



**THE 26TH FETUS AS A PATIENT
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Thyroid Function and Pregnancy Outcome



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Thyroid Function and Pregnancy Outcome



- Numerous hormonal changes and metabolic demands occur during pregnancy, resulting in profound and complex effects on thyroid function.
- Thyroid diseases are more prevalent in women (than in men) during the childbearing period.

Despite the new insights gained over the last two decades , many uncertainties remain and important questions remain incompletely elucidated.





Thyroid Function and Pregnancy Outcome

The Thyroid in Normal Pregnancy

The main changes that occur during a normal pregnancy:

Physiologic Change	Thyroid-related consequences
Increased renal I- clearance	Increased 24-hr RAIU
Decreased plasma I- and placental I- transport to the fetus	In I- deficient women, decreased T4, increased TSH, and goiter formation
Increased O ₂ consumption by fetoplacental unit, gravid uterus and mother	Increased BMR <i>(basal metabolic rate)</i>
First-trimester increase in hCG	Increased free T4 and T3 Decreased basal TSH (partial blunting of the pituitary-thyroid axis)
Increased serum TBG	Increased total T4 and T3
Increased plasma volume	Increased T4 and T3 pool size
Inner-ring deiodination of T4 and T3 by placenta	Accelerated rates of T4 and T3 degradation and production



Thyroid Function and Pregnancy Outcome

Iodine Metabolism



In the mother:

-Increased uptake of radioactive iodine: by hCG increased renal clearance of iodine by TSH



In the fetus:

- Iodine crosses the placenta by passive diffusion.
- Lack of regulation of the uptake of iodine.
- Deposits decreased iodine fetus and neonates.



Thyroid Function and Pregnancy Outcome

The Thyroid in Normal Pregnancy

In regions where the iodine supply is borderline or low, the situation is clearly different and significant changes occur during pregnancy

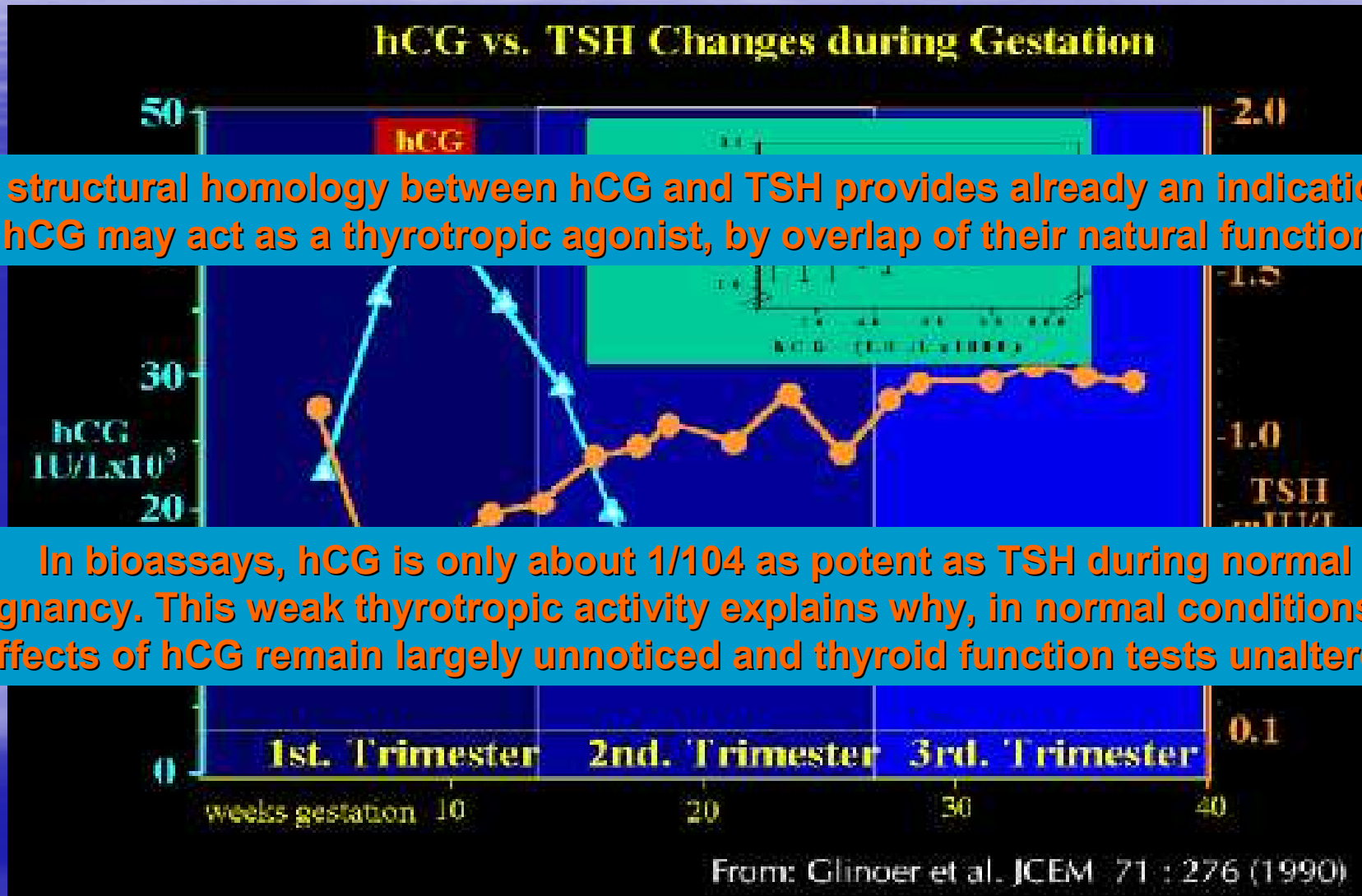
- Glinoe D, De Nayer P, Bourdoux, et al: Regulation of maternal thyroid function during pregnancy. J Clin Endocrinol Metab 71:276, 1990
- Glinoe D, Delange F, Laboureur I, De Nayer P: Maternal and neonatal thyroid function at birth in an area with of marginally low iodine intake. J Clin Endocrinol Metab 75:800, 1992
- Glinoe D: The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. Endocr Rev 18:404, 1997

When a pregnancy takes place in conditions with borderline iodine availability, significant increments in both the maternal and fetal thyroid volume occur, if no supplemental iodine is given during early pregnancy .

- Crooks J, Tulloch MI, Turnbull AC, et al: Comparative incidence of goitre in pregnancy in Iceland and Scotland. Lancet 2:625, 1969
- Glinoe D, Lemone M: Goiter and pregnancy: a new insight into an old problem. Thyroid 2:65, 1992
- Glinoe D, De Nayer P, Delange F, et al: A randomized trial for the treatment of mild iodine deficiency during pregnancy: maternal and neonatal effects. J Clin Endocrinol Metab 80:258, 1995

Thyroid Function and Pregnancy Outcome

Effects of human chorionic gonadotropin on thyroid function.



The structural homology between hCG and TSH provides already an indication that hCG may act as a thyrotropic agonist, by overlap of their natural functions.

In bioassays, hCG is only about 1/104 as potent as TSH during normal pregnancy. This weak thyrotropic activity explains why, in normal conditions, the effects of hCG remain largely unnoticed and thyroid function tests unaltered.



Thyroid Function and Pregnancy Outcome

Thyroid Status in Pregnancy



First trimester:

- Increased Free T4
- TSH decreased
- Assess gestational thyrotoxicosis



Third trimester:

- Free T4 and T3 decline (hCG decreased)



Thyroid Function and Pregnancy Outcome

Transplacental passage



1) Transplacental passage easy

- Iodides
- Thionamides
- Immunoglobulin tiroestimulantes
- TSH-releasing hormone

2) Limited transplacental passage

- Triiodothyronine
- Thyroxine

3) Transplacental passage zero

- TSH

Thyroid Function and Pregnancy Outcome

Thyroid function tests in pregnancy

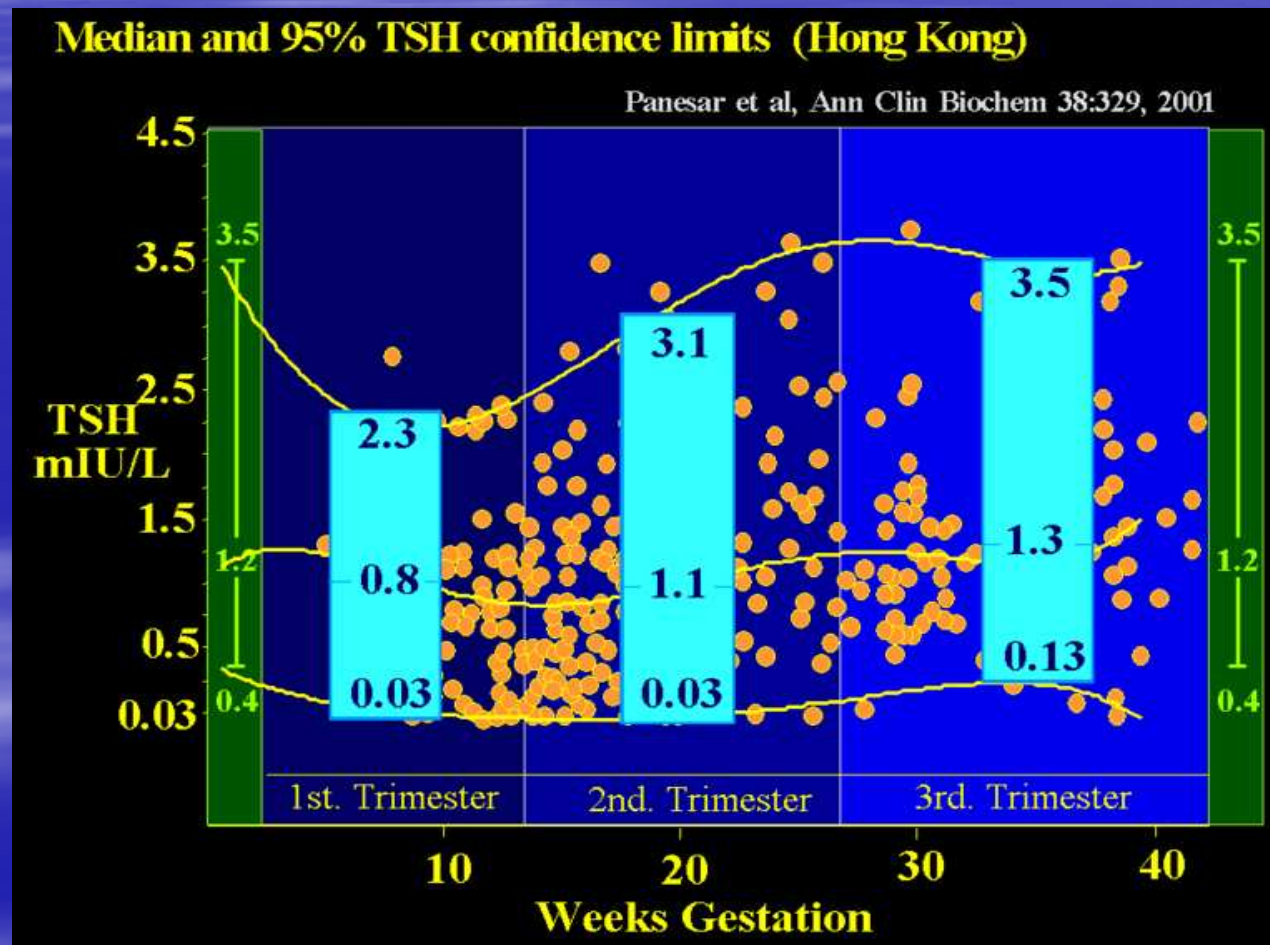


T4 Total	↑
T4 Libre	↔ ó ↓
T3 Total	↑
TSH	↔
TG	↑

Thyroid Function and Pregnancy Outcome

Serum TSH

(Thyroid function parameters in normal pregnancy)



Panesar NS, Li CY, Rogers MS: Reference intervals of thyroid hormones in pregnant Chinese women. Ann Clin Biochem 38:329, 2001

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Thyroid Function and Pregnancy Outcome

Other tests

(Thyroid function parameters in normal pregnancy)

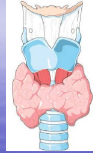
Isotopic tracers should not be administered during pregnancy and therefore the altered iodine kinetics in the pregnant patient will not be a source of confusion.

It should be recalled that clinical findings suggestive of mild hyperthyroidism on women during gestation are:

- Increased pulse pressure
- Tachycardia
- Heat intolerance
- Decreased peripheral vascular resistance



Thyroid Function and Pregnancy Outcome



Thyroid Pathologies

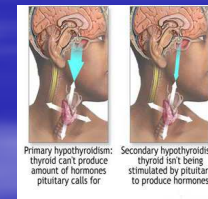
PREGNANCY AND IODINE DEFICIENCY



AUTOIMMUNE THYROID DISEASE AND PREGNANCY



PRIMARY HYPOTHYROIDISM



THYROTOXICOSIS





Thyroid Function and Pregnancy Outcome

PREGNANCY AND IODINE DEFICIENCY



The pregnancy should be viewed as an “environmental” factor to trigger the thyroid machinery and, in turn, induce thyroid pathology in areas with a marginally reduced iodine intake.



Thyroid Function and Pregnancy Outcome

AUTOIMMUNE THYROID DISEASE AND PREGNANCY

Consequential Changes

- Decreases Ab during pregnancy.
- Exacerbation and recurrences after parturition.



Thyroid Function and Pregnancy Outcome

AUTOIMMUNE THYROID DISEASE AND PREGNANCY

Disorders of Female Reproduction:

- Infertility.
- Miscarriage
- Recurrent Abortion



Thyroid Function and Pregnancy Outcome

AUTOIMMUNE THYROID DISEASE AND PREGNANCY

Effects of Pregnancy :

1. Primary hypothyroidism

- a) Thyroid destruction (Hashimoto's disease)
- b) Circulating TSH-receptor-blocking antibody

2. Asymptomatic (euthyroid) autoimmune disease Increased risk:

- a) of developing subclinical hypothyroidism during pregnancy
- b) of spontaneous miscarriage

3. Postpartum thyroid disease

- a) Hyperthyroidism
- b) Hypothyroidism
- c) Combinations

4. Graves' Disease

- a) Pre-existing
- b) Gestational exacerbation and Remission
- c) Postpartum exacerbation



Thyroid Function and Pregnancy Outcome

AUTOIMMUNE THYROID DISEASE AND PREGNANCY

SUMMARY

- ✓ During pregnancy cell-mediated and humoral immune responses are reduced.
- ✓ After delivery these conditions are reestablishment and exacerbations.
- ✓ Thyroid autoimmunity are associated with infertility, miscarriage and maternal hypothyroidism

✓ As a consequence:



Systematic screening for:

- Thyroid Dysfunction
- Antibody

In infertility patients and pregnancy



Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

Prevalence During Pregnancy:



- Hypothyroidism: 0.3-0.5 %

- Subclinical: 2-3%



Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

Maternal thyroid dysfunction can result in impaired psychoneurologic development of the fetus. Maternal hypothyroidism has been associated with mental retardation in the living euthyroid offspring as well as with increased fetal and neonatal losses.

Brent GA. Maternal hypothyroidism: recognition and management.
Thyroid. 1999;9:661-665.



Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

CAUSES:

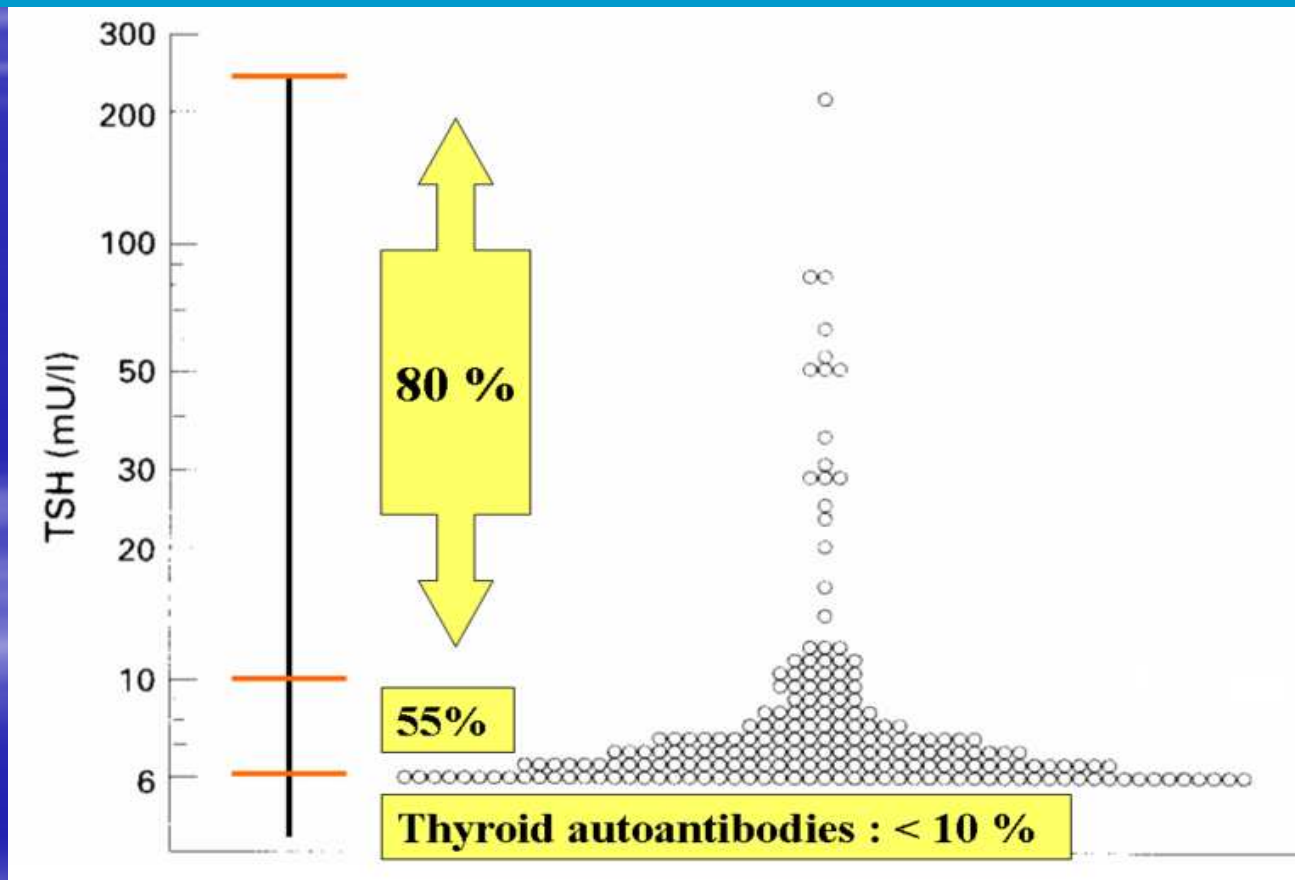


- Iodine deficiency.
- Chronic autoimmune thyroiditis.
- Radical treatment of hyperthyroidism.
- Surgery for thyroid tumors.
- TSH receptor “blocking” antibodies.

Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

A cohort of 10,857 women was screened for thyroid antibodies and serum TSH concentrations in the 2nd trimester of pregnancy

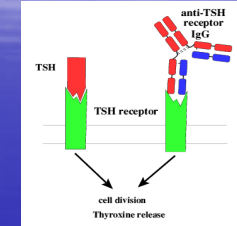


Allan WC, Haddow JE, Palomaki GE, et al: Maternal thyroid deficiency and pregnancy complications: implications for population screening. J Med Screen 7:127, 2000

Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

TSH receptor “Blocking” antibodies



Interference TSH-TSH receptor interaction

Transferred to the fetal

INTRAUTERINE OR TRANSIENT NEONATAL HYPHOTHYROIDISM

Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

DIAGNOSIS:

Clinical Features:

- Weight increase
- Sensitivity to cold
- Dry skin
- Asthenid
- Drowsiness
- Constipation
- Asymptomatic

Laboratory Test:

- Serum TSH
- Free T4
- Thyroid auto-antibodies





Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

OBSTETRICAL COMPLICATIONS

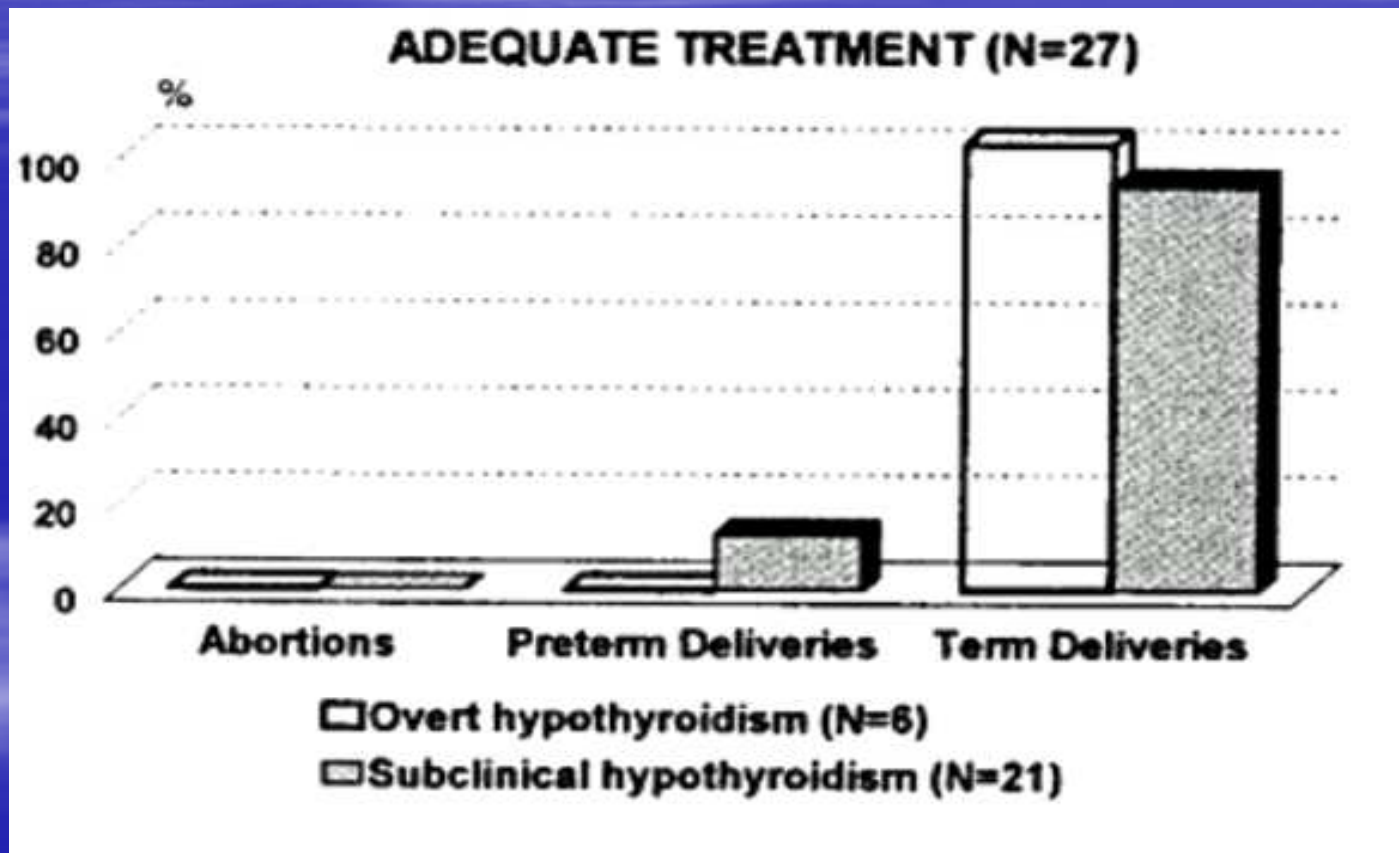


- ❖ ABORTION
- ❖ PRE-TERM DELIVERIES
- ❖ IUGR
- ❖ FETAL DEATH

Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

Abalovich et al.

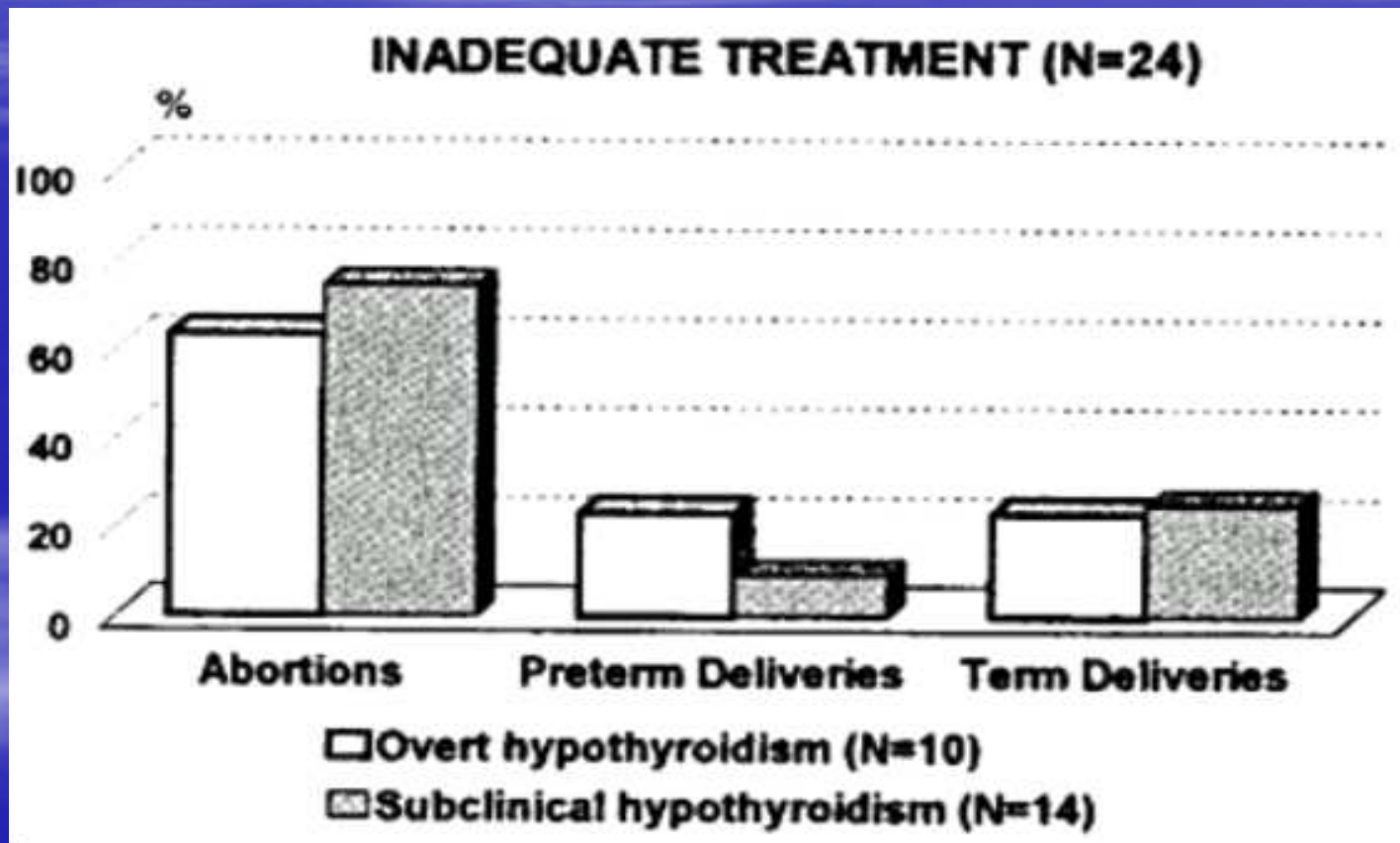


Abalovich M, Gutierrez S, Alcaraz G, et al: Overt and subclinical hypothyroidism complicating pregnancy. *Thyroid* 12:63, 2002

Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

Abalovich et al.



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Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

Screening for hypothyroidism during pregnancy

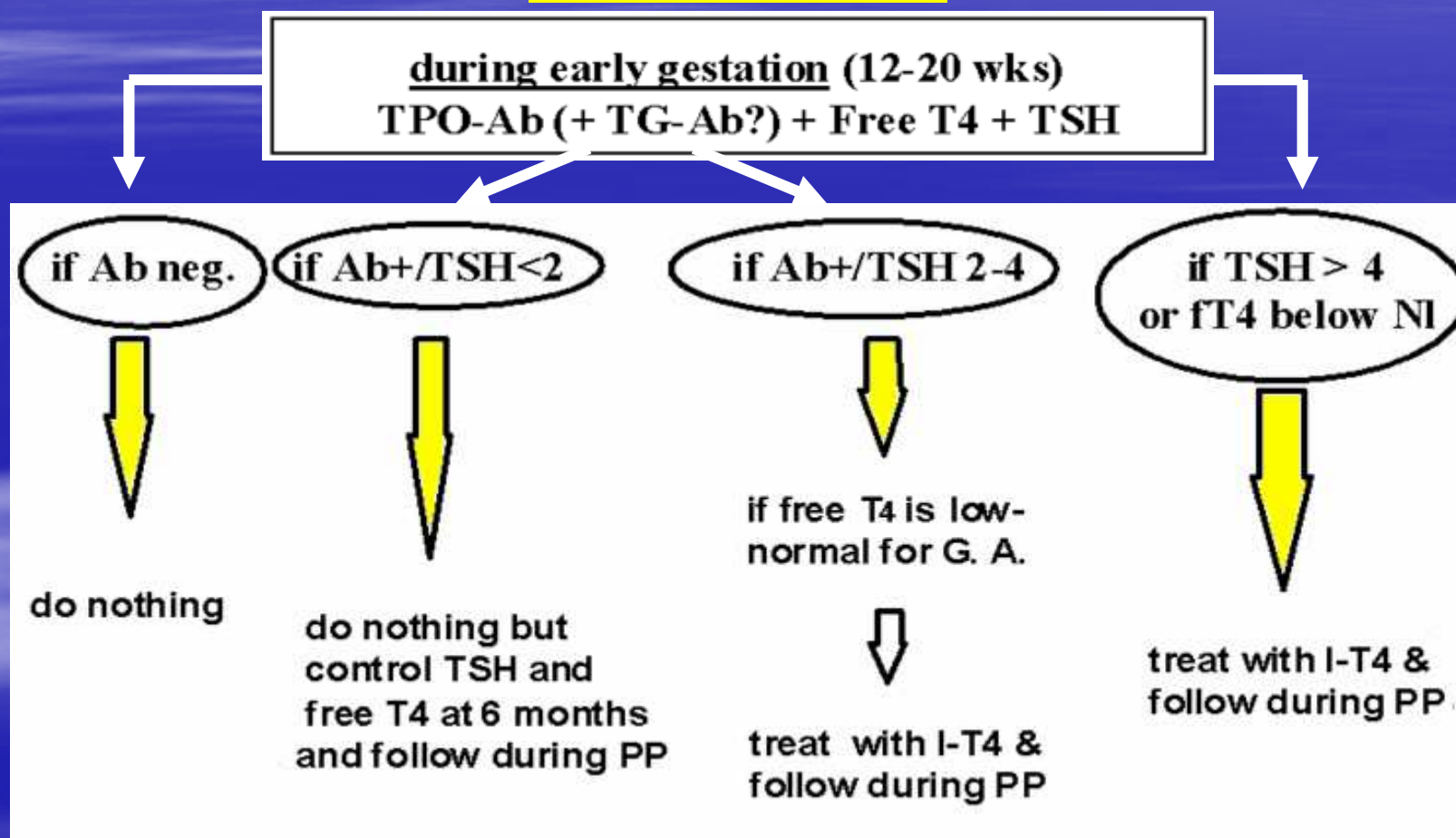
High risk women for whom screening is recommended

- 
- ✓ Women who already take thyroxine prior to conceptio.
 - ✓ History of hyperthyroid or hypothyroid disease, postpartum thryoiditis, or thyroid lobectomy.
 - ✓ Family history of thyroid disease.
 - ✓ Goiter.
 - ✓ Thyroid antibodies (when known).
 - ✓ Symptoms or clinical signs suggestive of thyroid underfunction.
 - ✓ Type I diabetes.
 - ✓ Other autoimmune disorders.
 - ✓ A history of neck irradiation.
 - ✓ Infertility should have screening with TSH as part oftheir infertility work-up.

Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

ALGORITHM





Thyroid Function and Pregnancy Outcome

PRIMARY HYPOTHYROIDISM

Therapeutic Considerations

	Patients with Hashimoto's disease (n = 15)		Patients with thyroid ablation (n = 18)	
	Before	During	Before	During
T4 dose (µg/ day)	111 +/- 25	139 +/- 52	114 +/- 33	166 +/- 64*
T4 dose (µg/ kg/ day)	1.7 +/- 0.6	1.9 +/- 0.9	1.8 +/- 0.5	2.3 +/- 0.8*
Serum TSH (mU/L)	2.0 +/- 1.8	1.8 +/- 1.1	1.5 +/- 1.3	1.9 +/- 1.1

* p<0.01. (from Kaplan ; Ref 60)

Thyroid Function and Pregnancy Outcome

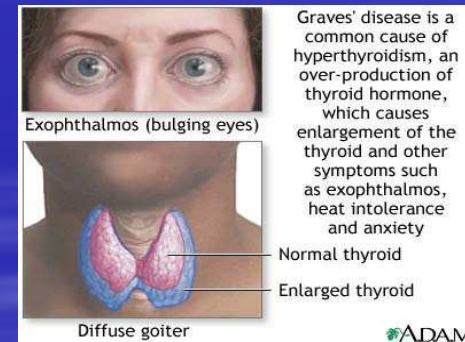
THYROTOXICOSIS



PREVALENCE: 1-4 X 1000 PREGNANCIES

CAUSES:

- Graves' Disease
- HCG-induced Hyperthyroidism
or
Gestational Hyperthyroidism



Thyroid Function and Pregnancy Outcome

THYROTOXICOSIS



Clinical Diagnosis

➤ Previous History:



- ✓ Hyperthyroidism or autoimmune thyroid disease in the patient or her family.
- ✓ Symptoms of hyperthyroidism including weight loss (or failure to gain weight), palpitations, proximal muscle weakness, or emotional lability.
- ✓ Symptoms suggesting Graves' disease (ophthalmopathy or pretibial myxedema).
- ✓ Thyroid enlargement.
- ✓ Accentuation of normal symptoms of pregnancy such as heat intolerance, diaphoresis, and fatigue.
- ✓ Pruritis.



Thyroid Function and Pregnancy Outcome

THYROTOXICOSIS



Clinical Diagnosis

➤ Physical Examination:

- ✓ Pulse rate > 100 .
- ✓ Widened pulse pressure.
- ✓ Eye signs of Graves' disease or pretibial myxedema.
- ✓ Thyroid enlargement especially in iodine sufficient geographical areas.
- ✓ Onycholysis.





Thyroid Function and Pregnancy Outcome

THYROTOXICOSIS

Laboratory Diagnosis



✓ TSH (< 0.1 mU/l)

✓ T3

✓ T4

TSH < 0.4 mU/l in 10-20% of euthyroid women near the end of 1st Trimester.



Thyroid Function and Pregnancy Outcome

THYROTOXICOSIS

Adverse pregnancy outcome and lack of control of maternal hyperthyroidism

	Poor control	Less than adequate control	Adequate control	Ref N°
Preeclampsia	14-22%		7%	252
	Poor control	Less than adequate control	Adequate control	Ref N°
CHF *	60%		3%	251
Thyroid storm	21%		2%	248
Preterm delivery	88%	25%	8%	251
LBW **	23%		10%	253

* CHF: congestive heart failure; ** LBW: low birth weight (< 2500 g)



Thyroid Function and Pregnancy Outcome

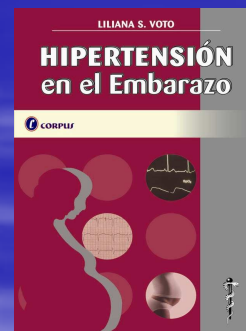
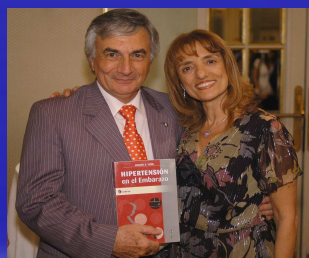
Better understanding of the complex maternal-fetal interrelationships related to the ongoing thyroid processes must remain our constant quest, in order to ensure the best possible health status of mother and progeny.



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THANK YOU FOR YOUR ATTENTION !!



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