Dysthyroïdie et Grossesse

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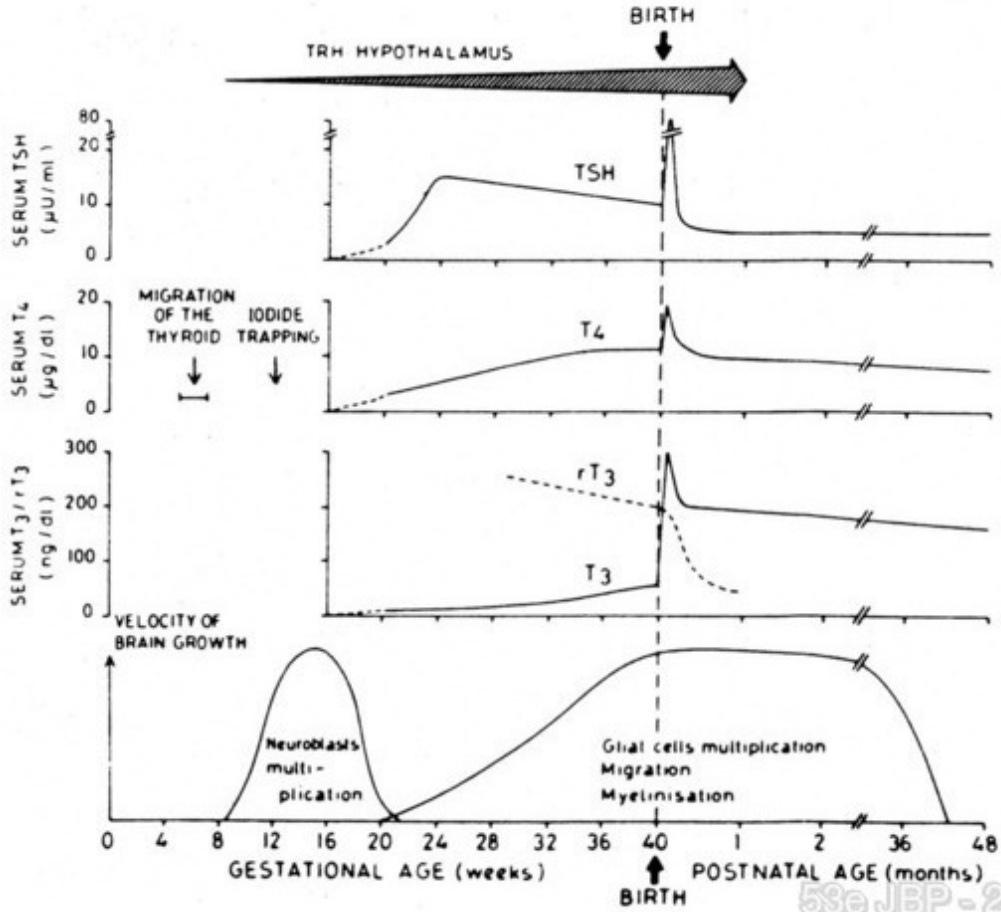
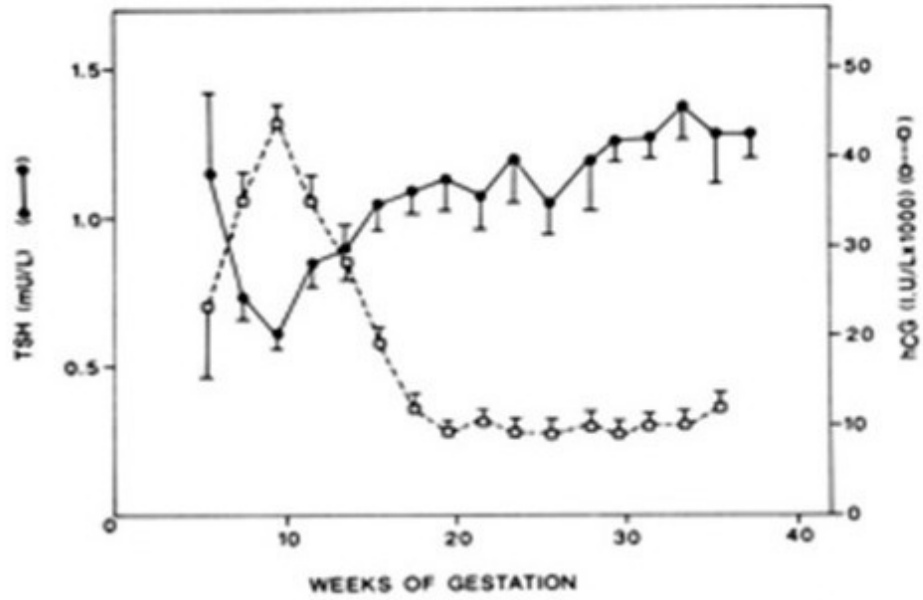
Définition des dysthyroïdies maternelles

- Les hypothyroïdies
  - Hypothyroïdies « vraie »: TSH augmentée FT4 Abaissée
  - Hypothyroïdie infra clinique (frustre) : TSH augmentée et FT4 normale
  - Hypothyroxinémie: TSH normale et FT4 abaissée
- L'hyperthyroïdie type Basedow
  - Hyperthyroïdie « vraie » : TSH abaissée et T4 augmentée
  - Hyperthyroïdie infra-clinique : TSH abaissée et T4 normale
  - Hyperthyroxinémie : TSH normale et T4 augmentée





Glinoer D, J Clin Endocrinol Metab 1990, 71, 276

- **La TSH s'abaisse au 1er trimestre chez 10-20% des femmes** et parfois augmente discrètement en fin de grossesse.
- Des **normes spécifiques à la grossesse** propres à chaque laboratoire seraient souhaitables.
- À défaut, limite supérieure TSH < 4 mUI/L
- Ou baisse de la limite inférieure TSH de 0,1-0,2 mUI/L et de la limite supérieure de 0,5-1 mUI/L (ATA 2017)

A study to establish gestation-specific reference intervals for thyroid function tests in normal singleton pregnancy.

Christina Cotzias (1), Sarah-Jane Wong (2), Erica Taylor (3), Paul Seed (4) and Joanna Girling (5).

Figure 1.

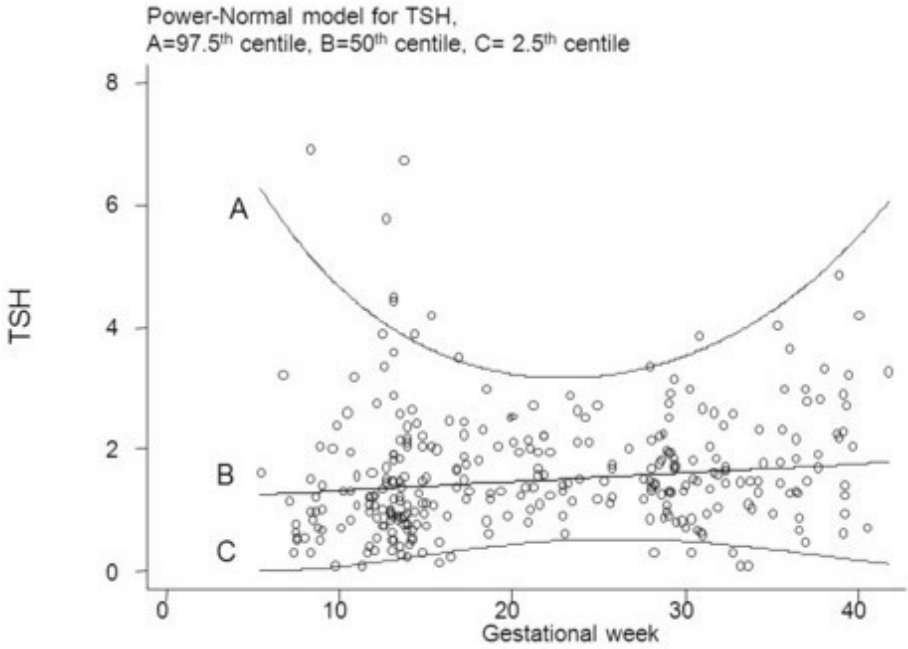
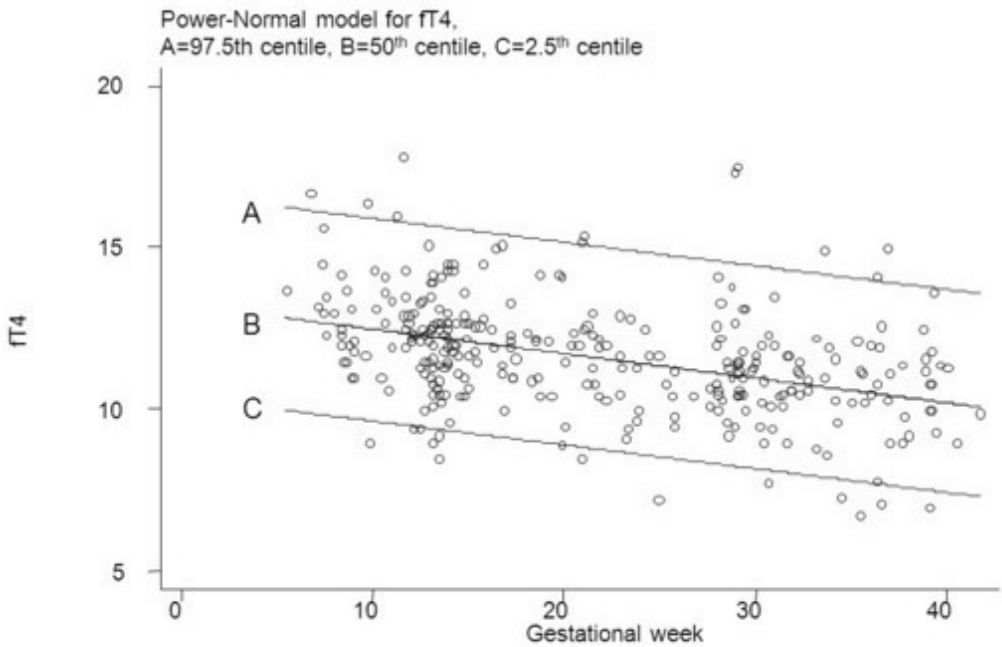


Figure 3.



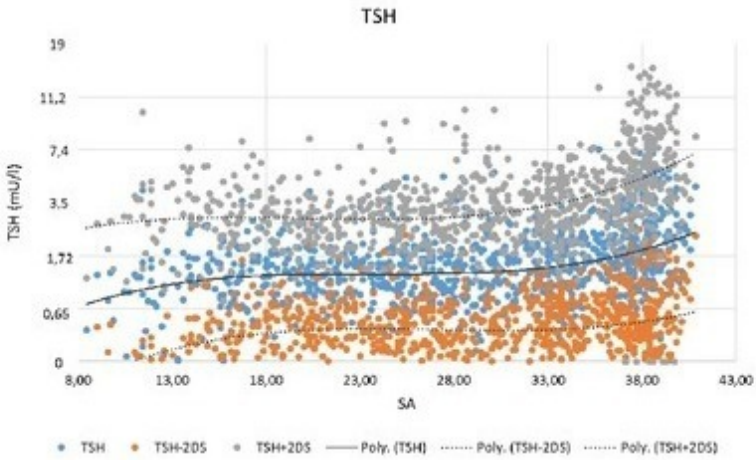
Endocrinologie

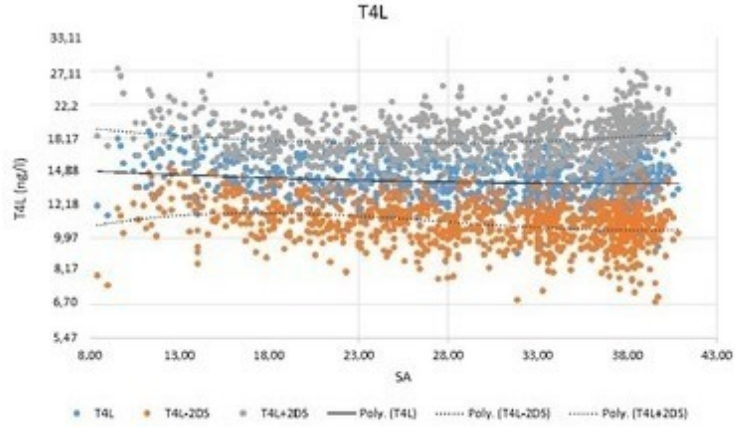
			TSH, mU/L	
Auteur, pays (référence) (méthode d'analyse)	N	Gestation (semaines)	Médiane	IC 95 %
Bestwick *et al.*, Italie (24) (AutoDELFIA)	5505	<16	1,07	0,04-3,19
Bestwick *et al.*, Royaume-Uni (24) (Advia Centaur)	16334	<16	1,11	0,06-3,50
Bocos-Terraz *et al.*, Espagne (264) (Architect)	481	<14	0,94	0,41-2,63
Gilbert *et al.*, Australie (271)[b] (Architect)	1817	9-13	0,74	0,02-2,15
Lambert-Messerlian *et al.*, États-Unis (270)[c]	8351	T1	1,00	0,12-3,37
(Immulite 2000)	8415	T2	1,19	0,35-3,35
La'ulu *et al.*, États-Unis (139,265)[c]	2172	10-13	0,94	0,02-2,69
	2683	14-20	1,14	0,15-3,11
Li *et al.*, Chine (17) (Cobas Elesys 601)	640	7-12	1,47	0,10-4,34
Männisto *et al.*, Finlande (266)	4333	T1	1,11	0,08-3,54
(Architect i2000)	747	T2	1,37	0,11-4,24
Medici *et al.*, Pays-Bas (267) (Vitros ECI)	5186	8-18	1,30	0,03-4,04
Pearce *et al.*, États-Unis (142) (Advia Centaur)	585	<14	1,1	0,04-3,60
Quinn *et al.*, Russie (272)	380	T1	1,66	0,09-4,67
(Abbott AxSYM)	549	T2	2,00	0,20-4,68
Springer *et al.*, République tchèque (268)[h] (ADVIA Centaur)	4337	9-11	1,21	0,06-3,67
Stricker *et al.*, Suisse (262)	575	6-12	0,95	0,07-2,82
(Architect i2000SR)	528	T2	1,02	0,20-2,79
Vaidya *et al.*, Royaume-Uni (Modular E 170) (274)	1089	<12	1,08	0,14-3,19

Tableau I : Taux de TSH dans différents pays en début de grossesse (d'après [2]).

V. CASTAIGNE
Service de Gynécologie-obstétrique du Centre Hospitalier Intercommunal de Créteil, coordonnateur du CPDPN.

Evolution en fonction du terme
Bilan thyroïdien





➡ Corrélation TSH et terme de grossesse (Rho= 0,34, p<0,01)

PARIS DIDEROT

THESE
POUR LE DIPLOME D'ETAT
DE DOCTEUR EN MEDECINE

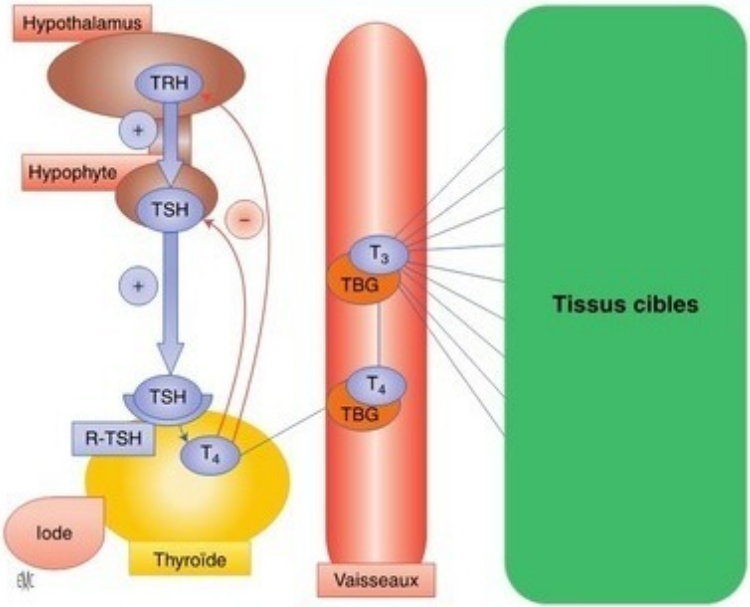


Figure 1. Axe thyroïdien. TRH : *thyroïd releasing hormone* ; TSH : *thyroïd stimulating hormone* ; T3 : triiodothyronine ; T4 : thyroxine ; TBG : *thyroid binding globuline* ; R-TSH : récepteur à la TSH.

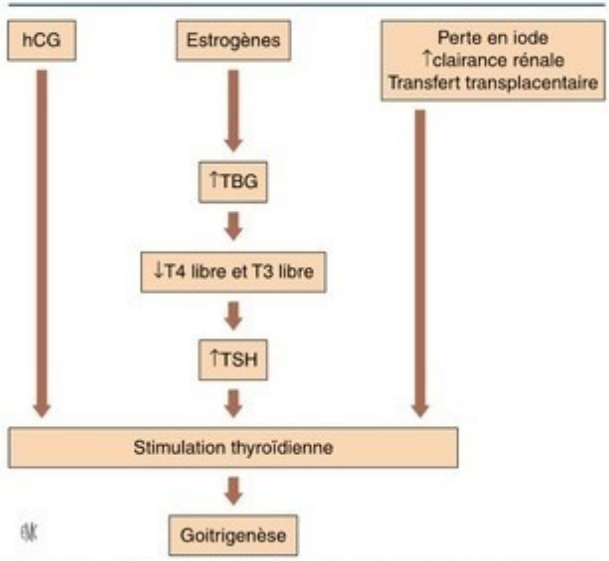


Figure 2. Effets des modifications physiologiques sur la thyroïde au cours de la grossesse. hCG : *human chorionic gonadotrophin* ; TBG : *thyroid binding globuline* ; T3 : triiodothyronine ; T4 : thyroxine ; TSH : *thyroïd stimulating hormone*.

Tableau 1.
Changements physiologiques thyroïdiens au cours de la grossesse avec leur traduction biologique.

Changements physiologiques	Changements de la fonction thyroïdienne
Augmentation de TBG	Augmentation des taux sériques de T4 totale et T3 totale
hCG	Augmentation de T4 libre et baisse de TSH
Augmentation du volume plasmatique	Augmentation du pool de T4 et T3
Augmentation de désiodase de type III	Augmentation de dégradation T4 et T3
Augmentation de clairance urinaire de l'iode	Baisse de production hormonale (zones de déficit iodé)
Augmentation du volume thyroïdien maternel (inconstant)	Augmentation de TG sérique

TBG : *thyroid binding globuline* ; T_4 : thyroxine ; T_3 : triiodothyronine ; hCG : *human chorionic gonadotrophin* ; TSH : *thyroïd stimulating hormone* ; TG : thyroglobuline.

- **Quelques rappels:**
  - Les h. thyr. ont un rôle capital dans le développement cérébral (organisation, prolifération, migration neuronales)
  - Le placenta est perméable :
    - à l 'iode, au TRH
    - aux drogues antithyroïdiennes
    - aux anticorps anti-récepteurs à la TSH (IgG)
    - faiblement aux hormones thyroïdiennes, probablement dans les deux sens
  - Mais, il est imperméable à la TSH

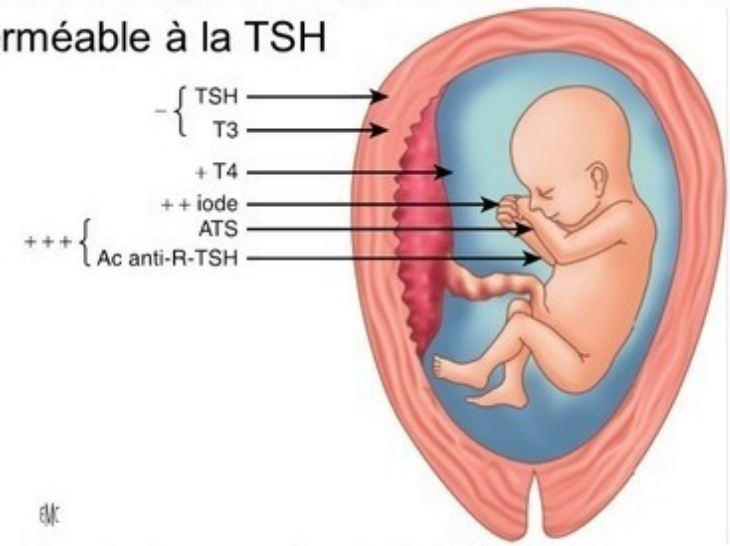
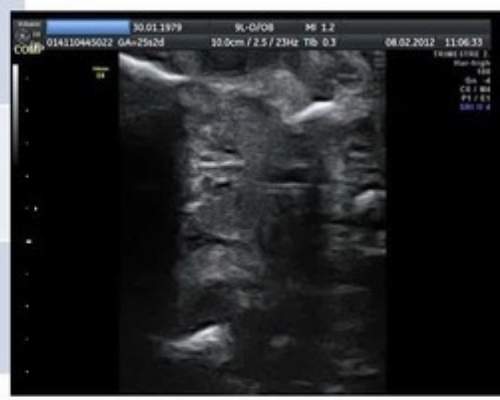


Figure 3. Passage transplacentaire des différents paramètres au cours du traitement de la maladie de Basedow. TSH : *thyroïd stimulating hormone* ; T3 : triiodothyronine ; T4 : thyroxine ; ATS : antithyroïdiens de synthèse ; Ac : anticorps ; R-TSH : récepteur à la TSH.

Complications Dysthyroïdies

	Hyperthyroïdie maternelle	Hypothyroïdie maternelle	Hyperthyroïde foetale	Hypothyroïdie foetale
Thyrotoxicose maternelle	+			
Mort fœtale in utero	+	+	+	+/-
Prématurité	+	+	+	+/-
Prééclampsie	+	+		
RCIU	+	+		
Insf cardiaque foetal			+	+/-
Maturation osseuse foetale			Avancée (craniosténose)	Retardée
Atteinte cérébrale Fœtale		+	+/-	+
Goitre et complications mécaniques			+	+



Lancet Diabetes Endocrinol 2016; 4: 35–43

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Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study

Tim I M Korevaar, Ryan Muetzel, Marco Medici, Layal Chaker, Vincent W V Jaddoe, Yolanda B de Rijke, Eric A P Steegers, Theo J Visser, Tonya White, Henning Tiemeier, Robin P Peeters

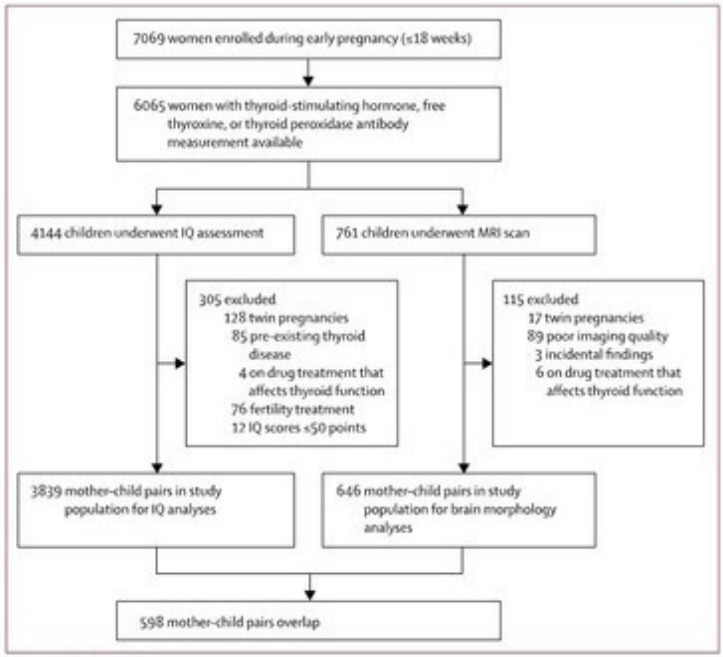


Figure 1: Study profile
IQ=intelligence quotient.

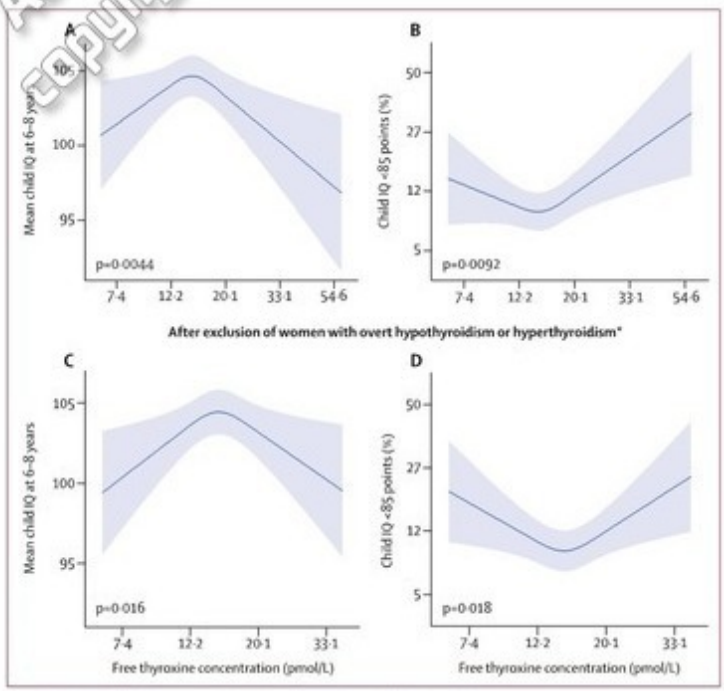


Figure 2: Association between maternal free thyroxine and offspring IQ
(A, C) Association between maternal free thyroxine concentrations during pregnancy and child IQ as predicted mean and 95% CI in the whole population (A) and after the exclusion of women with overt thyroid disease (C). (B, D) Association of maternal free thyroxine levels during pregnancy and the risk of child IQ below 85 as predicted back-transformed log odds with 95% CI in the whole population (B) and after the exclusion of women with overt thyroid disease (D). Scales for the x-axis might differ between the upper and lower graphs because of exclusions of women with overt, but not subclinical, disease entities. Appendix p 5 provides effect estimates from standard linear regression models. IQ=intelligence quotient. *Overt hypothyroidism and hyperthyroidism are defined as the biochemical diagnosis made during pregnancy, based on the central 95% reference range, as advocated in international guidelines.

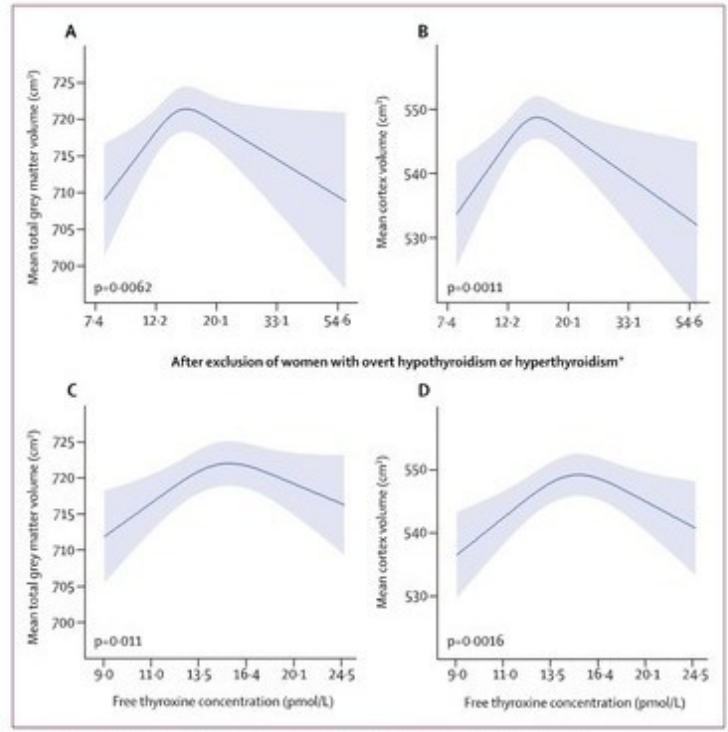


Figure 3: Association between maternal free thyroxine and offspring brain morphology
Plots show the association between maternal free thyroxine concentrations during early pregnancy and child MRI brain morphology outcomes (mean total grey matter volume [A, C] and mean cortex volume [B, D]) as predicted mean and 95% CI for the whole population (A, B) and after the exclusion of women with overt thyroid disease (C, D). Scales for the x-axis might differ between the upper and lower graphs because of exclusions of women with overt, but not subclinical, disease entities. Appendix p 10 provides effect estimates from standard linear regression models. *Overt hypothyroidism and hyperthyroidism are defined as the biochemical diagnosis made during pregnancy, based on the central 95% reference range, as advocated in international guidelines.

Seule la FT4 est impliquée ; pas la TSH
Médiane évaluation à 6 ans

Maternal thyroid function during pregnancy and child brain morphology: a time window-specific analysis of a prospective cohort

Tova F. Chaker, Tim I M Korevaar, Tessa A Mulder, Tonya White, Ryan L Muetzel, Robin P Peeters, Henning Tiemeier

www.thelancet.com/diabetes-endocrinology Vol 7 August 2019

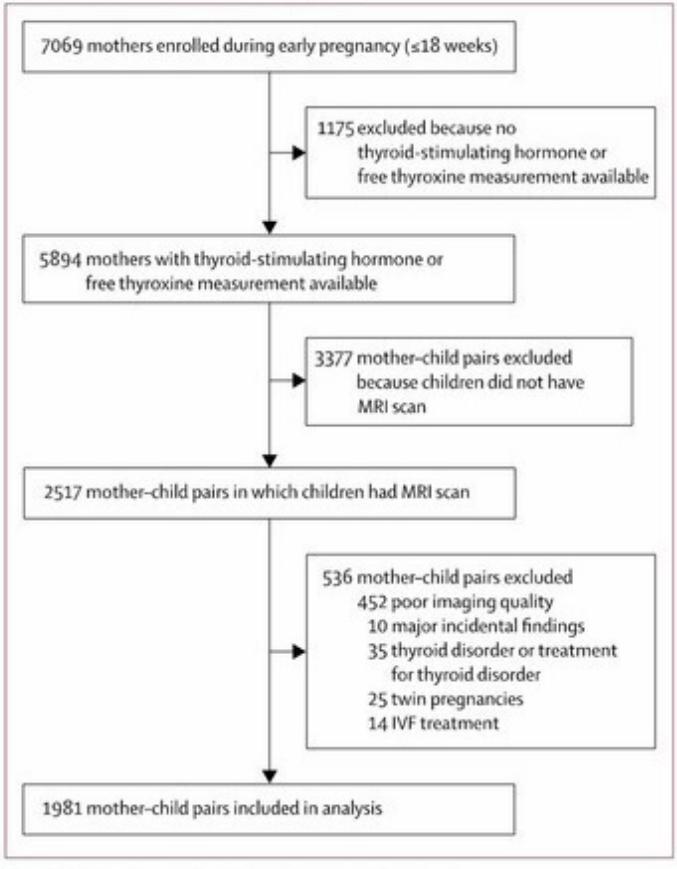


Figure 1: **Flowchart of participants through the study**

	All participants (n=1981)
Maternal characteristics	
Thyroid-stimulating hormone, mU/L*	1·33 (0·85–2·01)
Free thyroxine, pmol/L*	14·8 (13·2–16·6)
Thyroid peroxidase antibody positive	110 (6%)
Gestational age at blood sampling, weeks	13·1 (12·1–14·5)
Urinary iodine-to-creatine ratio, µg/g†	212·3 (142·1–308·9)
Urinary iodine-to-creatine ratio less than 150 µg/g†	242 (28%)
Age at intake, years	31·2 (27·9–33·9)
BMI	23·3 (21·4–26·0)
Parity	
0	1219 (62%)
1	560 (28%)
2	155 (8%)
≥3	47 (2%)
Smoking status	
No	1505 (76%)
Until pregnancy was known	192 (10%)
Yes	284 (14%)
Education level	
None or primary only	128 (6%)
Secondary phase 1 (3–4 years)	208 (10%)
Secondary phase 2 (4–5 years)	589 (30%)
Higher phase 1 (6–8 years)	484 (24%)
Higher phase 2 (>8 years)	572 (29%)
Ethnicity	
Dutch	1162 (59%)
Indonesian	75 (4%)
Cape Verdian	91 (5%)
Moroccan	94 (5%)
Dutch Antilles	39 (2%)
Surinamese	155 (8%)
Turkish	111 (6%)
Other European, North American, or Oceanian	172 (9%)
Other Asian, African, or South American	82 (4%)
Child characteristics	
Gestational age at birth, weeks	40·3 (39·3–41·0)
Birthweight, g	3460 (3100–3803)
Age at MRI, years	9·9 (9·7–10·2)
Sex	
Female	1003 (51%)
Male	978 (49%)

Data are median (IQR) or n (%). Data shown are after imputation of missing data. *Thyroid hormone measurements are available for n=1961 (TSH) and n=1971 (FT_4). †Urinary iodine-to-creatinine ratio available for 867 participants.

Table: **Descriptive characteristics of the study population**

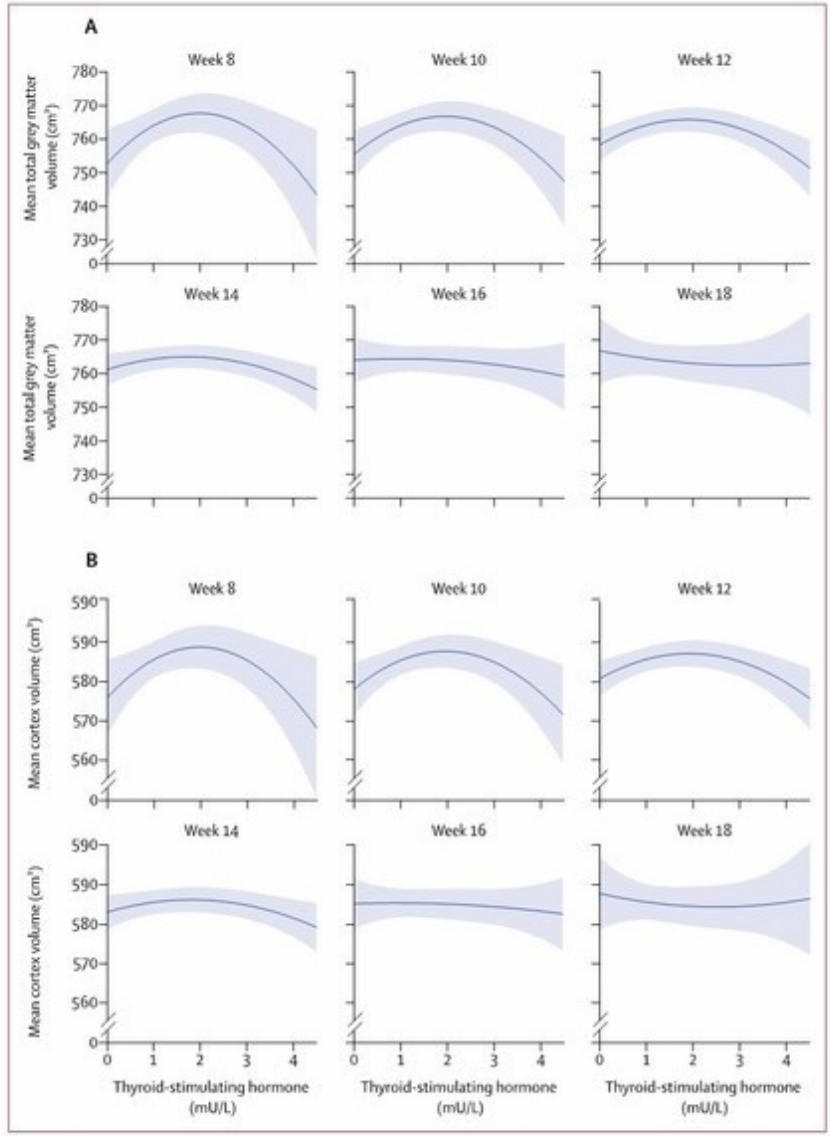


Figure 3: **The association of maternal thyroid stimulating hormone with child grey matter volume (A) or cortical grey matter volume (B) stratified by gestational age at blood sampling**

Analyses were adjusted for gestational age at blood sampling, maternal age, ethnicity, education level, smoking, thyroid peroxidase antibody positivity (>60 IU/mL), child sex, age at MRI, and total intracranial volume.

Human Thyroidian Fœtus Dysfunction

Illness	Aproximative Frequency	Goiter	Transmission
Dysgenesia - Athyreosis - Ectopia - Hypoplasia	1/4000	no	Sporadic, Familial, AD AR Syndromic
Hormogenesis Failure	1/40000	yes	AR
HT Pit axis dysfunction - Pit 1 mutation - TSH B chain mutation	1/100000	no	AR
TSHr Mutation - Inactivation - Activation		 no yes	 AR AD AD- sporadic (neo)
Resistance to Thyr Hormones		yes	AD
Positive Maternal Trab - Inhibiting Hypo - Stimulating hyper		 no yes	Maternal through the placenta
ATS Toxic or Iodine overload		yes	Maternal through the placenta
Iodine Deficiency	++++	yes	environemental

Hyperthyroïdie maternelle

- 1 à 3% des grossesses
  - 0,2% cliniquement parlantes
- Cliniquement:
  - Amaigrissement, asthénie, tachycardie, sueurs, tremblement, diarrhées, énervement, anxiété, insomnie, signe du tabouret, (aménorrhée)

- Principales étiologies:
  - Thyrotoxicose gestationnelle
  - Basedow (Graves)
  - Thyroïdite
  - Adénome toxique
  - Thyrotoxicose factice
  - Grossesse molaire
  - Mutation de TSH-R

Maladie de Basedow

1ère cause d'hyperthyr.
1 femme sur /1500 à 2000
Thyroïde hypervascularisée soufflante

Signes oculaires
- Bénins : rétraction palpébrale, gène oculaire
- Exophtalmie +++

- Pas de scintigraphie
- Ac anti TSH-R
- Amélioration en cours de grossesse possible
- Rebond post partum +++
- Prééclampsie, crise aigue thyrotoxique, ins cardiaque
- Traitement médical / chirurgie au 2ème trimestre

Hyperthyroïdie maternelle: conséquences fœtales

Type 3 deiodinase is critical for the maturation and function of the thyroid axis.

- Modèle animal d'hyperthyroïdie fœtale à mère hyperthyroïdienne
  - Hypothyroïdie centrale post natale par surexposition in utero
  - RCIU

Fœtal Loss Associated with excess Thyroid Hormone Exposure
Anselmo J et al JAMA Aug 2004

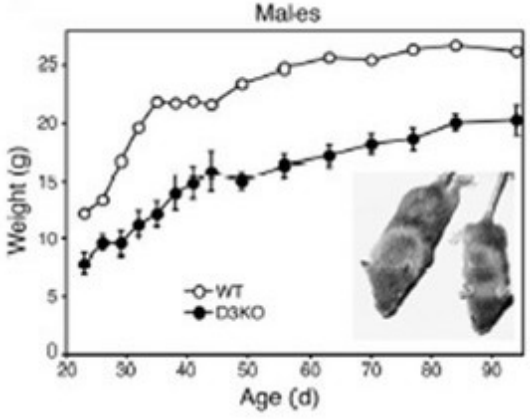


Figure 3
Postweaning growth curves of WT and D3KO male mice. Each point represents the mean ± SEM of measurements recorded in 7 to 58 animals at each age. Mean and median group size per data point were 18 and 12, respectively. Only data from animals born in litters of 3 to 7 pups are included. Data from extremely growth retarded D3KO mice, which typically do not survive through weaning, are not included. A picture of representative WT and D3KO weanlings is shown. Body length appear to be proportional to body weight.

Hernandez et al. J. Clin. Invest. 2006

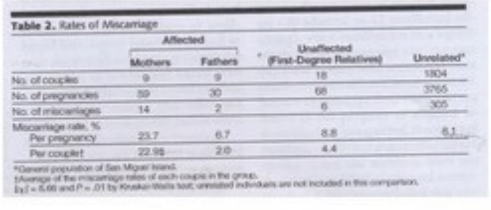
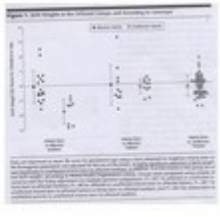


Table 2. Rates of Miscarriage

	Affected		Unaffected (First-Degree Relatives)	Unrelated*
	Mothers	Fathers		
No. of couples	9	9	18	1804
No. of pregnancies	59	30	68	3765
No. of miscarriages	14	2	6	305
Miscarriage rate, %				
Per pregnancy	23.7	6.7	8.8	8.1
Per couple†	22.9§	2.0	4.4	

*General population of San Miguel Island.
†Average of the miscarriage rates of each couple in the group.
§χ^2 = 6.68 and P = .01 by Kruskal-Wallis test; unrelated individuals are not included in this comparison.



Maladie de Basedow: conséquence fœtale

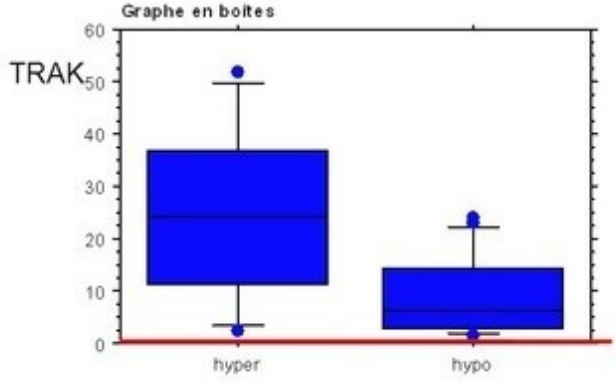
- Les TRAK peuvent persister pouvant passer la barrière placentaire
- Risque fœtal:
  - RCIU
  - Prématurité
  - MFIU
  - Basedow fœtal:
    - TRAK + (cut off 10)
- 2 à 10% des fœtus de mère Basedowienne ACTUELLE OU PASSEE (1/5000 N)

THYROIDECTOMIE ANTERIEURE*	TRAK +	TRAK -
OUI	14 (42%)	19
NON	10 (28%)	26

Test-t séries appariées
Ecart théorique = 0

	Ecart moyen	DDL	t	p
hyper, hypo	18,577	6	3,576	,0117

Graphe en boîtes



Statistiques descriptives

	Moy.	Dév. Std	Erreur Std	Nombre	Minimum	Maximum	# Manquants
hyper	25,067	17,207	6,504	7	2,470	52,000	10
hypo	9,302	7,647	1,855	17	1,500	24,000	0

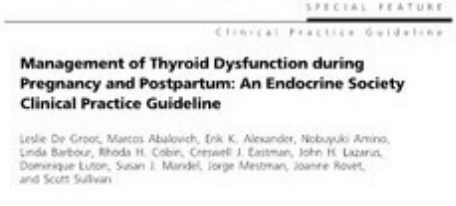
	TRAK +,+	TRAK +,-	TRAK -,-	TRAK -,+
ATS	15	0	8	1
LT4	5	1	17	0
ATS, LT4	3	0	0	0
Aucun	5	2	15	0
Total 3 dossiers incomplets	28	3	40	1

Maladie de Basedow: traitement maternel

- Surveillance biologique : FT4 TSH / 4 semaines
- Maintien d'une « hyperthyroïdie limite »
  - PTU pour maintenir les taux de T4l à la limite sup.
    - Chirurgie en cas d'échec ou d'intolérance du traitement
  - Risque d'hypothyr. foetale par passage placentaire des ATS et d'hyperthyr fœtale par passage des TRAK, d'où monitorage échographique de la thyroïde foetale
- Tt symptomatique: ß bloquant, …
- Pas de Lévothyrox en add back therapy sauf hyperthyroïdie fœtale résistante
- NFS de contrôle
- BHC de contrôle PTU

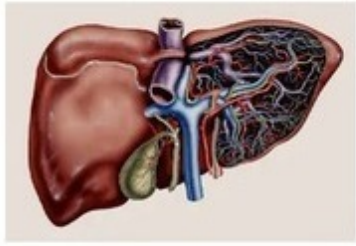
Choix de l'ATS

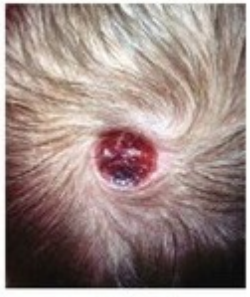
- 1er trimestre = PTU
- 2ème et 3ème trimestre = on peut maintenir le PTU mais envisager NMZ


SPECIAL FEATURE
Clinical Practice Guideline

Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline

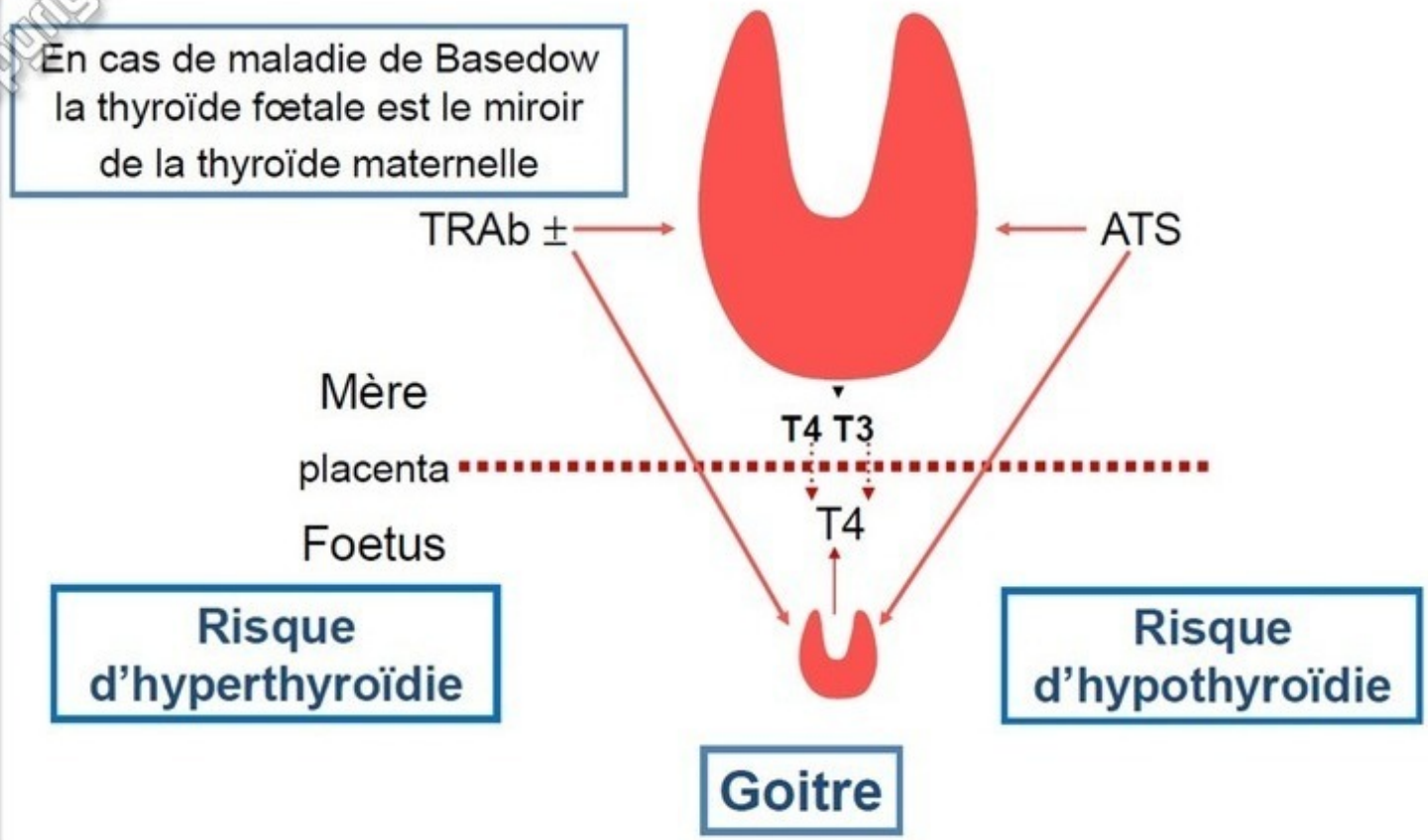
Leslie De Groot, Marcos Abalovich, Erik K. Alexander, Nobuyuki Amino, Linda Barbour, Rhoda H. Cobin, Creswell J. Eastman, John H. Lazarus, Dominique Luton, Susan J. Mandel, Jorge Mestman, Joanne Rovet, and Scott Sullivan





Author: Mark A Crowe, MD, Assistant Clinical Instructor, Department of Medicine, Division of Dermatology, University of Washington School of Medicine

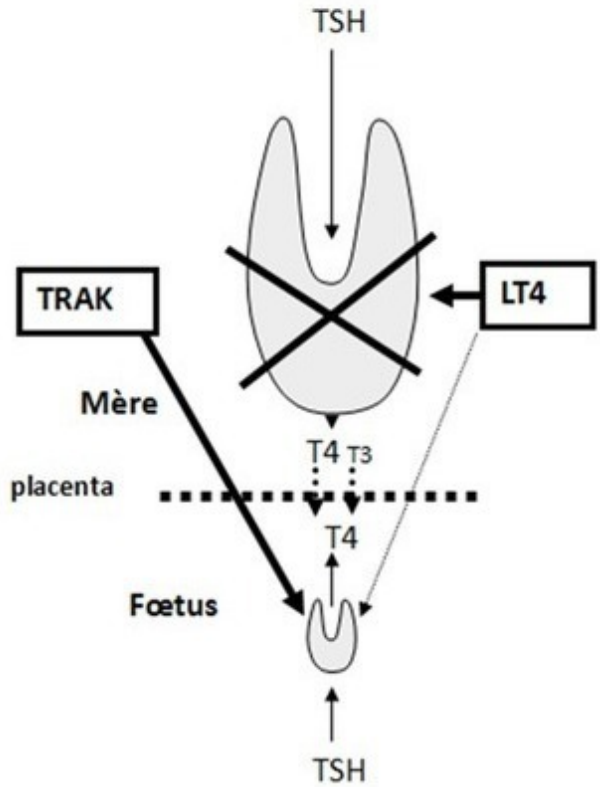
Thyroxinémie Maternelle



Juliette Abeillon du Payrat, Symposium « la Thyroïde dans tous ses états » 2015

Maladie de Basedow traitée par iode 131 ou chirurgie

- Risque d'hyperthyroïdie fœtale sans hyperthyroïdie maternelle
- Interroger les patientes
- Doser les TRAK en début de grossesse et au 2è trimestre (étude lyonnaise)



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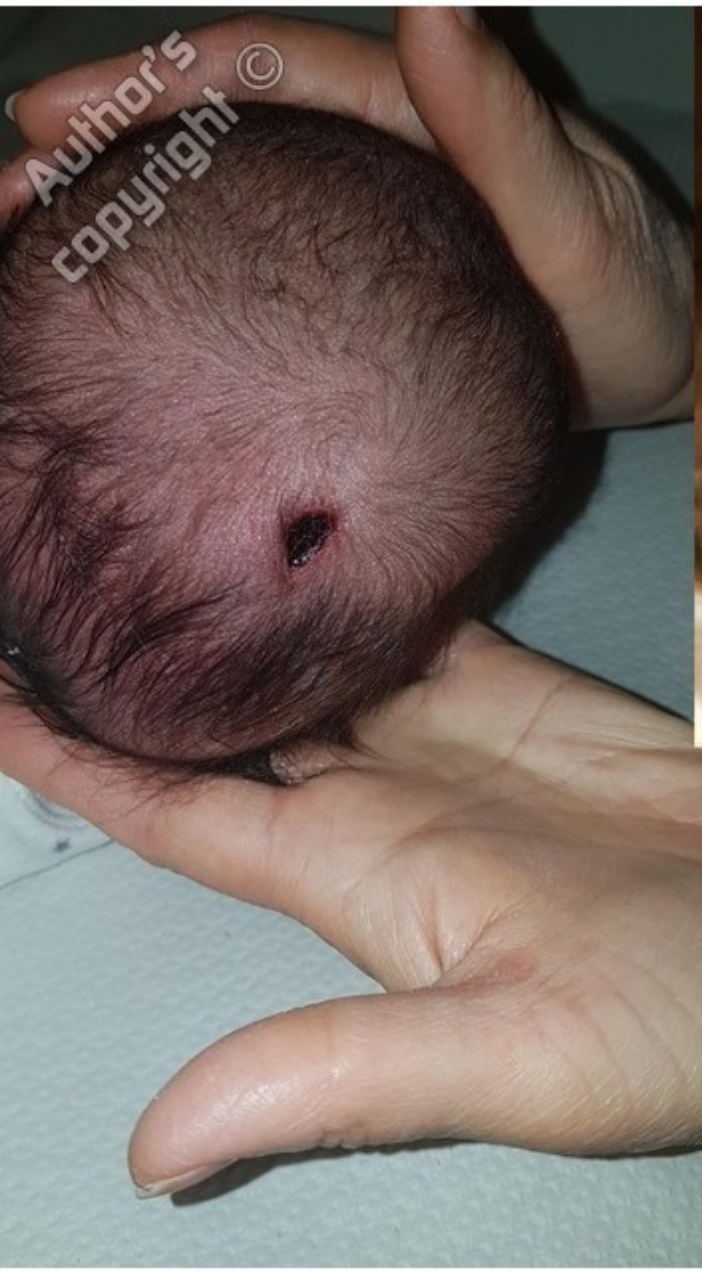
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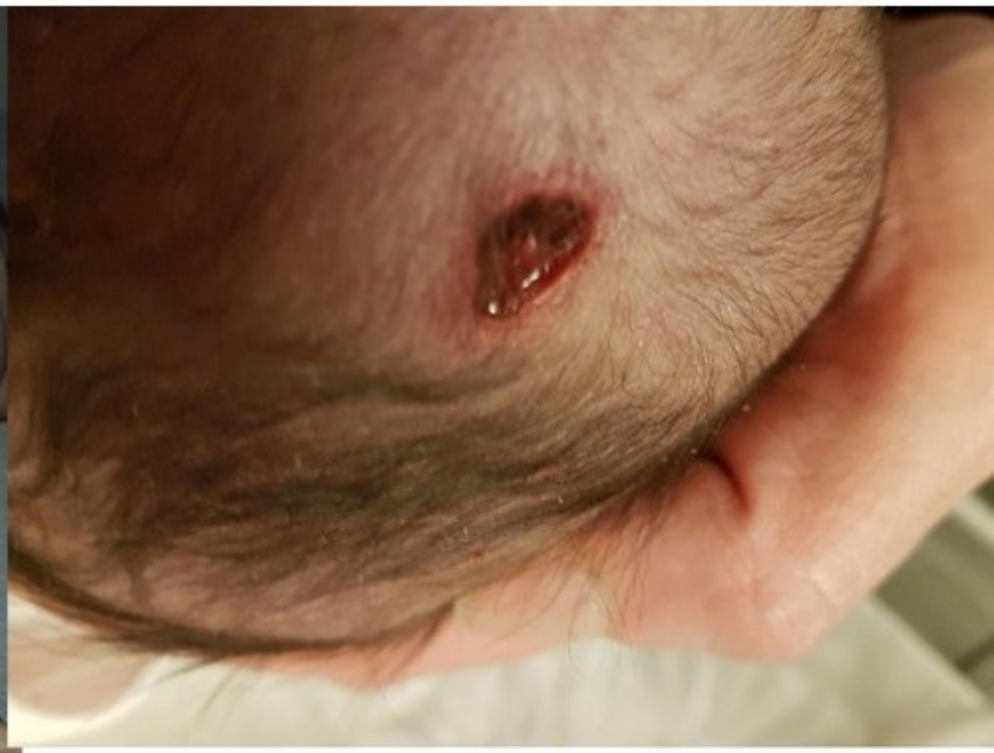

Tableau 1. Cas publiés d'embryopathies après exposition *in utero* au MMI ou au CMZ (1972 - 2010)

		n		Malformations associées
		MMI	CMZ	
Nombre de cas = 67		**43**	**24**	
ACC	Isolée	14	4	
	Associée	9	2	DF (n=6), AC (n=2) RPM, épilepsie, hypertonie Hypoacousie Athélie, hélix anormal, autres anomalies ectodermiques (syndactylie, mamelons surnuméraires, ongles dystrophiques) Hypospade Omphalocèle, hernie ombilicale, imperforation anale, canal vitello-intestinal persistant, canal de l'Ouraque persistant, sinus pilonidal sacré Scalp-ear-nipple syndrome, syndrome de Roviralta Trachéomalacie
AC	Isolée	1	2	
	Associée	7	6	DF (n=10) RPM (n=4), hypotonie, hypertonie, troubles de la succion Colobome, hypoacousie (n=3) ACC (n=2), hypoplasie mamelonnaire (n=2), athélie Rein pelvien CIV, coarctation de l'aorte, canal artériel persistant AE (n=2), hernie ombilicale, canal vitello-intestinal persistant (n=2), sinus pilonidal sacré
AE +/- FTO	Isolée	1	0	
	Associée	6	0	DF (n=2), AC (n=2) RPM, hypotonie CIV (n=2), CIV-malposition aortique, canal artériel persistant Omphalocèle (n=2)
Autres		8	10	DF (n=5), fente palatine, luette bifide, palais ogival RPM (n=2), atrophie cérébrale, syndrome de West Cataracte congénitale bilatérale Athélie unilatérale Agénésie rénale bilatérale (syndrome de Potter) (n=2), hypospade (n=3), urétérocèle droite, HH CIV, CAV Spina bifida, hémivertèbre, synostose radio-ulnaire, adactylie partielle du pied, craniosténose Laparoschisis (n=2), omphalocèle, canal vitello-intestinal persistant

ACC : Aplasia Cutis Congenita ; AC : Atrésie des Choanes ; AE : Atrésie de l'œsophage ; FTO : Fistule Trachéo-Oesophagienne ; MMI : Méthimazole ; CMZ : Carbimazole ; DF: Dysmorphie Faciale ; RPM : Retard Psycho-Moteur ; CIV : Communication Inter-Ventriculaire ; CAV : Canal Atrio-Ventriculaire ; HH : Hypogonadisme Hypogonadotrope

Choix de l'ATS

- 1er trimestre = PTU

- 2ème et 3ème trimestre = on peut maintenir le PTU mais envisager NMZ

SPECIAL FEATURE

Clinical Practice Guideline

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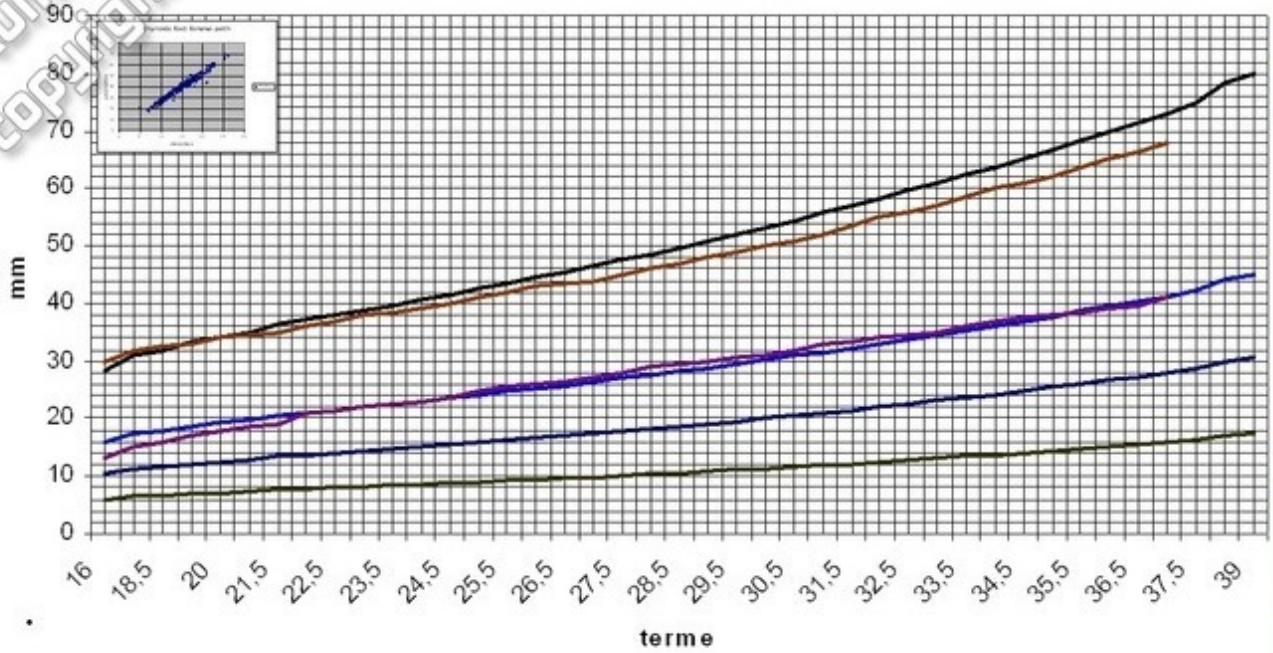
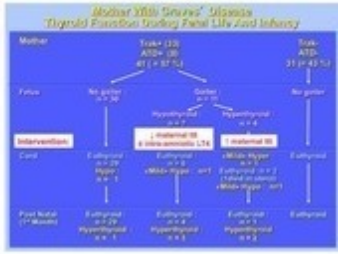
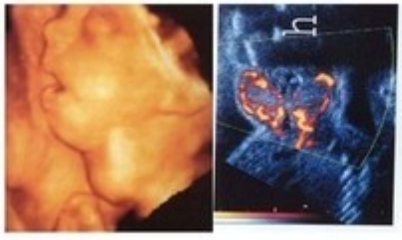
Comment détecter et traiter une dysfonction thyroïdienne foetale ?

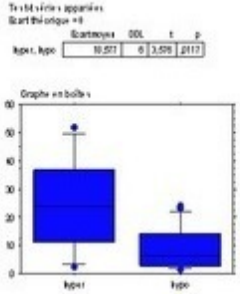
Courbes de thyroïdes foetales





Oyelese et al Ultrasound Obs Gynecol 2005; 25;312-314

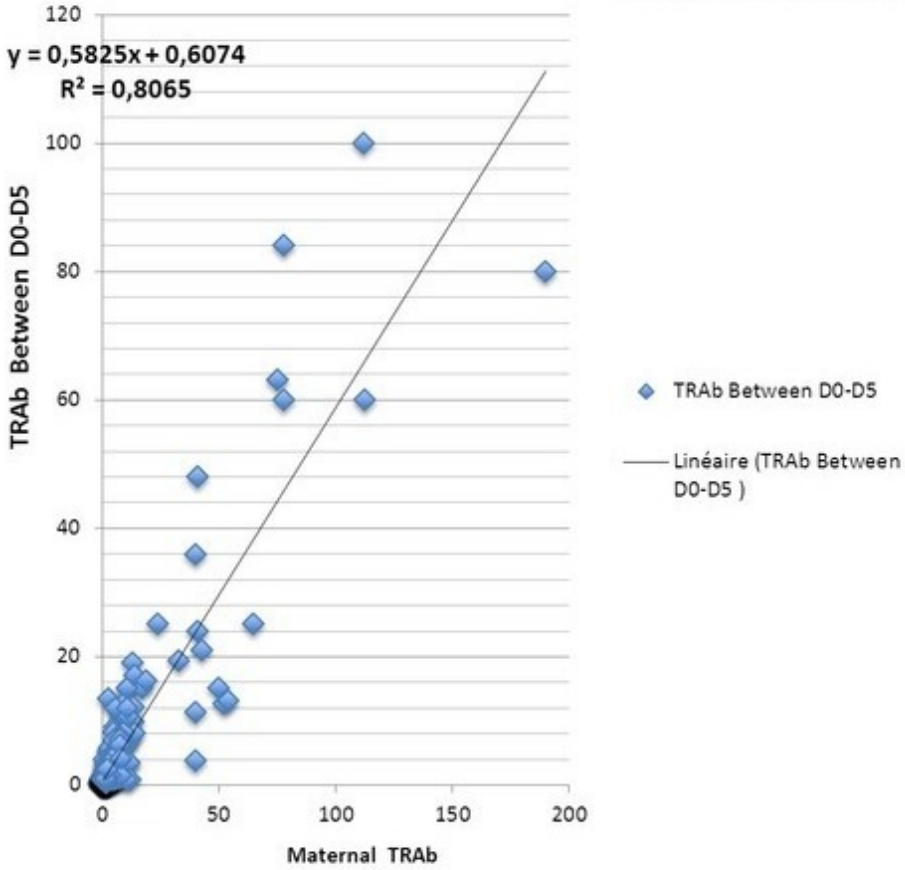


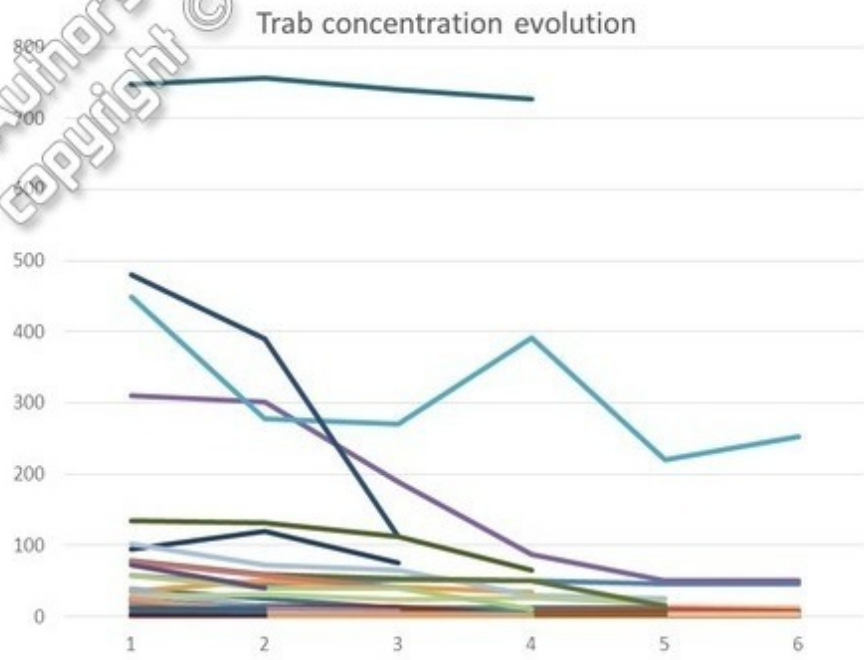


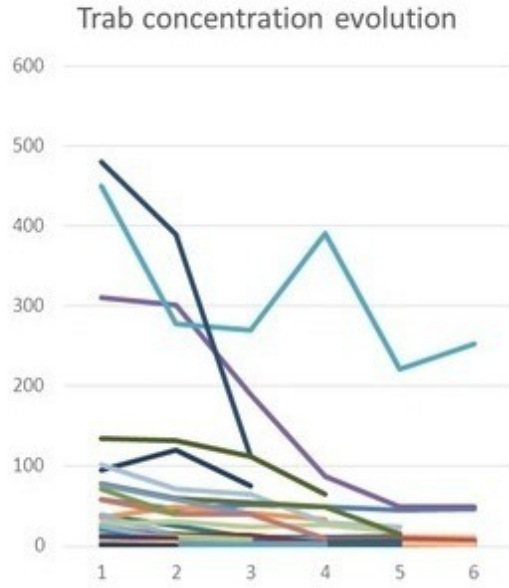
Thyroxinémie Maternelle

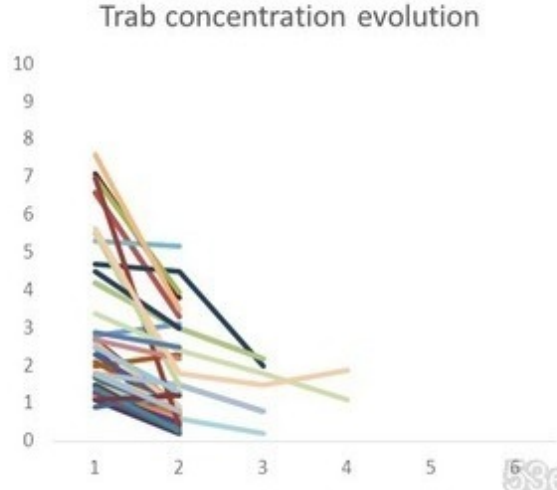
Association between the maternal TRAb value during pregnancy and TRAb (child) D0-D5

Data non encore publiée: Dr Banigé, Pr Luton









ENDOCRINE SOCIETY

[illegible]Study of the factors leading to foetal and neonatal dysthyroidism in children of [illegible] with Graves' disease

Maia Ban[illegible], [illegible] Estellat, Valerie Biran, Luc Desfrere, Valerie Champion, Alexandra Bena[illegible], [illegible] Ville, Marc Dommergues, Pierre-Henri Jarreau, Mostafa Mokhtari, Claire Bo[illegible], [illegible] Brioude, Laurent Mandelbrot, Pierre François Ceccaldi, Delphine [illegible], Michel Polak, Dominique Luton

Table 4. Relationship between neonatal dysthyroidism and the predictor variable (Maternal or neonatal TRAb level).

Predictor Variable	Optimal Cut-off IU/L	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	correctly classified %	AUC (95% CI)
	In the population of all women N=417						
Max maternal TRAb	5.9	100 [100-100]	82 [78-86]	26 [22-30]	100 [100-100]	83	0.97 [0.95-0.99]
Neonatal TRAb Between D0-D5	6.8	100 [100-100]	94 [92-96]	50 [45-55]	100 [100-100]	92	0.98 [0.97-0.99]
	In the population of women receiving ATDs during pregnancy N=145(35.0%)						
Max maternal TRAb	5.9	100 [100-100]	61 [53-69]	29 [22-36]	100 [100-100]	66	0.93 [0.87-0.98]
Neonatal TRAb Between D0-D5	6.8	100 [100-100]	89 [84-94]	59 [51-67]	100 [100-100]	90	0.97 [0.94-0.99]
	In the population of women not receiving ATDs during pregnancy N=272(65.0%)						
Max maternal TRAb	5.9	100 [100-100]	92 [89-95]	19 [15-23]	100 [100-100]	92	0.99 [0.97-1.0]
Neonatal TRAb Between D0-D5	6.8	100 [100-100]	96 [94-98]	31 [25-37]	100 [100-100]	96	0.99 [0.99-1.0]

Table 3. Relationship between foetal thyroid hypertrophy and the level of maternal TRAb.

Predictor Variable	Optimal Cut-off IU/L	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Cor-rectly classified %	AUC (95% CI)
	In the population of all women N=417						
Max maternal TRAb	2.5	100 [100-100]	64 [60-68]	26 [22-30]	100 [100-100]	68	0.91 [0.87-0.94]
	In the population of women receiving ATDs during pregnancy N=145(35.0%)						
Max maternal TRAb	2.5	100 [100-100]	39 [31-47]	38 [30-46]	100 [100-100]	40	0.83 [0.76-0.90]
	In the population of women not receiving ATDs during pregnancy N=272 (65.0%)						
Max maternal TRAb	2.5	100 [100-100]	73 [68-78]	8 [5-11]	100 [100-100]	74	0.91 [0.87-0.94]

Prediction of Neonatal Hyperthyroidism

Maïa Banigé, MD[1], Michel Polak, MD, PhD[2], Dominique Luton, MD, PhD[3], and Research Group for Perinatal Dysthyroidism (RGPD) Study Group*

Table I. Risk factors for development of NH*

	Univariate analysis		Multivariate analysis	
Predictor variables	**OR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**
Log(FT4), days 3-7, pmol/L	17.58 (4.92-62.86)	<.0001	0.13 (0.01-1.67)	.12
Log(TSH), days 3-7, mU/L	0.23 (0.14-0.38)	<.0001	0.47 (0.28-0.80)	.005
Log(TRAb), day 0-5, IU/L	31.73 (6.67-150.96)	<.0001	26.70 (3.48-204.81)	.002
TSH cutoff (days 3-7) = 0.90 mU/L (N = 415)				
Sensitivity, % (95% CI)				78 (74-82)
Specificity, % (95% CI)				99 (99-100)
Positive predictive value, % (95% CI)				90 (87-93)
Negative predictive value, % (95% CI)				98 (97-99)
Correctly classified, %				98

*In the population of all women (N = 415), according to univariate and multivariate logistic regression model analyses showing the aOR.

ENDOCRINE SOCIETY

Study of the factors leading to foetal and neonatal dysthyroidism in children of patients with Graves' disease

Maïa Banigé Candice Estellat, Valerie Biran, Luc Desfrere, Valerie Champion, Alexandra Benachi, Yves Ville, Marc Dommergues, Pierre-Henri Jarreau, Mostafa Mokhtari, Claire Boithias, Frederic Brioude, Laurent Mandelbrot, Pierre-François Ceccaldi, Delphine Mitanchez, Michel Polak, Dominique Luton

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Endocrine Society

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Table 6: In the population of all women (N=417) : Risk factors for development of neonatal dysthyroidism based on univarante and multivariante logistic regression model analyses showing adjusted odds ratio (aOR) and 95% confidence interval (CI)

Predictor Variable	Univariate analysis		Multivariante analysis	
	OR (95% CI)	P value	aOR (95% CI)	P value
TRAb between D0-D5 IU/L	1.45[1.29-1.63]	p<0.0001	1.41[1.22-1.62]	p<0.0001
Bio.Imbalance (mother)	17.58[7.25-42.62]	p<0.0001	2.56[0.52-12.49]	p=0.24
Foetal thyroid hypertrophy	42.81[15.79-116.08]	p<0.0001	8.35[1.66-42.03]	(p)<0.01
AUC (95% CI)	0.98 [0.97-0.99]		0.97 [0.83-1.00]	

Table 3. Relationship between foetal thyroid hypertrophy and the level of maternal TRAb.

Predictor Variable	Optimal Cut-off IU/L	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Correctly classified %	AUC (95% CI)
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Table 4. Relationship between neonatal dysthyroidism and the predictor variable (Maternal or neonatal TRAb level).

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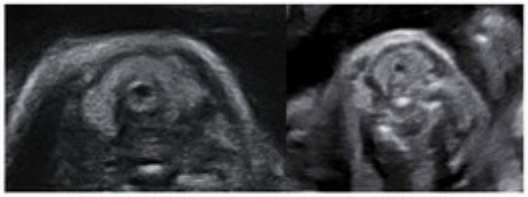
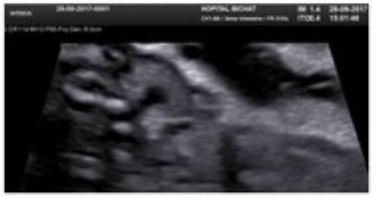
Monitorage de la thyroïde fœtale

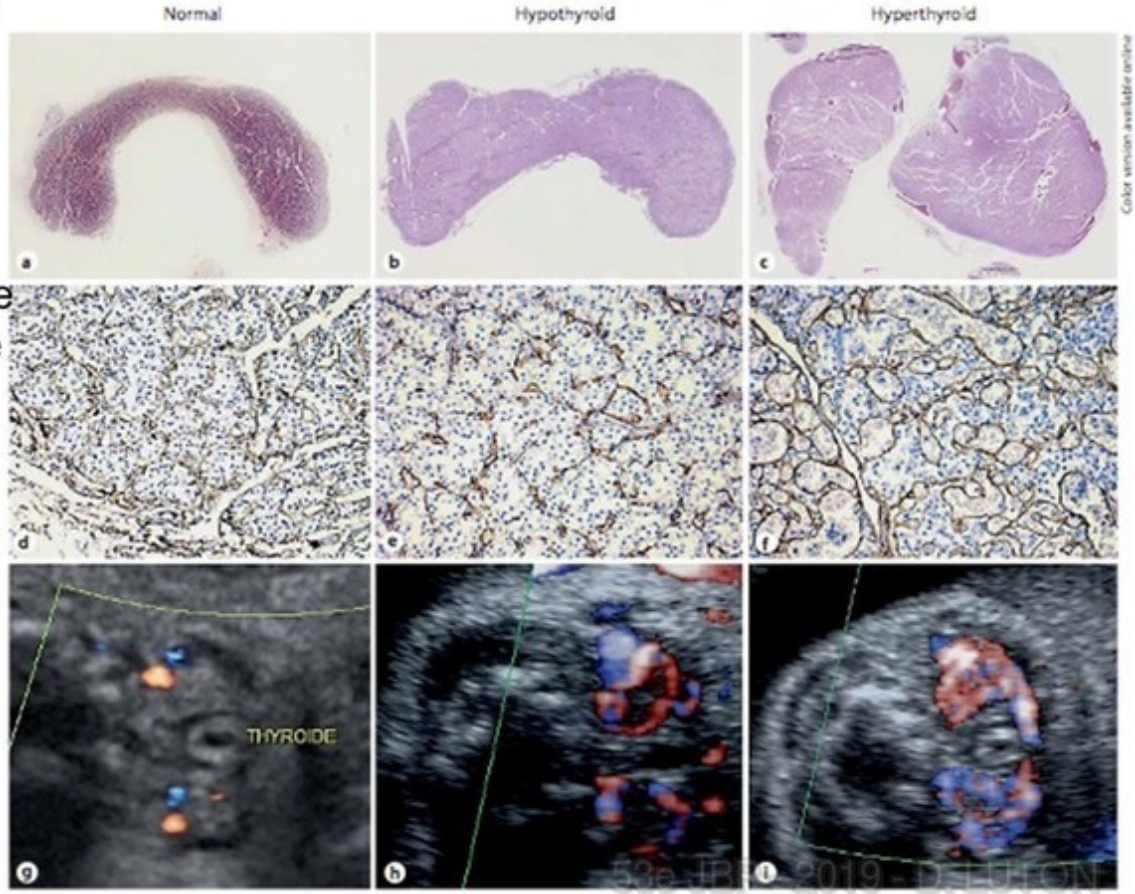
Correlation between Colored Doppler Echography of Fetal Thyroid Goiters and Histologic Study

Pierre-François Ceccaldi[a] Sandra Cohen[b] Edith Vuillard[a] Fabien Guimiot
Anne-Lise Delezoide[c] Olivier Poujade[a] Guillaume Ducarme[a]
Jean-François Oury[a] Dominique Luton[a]

Intérêts de l'échographie:
- FC fœtale
- maturation osseuse
- vascularisation thyr. fœtale
- diamètre de la thyr. fœtale
- mouvements fœtaux



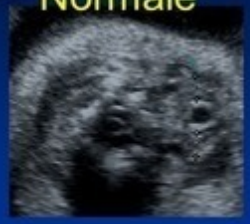




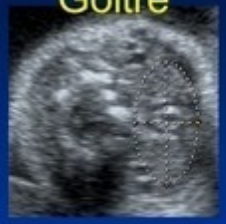
Fetal Diagn Ther 2010;27:233–235

Thyroïde fœtale : étude doppler du fonctionnement

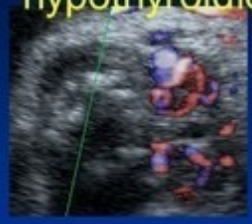
Normale



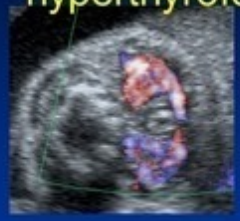
Goitre

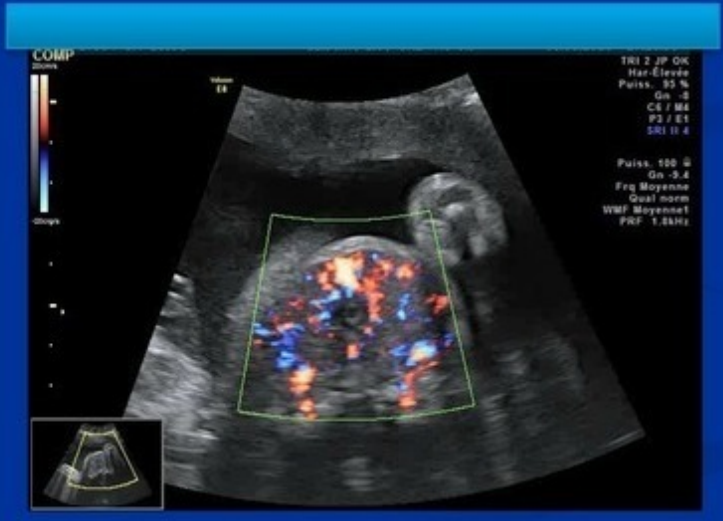


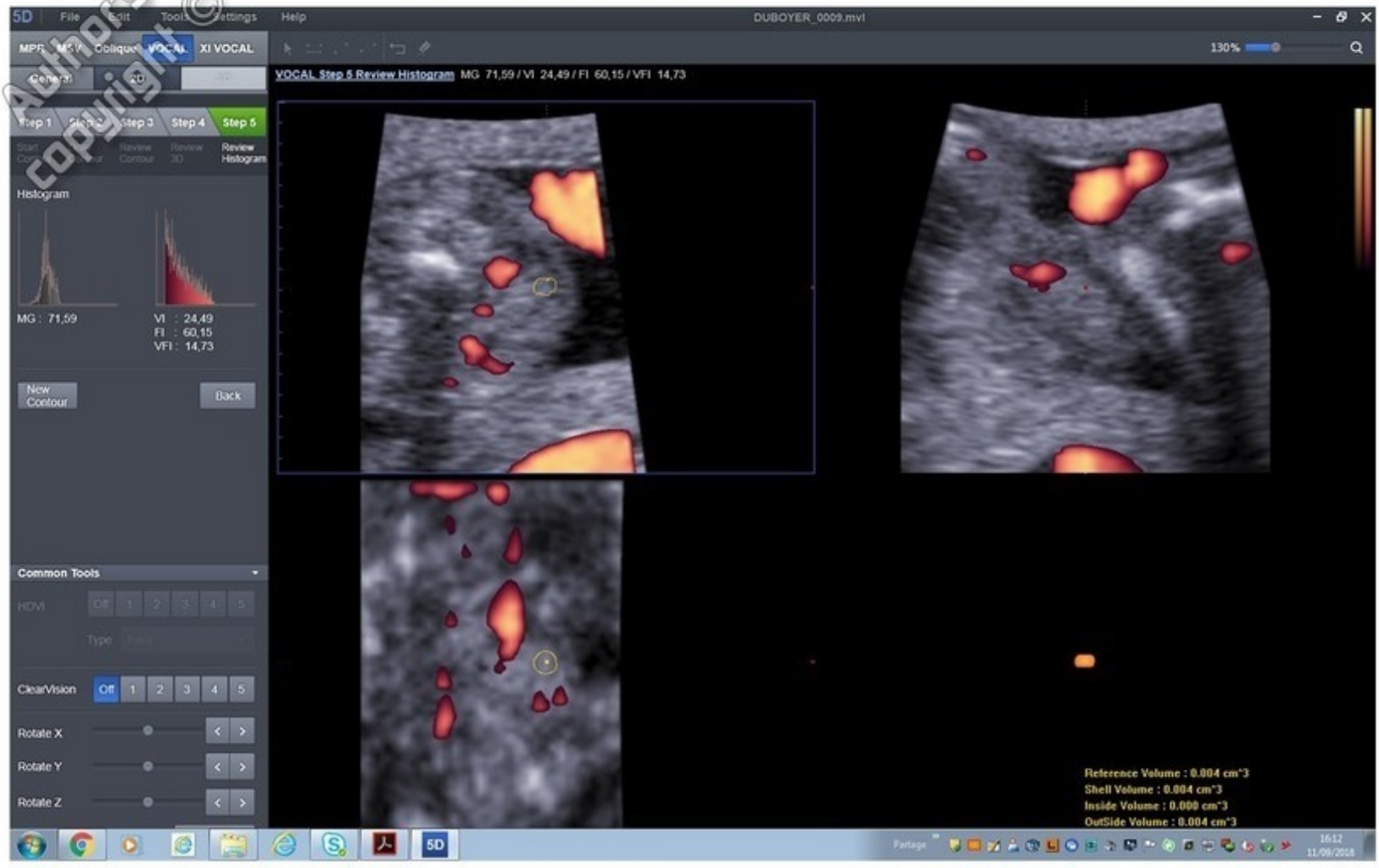
hypothyroidie



hyperthyroïdie







Mother With Graves' Disease
Thyroid Function During Fetal Life And Infancy

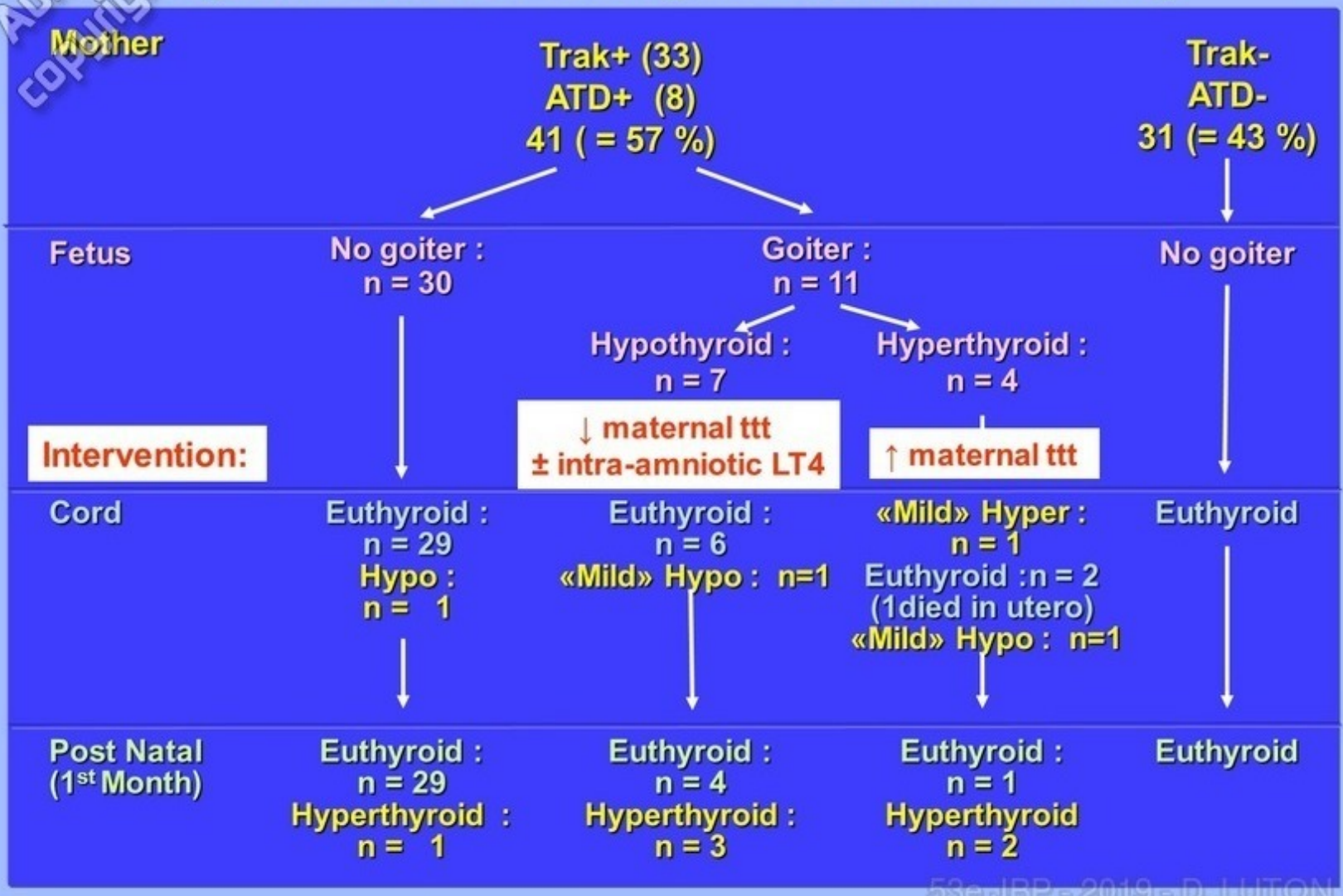


TABLE 2. Fetuses at 32 WG: seven with hypothyroidism (cases 1–7) and four with hyperthyroidism (cases 8–11)

Case no.	32 WG							Birth			
				Fetal blood sampling[c]					Cord blood[e]		
	TRAK ULN[a]	Treatment dose (mg/d)	Doppler[b]	FT_4 (pmol/liter)	TSH (mIU/liter)	IAT_4	FHR	Bone[d]	FT_4 (pmol/liter)	TSH (mIU/liter)	Neonatal hyperthyroidism
1	0	PTU 300	Periph	5.2	445	Yes	Normal	Normal	13.9	10.8	No
2	0	PTU 100	Periph	7	56	No	Normal	Normal	12	13.5	No
3	20	PTU 300	Periph				Normal	Delayed	9.7	5	Yes
4	1.8	PTU 100	Total				Normal	Normal	12.8	10.5	Yes
5	4	PTU 300	Total	3.9	483	Yes	Normal	Normal	13.9	12	No
6	1.8	PTU 50	Periph				Normal	Normal	12	2.5	No
7	8	NCZ 30	No	5.3	323	Yes	Normal	Delayed	16.4	2.4	Yes
8	37	PTU 200	Total				Normal	Advanced	8.4	6.6	Yes
9	325	NCZ 30	Total	51.7	<0.05		>160	Normal	19.3	<0.05	Death
10	19	PTU 250	Total				Normal	Advanced	12.9	<0.05	Yes
11	3.3	PTU 250	Total	14.8	<0.05		Normal	Normal	15.2	4.4	No

[a] Number of times the upper limit of normal.
[b] Periph, Peripheral signal; Total, signal throughout the thyroid gland; IAT_4, intraamniotic L-T_4 injection.
[c] A value of 14 pmol/liter is the upper limit of our normal data [the fetus with FT_4 of 14.8 pmol/liter had FT_3 of 7.5 pmol/liter for an upper limit of normal of 1.9 pmol/liter (25)].
[d] Bone maturation.
[e] Normal ranges for cord blood values were: FT_4, 10.4–16.4 pmol/liter; and TSH, 2.6–11.8 mU/liter (25).

Luton et al. Management of Graves' Disease during Pregnancy: The Key Role of Fetal Thyroid Gland Monitoring (J Clin Endocrinol Metab 90: 6093–6098, 2005)

Ultrasound Obstet Gynecol 2009; **33**: 412–420
Published online in Wiley InterScience (www.interscience.wiley.com). **DOI:** 10.1002/uog.6315

Use of ultrasound to distinguish between fetal hyperthyroidism and hypothyroidism on discovery of a goiter

C. HUEL*, J. GUIBOURDENCHE†, E. VUILLARD*, J. OUAHBA*, M. PIKETTY*, J. F. OURY* and D. LUTON*

*Departments of *Perinatology and †Endocrine Biochemistry, Robert Debré Hospital, Paris, France*

Table 1 Characteristics of the study population of 39 fetuses with goiter

	Maternal characteristics				*Fetal characteristics*			
Case	*Maternal thyroid disease*	*Antithyroid drugs**	*TRAb maximum†*	*Maternal thyroid status‡*	*Fetal thyroid status§*	*GA (weeks)¶*	*FBS (n)*	*Cord blood sampling at delivery*
1	Graves' disease	Yes	21N	Hypo.	Hyper.	23.5	2	Euthyroid (TSH unmeasurable)
2	Graves' disease	Yes	78N	Hypo.	Hyper.	29	1	Euthyroid (TSH unmeasurable)
3	Graves' disease	Yes	8N	Euthyroid**	Hyper.	34	0	Hypo.
4	Graves' disease	Yes	Negative	Euthyroid**	Hypo.	34.5	0	Hypo.
5	Graves' disease	Yes	2.8N	Euthyroid**	Hypo.	38	0	Compensated hypo.
6	No	No	Negative	Euthyroid	Hypo.	25.5	2	Hypo.
7	Graves' disease	Yes	Positive	Hypo.	Hypo.	36	0	ND
8	Graves' disease	No	Negative	Hypo.	Hypo.	35	0	Compensated hypo.
8a	Graves' disease	No	Negative	Hypo.	Hypo.	36	0	Compensated hypo.
9	Graves' disease	Yes	8N	Hypo.	Hypo.	38	0	Compensated hypo.
10	Graves' disease	Yes	Negative	Euthyroid	Hypo.	36	0	Compensated hypo.
11	Toxic nodular goiter	Yes	Negative	Euthyroid	Hypo.	29	1	Euthyroid
12	Graves' disease	Yes	Negative	Euthyroid**	Hypo.	23	0	Stillborn (hypo.)
13	Graves' disease	Yes	3.33N	Euthyroid**	Hypo.	26.5	0	Euthyroid
14	Graves' disease	Yes	Negative	Hypo.	Hypo.	23	2	Euthyroid
15	Graves' disease	Yes	23N	Hypo.	Hypo.	33.5	0	Euthyroid
16	Graves' disease	Yes	1.5N	Euthyroid**	Hypo.	32	1	Hypo. changed to hyper.
17	Graves' disease	Yes	4N	Euthyroid	Hypo.	23	1	Euthyroid
18	Graves' disease	Yes	52N	Euthyroid	Hyper.	22.5	1	Intrauterine death (TSH unmeasurable)
19	Graves' disease	No	40N	Euthyroid	Hyper.	28	1	Euthyroid
20	Graves' disease	No	24N	Euthyroid	Hyper.	32.5	1	Euthyroid (TSH unmeasurable)
21	Graves' disease	Yes	2.8N	Hypo.	Hypo.	26.2	1	Euthyroid
22	No	No	Negative	Euthyroid	Hypo.	22.5	1	ND
23	Graves' disease	Yes	2N	Euthyroid**	Hypo.	29	1	Euthyroid
24	Unclassified hyper.	Yes	Negative	Euthyroid	Hypo.	27	0	ND
25	Hyper. in pregnancy	Yes	Negative	Hypo.	Hypo.	26	1	Euthyroid
26	Hashimoto's disease	No	Negative	Euthyroid**	Hypo.	28.5	0	Euthyroid
27	Graves' disease	Yes	13.3N	Hypo.	Hypo.	32	1	Euthyroid
28	Graves' disease	Yes	1.7N	Euthyroid**	Hypo.	27	0	ND
29	Graves' disease	Yes	13N	Hypo.	Hypo.	22.5	2	Euthyroid
30	Graves' disease	Yes	2.47N	Hyper.	Hyper.	28.5	1	Euthyroid
31	Graves' disease	Yes	19N	Hyper.	Hypo.	23	2	Euthyroid
32	Graves' disease	Yes	24N	Hypo.	Hypo.	31	1	Euthyroid
33	Graves' disease	Yes	Negative	Euthyroid	Hypo.	29.5	1	Hypo.
34	Graves' disease	Yes	6.2N	Euthyroid	Hypo.	25.5	1	Compensated hypo.
35	Graves' disease	Yes	11.8N	Euthyroid**	Hypo.	32.5	1	ND
36	Graves' disease	Yes	17.2N	Hypo.	Hypo.	22	2	Compensated hypo.
37	Graves' disease	Yes	5.5N	Euthyroid	Hypo.	28	1	Compensated hypo.
38	Unclassified hyper.	Yes	Negative	Hypo.	Hypo.	33.5	0	Euthyroid

Case numbers correspond to pregnancies; Cases 1 and 2 were two different pregnancies in the same woman and Case 8/8a was a twin pregnancy with two affected fetuses. *Mother using antithyroid drugs when fetal goiter was discovered. †TRAb results are presented as multiples of the normal (N) value. ‡Thyroid status of mother when fetal goiter discovered. §Prenatal diagnosis. ¶GA at discovery of fetal goiter. **Thyroxine in normal low range. FBS, fetal blood sampling; GA, gestational age; Hypo, hypothyroid; Hyper, hyperthyroid; ND, not determined; TRAb, antibodies against TSH receptor; TSH, thyroid-stimulating hormone.

Table 2 Ultrasound findings according to fetal thyroid status in 39 fetuses with goiter

	Vascularization of goiter			*Bone maturation*		
Fetal thyroid status	*Peripheral*	*Central*	*Tachycardia*	*Delayed*	*Accelerated*	*Fetal movements increased*
Hypothyroidism	22/32 (68.8)	0	2/32 (6.3)	15/32 (46.9)	0	14/32 (43.8)
Hyperthyroidism	1/5 (20)	3/5 (60)	4/7 (57.1)	0	6/7 (85.7)	0
P^*	0.0574	0.0013	0.0055	0.0307	< 0.0001	0.0364

Values given as n (%). *Fisher's exact test, significance threshold: $P < 0.05$.

Table 3 Ultrasound score to distinguish hypo- from hyperthyroidism in fetuses with goiter

Ultrasound finding	*Weighting*
Vascularization	
Peripheral or absent	0
Central	1
Fetal heart rate	
Normal	0
Tachycardia	1
Bone maturation	
Delayed	−1
Normal	0
Accelerated	1
Fetal movements	
Normal	1
Increased	0

An overall score ≥ 2 is suggestive of hyperthyroidism and a score < 2 is indicative of hypothyroidism.

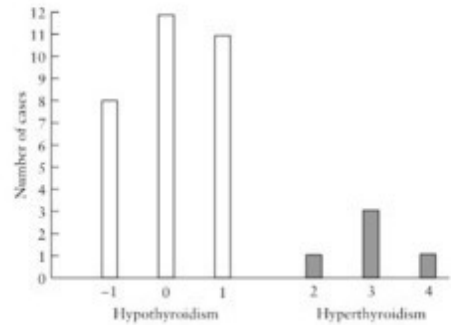
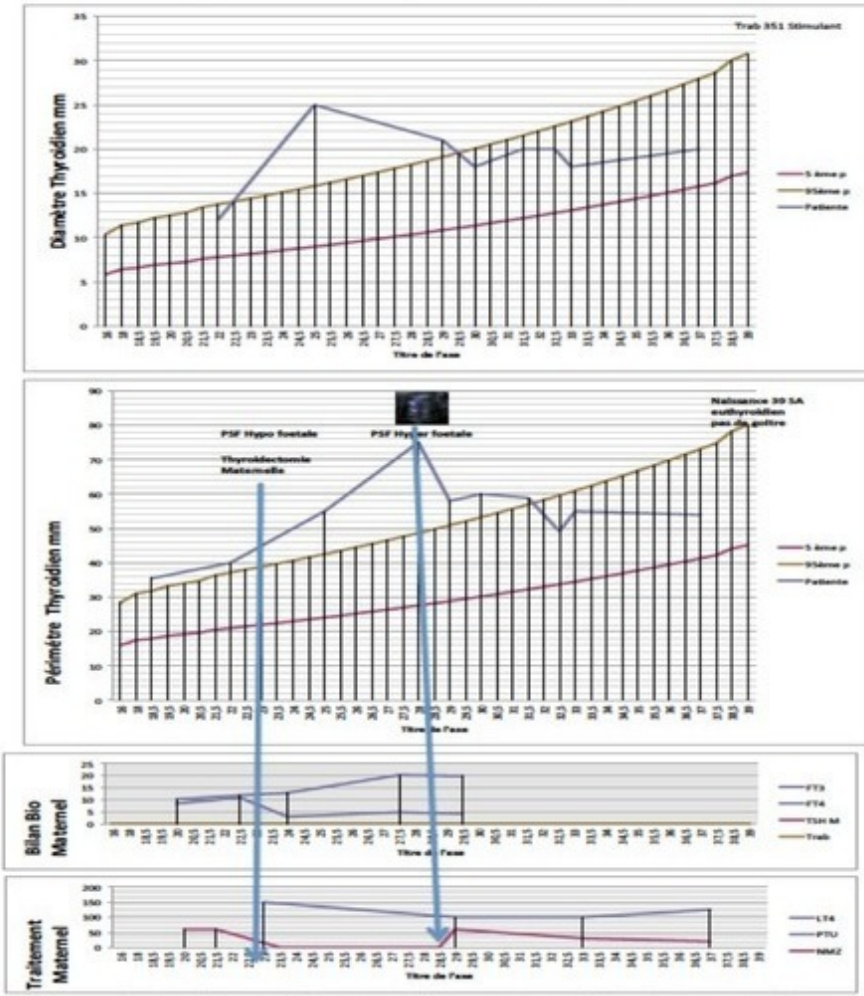


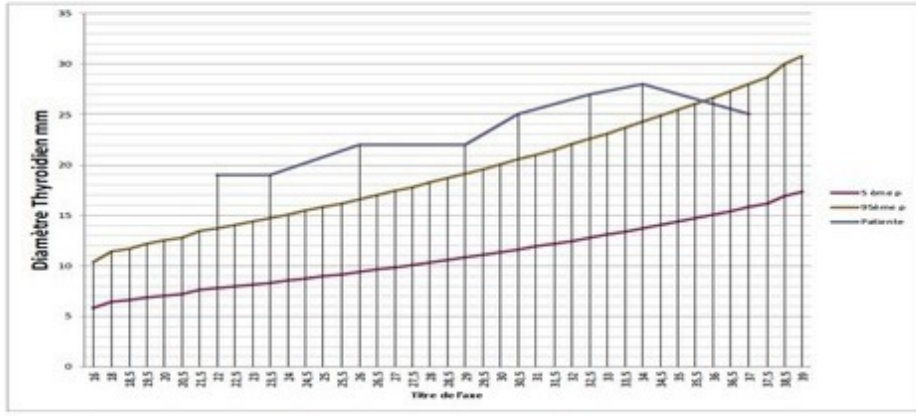
Figure 4 Distribution of scores as a function of fetal thyroid status (χ^2 test, $P < 0.0001$).

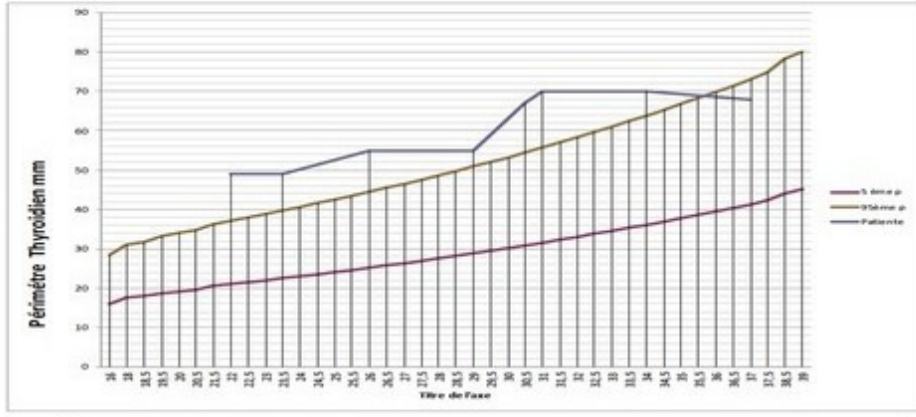
Cas N°1 Fœtus hypo puis hyperthyroidien avec traitement antenatal

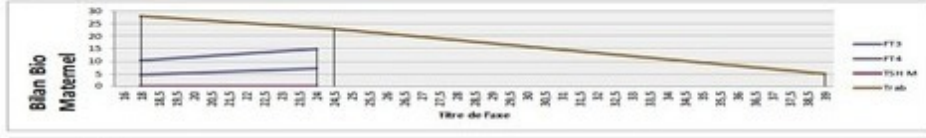


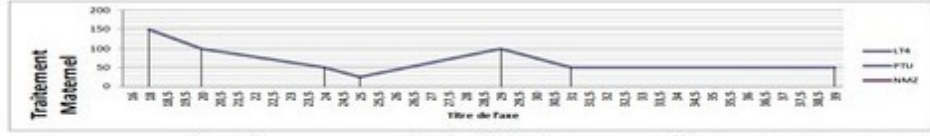
Patiente présentant une maladie de Basedow traitée par NMZ difficile à contrôler . Trab à 350. Fortes doses de Neomercazole avec induction d'une hypothyroidie fœtale (prouvée à la PSF). Thyroidectomie maternelle et substitution par LT4. Persistance puis aggravation du goitre chez le fœtus (la nouvelle PSF prouve qu'il s'agit bien d'une hyperthyroidie fœtale. Mise de la mère sous NMZ à visée fœtale uniquement. Naissance à 39 SA d'un fœtus euthyroidien sans goitre.

Cas N°2 : Fœtus hypothyroidien par surdosage en ATS, traitement par adaptation des doses chez la mère et injection de LT4 in utero









Hypo fœtale PSP Baisse PTU mat

Injection LT4 Reprise PTU

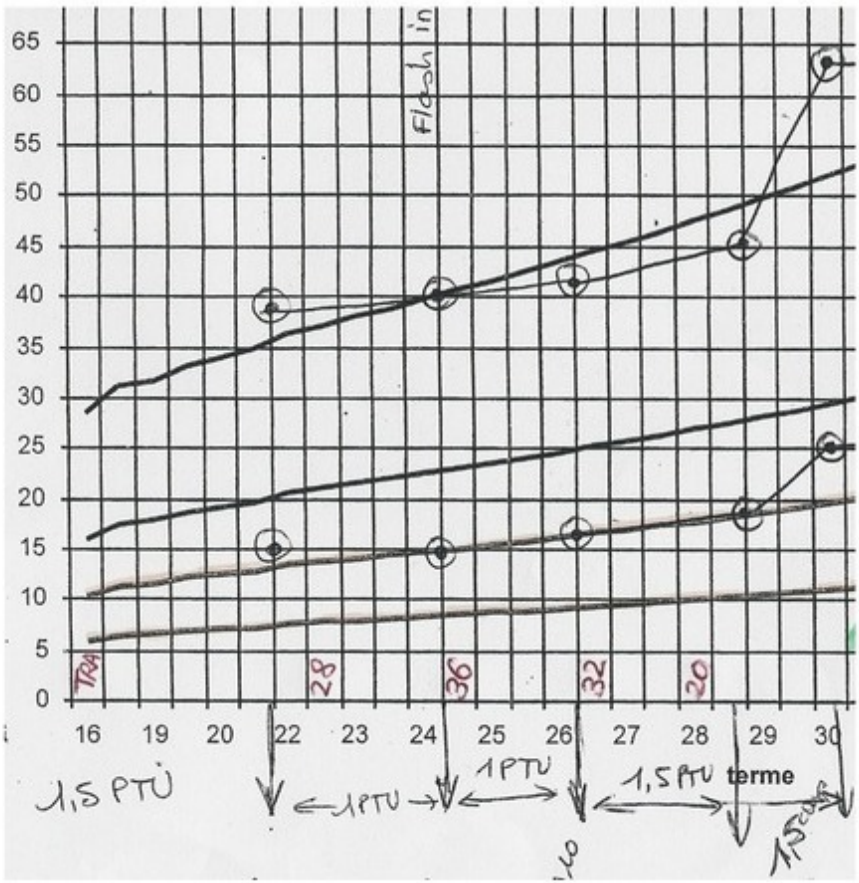
Réacutisation des prises fœtal

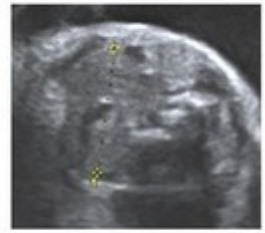
Renforcement du PTU

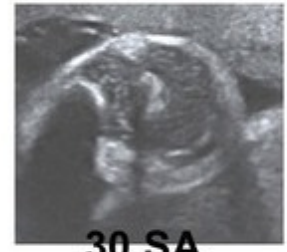
Normalisation du bilan

Vers un Euthyroïdisme

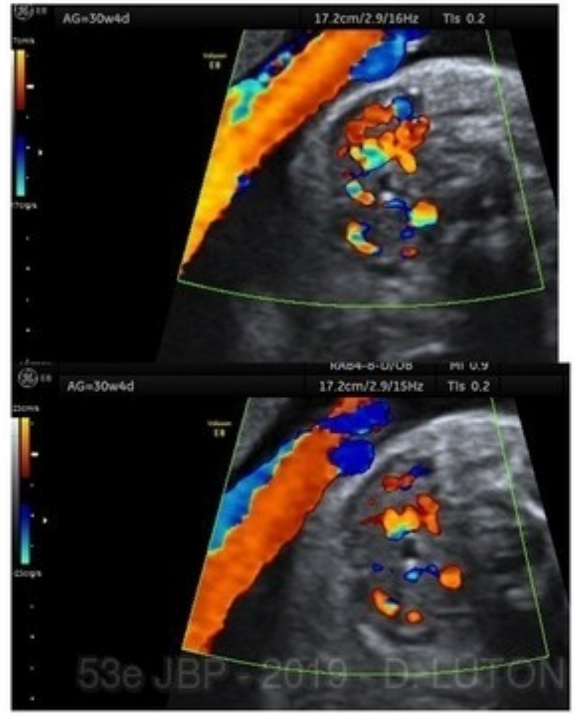
Cas N°3 :Mère basedow, trak++, exophtalmie sévère sous 1,5 PTU.
22 sa fœtus hypothyroïdien; baisse à 1PTU pour le foetus
26 sa, pour raison endocrino et ophtalmique, on remonte à 1,5 PTU,

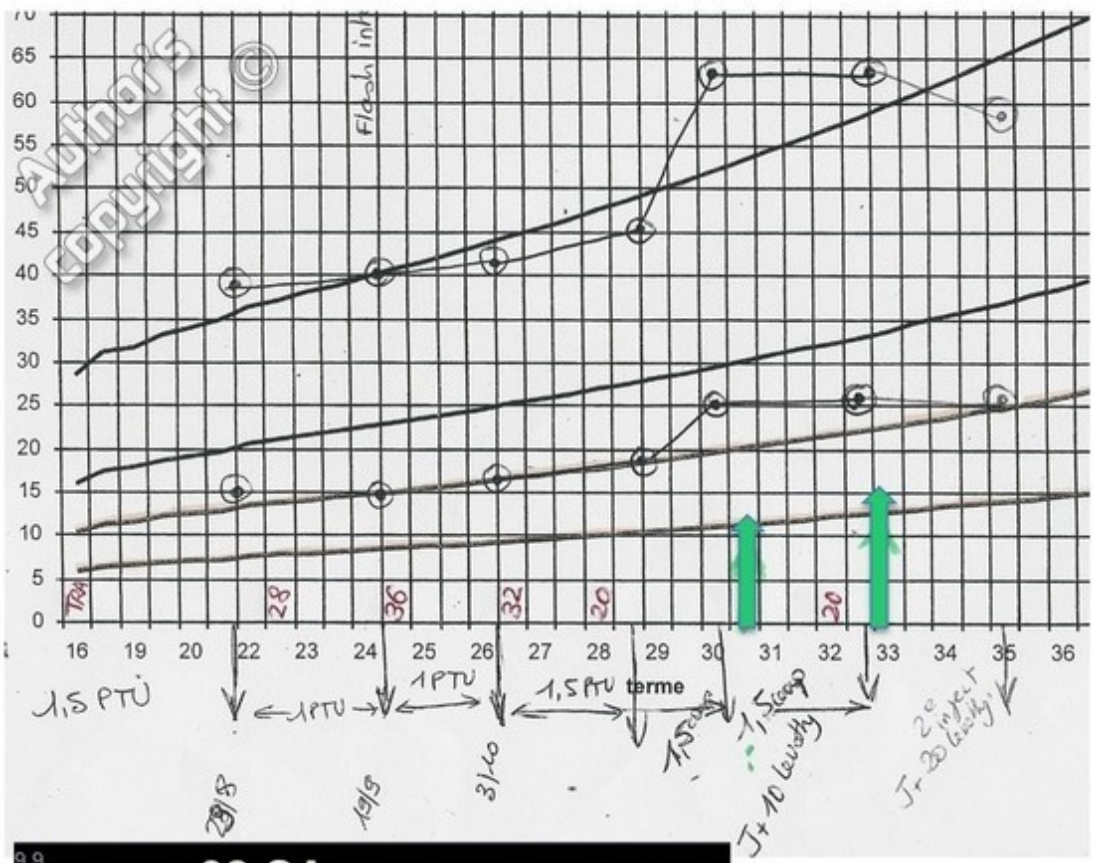






30 SA





30 sa

Injection de levothyrox

toutes les 2sem

32 sa

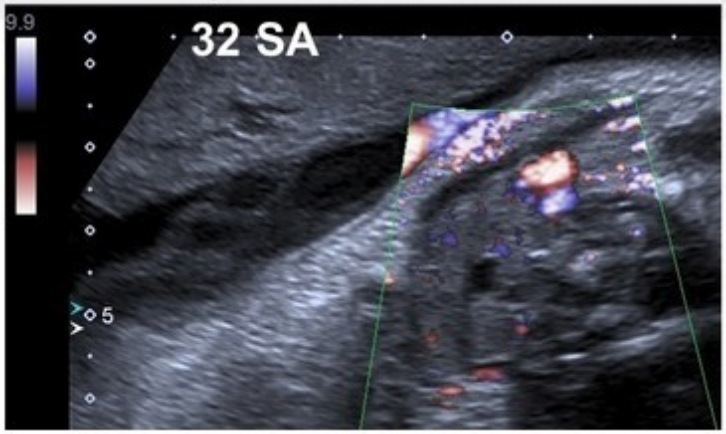
Patiente sous 1,5 PTU

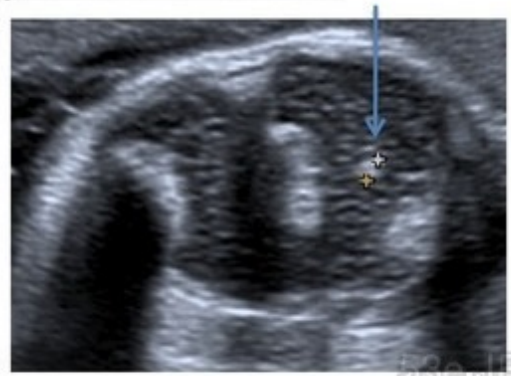
Injection de levothyrox

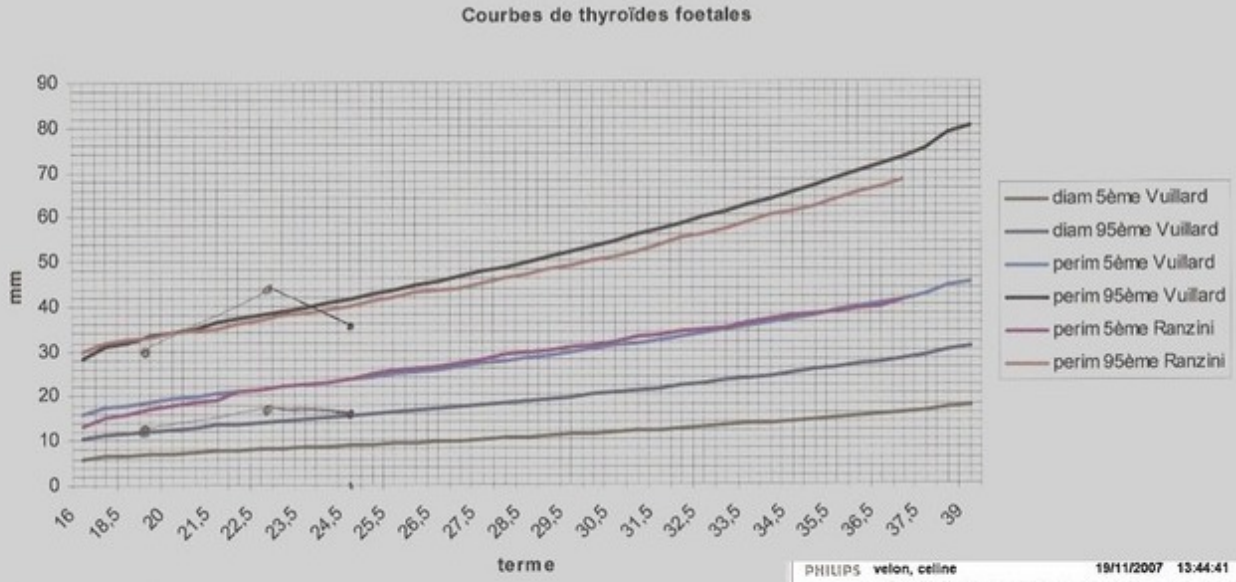
toutes les 2sem

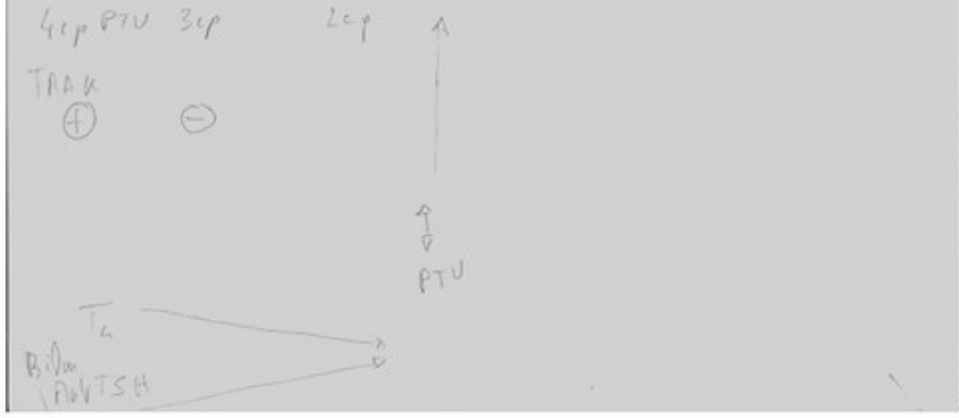
35 sa

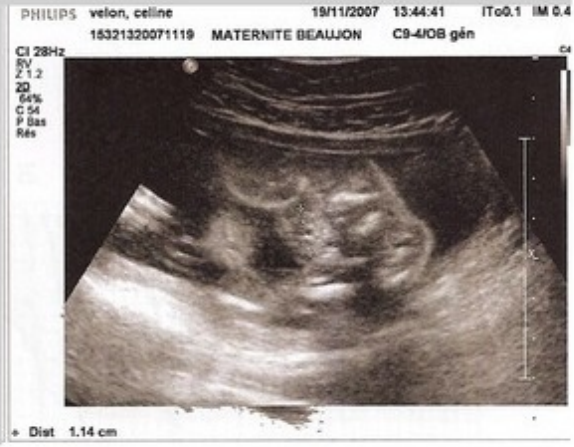
thyroïde normalisée



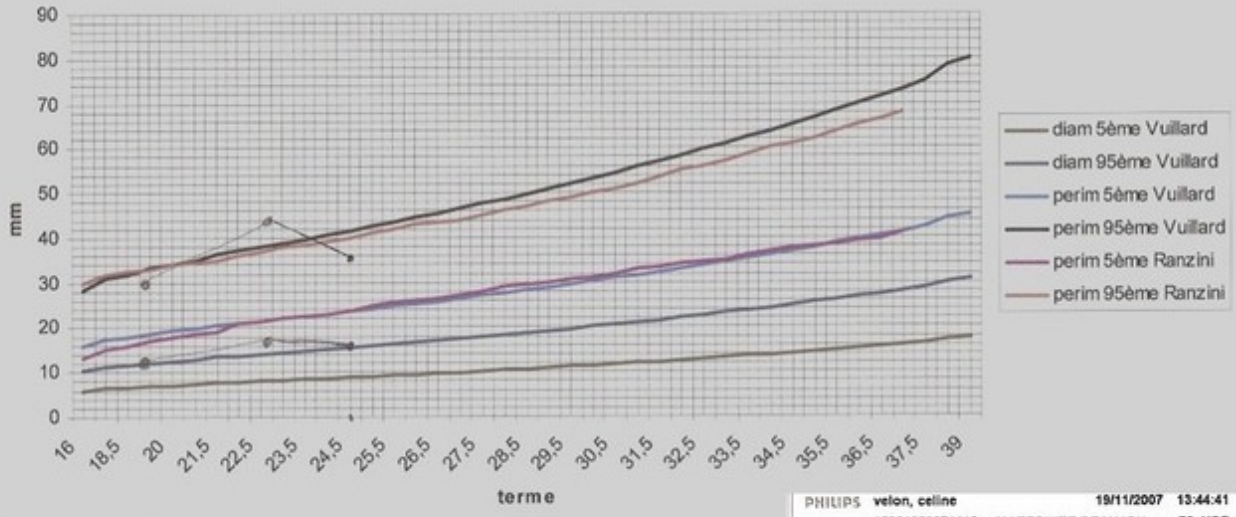


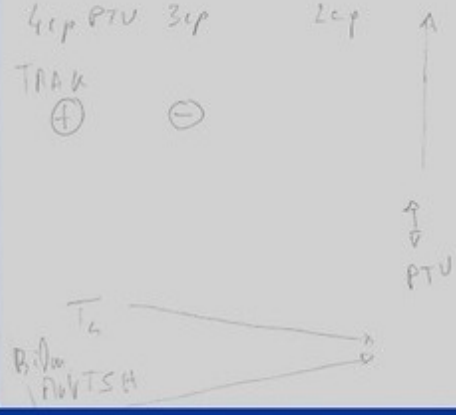


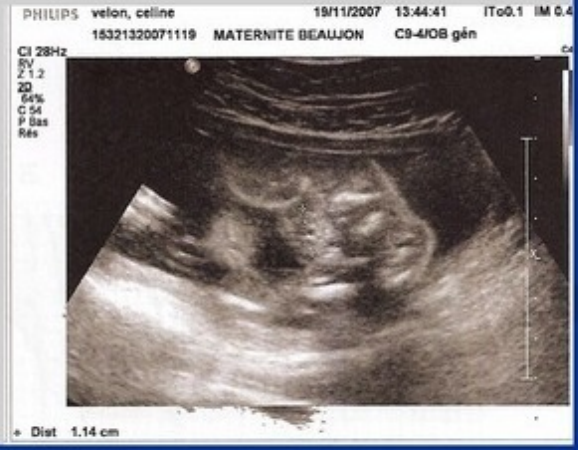




Courbes de thyroïdes foetales







Résumé

- **La mesure de la thyroïde fœtale permet de repérer les fœtus avec dysfonction thyroïdienne**

- **En cas de goitre fœtal une combinaison de critère permet de distinguer entre hypo ou hyperthyroïdie fœtale**
  - Maternelle
    - Taux des TRAK, valeur de la T4
    - Prise et doses d'ATS
  - Fetal
    - Fréquence cardiaque
    - Maturation osseuse
    - Doppler
    - Mouvements fœtaux
    - Taux des Trak

- **La PSF doit être réservée aux cas sévères, aux cas douteux, at avant injection de LT4 (50%)**

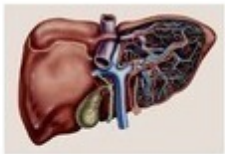
- **Le traitement prénatal est efficace pour améliorer la fonction thyroïdienne fœtale**

Hyperthyroïdie Aspect Maternel et Foetal

- Pas de preuve pour le traitement d'une hyperthyroïdie frustre (USPSTF Recommendation level: C, Evidence-fair) (2|⊕○○○)
- Les Trab doivent être mesurés avant 22 SA en cas de:
  - Maladie de Basedow en cours
  - Atcd de Maladie de Basedow avec ou sans tt par iode 131 ou thyroidectomie
  - Un enfant precedent avec Basedow néonatal
  - Un Atcd de Trak +
  - Celle avec des Trak + et sans ATD présentent peu de risque pour leur enfants
  - (USPSTF Recommendation level: B, Evidence-fair) (1|⊕⊕⊕○)

Hyperthyroïdie Aspect Maternel et Foetal

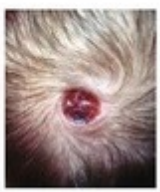
- Hyperthyroïdie avérée (quelque soit la cause)
  - le traitement par ATS doit maintenir le niveau de FT4 à la limite supérieure (dernier quartile) (USPSTF Recommendation level: B, Evidence-fair) (1|⊕⊕○○)



- PTU en première ligne au 1er trimestre

Methimazole 10mg is considered to be approximately equal to 100-150 mg of Propylthiouracil.

  - risque de toxicité hépatique du PTU, si possible changer pour du NMZ à partir du second Trimestre (USPSTF Recommendation level: B, Evidence-fair) (1|⊕⊕○○)
  - Si maintient du PTU surveiller la fonction hépatique toute les 3-4 semaines et être vigilant sur les symptomes (USPSTF Recommendation level: C, Evidence-poor) (2|⊕○○○)



Hyperthyroïdie Aspect Fœtal et Néonatal

- Patientes avec Traks positifs (+, 2à 3N, >10) ou les femmes sous ATD il faut rechercher une dysfonction de la thyroïde foetale par échographie centrée sur la thyroide foetale dès 18-20 SA et répété toute les 4 à 6 semaines. (USPSTF Recommendation level: B, Evidence-fair) (1|⊕⊕⊕O)

- Tous les nouveau nés de patientes avec Basedow (sauf celles avec TRAKS <0 et celles sans ATD) doivent êtres évalués spécifiquement à la naissance. (USPSTF Recommendation level: B, Evidence-fair) (1|⊕⊕⊕O)

ENJEUX POUR L'ENFANT – SURVEILLANCE

R62. Un dosage de TRAb doit être réalisé au début de la grossesse. Les mères avec TRAb positifs seront surveillées de façon intensive. 1 / +++

R63. Un taux de TRAb >5 UI/l (par technique de 2e génération) au deuxième trimestre de grossesse indique un risque d'hyperthyroïdie fœtale et néonatale; le suivi échographique doit être intensifié avec des échographies de la thyroïde fœtale répétées tous les mois à partir de 22SA. Ce rythme sera adapté à la survenue ou non d'une hypertrophie de la glande thyroïdienne fœtale. 1 / ++

SUIVI NÉONATAL ET POST-PARTUM - EVALUATION NÉONATALE

R68. Les nouveau-nés de mères ayant des TRAb positifs pendant la grossesse sont à risque d'hyperthyroïdie néonatale, en particuliers si les TRAb sont >5 UI/l par technique de 2e génération. 1 /+++

R69. Les TRAb, TSH et T4L doivent être prélevés au sang de cordon chez tous les nouveau-nés de mère avec TRAb positifs ou traitée; ils reflètent le statut et/ou le traitement anténatal et orientent la surveillance postnatale. 1 / ++

Dysthyroïdie et allaitement maternel

- L'hypothyroïdie peut altérer l'allaitement: traiter si hypothyroïdie même infraclinique
- ATA 2017: Impact négligeable des hormones thyroïdiennes maternelles et des ATS sur le nourrisson allaité: traitement possible par NZ < 20 mg/j ou PTU < 450 mg/j, à dose minimale efficace, pas de surveillance spécifique du nourrisson
- SFE 2016: données expérimentales rassurantes mais RCP des ATS
  - Éviter l'allaitement sous PTU; si impossible, surveillance du nourrisson,
  - NZ contre-indiqué
  - Thyrozol < 10 mg/j avec surveillance du nourrisson
- **Supplémenter en iode** (sauf si dysthyroïdie traitée)

Hypothyroïdie maternelle

- Parfois difficile
  - Signes peu spécifiques:
    - crampes musculaires
    - constipation
    - asthénie
    - rétention hydrique
- Mais:
  - Bradycardie
  - prise pondérale excessive
  - sécheresse cutanée
  - Goitre
  - antécédents familiaux
- TSH , T4L

- Principales étiologies:
  - Thyroïdite de Hashimoto
    - Contexte auto immun
    - Famille
    - Ac Anti thyroperoxydase (TPO) (microsome , thyroglobuline)
  - Carence en iode
  - Piège de l'hypothyroïdie résiduelle post Basedow

Hypothyroïdie maternelle: retentissement maternel

- Prévalence de l'insuff. thyroïdienne:
  - clinique 0,3 à 0,7%
  - subclinique de 2,2 à 2,5%

- Les besoins en thyroxine
  - peuvent augmenter chez près de 80% des patientes présentant une hypothyroidie avant la grossesse
    - par augmentation de la TBG
    - augmentation du Vplasm
    - augmentation de l'activité de la desiodase placentaire de type 3

- Retentissements:
  - Fertilité
  - Obstétricaux classiques et historiques:
    - Mort in utero
    - Préeclampsie
    - HRP
    - «souffrance fœtale»…

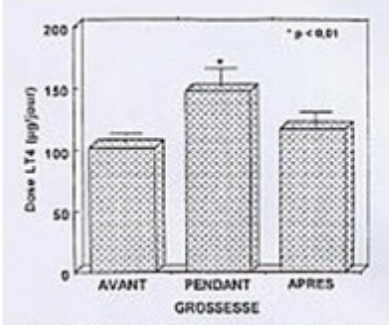


Figure 91-4. Variation de la dose de lévothyroxine au cours de la grossesse chez 12 patientes présentant une hypothyroïdie périphérique (d'après Mandel [22]).

Hypothyroïdie maternelle: retentissement fœtal

- Fœtus dépendant de l'apport hormonal maternel durant le 1er trimestre de la grossesse
- T4 convertie en T3 , récepteurs sur le cerveau fœtal, importance d'un transfert maternofœtal hormonal (longtemps ignoré)
- Enfants athyreotiques normaux à la naissance avec concentration en T4 réduite (de ½ à ⅓)

– Enfants de femmes ayant une TSH élevée durant la grossesse (Moy:13,2 mU/L)
– Diminution modérée mais significative des performances générales
– Baisse de 4 points du QI
– 15% des enfants avaient un score inférieur à 85 contre 5% chez les témoins

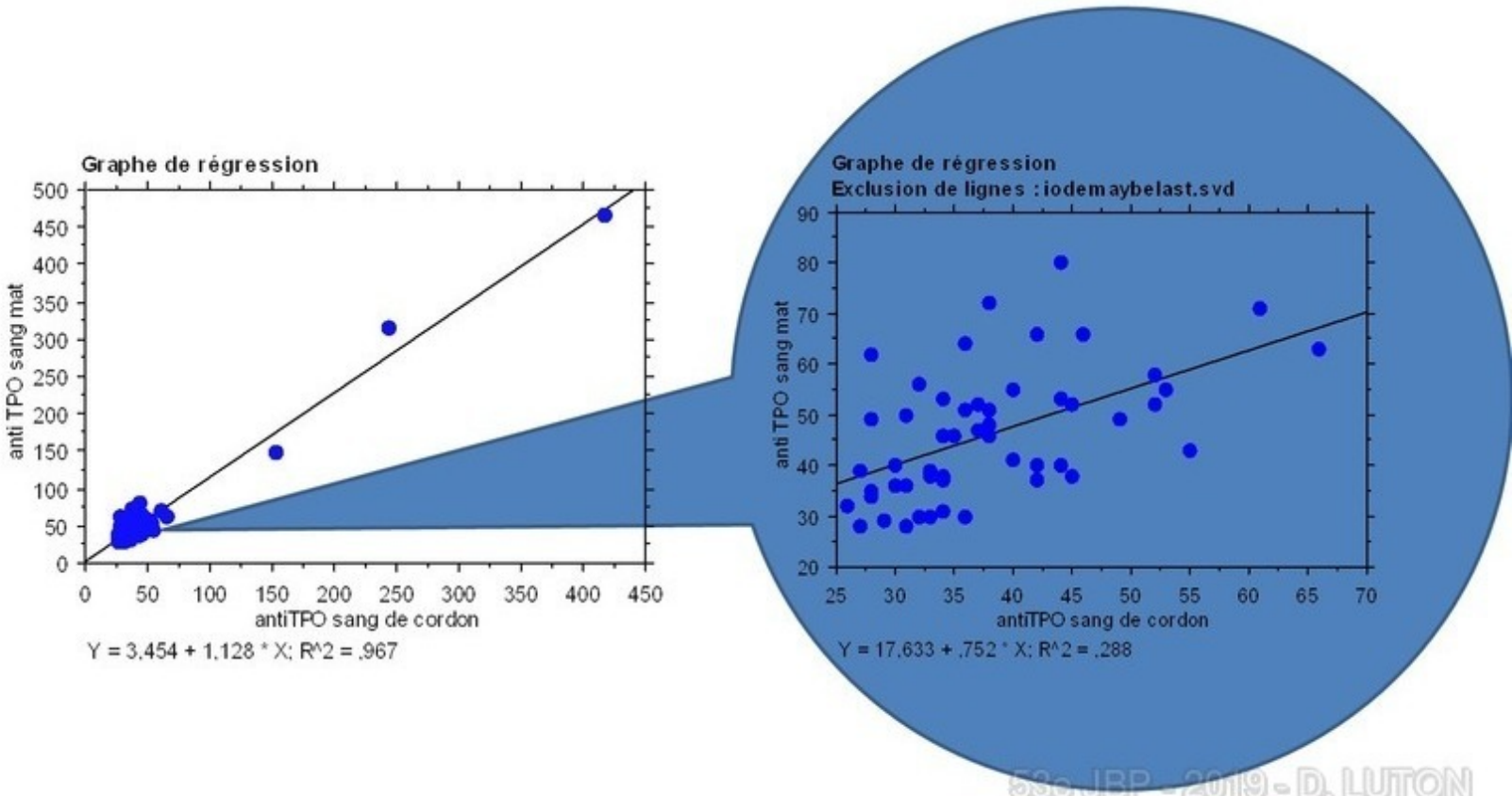
Haddow et al NEJM 1999

OPEN ACCESS Freely available online

Anti-TPO Antibodies Diffusion through the Placental Barrier during Pregnancy

Jérémy Seror[1,2]*, Gaëlle Amand[1,2], Jean Guibourdenche[3], Pierre-François Ceccaldi[1,2], Dominique Luton[1,2]

1 Paris Diderot, Université Paris VII, Paris, France, **2** Department of Gynecology and Obstetrics, Beaujon-Bichat Hospital, AP-HP, Clichy, France, **3** Department of Hormonal and Metabolic Biology, Cochin Hospital, AP-HP, Paris, France



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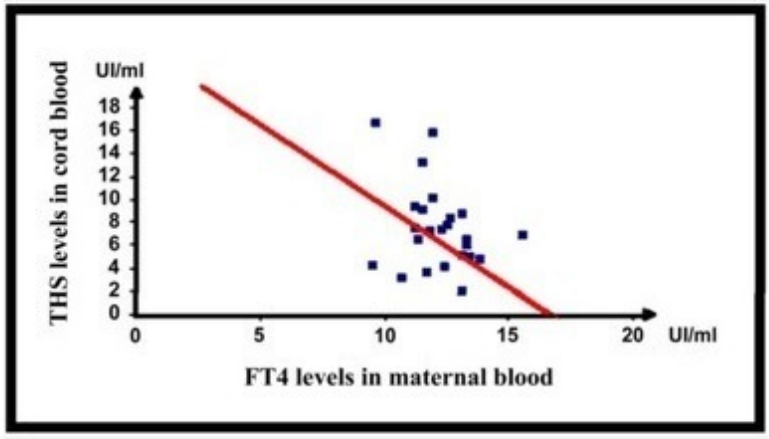

Figure 4. Correlation between FT4 levels in maternal blood and TSH levels in cord blood at delivery.
doi:10.1371/journal.pone.0084647.g004

Hypothyroïdie Maternelle

- Correctement équilibrée : RAS
  - attention au piège classique de l'hypothyroïdie résiduelle post Basedow
- Doute sur certains anticorps.....
- En cas de mauvais équilibre avec hypothyroïdie il existe un risque de retentissement sur le cerveau fœtal mais difficile à apprécier dans son ampleur et sa fréquence

Hypothyroïdie maternelle: faut-il dépister en anténatal ?

Hypothyroïdie et TPO: intérêt de la recherche préconceptionnelle

Levothyroxine Treatment in Euthyroid Pregnant Women with Autoimmune Thyroid Disease: Effects on Obstetrical Complications

Roberto Negro, Gianni Formoso, Tiziana Mangieri, Antonio Pezzarossa, Davide Dazzi, and Haslinda Hassan

TABLE 2. Pregnancy outcome

Pregnancy complications	Group A TPOAb$^+$ LT_4 (n = 57)	Group B TPOAb$^+$ (n = 58)	Group C TPOAb$^-$ (n = 869)
Hypertension	5 (8.8)	7 (12)	63 (7.2)
Preeclampsia	2 (3.5)	3 (5.2)	32 (3.7)
Placental abruption	0	1 (1.7)	4 (0.5)
Miscarriage	2 (3.5)	8 (13.8)	21 (2.4)
Preterm delivery	4 (7)	13 (22.4)	71 (8.2)

Numbers in parentheses represent percentage.

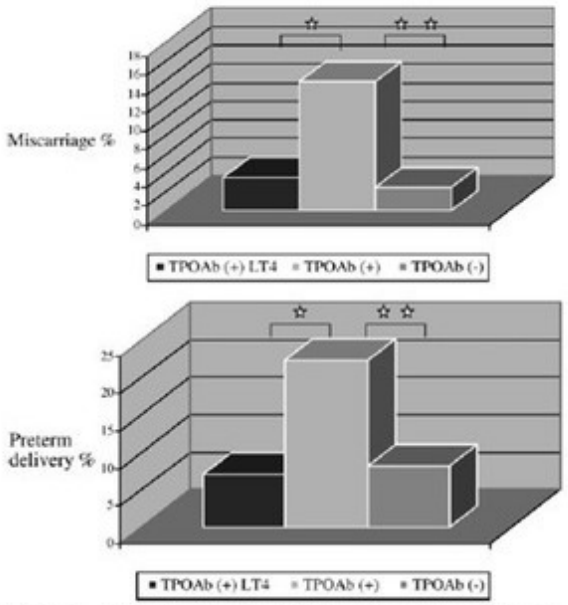

FIG. 4. Percentage of miscarriages (*top*) and premature deliveries (*bottom*) in group A (TPOAb$^+$ treated with LT_4), group B (TPOAb$^+$), and group C (TPOAb$^-$). *, $P < 0.05$; * *, $P < 0.01$.

TABLE 1. Characteristics of patients at 10, 20, and 30 wk gestation and delivery (D)

	n	Age (yr)	TSH (mIU/liter) 10 wk	20 wk	30 wk	D	FT_4 (ng/liter) 10 wk	20 wk	30 wk	D
TPOAb$^+$ LT_4	57	30 ± 5	1.6 ± 0.5	1.1 ± 0.4	1.2 ± 0.4	1.9 ± 0.5	14.8 ± 4.2	14.2 ± 3.8	14.3 ± 3.6	14.3 ± 3.2
TPOAb$^+$	58	30 ± 6	1.7 ± 0.5	2.3 ± 0.5	2.5 ± 0.6	3.5 ± 0.7	14.6 ± 4.3	13.8 ± 4.8	12.4 ± 4.9	10.2 ± 4.5
TPOAb$^-$	869	28 ± 5	1.1 ± 0.4	1.2 ± 0.4	1.4 ± 0.4	2.1 ± 0.6	15.2 ± 4.1	14.3 ± 4.0	13.8 ± 4.2	14.6 ± 3.8

Data are expressed as mean ± SD.

Adaptation thérapeutique précoce systématique +++

Hypothyroïdie maternelle: faut-il dépister en anténatal ?

- Dépistage de **routine** à la recherche d'une hypothyroïdie **subclinique:** n'est pas d'actualité

Mais:
Identification de patientes à risque

Table 1. Maternal Characteristics of Women Who Underwent Thyroid-Stimulating Hormone Screening at or Before 20 Weeks of Gestation

Maternal Demographics	Subclinical Hypothyroidism (n = 404)	Normal TSH (n = 15,689)	P
Age (y)	26.9 ± 5.9	25.5 ± 5.6	< .001
≥ 35	44 (11)	1,161 (7)	.009
Race or ethnicity:			< .001
Hispanic	341 (84)	13,472 (86)	
African American	27 (7)	1,588 (10)	
White	16 (4)	321 (2)	
Other	20 (5)	308 (2)	
Nulliparity	145 (36)	5,672 (36)	.915
Weeks at enrollment	12.2 ± 4.0	11.9 ± 3.8	.211
Body mass index (kg/m^2)	32.1 ± 6.3	31.7 ± 5.5	.163

TSH, thyroid-stimulating hormone.
Values are mean ± standard deviation or n (%). Women with a TSH value at or above the 97.5th percentile and normal free thyroxine (subclinical hypothyroidism) are compared with those with a TSH between the 5th and 95th percentiles (normal).

Aux conséquences obstétricales bien présentes

Table 2. Pregnancy Outcomes in Women Who Underwent Thyroid-Stimulating Hormone Screening at or Before 20 Weeks of Gestation.

Pregnancy Outcome	Subclinical Hypothyroidism (n = 404)	Normal TSH (n = 15,689)	P
Hypertension			
Gestational	41 (11)	1,400 (9)	.397
Severe preeclampsia	23 (6)	842 (5)	.774
Placental abruption	4 (1)	52 (0.3)	.026
Weeks gestation at delivery	39.3 ± 2.2	39.4 ± 1.9	.226
36 or less	27 (7)	891 (6)	.390
34 or less	18 (4)	385 (2.5)	.011
32 or less	10 (2.5)	218 (1)	.068
Cesarean delivery	108 (27)	3,853 (25)	.316
Repeat	59 (15)	1,923 (12)	.156
Primary			
Dystocia	16 (4)	716 (5)	0.566
Fetal distress	17 (4)	647 (4)	0.933
Other	16 (4)	567 (4)	0.713

TSH, thyroid-stimulating hormone.
Values are mean ± standard deviation or n (%). Women with a TSH value at or above the 97.5th percentile and normal free thyroxine levels (subclinical hypothyroidism) are compared with those with a TSH between the 5th and 95th percentiles (normal).

Casey BM et al. Obstet Gynecol Surv. 2006 Jun;61(6):415-20
Casey BM et al. Obstet Gynecol 2005;105:239–45.

Subclinical Thyroid Disease and the Incidence of Hypertension in Pregnancy

Karen L. Wilson, MD, Brian M. Casey, MD, Donald D. McIntire, PhD, Lisa M. Halvorson, MD, and F. Gary Cunningham, MD

VOL. 119, NO. 2, PART 1, FEBRUARY 2012 **Wilson et al** *Subclinical Thyroid Disease and Hypertension*

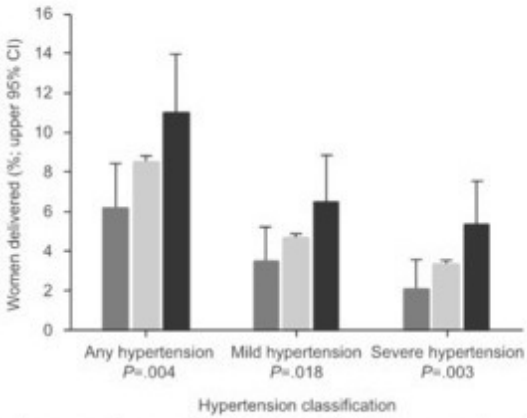

Fig. 1. Incidence of hypertension during pregnancy and mild or severe preeclampsia according to classification of subclinical hyperthyroidism (*dark gray bars*), euthyroid (*light gray bars*), and subclinical hypothyroidism (*black bars*) in 24,883 pregnant women who were screened during the first prenatal visit.

Wilson. Subclinical Thyroid Disease and Hypertension. Obstet Gynecol 2011.

Table 1. Maternal Demographics in Women With Subclinical Thyroid Dysfunction Compared With Euthyroid Women

	Subclinical Hyperthyroid (n=584)	P*	Euthyroid (n=23,771)	P†	Subclinical Hypothyroid (n=528)
Race		<.001		<.001	
African American	100 (17)		2,690 (11)		31 (6)
White	10 (2)		558 (2)		20 (4)
Hispanic	449 (77)		20,002 (84)		455 (86)
Other	25 (4)		521 (2)		22 (4)
Parity		.415		.845	
0	195 (33)		8,737 (35)		184 (35)
1	179 (31)		7,561 (32)		165 (31)
2	117 (20)		4,757 (20)		113 (21)
More than 2	93 (16)		3,221 (14)		68 (13)
Age (y)	25.8±5.5	.009	25.2±5.6	<.001	26.7±5.7
Weight	162±30	<.001	170±34	.057	176±38

Data are n (%) or mean±standard deviation unless otherwise specified.
* Compares hypothesis of equality of subclinical hyperthyroid and euthyroid.
† Compares hypothesis of equality of subclinical hypothyroid and euthyroid.

0.03 to 4.13

CONCLUSION: Women with subclinical hypothyroidism identified during pregnancy have an increased risk for severe preeclampsia when compared with euthyroid women.

(Obstet Gynecol 2012;119:315–20)

DOI: 10.1097/AOG.0b013e318240de6a

LEVEL OF EVIDENCE: II

Pathologies obstétricales

	Patientes normales n=197, moyenne [IC95%]	DIABETE GESTATIONNEL n=22	p	MENACE D'ACCOUCHEMENT PREMATURE, n=35	p	PREECLAMPSIE, n=8	p
T4L ng/l	14,22 [14,1 ; 14,3]	13,8 [13,4 ; 14,1]	0,03	13,79 [13,46 ; 14,11]	0,08	13,5 [13,0 ; 14,0]	0,02
TSH mU/l	1,63 [1,56 ; 1,69]	1,45 [1,31 ; 1,59]	0,08	2,2 [1,69 ; 2,72]	<0,01	2,73 [1,86 ; 3,6]	<0,01
Sodium mmol/l	136 [136 ; 137]	137 [136 ; 137]	0,16	137 [137 ; 137]	0,5	136 [135 ; 137]	0,8
Chlore mmol/l	104 [104 ; 105]	105 [104 ; 105]	0,5	105 [104 ; 105]	0,3	104 [103 ; 105]	0,3
Calcium mmol/l	2,28 [2,27 ; 2,29]	2,32 [2,29 ; 2,36]	0,05	2,27 [2,25 ; 2,30]	0,5	2,3 [2,26 ; 2,33]	0,5
Phosphore mmol/l	1,15 [1,13 ; 1,16]	1,14 [1,10 ; 1,19]	0,2	1,17 [1,11 ; 1,24]	0,2	1,15 [1,08 ; 1,22]	0,9
Magnésium mmol/l	0,79 [0,78 ; 0,79]	0,8 [0,78 ; 0,81]	0,2	0,77 [0,76 ; 0,78]	0,1	0,77 [0,76 ; 0,8]	0,3
Protides g/l	68 [68 ; 69]	68 [67 ; 69]	0,2	67 [66 ; 68]	0,1	68 [67 ; 70]	0,8
Albumine g/l	32 [31 ; 32]	32 [31 ; 32]	0,9	32 [31 ; 32]	0,6	31 [29 ; 32]	0,2
Créatinine µmol/l	44 [43 ; 44]	45 [43 ; 47]	0,3	46 [45 ; 48]	0,1	51 [48 ; 54]	<0,01
Acide urique µmol/l	221 [217 ; 225]	212 [200 ; 223]	0,1	220 [207 ; 233]	0,87	282 [244 ; 320]	<0,01
ASAT UI/l	23 [22 ; 23]	25 [10 ; 30]	0,07	23 [21 ; 25]	0,95	23 [20 ; 26]	0,8
ALAT UI/l	17 [16 ; 17]	18 [16 ; 18]	0,1	16 [15 ; 17]	0,2	22 [19 ; 25]	<0,01
GGT UI/l	13 [12 ; 14]	18 [14 ; 22]	0,01	17 [13 ; 22]	<0,01	16 [8 ; 25]	0,09
PAL UI/l	104 [101 ; 108]	109 [97 ; 120]	0,5	102 [92 ; 112]	0,7	88 [76 ; 100]	0,07
Bilirubine C µmol/l	5 [4,9 ; 5]	4,9 [4,5 ; 5]	0,2	5 [4,5 ; 5]	0,8	5 [4,5 ; 5]	0,5
Bilirubine T µmol/l	7,6 [7,4 ; 7,8]	8 [7,1 ; 9,3	0,1	8 [7 ; 9]	0,34	7 [6 ; 8]	0,3
Amylase UI/l	76 [74 ; 78]	71 [65 ; 76]	0,2	72 [69 ; 75]	0,1	77 [60 ; 94]	0,8
Fer sérique g/l	15,32 [14,71 ; 15,95]	16,5 [14,23 ; 18,9]	0,3	14,55 [13,22 ; 15,89]	0,34	15,5 [11,8 ; 19,22]	0,9
Ferritine µg/l	19 [18 ; 20]	28 [20 ; 37]	<0,01	27 [22 ; 32,5]	<0,01	38 [20 ; 57]	<0,01
Transferrine µmol/l	3,35 [3,31 ; 3,41]	3,45 [3,29 ; 3,68]	0,2	3,42 [3,28 ; 3,56]	0,4	3,36 [3,31 ; 3,41]	0,2
Triglycérides g/l	2,16 [2,1 ; 2,23]	2,29 [2,1 ; 2,53]	0,2	2,16 [2,00 ; 2,33]	0,99	1,96 [1,64 ; 2,27]	0,2
Apo-lipo A1 g/l	1,85 [1,82 ; 1,87]	1,72 [1,65 ; 1,78]	<0,01	1,78 [1,73 ; 1,82]	0,03	1,98 [1,85 ; 2,10]	0,02
Haptoglobine g/l	0,95 [0,93 ; 0,98]	0,68 [0,60 ; 0,76]	<0,01	0,86 [0,78 ; 0,93]	0,01	0,95 [0,80 ; 1,10]	0,99

BMJ

RESEARCH

Association between thyroid autoantibodies and miscarriage and preterm birth: meta-analysis of evidence

Shakila Thangaratinam, senior lecturer/consultant in obstetrics and gynaecology and clinical epidemiology,[1] Alex Tan, academic foundation trainee,[2] Ellen Knox, consultant obstetrician/subspecialist in fetal medicine,[3] Mark D Kilby, professor of fetal medicine,[2,3] Jayne Franklyn, professor of medicine,[2] Arri Coomarasamy, reader/consultant gynaecologist/subspecialist in reproductive medicine and surgery[2]

BMJ 2011;342:d2616

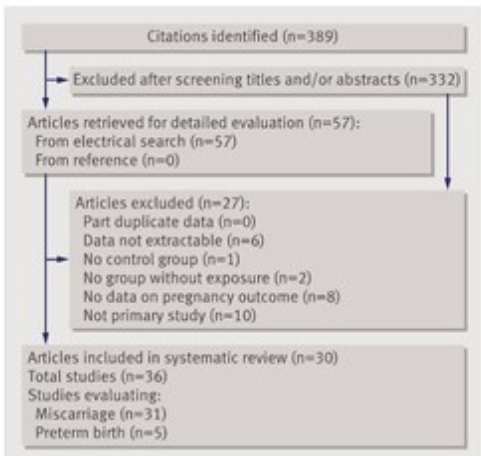

Fig 1| Flow chart of study selection in review of association between thyroid autoantibodies and adverse pregnancy outcome

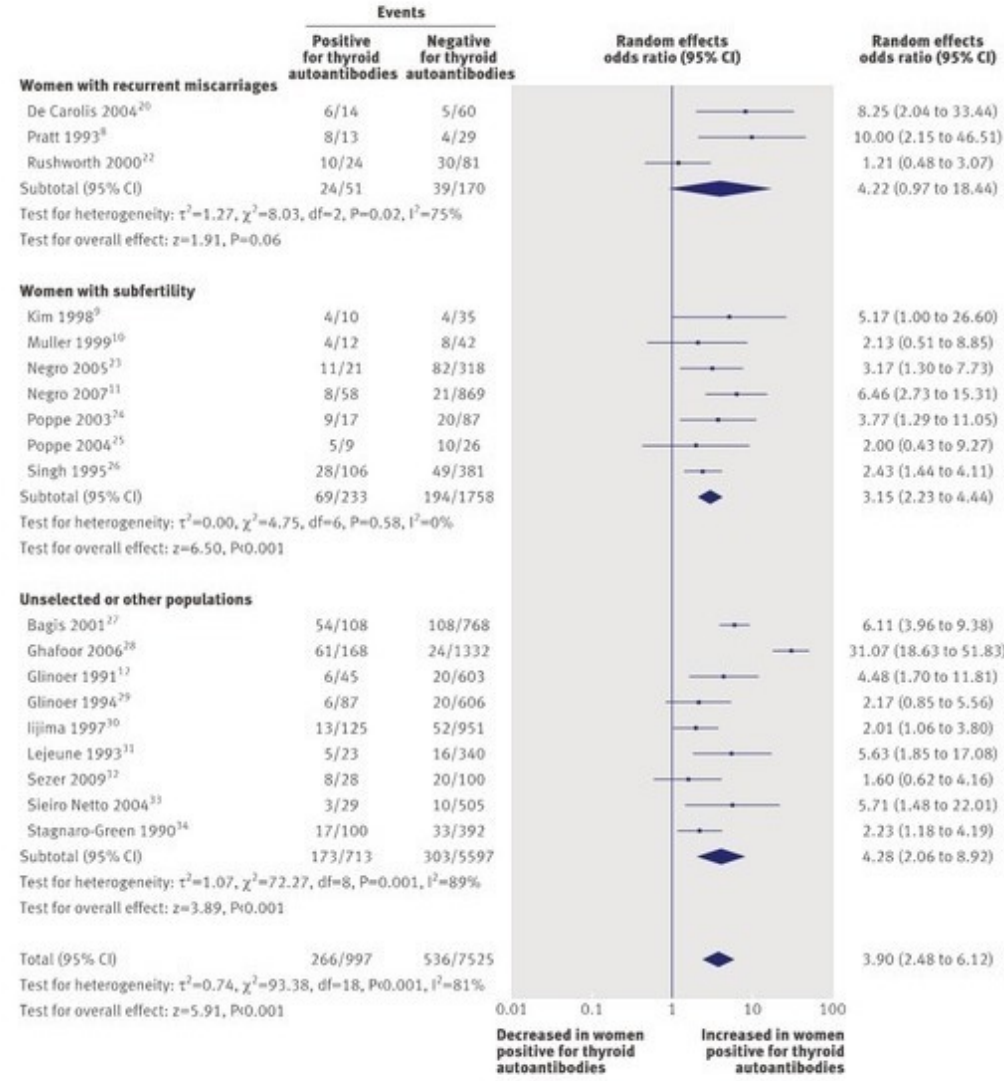

Fig 2 | Association between thyroid autoantibodies and miscarriage in cohort studies

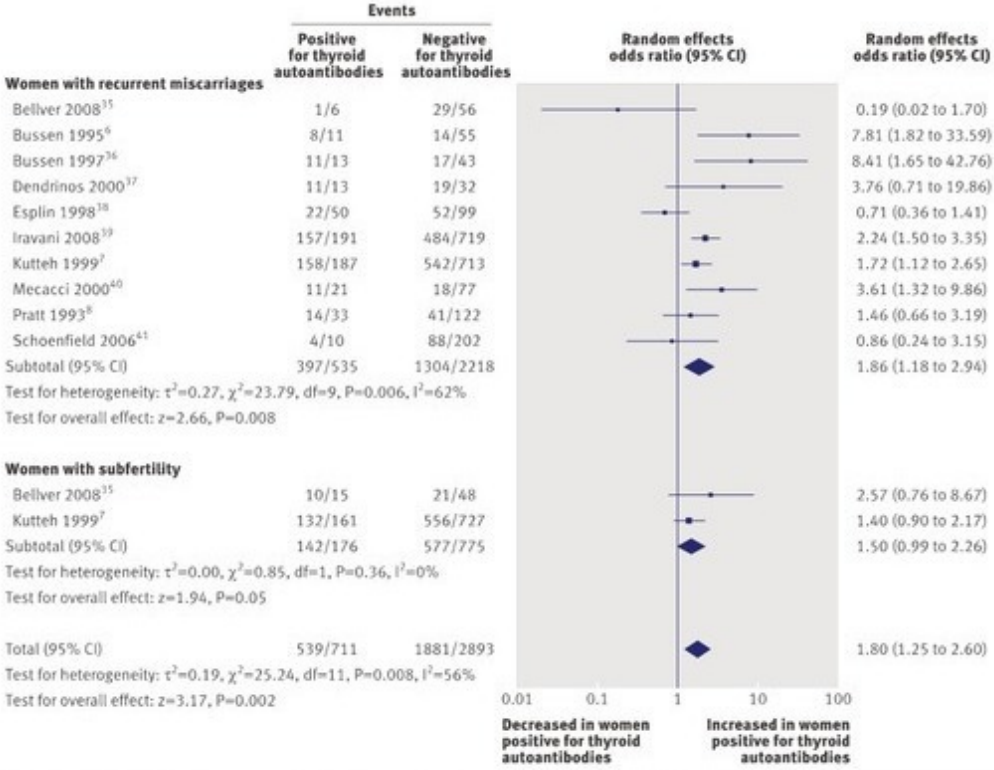

Fig 3 | Association between thyroid autoantibodies and miscarriage in case-control studies

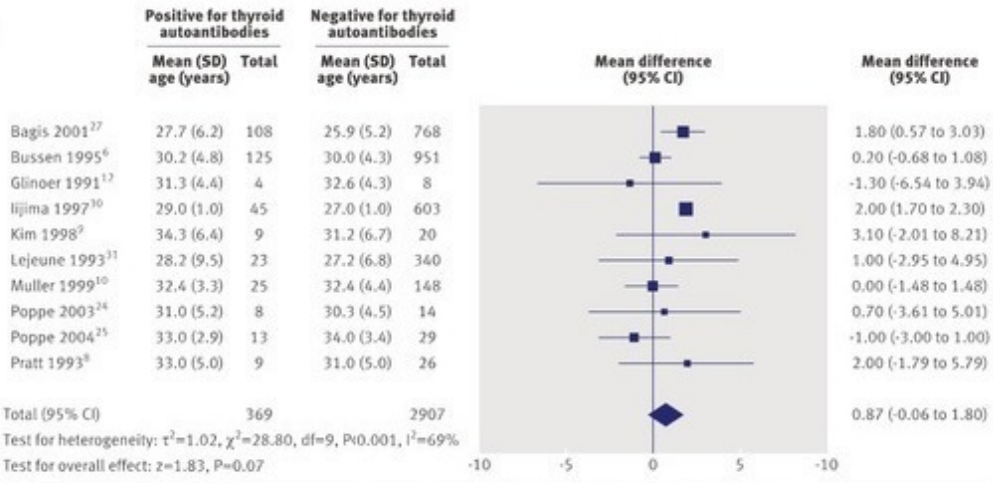

Fig 4 | Comparison of age between women postive and negative for thyroid autoantibodies in included studies

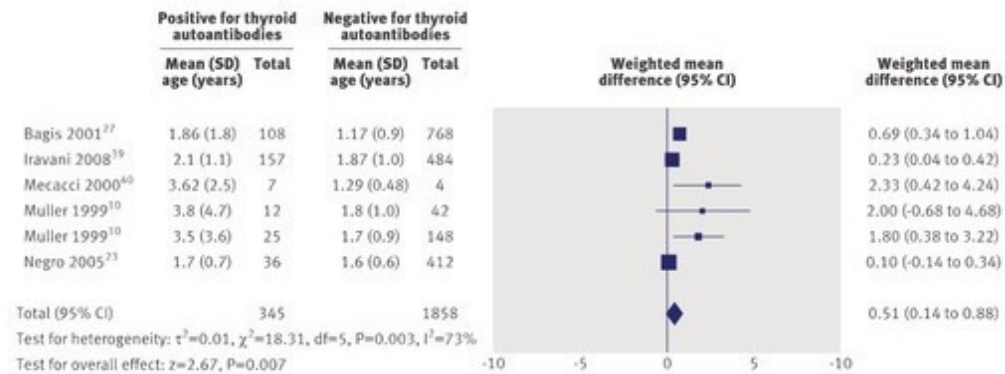

Fig 5 | Comparison of serum thyroid stimulating hormone (TSH) concentration between women positive and negative for thyroid autoantibodies in included studies

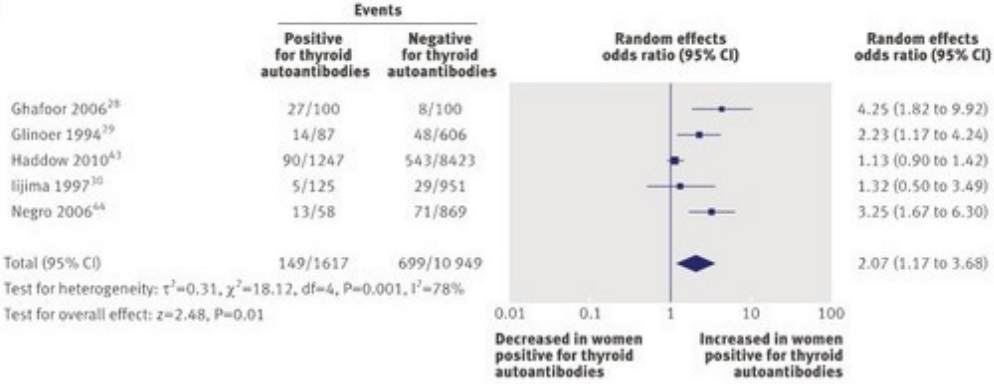

Fig 6 | Association between thyroid autoantibodies and preterm births

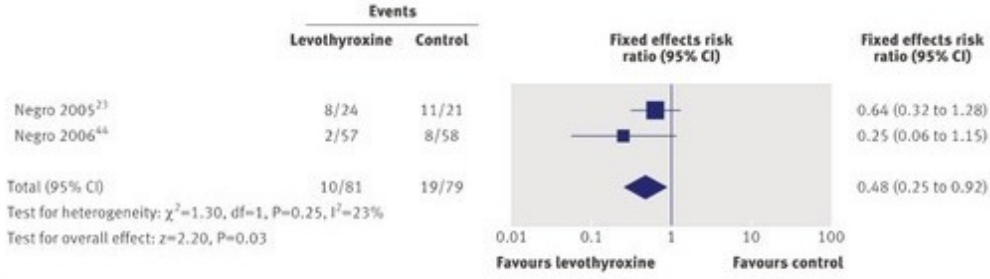

Fig 7 | Effect of levothyroxine treatment in reducing miscarriage in women with normal thyroid function and thyroid autoantibodies

To obtain a definitive answer on the role of levothyroxine in reducing miscarriages and preterm births a large placebo controlled rando- mised trial is needed with live births as the primary outcome.

The NEW ENGLAND JOURNAL of MEDICINE

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Antenatal Thyroid Screening and Childhood Cognitive Function

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N ENGL J MED 366;6 NEJM.ORG FEBRUARY 9, 2012

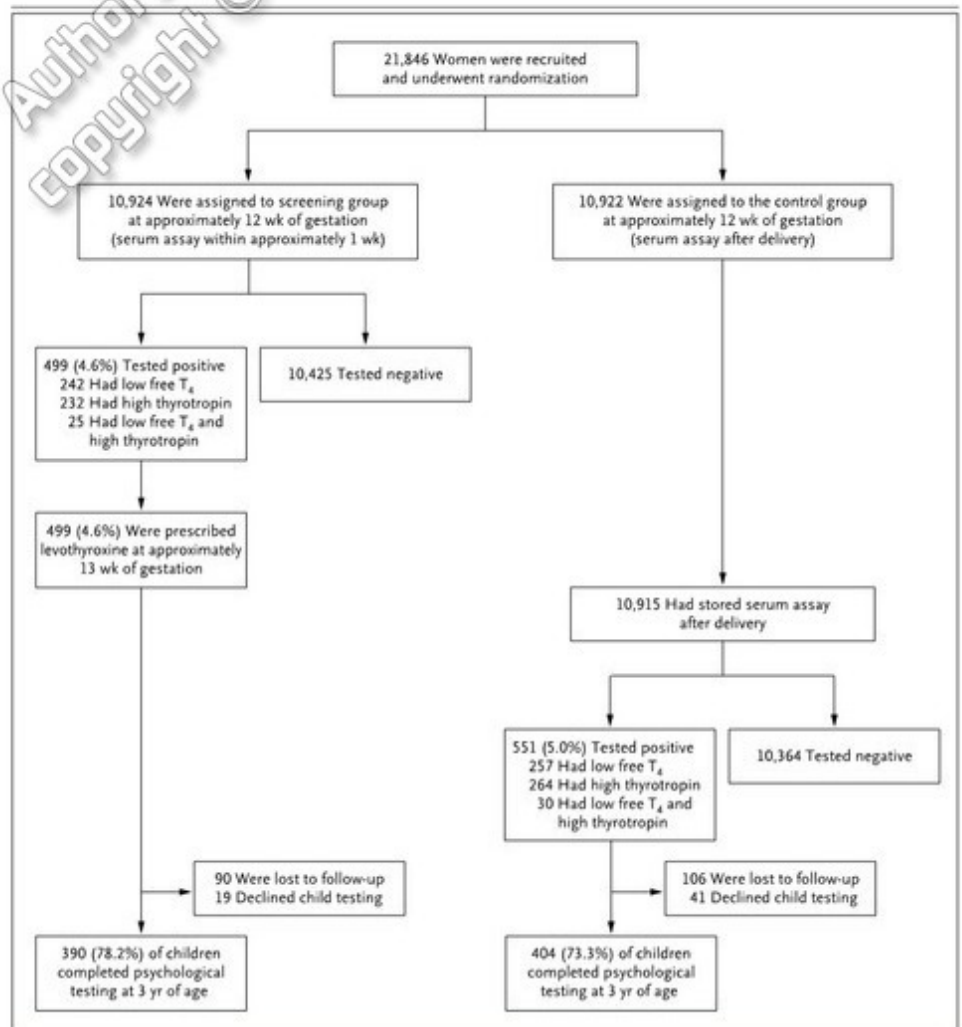


Figure 1. Randomization and Follow-up of the Study Participants.

Table 1. Characteristics of Women with Positive Screening Results and Their Children Who Completed Psychological Testing.*

Characteristic	Screening Group (N = 390)	Control Group (N = 404)
Gestational age at screening (weeks, days)		
Median	12, 3	12, 3
Interquartile range	11, 6–13, 6	11, 6–13, 5
Thyrotropin (mIU/liter)†		
United Kingdom‡		
Median	3.8	3.2
Interquartile range	1.5–4.7	1.2–4.2
Turin		
Median	3.1	2.4
Interquartile range	1.3–4.0	1.3–3.9
Free T_4†		
United Kingdom (pmol/liter)		
Median	11.1	11.2
Interquartile range	10.5–13.3	10.5–13.2
Turin (pg/ml)		
Median	7.4	7.4
Interquartile range	7.1–8.6	7.2–8.3
Maternal smokers (%)	17	14
Maternal weight (kg)		
Median	68	67
Interquartile range	59–78	59–80
Age when mother left full-time education (%)¶		
≤16 yr	34	33
17–18 yr	27	26
≥19 yr	39	41
Age when father left full-time education (%)¶		
≤16 yr	51	42
17–18 yr	18	23
≥19 yr	31	35
Maternal age at delivery (yr)	30±5.4	31±5.3
Paternal age at delivery (yr)¶	32±5.9	33±6.3
Male children (%)	55	51
Age at psychological testing (yr)		
Median	3.2	3.2
Interquartile range	3.2–3.3	3.2–3.3

* Plus–minus values are means ±SD. In the screening group, the women were assigned to treatment with levothyroxine. To convert the values for free thyroxine (T_4) from picomoles per liter to nanograms per deciliter, divide by 12.87.
† Values for thyrotropin and free T_4 levels are provided separately for the United Kingdom and Turin because different assays were used (ADVIA Centaur in the United Kingdom and AutoDELFIA in Turin, Italy).
‡ The difference between the screening and control groups was significant ($P = 0.009$); there were no other significant differences.
¶ Data shown are for the United Kingdom only (parents in Turin were not asked about educational status or age at delivery).

Table 2. Standardized Full-Scale Child IQ and Scores on the Child Behavior Checklist (CBCL) and the Behavior Rating Inventory of Executive Function, Preschool Version (Brief-P), According to Study Group.*

Test	Screening Group (N=390)	Control Group (N=404)	Difference (95% CI) (Control Group – Screening Group)†	P Value
IQ				
Mean	99.2±13.3	100.0±13.3	0.8 (−1.1 to 2.6)	0.40
<85 (% of children)	12.1	14.1	2.1 (−2.6 to 6.7)	0.39
CBCL T score‡				
Mean	44.4±12.4	45.1±13.6	0.7 (−1.2 to 2.5)	0.49
Brief-P T score§				
Median	40	40	0	0.59
Interquartile range	47–55	47–55		

* Plus–minus values are means ±SD. The full-scale child IQ test was standardized so that for each psychologist, the mean score among the children in the control group whom they tested was 100. In the screening group, the women were assigned to treatment with levothyroxine.
† For percentages of children with an IQ below 85, the absolute (percentage-point) differences are shown.
‡ For the CBCL, a T score above the 98th percentile is indicative of a clinically significant problem.
§ For the Brief-P, a T score above 65 is indicative of a clinically significant problem.

Terme trop tardif de LT4 13 GA

24% de perdu de vue

Rima K. Dhillon-Smith et al . Levothyroxine in Women with Thyroid Peroxidase Antibodies before Conception. N Engl J Med 2019;380:1316-25. DOI: 10.1056/NEJMoa18

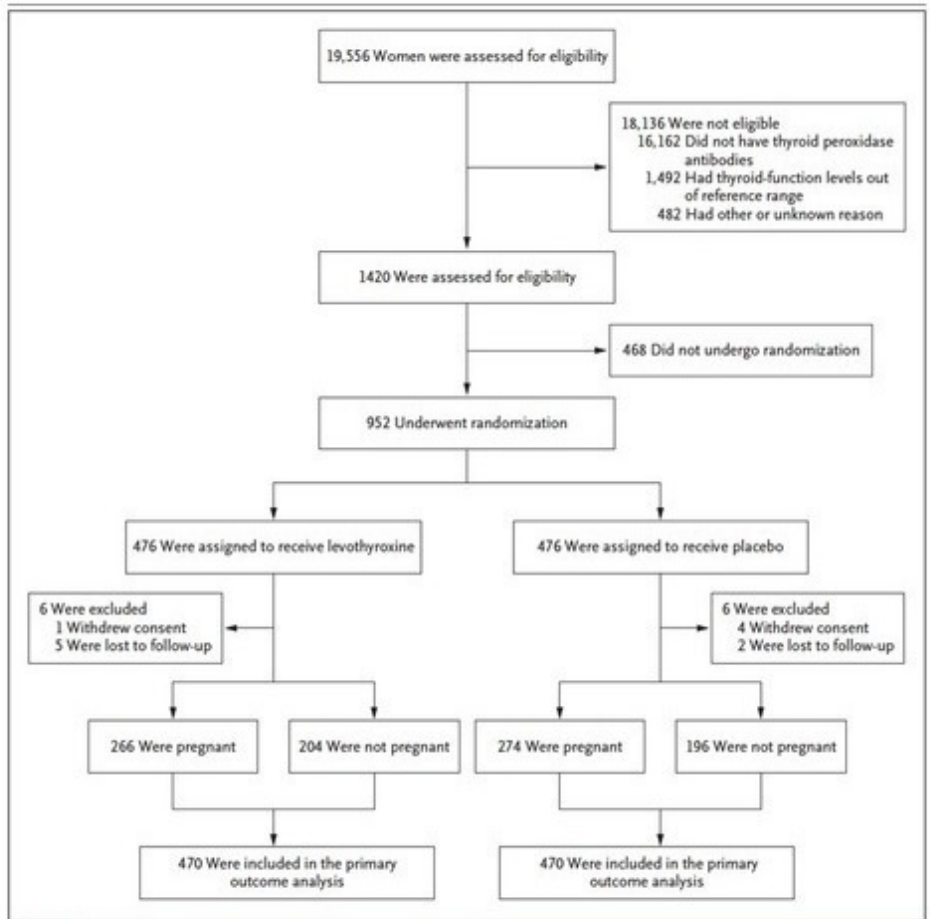


Figure 1. Enrollment, Randomization, Follow-up, and Analysis.

Table 1. Baseline Characteristics of the Participants.*

Characteristic	Levothyroxine Group (N = 476)	Placebo Group (N = 476)
General demographic characteristics		
Maternal age†		
<35 yr — no. (%)	306 (64.3)	306 (64.3)
Mean age — yr	32.5±4.9	32.7±4.9
BMI		
BMI ≥25 — no./total no. (%)	240/462 (51.9)	240/464 (51.7)
Mean BMI	26.4±5.6	26.5±5.5
Race or ethnic group — no. (%)‡		
White	328 (68.9)	337 (70.8)
Chinese	4 (0.8)	4 (0.8)
South Asian	110 (23.1)	94 (19.7)
Black	16 (3.4)	23 (4.8)
Other	18 (3.8)	18 (3.8)
Pregnancy history		
Nulliparous — no./total no. (%)	141/476 (29.6)	131/473 (27.7)
Previous miscarriages — no./total no. (%)†		
0	166/476 (34.9)	165/476 (34.7)
1 or 2	219/476 (46.0)	213/473 (45.0)
≥3	91/476 (19.1)	95/476 (20.0)
No. of previous miscarriages — median (IQR)		
In women with ≥1 miscarriage	2 (1–3)	2 (1–3)
First-trimester miscarriage (<14 wk) in women with ≥1 miscarriage	2 (1–3)	2 (1–3)
Previous preterm births at <34 wk — no./total no. (%)	11/476 (2.3)	10/473 (2.1)
Current treatment for infertility — no. (%)†	216 (45.4)	213 (44.7)
Prerandomization thyroid hormone concentrations		
Serum thyrotropin level†		
≤2.5 mIU/liter — no. (%)	329 (69.1)	330 (69.3)
>2.5 mIU/liter — no. (%)	147 (30.9)	146 (30.7)
Median level (IQR) — mIU/liter	2.10 (1.51–2.74)	2.01 (1.45–2.70)
Level on log scale — mIU/liter	0.674±0.422	0.652±0.418
Mean serum free thyroxine level — pmol/liter	14.6±1.9	14.5±2.0
Median serum thyroid peroxidase antibody level (IQR) — IU/ml§	170 (83–428)	202 (94–417)

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. There were no significant differences between the groups in the listed characteristics at baseline. To convert the values for free thyroxine to nanograms per deciliter, divide by 12.87. BMI denotes body-mass index, and IQR interquartile range.
† This variable was a minimization variable.
‡ Race or ethnic group was reported by the participants.
§ Data were missing for six women in the levothyroxine group and four women in the placebo group.

Table 2. Primary Outcome and Secondary Outcomes.*

Outcome	Levothyroxine Group	Placebo Group	Relative Risk or Mean Difference (95% CI)†
Primary outcome			
Live birth at ≥34 wk — no./total no. (%)	176/470 (37.4)	178/470 (37.9)	0.97 (0.83 to 1.14)
Secondary outcomes			
Pregnancy at ≤12 mo after enrollment — no./total no. (%)	266/470 (56.6)	274/470 (58.3)	0.97 (0.88 to 1.07)
Pregnancy outcomes — no./total no. (%)			
Clinical pregnancy at 7 wk‡	237/266 (89.1)	248/274 (90.5)	0.98 (0.93 to 1.04)
Ongoing pregnancy at 12 wk‡	194/266 (72.9)	200/274 (73.0)	1.00 (0.90 to 1.11)
Miscarriage at <24 wk§	75/266 (28.2)	81/274 (29.6)	0.95 (0.73 to 1.23)
Stillbirth: intrauterine death at ≥24 wk	1/266 (0.4)	0/274	—
Ectopic pregnancy	3/266 (1.1)	6/274 (2.2)	0.50 (0.13 to 1.99)
Termination of pregnancy¶	1/266 (0.4)	0/274	—
Live birth			
At <34 wk	10/266 (3.8)	10/274 (3.6)	1.02 (0.43 to 2.42)
At ≥34 wk	176/266 (66.2)	178/274 (65.0)	1.02 (0.90 to 1.15)
Neonatal outcomes among women with live births at ≥24 wk			
Gestational age at delivery			
Wk of gestation	38 wk 6 days±2 wk 3 days	39 wk±2 wk 4 days	1 day (−0 wk 4 days to 0 wk 3 days)
No. of women	186	188	
Birth weight			
Mean weight — g‖	3226±660	3262±668	−35 (−168 to 97)
No. of infants	187	188	
Apgar score			
At 1 min			
Median (IQR)	9 (9–9)	9 (8–9)	0.1 (−0.2 to 0.4)
No. of infants	179	178	
At 5 min			
Median (IQR)	9 (9–10)	9 (9–10)	0.0 (−0.2 to 0.2)
No. of infants	178	178	

* Plus–minus values are means ±SD. There were no significant differences between the groups.

† Relative risks are shown for the primary outcome and all pregnancy outcomes listed as secondary outcomes. The mean difference is shown for all neonatal outcomes listed as secondary outcomes. For binary outcomes, a relative risk of less than 1 favors the levothyroxine group, except for live birth after at least 34 weeks of gestation, clinical pregnancy at 7 weeks, and ongoing pregnancy at 12 weeks, for which a relative risk greater than 1 would favor levothyroxine. For continuous outcomes, mean differences greater than 1 favor the levothyroxine group. The widths of the confidence intervals have not been adjusted for multiple comparisons.

‡ Nine ectopic pregnancies were considered to be unviable and so were assumed to have ended on day 0. One pregnancy was terminated at 12 weeks, so it was counted as survival to this time. One missing date of miscarriage was assumed in this analysis to be between 7 and 12 weeks (the period during which miscarriage typically occurs).

§ The median gestational age in the levothyroxine group was 8 weeks (IQR, 6 to 10), and the median gestational age in the placebo group was 9 weeks (IQR, 7 to 10). One woman in the placebo group who was pregnant with twins and who had both a live birth at less than 34 weeks of gestation and a miscarriage was counted in both categories.

¶ The reason for termination of pregnancy was fetal abnormality (anencephaly).

‖ Eight birth weights were unknown in the levothyroxine group, and seven birth weights were unknown in the placebo group.

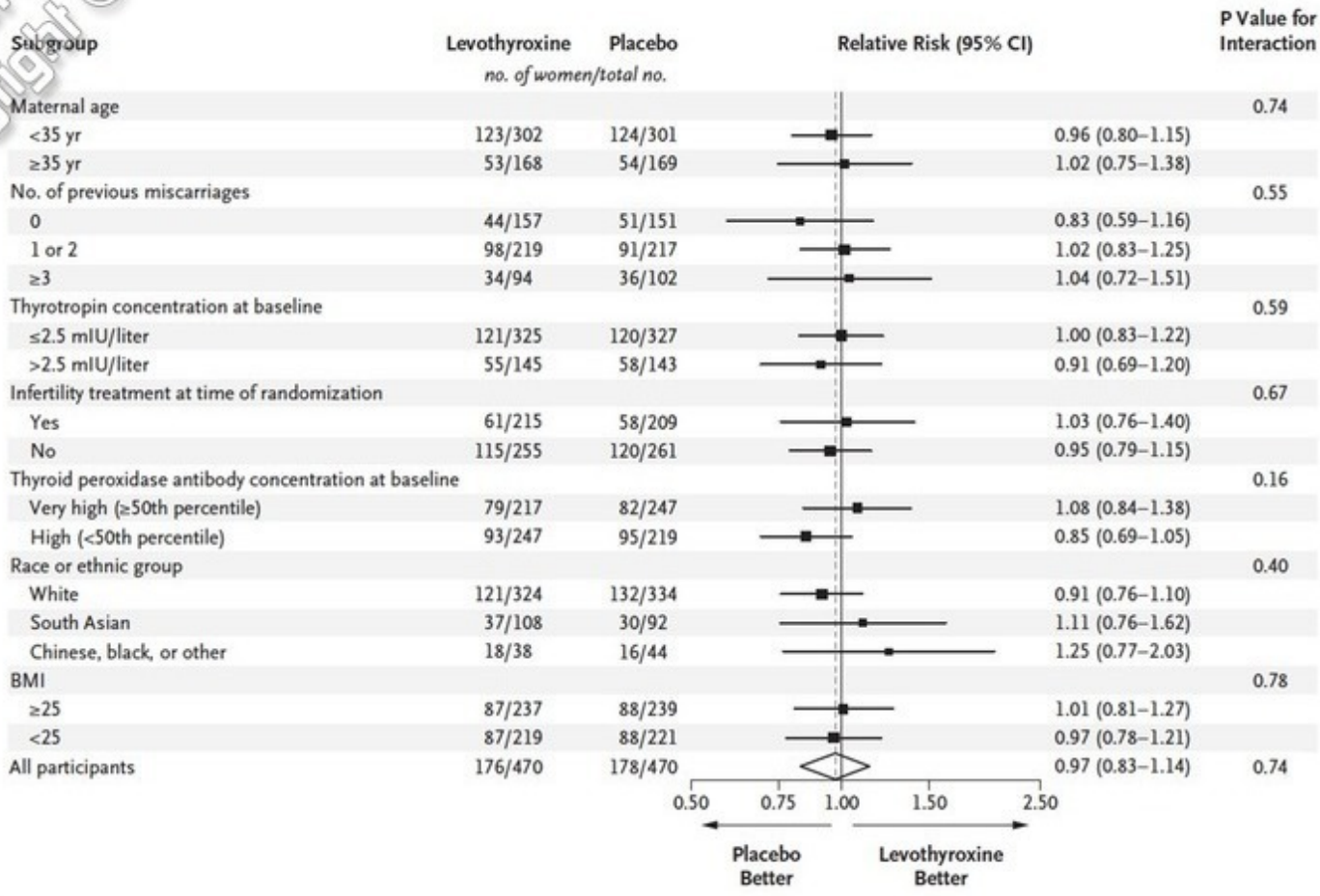


Figure 2. Prespecified Subgroup Analyses in Women Who Had a Live Birth after at Least 34 Weeks of Gestation.

The widths of the confidence intervals were not adjusted for multiple comparisons. The size of the black squares corresponds to the total number of women in the subgroup. Prespecified subgroup analyses included maternal age, the number of previous miscarriages, the thyrotropin concentration at baseline, and infertility treatment at the time of randomization. Prespecified "exploratory" subgroup analyses included the thyroid peroxidase antibody concentration at baseline, race and ethnic group, and the body-mass index (BMI, the weight in kilograms divided by the square of the height in meters).

Discussion

- LT4 limité à 50 µg/j , pas indexé sur le BMI par ex

Hypothyroïdie Aspect Maternel et Foetal

- Hypothyroïdie Fruste (TSH elevée, FT4 nle)
- Administration FT4
  - Hypo frustre antiTPO +
    - For obstetrical outcome: (USPSTF Recommendation level: B, Evidence-fair) (2|⊕⊕○○)
    - For neurological outcome: (USPSTF Recommendation level: I, Evidence-poor) (2|○○○○).
  - Hypo frustre antiTPO-
    - For obstetrical outcome: (USPSTF Recommendation level: C, Evidence-fair) (2|⊕⊕○○)
    - For neurological outcome: (USPSTF Recommendation level: I, Evidence-poor) (2|○○○○)

Hypothyroïdie Aspect Maternel et Foetal

- Hypothyroïdie préconceptionelle
  - Administration de FT4 Cible TSH < 2.5 mIU/L. (USPSTF Recommendation level: C, Evidence-poor) (2|⊕○○○)
- Hypothyroïdie en cours de Grossesse
  - Augmentation des doses toute les 4 à 6 semaines (30%). (USPSTF Recommendation level: A, Evidence-good) (1|⊕⊕⊕⊕)
  - Cible TSH < 2,5 T1 ou TSH <3 T2T3 – contrôle toutes les 4 à 6 semaines (USPSTF Recommendation level: A, Evidence-good) (1|⊕⊕⊕⊕)
  - Euthyroïdie et Anti TPO + , monitorage toutes les 4 à 6 semaines (USPSTF Recommendation level: A, Evidence-fair) (1|⊕⊕⊕○)
- Post Partum
  - Retour aux dosages antérieurs (USPSTF Recommendation level: A, Evidence-good) (1|⊕⊕⊕⊕)

Iode

Carence iodée maternelle: conséquence fœtale

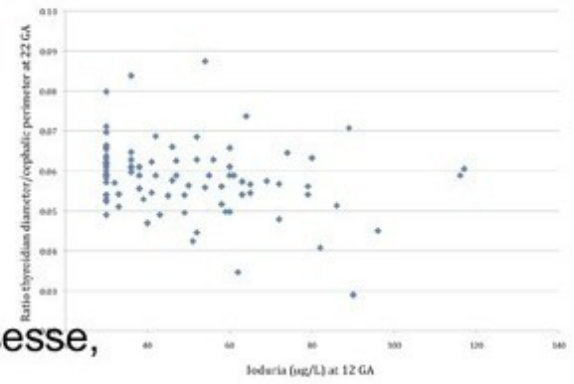
Iodine Deficiency in Northern Paris Area: Impact on Fetal Thyroid Mensuration

Dominique Luton[1]*, Corinne Alberti[4], Edith Vuillard[2], Guillaume Ducarme[1], Jean François Oury[2], Jean Guibourdenche[3]

Table 1. Changes in maternal serum levels of free triiodothyronine, free thyroxine, and TSH from 12 weeks' gestational age to delivery; cord blood values of the same parameters; and maternal serum iodine and urinary iodine excretion.

Maternal blood	Statistics	FT3 pmole/L	FT4 pmole/L	TSH IU/L	UIE µg/L	Serum iodine nmole/L
12 WGA	Mean (SD)	4.7 (0.4)	14.1 (1.49)	1.29 (0.63)	48.02 (2)	NA
	Min-Max	3.8–5.7	10.4–18.2	0.08–3.17	30–117	
	N	116	116	116	102	
32 WGA	Mean (SD)	4.2 (0.4)	12.1 (1.5)	1.62 (0.73)	52.4 (4)	695 (41)
	Min-Max	3.3–5.3	8.8–15.5	0.46–4.5	30–233	271–1900
	N	96	96	96	63	76
Delivery	Mean (SD)	4.1 (0.6)	12.2 (1.7)	2.87 (1.5)	NA	NA
	Min-Max	1.5–5.2	8.7–16.7	0.22–9.8		
	N	85	85	85		
Cord Blood	Mean (SD)	2.53 (0.08)	14.1(0.2)	7.7 (0.8)	NA	NA
	Min-Max	1.5–4.7	9.5–19.2	0.5–27		
	N	72	72	72		

FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; UIE, urinary iodine excretion; WGA, weeks' gestational age; NA, not available.
doi:10.1371/journal.pone.0014707.t001



Plus la iodurie maternelle est basse en début de grossesse,
Plus le ratio fœtal diam. thyr./PC est élevé à 22SA.
Région parisienne, carencée en iode

R=0,25 p<0,02 n=90

Figure 2. Correlation between maternal urinary iodine excretion at 12 weeks gestational age (WGA) and the ratio of fetal thyroid gland diameter over fetal head circumference at 22 weeks gestational age (n = 90). R = 0,25 p<0,02 n = 90.
doi:10.1371/journal.pone.0014707.g002

Carence iodée maternelle: conséquence fœtale

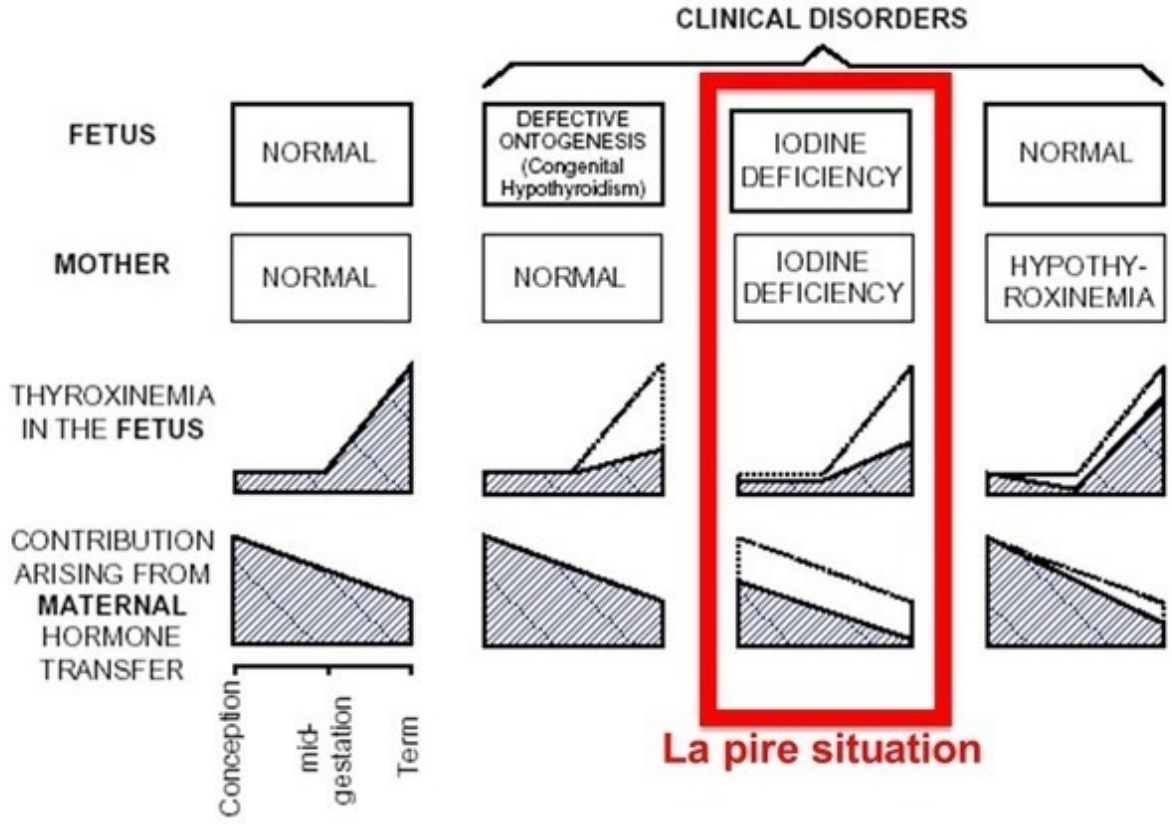
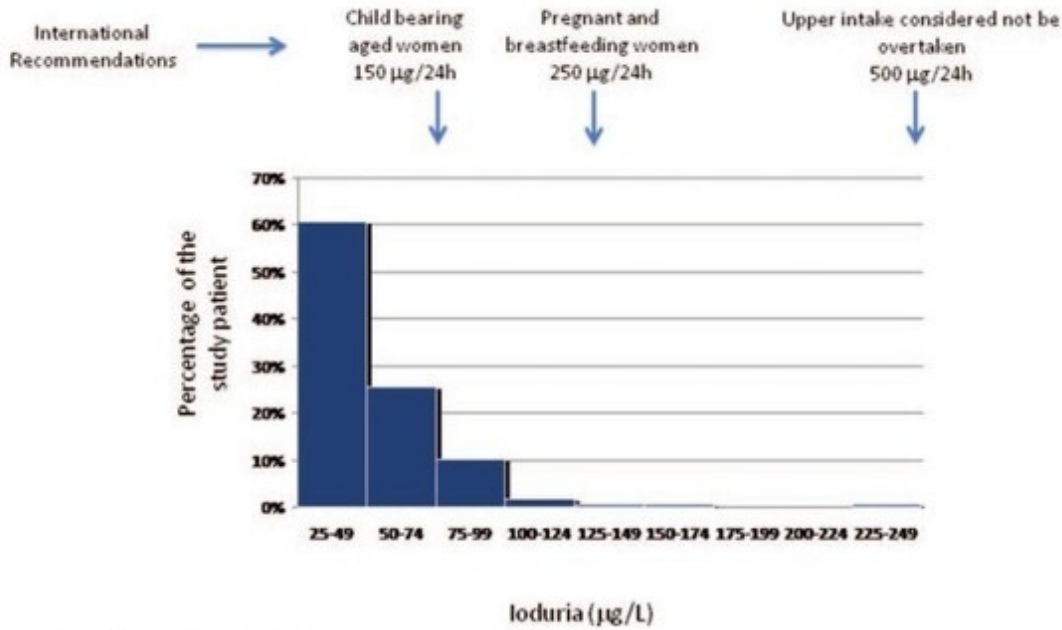


Figure 5. A schematic representation of the three sets of clinical conditions that may affect thyroid function in the mother alone, the fetus alone, or the fetal–maternal unit, showing the relative contributions of an impaired maternal and/or fetal thyroid function, that may eventually lead to alterations in fetal thyroxinemia. Reproduced with permission from Ref. 24.

Results in Paris



Mean ioduria is 49,8 µg/l +/- 2,1 among 165 samples

Figure 2. Urinary iodine excretion in pregnant women at 12 GA in the northern part of the Paris conurbation in 2006-2007 (pooled data). Mean ioduria is 49,8 mg/l +/2 2,1 among 165 samples.

OPEN ACCESS Freely available online PLOS one

Iodine Deficiency in Northern Paris Area: Impact on Fetal Thyroid Mensuration

Dominique Luton[1*], Corinne Alberti[4], Edith Vuillard[2], Guillaume Ducarme[1], Jean François Oury[2], Jean Guibourdenche[3]

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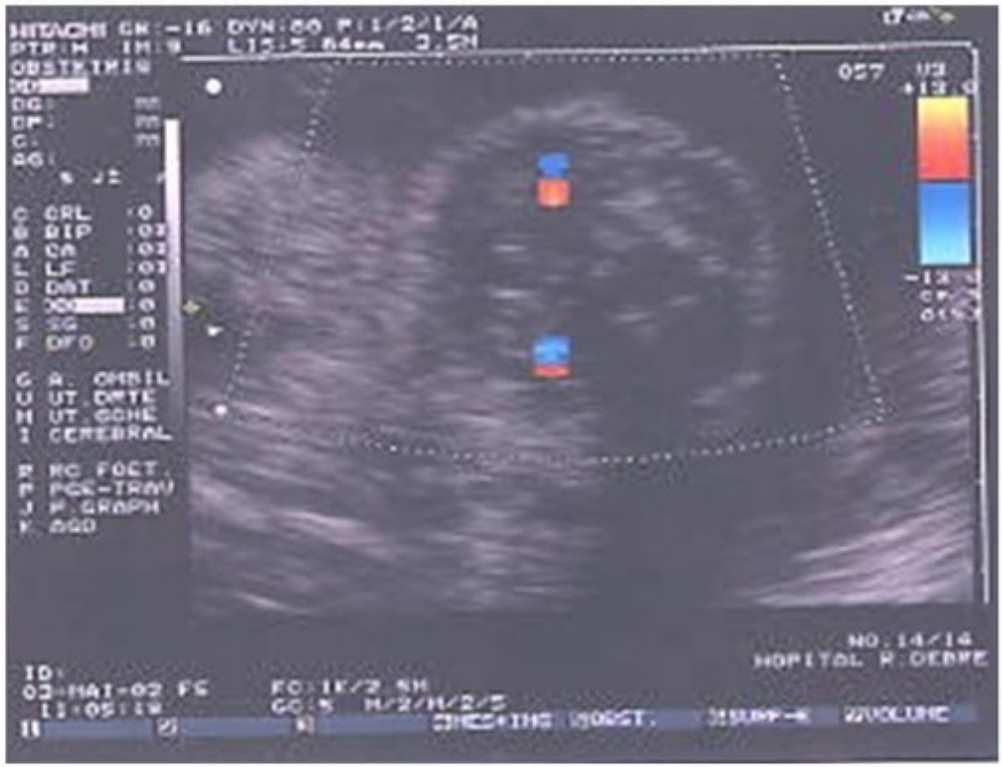
Recommandations

- Femmes en age de procréer : 150 µg par jour Pendant la grossesse et l'allaitement : 250 µg par jour (Niveau A)
- Pendant la grossesse et l'allaitement ne pas dépasser. 500 µg par jour (Niveau I)
- Pour mesurer l'état d'apport en iode d'une population , faire une iodurie sur une cohorte , idéalement entre 150 et 250 µg/L. (Niveau A)

- Potassium iodide, goiter, prenatal diagnosis.
-
-

Abstract

Background : Supra physiological maternal exposure to iodine may induce hypothyroidism and goiter in the offspring. Potassium Iodide (PI) prescribed to treat Erythema nodosum during pregnancy can inhibit fetal thyroid uptake of radioactive iodine. A case of fetal goiter is described after a maternal exposure of Potassium Iodide. **Case :** We report the case of a euthyroid patient with Erythema nodosums disease who received a cumulative dose of 8400 mg PI during the 2nd trimester of her third pregnancy. Echography showed a fetal goiter at 22 weeks of gestation (WG). The foetus was euthyroid as diagnosed by funipuncture. At 32 WG fetal thyroid was normal. The patient was delivered of a euthyroid newborn at 39 WG. Neonatal ultrasonography showed a midly goiter with an euthyroid status by biological assesments. Clinical assessments were normal at two month. **Conclusion :** Teratovigilance require fetal thyroid assessment by echography in the management of potential fetal thyroid dysfunction, particularly after massive maternal iodine exposure.



Thyroïdite du post partum

- Survient (def) dans l'année qui suit l'accouchement
- 2 à 16% des patientes
- Thyrotoxicose 2 à 3 mois après l'accouchement
- En générale modérée
- Goitre simple
- Hypothyroïdie 4 à 8 mois après l'accouchement
- Puis normalisation

Thyroïdite du post partum

- Hashimoto « like »
- Terrain= goitre et taux élevé d'AC anti thyroglobulines et anti microsomes
- Tt symptomatique
  - Hyper : B- , pas d'ATS
  - Hypo : substitution dans 1/3 des cas
- Récidive aux grossesses ultérieures
- 20 à 30 % d' hypothyroïdie définitive dans les 3-4 ans
- ----→ suivie +++

Nodules thyroïdiens

- Fréquents
- Scintigraphie contre indiquée
- Dans certains contexte (nodule suspect cliniquement, antécédent familial de néoplasie endocrine multiple de type 2, symptomes évocateurs de tumeur médullaire) le dosage de calcitonine peut être proposé
- Eliminer adénome toxique (clinique + dosages)
  - Si oui -> chir
- Sinon
  - Contexte familiale et caractéristiques cliniques
  - Aspect échographique
  - Cytoponction
- Si pas de décision chir: traitement freinateur LT4 et surveillance echo et clinique

Goitre simple

- Être sur de la fonction thyroïdienne

- Laisser le traitement freinateur

Cancer de la thyroïde

- Traité : pas de CI à la grossesse
- Attendre 12 mois après arrêt de l'iode 131
- Surveillance pluridisciplinaire
- Dosage de la thyroglobuline
- Le cancer médullaire de la thyroïde représente environ 10 % des cancers thyroïdien
    - Dosage de la calcitonine
- La mutation de RET expose aussi au phéochromocytome et à l'hyperparathyroïdie dans le cadre de la Néoplasie Endocrinienne Multiple de type 2. La forme 2B est plus agressive et entraîne aussi des névromes
- consultation multidisciplinaire d'oncogénétique et un conseil génétique pour informer et expliquer du risque de transmission de l'affection à la descendance. Il est maintenant proposé une thyroïdectomie prophylactique chez les enfants porteurs de mutations germinales de RET

Qui dépister ?

Human Thyroidian Fœtus Dysfunction: echographic scanning

illness	Aproximative Frequency	Goiter	Transmission	Fœtal echographic interest ?
Dysgenesis - Athyreosis - Ectopia - Hypoplasia	1/4000	no	Sporadic, Familial, AD AR Syndromic	Could Be
Hormogenesis Failure	1/40000	yes	AR	Yes Recurrence
HT Pit axis dysfunction - Pit 1 mutation - TSH B chain mutation	1/100000	no	AR	
TSHr Mutation - Inactivation - Activation		 no yes	 AR AD AD- sporadic (neo)	
Resistance to Thyr Hormones		yes	AD	
Positive Maternal Trab - Inhibiting Hypo - Stimulating hyper		 no yes	Maternal through the placenta	Yes
ATS Toxic or Iodine overload		yes	Maternal through the placenta	Yes
Iodine Deficiency	++++	yes	environemental	Could be
Maternal Hypo excluding post thyroidectomy with persistant TRAb TPO and TG ab				No or not yet

Dépistage de l'hypothyroïdie

- Toute patiente avec dysfonction thyroïdienne doit avoir une TSH en préconceptionel (USPSTF Recommendation level: B, Evidence-fair) (1|????)

- Pas de dépistage universel des anti TPO (USPSTF Recommendation level: C, Evidence level-fair) (2|????)

- Dépistage universel pendant la grossesse reste débattu (avant 9SA)
  - Contre et pour un dépistage ciblé : (USPSTF Recommendation level: I, Evidence-poor) (2|????) (Authors supporting – MA, EA, JM, LB, SS, SM, DL, RC)
  - Pour systématique : (USPSTF Recommendation level: C, Evidence-fair) (2|????) (Authors supporting – LD, JR, JL, NA, CE)

Dépistage de l'hypothyroïdie

- Dépistage universel avant la grossesse n'est pas recommandé (USPSTF Recommendation level: I, Evidence-poor) (2|⊕○○○)
- Par contre un dépistage des individus à haut risque est nécessaire
  - Women over age 30 years
  - Women with a family history or autoimmune thyroid disease or hypothyroidism
  - Women with a goiter
  - Women with thyroid antibodies, primarily thyroid peroxidase antibodies
  - Women with symptoms or clinical signs suggestive of thyroid hypofunction
  - Women with type 1 diabetes mellitus, or other autoimmune disorders
  - Women with infertility
  - Women with a prior history of preterm delivery
  - Women with prior therapeutic head or neck irradiation or prior thyroid surgery
  - Women currently receiving levothyroxine replacement
- Doser TSH ou FT4 TSH et traiter avec une cible dTSH<2,5 UI /l le cas échéant
- (USPSTF Recommendation level: I, Evidence-poor) (2|⊕○○○)