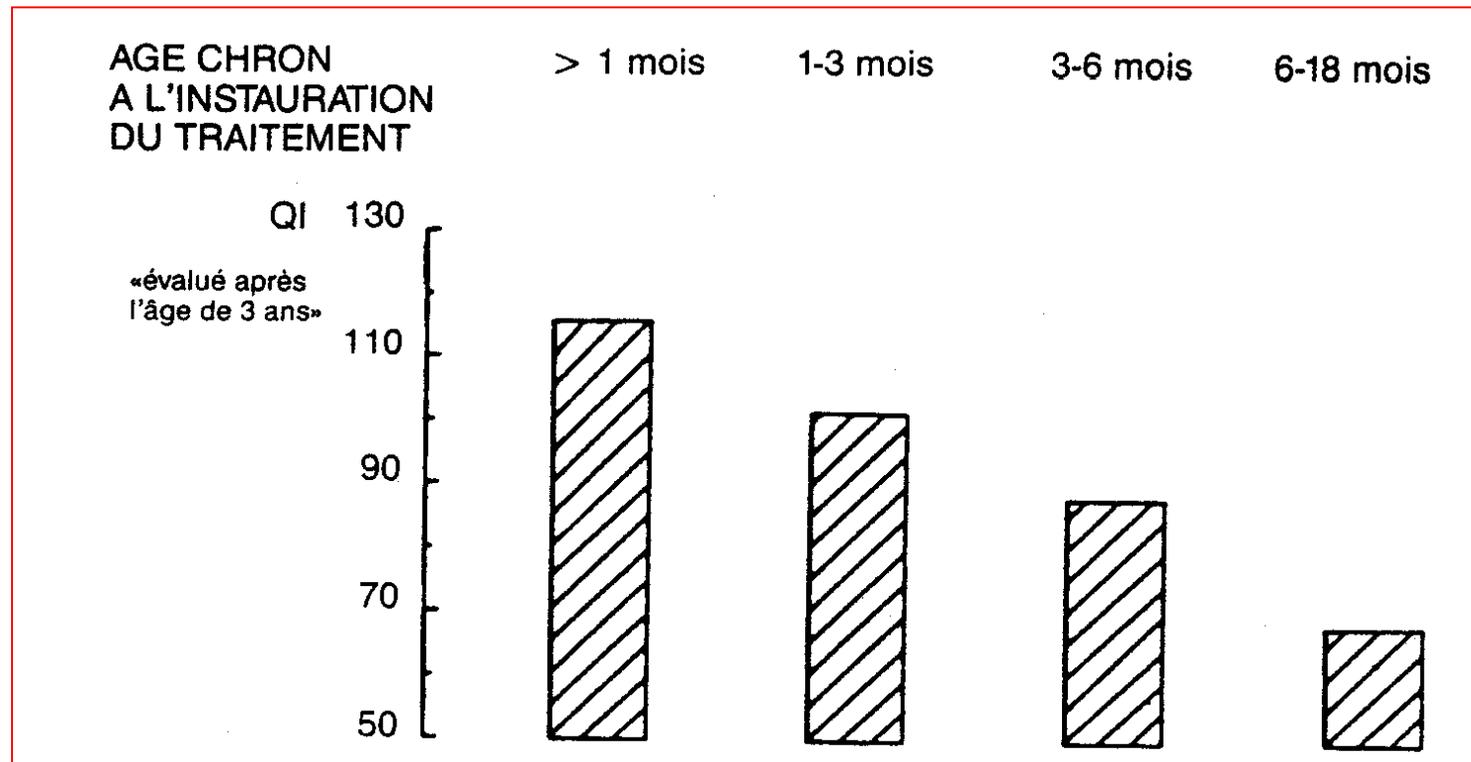
- [Postgrad Med J](#). 2015 Dec;91(1082):681-4. doi: 10.1136/postgradmedj-2015-133540. Epub 2015 Oct 26.

Iodine-containing disinfectants in preparation for caesarean section: impact on thyroid profile in cord blood.

[Nili F¹](#), [Hantoushzadeh S¹](#), [Alimohamadi A²](#), [Shariat M³](#), [Rezaeizadeh G³](#)

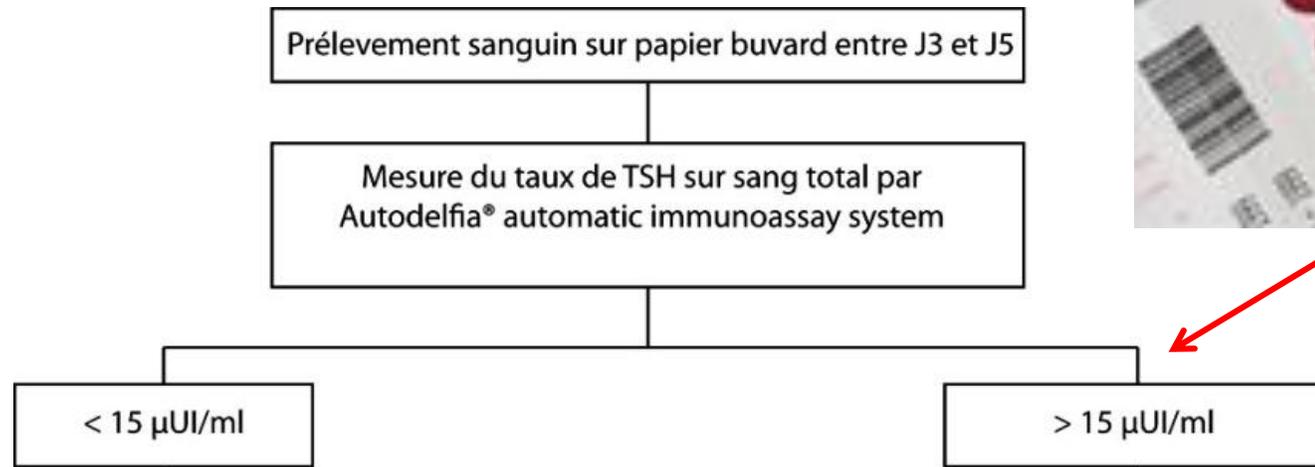
Congenital Hypothyroidism: what is it?

- Intellectual Disability if not detected and treated promptly
- Before newborn screening:



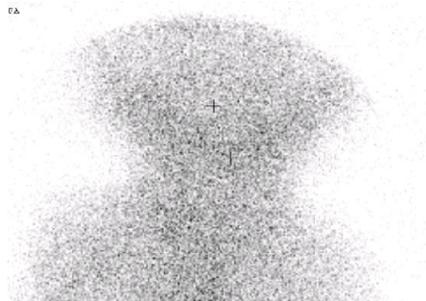
Wolter, R 1979

Neonatal Screening for congenital hypothyroidism



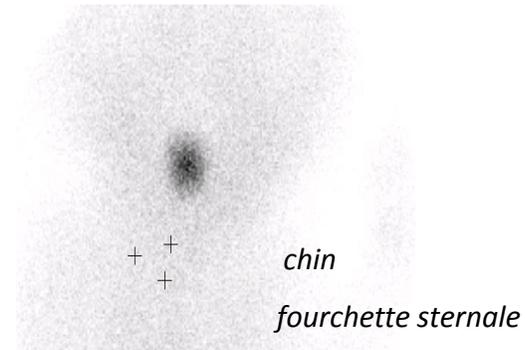
Management : emergency

- History
- Clinical exam and laboratory investigations :
 - TSH, freeT₄
 - Thyroglobuline , R-TSH blocking
- Bone age: assessment of the severity of prenatal hypothyroidism
- Thyroid ultra-sound
- thyroid Tc^{99m} ou I¹²³ SCAN



Athyreosis

=>start **Lévothyroxin** immediately



Ectopic thyroid

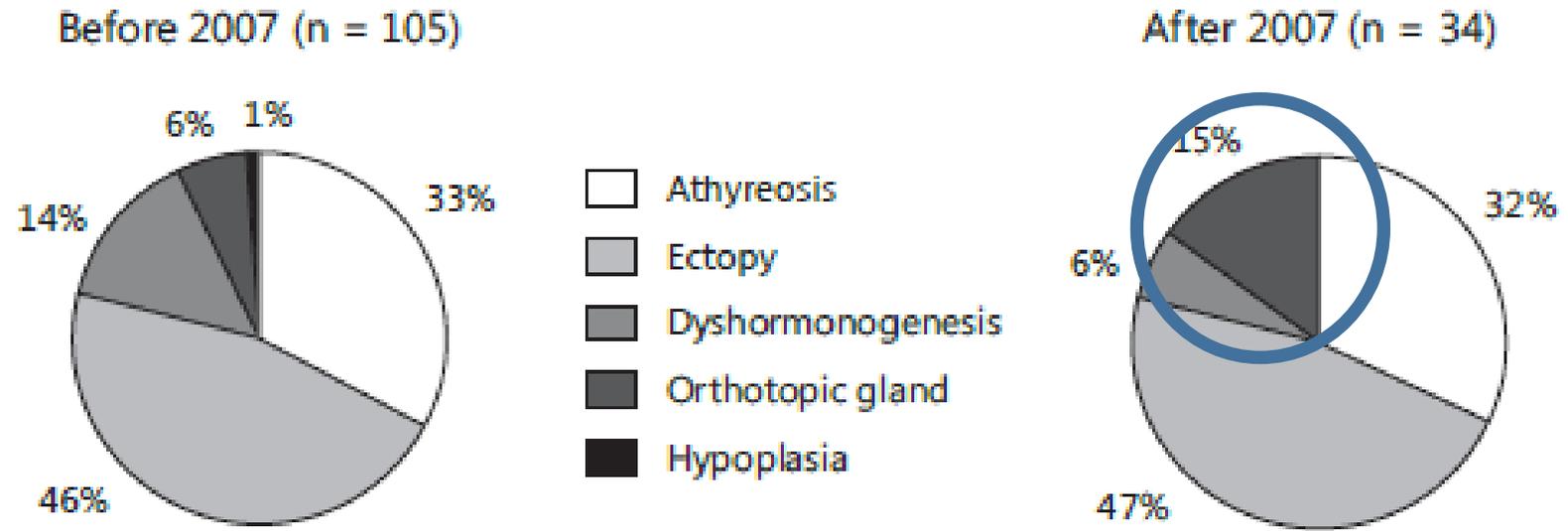
Congenital hypothyroidism

- The treatment is lifelong except for rare transient forms
- In transient forms, the Lthyroxin treatment is stopped after 3 years of age.
 - So in any case, a child with positive neonatal screening will be treated for at least 2-3 years

Congenital Hypothyroidism: Long-Term Experience with Early and High Levothyroxine Dosage

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France Ziereisen^b Guy Van Vliet^{c,d} Claudine Heinrichs^a Cécile Brachet^a

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Etiological classification of CH according to birth year before 2007 (left) and after 2007 (right).

We observed more eutopic thyroid glands

Arch Dis Child. 1988 Jan

Topical iodine, breastfeeding, and neonatal hypothyroidism.

F Delange, J P Chanoine, C Abrassart, and P Bourdoux

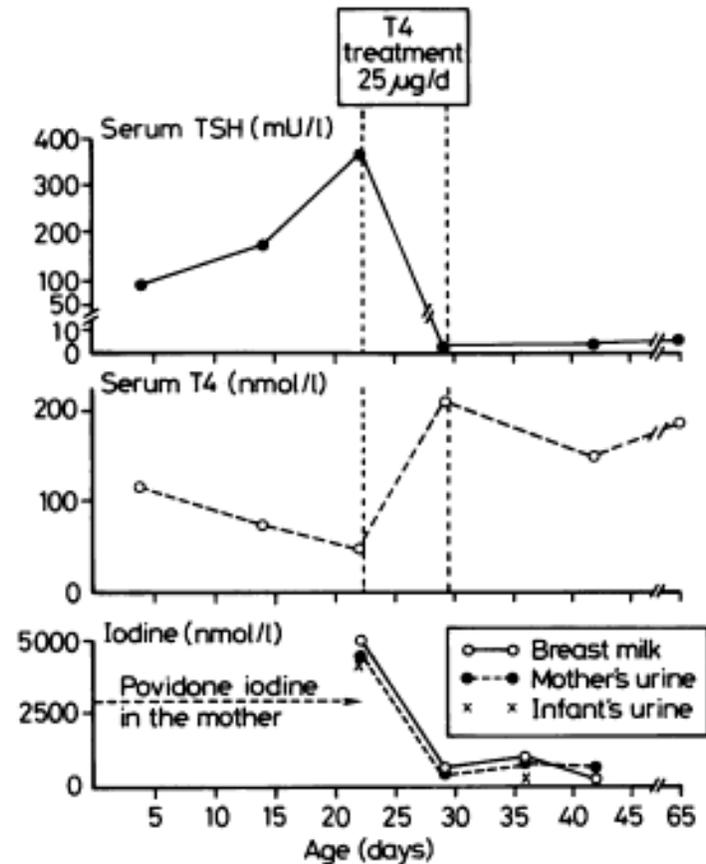


Figure Time course of the serum concentrations of thyroid stimulating hormone (TSH) and thyroxine (T4) in the infant and the iodine content of the urine of mother and infant and the mother's breast milk.

Increased recall rate at screening for congenital hypothyroidism in breast fed infants born to iodine overloaded mothers

J P CHANOINE,*‡ M BOULVAIN,† P BOURDOUX,‡ A PARDOU,* H V VAN THI,‡
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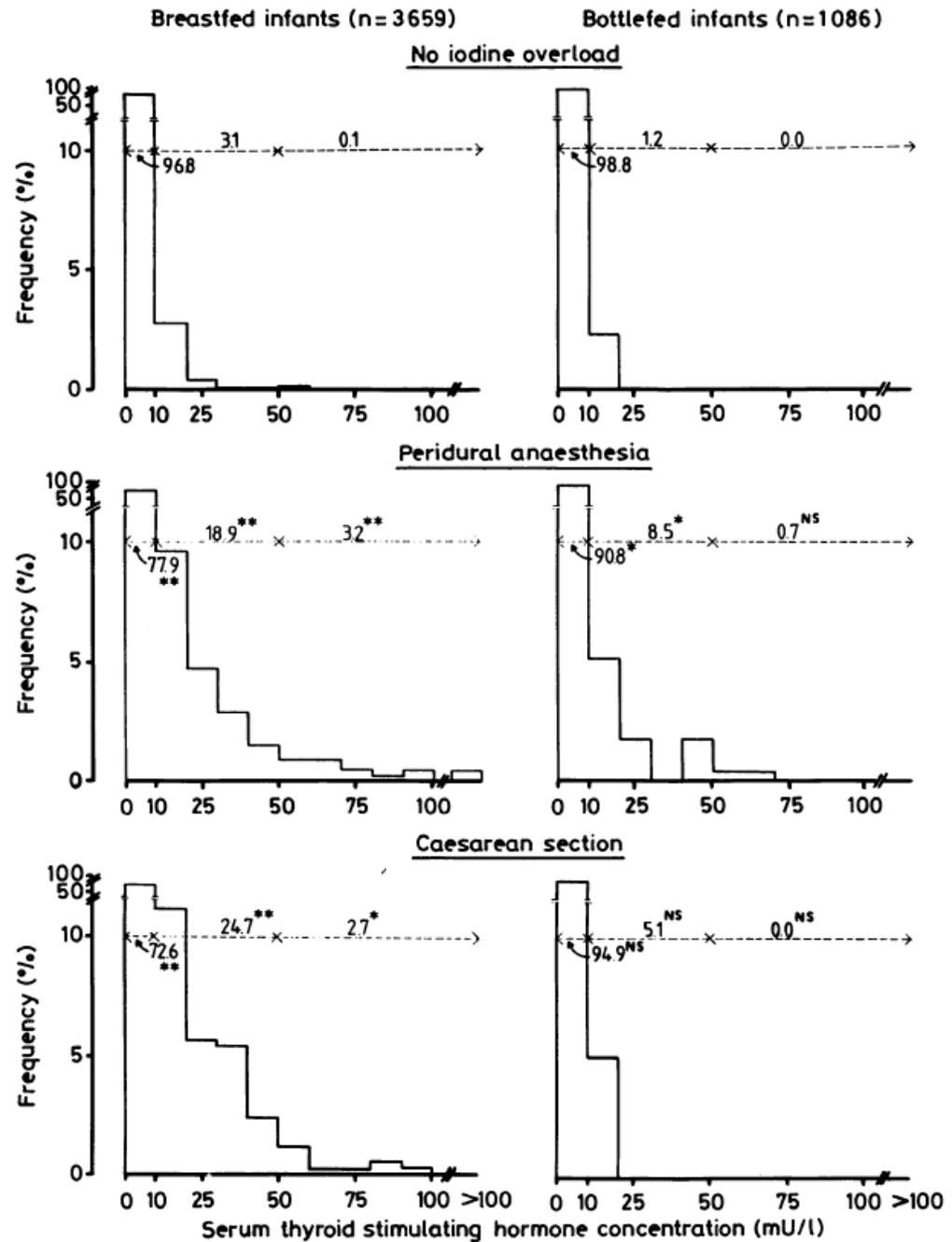
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- 4745 neonates, 77% breastfed
 - 3086 neonates with mothers not using povidone iodine
 - 1659 neonates whose mothers had received povidone iodine for either
 - C-section
 - peridural anesth

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SUMMARY Skin disinfection with povidine-iodine (PVP-I) is widely used in obstetrics. We evaluated the influence of PVP-I in mothers at delivery on the serum thyroid stimulating hormone concentrations of their infants at the time of screening for congenital hypothyroidism. The study covered 4745 infants who were either breast fed (3659, 77%) or bottle fed (1086, 23%); 3086 (65%) of them were born to mothers with no iodine overload (controls) and 1659 (35%) to mothers with iodine overload. Compared with the control group, the breast and bottle fed infants born to mothers with iodide overload had a shift of neonatal thyroid stimulating hormone concentration towards high values. The shift was maximal in the breast fed infants with a 25 to 30 fold increase in the recall rate at screening for congenital hypothyroidism (serum thyroid stimulating hormone >50 mU/l) while in the bottle fed infants, the recall rate was barely modified. In conclusion, the use of PVP-I in mothers at delivery induces a transient impairment of thyroid function in their infants, especially if breast fed. This situation is detrimental to screening for congenital hypothyroidism. Consequently PVP-I is not recommended in obstetrics.

Therefore, povidone was replaced by chlorhexidine and, in 1989:

Table Comparison of povidone-iodine (PVP-I) with chlorhexidine in isopropanolol (CHL) for skin disinfection

	Frequency (%) of serum thyroid stimulating hormone concentration (mU/l)			% Of serum thyroid stimulating hormone concentration >50 mU/l (recall)	
	<10	10-50	>50 (recall)	Breast fed	Bottle fed
PVP-I:					
Without skin Disinfection	97.2	2.7	0.1	0.1	0.0
With skin Disinfection	79.9*	17.6*	2.5*	3.1*	0.5
CHL:					
Without skin Disinfection	94.4	5.6	0.0	0.0	0.0
With skin Disinfection	94.0	5.7	0.3	0.3	0.0

*p<0.01.

References

- 1 Chanoine JP, Boulvain M, Bourdoux P, *et al.* Increased recall rate at screening for congenital hypothyroidism in breastfed infants born to iodine overloaded mothers. *Arch Dis Child* 1988;**63**:1207-10.
- 2 Chanoine JP, Bourdoux P, Pardou A, Delange F. Iodinated skin disinfectants in mothers at delivery and impairment of thyroid function in their breastfed infants. In: G A Medeiros-Neto

- 3 Delange F, Heidemann P, Bourdoux P, *et al.* Regional variations of iodine nutrition and thyroid function during the neonatal period in Europe. *Biol Neonate* 1986;**49**:322-30.

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Ce n'est pas le cas partout dans le monde?

1. Jeng MJ, Lin CY, Soong WJ, et al. Neonatal thyroid function is unaffected by maternal topical iodine disinfection for cesarean section or vaginal delivery. *Clin Pediatr.* 1997;36:109-111.
2. Chanoine JP, Boulvain M, Bourdoux P, et al. Increased recall rate at screening for congenital hypothyroidism in breastfed infants born to iodine overloaded mothers. *Arch Dis Child.* 1988; 63:1207-1210.
3. Lin HD, Lo JG, Ching KN. Amount of urinary iodine excretion in residents of Taipei City: a hospital-based study. *Chung-Hua-I-Hsueh-Tsa-Chih-Taipei.* 1991;48:20-24.
4. Delange FM, Ermans AM. Iodine deficiency. In: Braverman LE, Utiger RD, eds. *The Thyroid*, 7th ed. Philadelphia: Lippincott-Raven; 1996:296-316.
5. Brown RS, Bloomfield S, Bednarek FJ, et al. Routine skin cleansing with povidone-iodine is not a common cause of transient neonatal hypothyroidism in North America: a prospective, controlled study. *Thyroid.* 1997; 7:395-400.



done-iodine at the time of delivery for a cesarian section, the frequencies of thyrotropin values between 10 and 50 mIU/L and >50 mIU/L were, respectively, eight and 27 times higher than in breastfed neonates born to mothers without iodine overload.² To explain this discrepancy, although urinary and/or breast milk iodine concentrations were not measured, Jeng et al¹ hypothesized that the degree of iodine overload might be less severe in their patients than in ours.

We think that the difference in iodine nutrition can best explain this discrepancy: in Taiwan, the reported iodine intake in adults is two to three times higher than the WHO recommendation of 150 µg/day,³ while it is only 50–75 µg/day in Belgium.⁴ It is well known that the degree of iodine nutrition is a main determinant of the hypersensitivity of the thyroid gland to goitrogenic substances in the environment, like acute iodine overload.⁴ In Europe, there is an inverse relationship between the frequency of TSH >50 mIU/L

on the 5th day of life and the state of iodine nutrition.⁴ In Toronto, an area of high iodine intake, the iodine content of the neonatal thyroid is three to four times higher and the turnover rate of intrathyroidal iodine three to four times lower than in Brussels, where iodine intake is borderline.⁴ Thus, thyroid failure is more likely to occur in Brussels than in Toronto. In Massachusetts, an area where iodine intake is also high, Brown et al⁵ just reported findings similar to those from Jeng et al with a degree of iodine overload similar to ours.

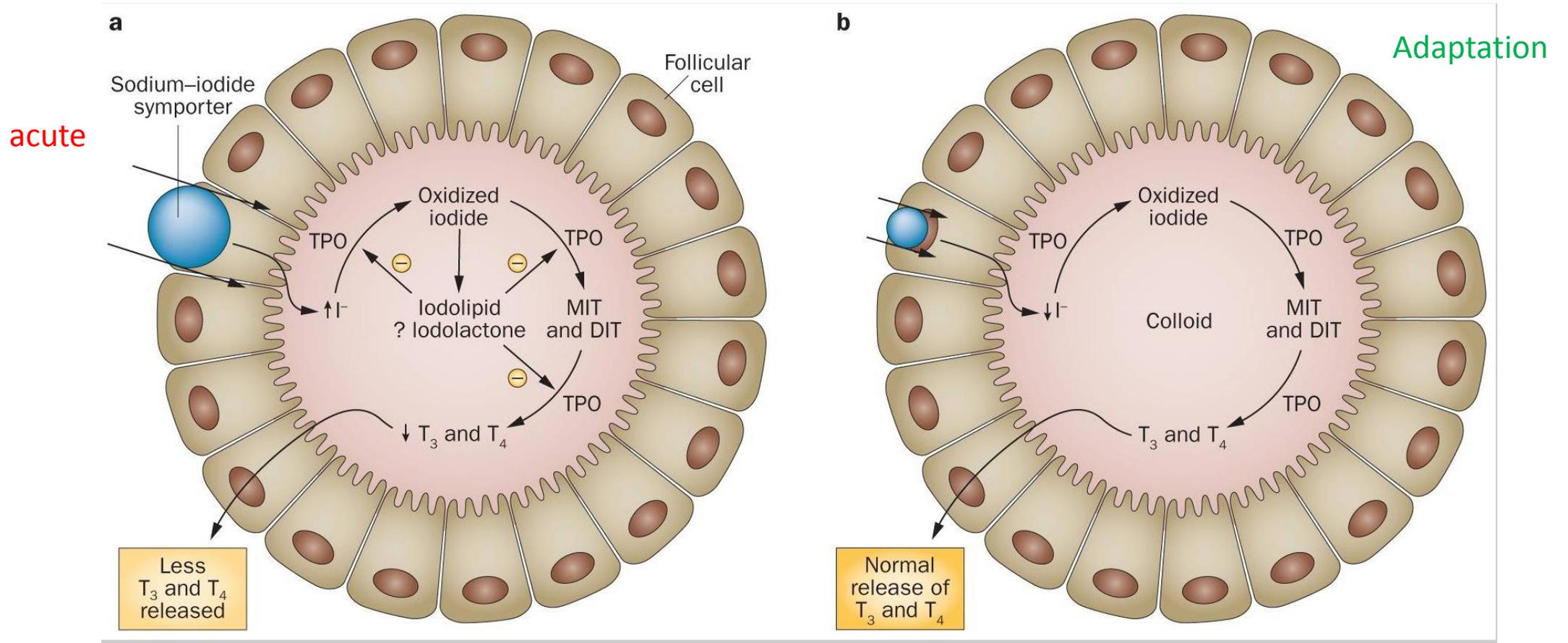
In conclusion, taken together, these data suggest that acute perinatal iodine overload is associated with transient impairment of the neonatal thyroid function only in areas where iodine nutrition is insufficient.

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REFERENCES

1. Jeng MJ, Lin CY, Soong WJ, et al. Neonatal thyroid function is unaffected by maternal topical iodine disinfection for cesarean section or vaginal delivery. *Clin Pediatr*. 1997;36:109-111.
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Iodine and the thyroid: Wolff and Chaikoff effect



Pediatric implications

- Povidone iodide topical application at delivery causes an increased TSH in the neonate
- This causes an increased recall rate at neonatal screening for congenital hypothyroidism
- The neonate presents transient hypothyroidism due to iodine overload but this is not known
- Because of elevated TSH, the neonate receives Lthyroxin supplements for 3 years!!!

hypothyroidism in breast fed infants born to iodine overloaded mothers

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BACK TO 1988's CONCLUSIONS: pvp-i is not recommended in obstrectics

