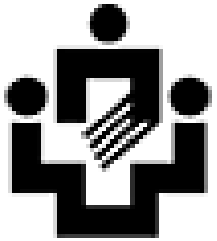
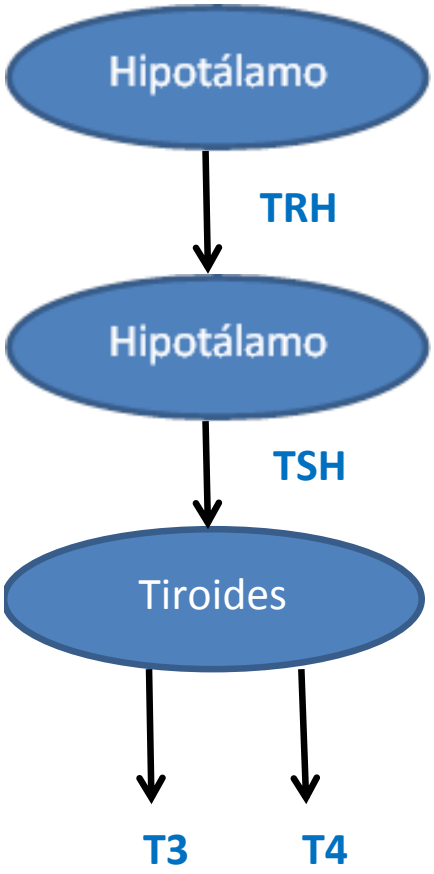
HIPOTIRODISMO EN EL EMBARAZO



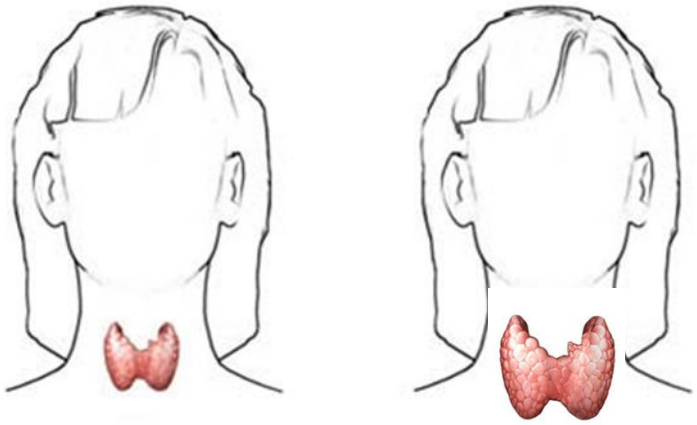
Inés Velasco
Grupo TiroSEEN
Barcelona-2015

Un poco de fisiología…

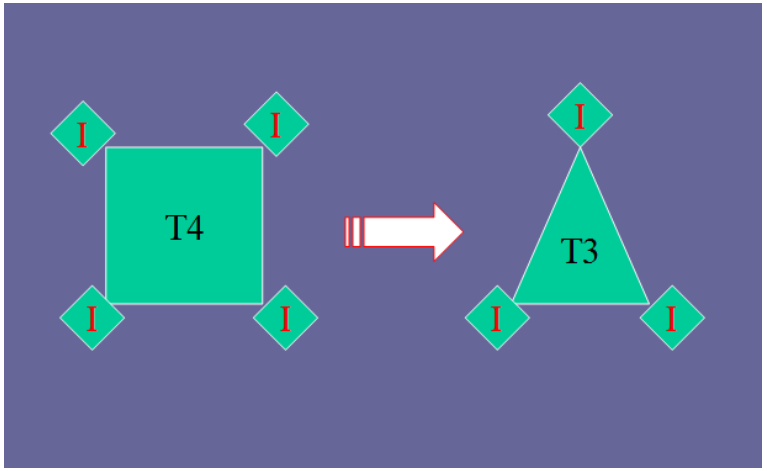


Mecanismos de adaptación

- Hiperplasia compensadora



- Secreción preferencial de T3



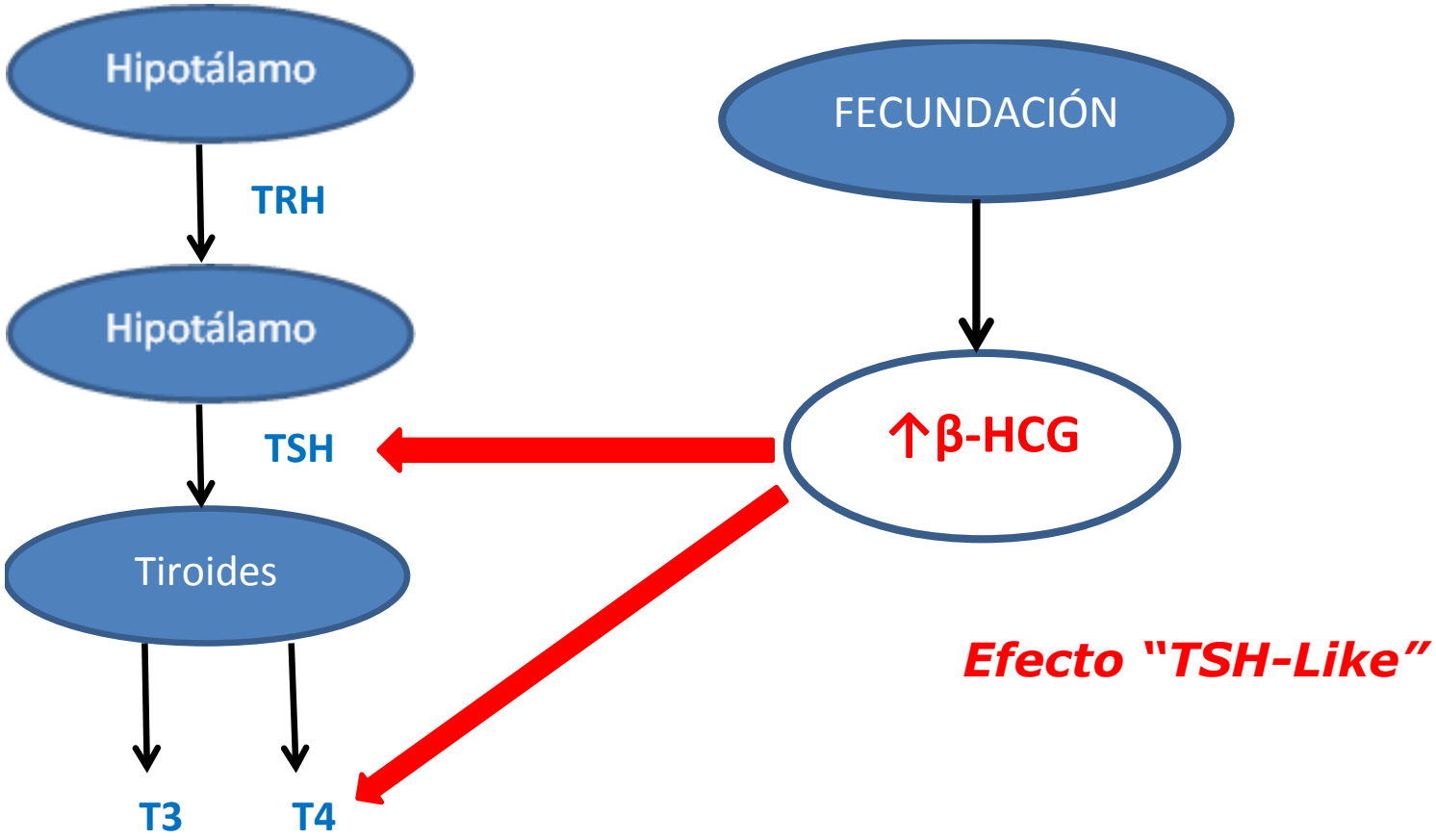
Funciones

- Hormonas tiroideas:
  - Crecimiento somático
  - Regulación metabólica
  - Neurodesarrollo.
- Gestación:
  - Aumento metabolismo basal.
  - Incremento gasto cardíaco.
  - Crecimiento celular y organogénesis.

El embarazo es una situación de estrés para el tiroides

Un poco MÁS de fisiología…

- Endocrinología
- Obstetricia



Efecto TSH-Like

- Los valores de referencia de TSH para población adulta ya no son válidos.
- La T3 no atraviesa la barrera placentaria.
- Los niveles de T4 libre en sangre durante el primer trimestre se han asociado a un pronóstico neurológico en la descendencia.

Tiroides y Gestación

ENFERMEDAD TIROIDEA GESTACIONAL

1. Cribado universal de la disfunción tiroidea en la mujer gestante.
2. Actitud ante el Hipotiroidismo Clínico
3. Actitud ante el Hipotiroidismo Subclínico.
4. Actitud ante la Autoinmunidad.
5. Actitud ante la Hipotiroxinemia.
6. Conclusiones.

CRIBADO DE FUNCIÓN TIROIDEA

Mayor riesgo de disfunción tiroidea.

- Aumento de los requerimientos
- Fracaso en los mecanismos de compensación

La disfunción tiroidea durante la gestación se asocia a:

- Infertilidad
- Abortos de repetición
- Parto pretérmino
- Alteraciones del neurodesarrollo

CRIBADO DE FUNCIÓN TIROIDEA

THYROID
Volume 21, Number 10, 2011

DOI: 10.1089/thy.2011.0087

Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum

The American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum

Alex Stagnaro-Green (Chair),[1] Marcos Abalovich,[2] Erik Alexander,[3] Fereidoun Azizi,[4] Jorge Mestman,[5] Roberto Negro,[6] Angelita Nixon,[7] Elizabeth N. Pearce,[8] Offie P. Soldin,[9] Scott Sullivan,[10] and Wilmar Wiersinga[11]

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

8.4a1. Some members recommended screening of all pregnant women for serum TSH abnormalities by the ninth week or at the time of their first visit. USPSTF recommendation level: C; evidence, fair (2⊕⊕◯◯) (6, 9, 22, 72, 137) (Authors supporting: L.D.G., J.R., J.H.L., N.A., C.I.E.).

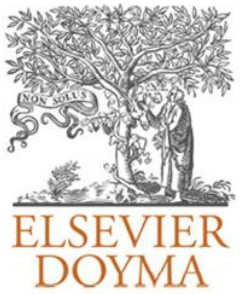
Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline

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

8.4a2. Some members recommended neither for nor against universal screening of all pregnant women for TSH abnormalities at the time of their first visit. These members strongly support aggressive case finding to identify and test high-risk women (Table 1) for elevated TSH concentrations by the ninth week or at the time of their first visit before or during pregnancy, and they recognize that in some situations ascertainment of the individual's risk status may not be feasible. In such cases, and where the local practice environment is appropriate, testing of all women by wk 9 of pregnancy or at the first prenatal visit is reasonable. USPSTF recommendation level: I; evidence, poor (2⊕OOO) (72, 80, 137, 138) (Authors supporting: M.A., E.K.A., J.M., L.B., S.S., S.J.M., D.L., R.H.C.).

CRIBADO DE FUNCIÓN TIROIDEA

Endocrinol Nutr. 2012;59(9):547–560



ENDOCRINOLOGÍA Y NUTRICIÓN

www.elsevier.es/endo

DOCUMENTO DE CONSENSO

Detección de la disfunción tiroidea en la población gestante: está justificado el cribado universal☆

Lluís Vila[a,*], Inés Velasco[b], Stella González[c], Francisco Morales[d], Emilia Sánchez[e], José Maria Lailla[f], Txanton Martinez-Astorquiza[g], Manel Puig-Domingo[h]
y el Grupo de Trabajo de Trastornos por Deficiencia de Yodo y Disfunción Tiroidea de la Sociedad Española de Endocrinología y Nutrición[◊,&]

CRIBADO DE FUNCIÓN TIROIDEA

CONTROVERSIES IN ENDOCRINOLOGY

On the need for universal thyroid screening in pregnant women

Lluís Vila, Inés Velasco[1], Stella González[2], Francisco Morales[3], Emilia Sánchez[4], Sara Torrejón, Berta Soldevila[5], Alex Stagnaro-Green[6] and Manuel Puig-Domingo[5]

European Journal of Endocrinology
(2014) **170**, R17–R30

Puntos críticos del cribado

- Necesidad de rangos de referencia propios para cada centro.

THYROID
Volume X, Number X, 2015

DOI: 10.1089/thy.2015.0309

LETTER TO THE EDITOR

Standardization of Free Thyroxine and Harmonization of Thyrotropin Measurements: A Request for Input from Endocrinologists and Other Physicians

Linda M. Thienpont,[1] James D Faix,[2,3] and Graham Beastall[4]

Otros puntos críticos del cribado..

- Guía consensuada con ginecólogos.
- Evidencias del beneficio terapéutico.

ENFERMEDAD TIROIDEA GESTACIONAL

1. Cribado universal de la disfunción tiroidea en la mujer gestante.
2. Actitud ante el Hipotiroidismo Clínico
3. Actitud ante el Hipotiroidismo Subclínico.
4. Actitud ante la Autoinmunidad.
5. Actitud ante la Hipotiroxinemia.
6. Conclusiones.

HIPOTIROIDISMO CLÍNICO

Clinical Endocrinology (2013) **79**, 297–304

doi: 10.1111/cen.12232

REVIEW ARTICLE

Screening for overt thyroid disease in early pregnancy may be preferable to searching for small aberrations in thyroid function tests

Peter Laurberg*, Stine L. Andersen*, Inge B. Pedersen*, Stig Andersent and Allan Carlé*

by screening. A number of studies indicate that untreated overt thyroid disease in pregnancy may lead to complications. The potential benefit of screening and early therapy is supported by evidence, indicating that even severe maternal hypothyroidism does not lead to neurocognitive deficiencies in the child, if the condition is detected and treated during the first half of pregnancy. Screening and therapy for overt thyroid dysfunction in early pregnancy may be indicated, rather than focusing on identifying and treating small aberrations in thyroid function tests.

HIPOTIROIDISMO CLÍNICO

THYROID
Volume 24, Number 10, 2014

DOI: 10.1089/thy.2014.0007

The Attitude Toward Hypothyroidism During Early Gestation: Time for a Change of Mind?

Victor Pop,[1] Maarten Broeren,[2] and Wilmar Wiersinga[3]

We feel that the high number of "healthy" pregnant women with unknown severe hypothyroidism according to recent reference criteria of trimester-specific normal thyroid function in an iodine sufficient area underlines the need of screening the thyroid function of the general pregnant population.

HIPOTIROIDISMO CLÍNICO: TRATAMIENTO

- **Hipotiroidismo conocido**:
  - Se incrementa la dosis de tiroxina en un 25-30% al conocer la gestación.

(Alexander EK et al. NEJM 2004)

- **Hipotiroidismo no conocido**:
  - Iniciar tto con 2.3 µg/kg/día para alcanzar un objetivo de TSH < 2,5 rápidamente (mujer de 60 kg: 138 µg)

(Abalovich M et al. Thyroid 2013)

ENFERMEDAD TIROIDEA GESTACIONAL

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HIPOTIROIDISMO SUBCLÍNICO

- Guía ATA (2011):

RECOMMENDATION 8

SCH has been associated with adverse maternal and fetal outcomes. However, due to the lack of randomized controlled trials there is insufficient evidence to recommend for or against universal LT_4 treatment in TAb− pregnant women with SCH. **Level I-USPSTF**

RECOMMENDATION 9

Women who are positive for TPOAb and have SCH should be treated with LT_4. **Level B-USPSTF**

Dissent from one committee member: There is no consistent prospective evidence demonstrating that women who are TPOAb+, but who have SCH only, achieve maternal or perinatal benefit from LT_4 treatment. Correspondingly, there is no indication to treat women who are TPOAb+ and have SCH with LT_4.

HIPOTIROIDISMO SUBCLÍNICO

- Guía Endocrine Society (2012):

given that the potential benefits outweigh the potential risks, the panel recommends T_4 replacement in women with SCH who are thyroid peroxidase antibody positive (TPO-Ab+). For obstetrical outcome: USPSTF recommendation level, B; evidence, fair (2⊕⊕○○); for neurological outcome, USPSTF recommendation level, I; evidence, poor (2○○○○). The panel also recommends T_4 replacement in women with SCH who are TPO-Ab negative (TPO-Ab−). For obstetrical outcome: USPSTF recommendation level, C; evidence, fair (2⊕⊕○○); for neurological outcome: USPSTF recommendation level, I; evidence, poor (2○○○○).

HIPOTIROIDISMO SUBCLÍNICO

Guidelines

European Thyroid Journal

Eur Thyroid J 2014;3:76–94
DOI: 10.1159/000362597

Received: February 13, 2014
Accepted after revision: April 1, 2014
Published online: June 7, 2014

2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children

John Lazarus[a] Rosalind S. Brown[c] Chantal Daumerie[d]
Alicja Hubalewska-Dydejczyk[e] Roberto Negro[f] Bijay Vaidya[b]

HIPOTIROIDISMO SUBCLÍNICO (ETA 2014)

Conclusions

- Current data indicate an increase in pregnancy loss, gestational diabetes, gestational hypertension, pre-eclampsia and preterm delivery in women with SCH in pregnancy.
- The association between SCH in pregnancy and impaired neuropsychological development of the offspring is inconsistent.

¿¿ ??

Recommendation

Further studies are required to determine the precise effects of SCH on obstetric outcome in addition to their effects on childhood neuro-intellectual development. (2S)

HIPOTIROIDISMO SUBCLÍNICO (ETA 2014)

Conclusions

Evidence for screening for SCH in pregnancy is equivocal.

The decision regarding screening for SCH must be reconsidered when new high-quality evidence becomes available.

¿¿ ??

Recommendations

SCH arising before conception or during gestation should be treated with levothyroxine. (2S)

HIPOTIRODISMO SUBCLÍNICO

Position Statement | G Brabant and others | Critical review of subclinical hypothyroidism in pregnancy | 173:1 | P1–P11

Management of subclinical hypothyroidism in pregnancy: are we too simplistic?

Georg Brabant[1,2], Robin P Peeters[3], Shiao Y Chan[4], Juan Bernal[5,6], Philippe Bouchard[7], Domenico Salvatore[8], Kristien Boelaert[9] and Peter Laurberg[10]

European Journal of Endocrinology (2015); ***173****: P1-P11.*

ENFERMEDAD TIROIDEA GESTACIONAL

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AUTOINMUNIDAD TIROIDEA POSITIVA

- Guía ATA (2011):

RECOMMENDATION 42

There is insufficient evidence to recommend for or against screening for anti-thyroid antibodies, or treating in the first trimester of pregnancy with LT_4 or IVIG, in euthyroid women with sporadic or recurrent abortion or in women undergoing *in vitro* fertilization (IVF). **Level I-USPSTF**

Question 53: Should euthyroid women who are known to be positive for anti-thyroid antibodies either before or during pregnancy be treated with LT_4 in order to decrease the chance of sporadic or recurrent miscarriage?

- **RECOMMENDATION 43**

  There is insufficient evidence to recommend for or against LT_4 therapy in TAb+ euthyroid women during pregnancy. **Level I-USPSTF**

AUTOINMUNIDAD TIROIDEA POSITIVA

- Guía Endocrine Society (2012):

1.2.6. Women with thyroid autoimmunity who are euthyroid in the early stages of pregnancy are at risk of developing hypothyroidism and should be monitored every 4–6 wk for elevation of TSH above the normal range for pregnancy. USPSTF recommendation level: A; evidence, fair (1⊕⊕⊕○).

4.1. A positive association exists between the presence of thyroid antibodies and pregnancy loss. Universal screening for antithyroid antibodies, and possible treatment, cannot be recommended at this time. As of January

TTO AUTOINMUNIDAD TIROIDEA

A Favor:

- Si existen malos antecedentes obstétricos.
- En tratamientos de reproducción asistida (empírico).

En Contra:

- No hay estudios concluyentes sobre la efectividad del tratamiento en reducir las complicaciones obstétricas y neonatales.

ENFERMEDAD TIROIDEA GESTACIONAL

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HIPOTIROXINEMIA MATERNA

Review Article

Doubts and Concerns about Isolated Maternal Hypothyroxinemia

Mariacarla Moleti, Francesco Trimarchi, and Francesco Vermiglio

From the above, it is clear that the criteria for defining normal levels of FT4 and TSH in pregnant women are far from homogeneous. This variance has obvious diagnostic and therapeutic implications. Indeed, depending on the FT4/TSH threshold considered to be normal, the same biochemical pattern may be variously defined as overt/subclinical hypothyroidism, which requires medical treatment, as isolated hypothyroxinemia, the treatment of which is advocated by some but not by others, or even as normal.

HIPOTIROXINEMIA MATERNA

- Guía ATA (2011):

Question 10: Should isolated hypothyroxinemia be treated in pregnancy?

RECOMMENDATION 7

Isolated hypothyroxinemia should not be treated in pregnancy. Level C-USPSTF

RECOMMENDATION 73

Because no studies to date have demonstrated a benefit to treatment of isolated maternal hypothyroximenia, universal FT_4 screening of pregnant women is not recommended. Level D-USPSTF

HIPOTIROXINEMIA MATERNA

- Guía Endocrine Society (2012):

Conclusions: Practice guidelines are presented for diagnosis and treatment of patients with thyroid-related medical issues just before and during pregnancy and in the postpartum interval. These include evidence-based approaches to assessing the cause of the condition, treating it, and managing hypothyroidism, hyperthyroidism, gestational hyperthyroidism, thyroid autoimmunity, thyroid tumors, iodine nutrition, postpartum thyroiditis, and screening for thyroid disease. Indications and side effects of therapeutic agents used in treatment are also presented. (*J Clin Endocrinol Metab* 97: 2543–2565, 2012)

  - No considera la hipotiroxinemia como enfermedad tiroidea.
  - No aparece incluida en la guía.

HIPOTIROXINEMIA MATERNA

¿¿ ??

- Guía ETA (2014):

Maternal hypothyroxinaemia is associated with impaired neuropsychological development of the offspring.

There is no evidence that screening specifically for isolated hypothyroxinaemia is indicated.

To date, no study of intervention is available to demonstrate a benefit from treating hypothyroxinaemic women in terms of obstetric complications. (1S)
However, levothyroxine therapy may be considered in isolated hypothyroxinaemia detected in the first trimester because of its association with neuropsychological impairment in children. (3W)

Resumen final

Recomendaciones

- Búsqueda dirigida (agressive case-finding).
- Identificación de pacientes de riesgo:
  - Hipotiroidismo clínico.
  - Malos antecedentes obstétricos:
    - Hipotiroidismo subclínico.
    - Autoinmunidad tiroidea.
- Tratamiento con tiroxina en casos de alto riesgo.

Recomendaciones

- Actitud conservadora en casos de bajo riesgo:
  - Ausencia de rangos de referencia propios.
  - Hipotiroxinemia materna.
  - Autoinmunidad tiroidea aislada.

- Identificación de pacientes de riesgo:
  - Hallazgo oportunista.
  - Daños colaterales del cribado.

Recomendaciones

- Abordaje multidisciplinar de la disfunción tiroidea en gestantes/ mujeres en edad fértil.

- Búsqueda de consenso:

GRACIAS!!