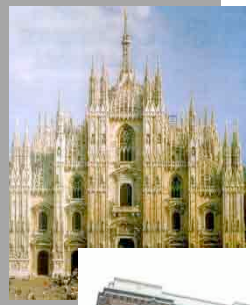
9° Congresso Nazionale AME

Associazione Medici Endocrinologi

Update in Endocrinologia Clinica

AIT - AME Position Statement

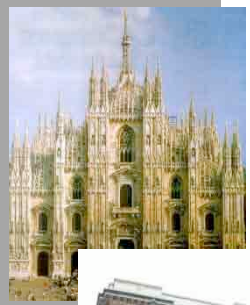
Thyroid Nodules and Differentiated Thyroid cancer
Management in Pregnancy



A. Baroli, P. Beck-Peccoz, L. Chiovato, R. Elisei, P. Garofalo, R. Guglielmi, R. Negro, E. Papini, M.P. Pisoni, M. Zini

Items

- **Background**
- Thyroid Nodules Management:
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- Discussion
- Differentiated Thyroid Cancer Management :
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- Discussion
- Conclusions



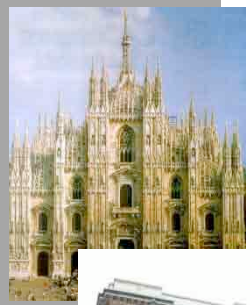
Background

- the detection of thyroid nodules in pregnant women is a frequent finding and their best management is sometimes controversial
- a repeat ultrasound performed within a week after delivery has been reported to reveal:

a. an up to 60% increase in the size of known nodules

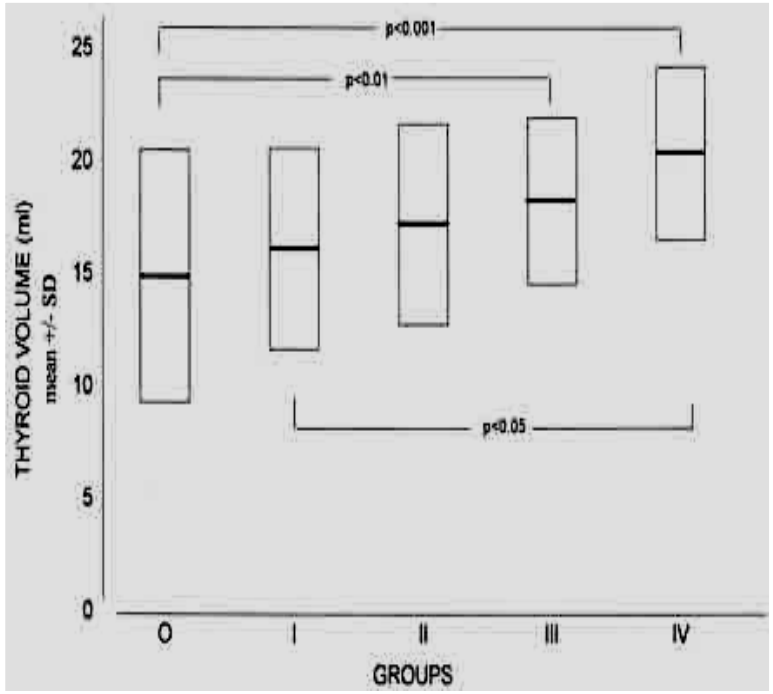
b. detection of new nodules in 20% of women

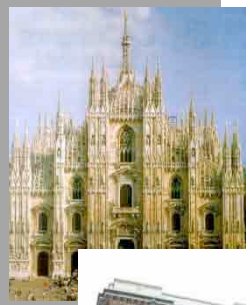
- prevalence of nodules is significantly higher in women with prior pregnancies compared to nulliparous ones (25% *vs* 9%) in areas at low iodine supply



Glinoer D et all. J Clin Endocrinol Metab 73:421, 1991
Struve C et all Thyroid 3:7, 1993

Parity as a thyroid size-determining factor in areas with moderate iodine deficiency

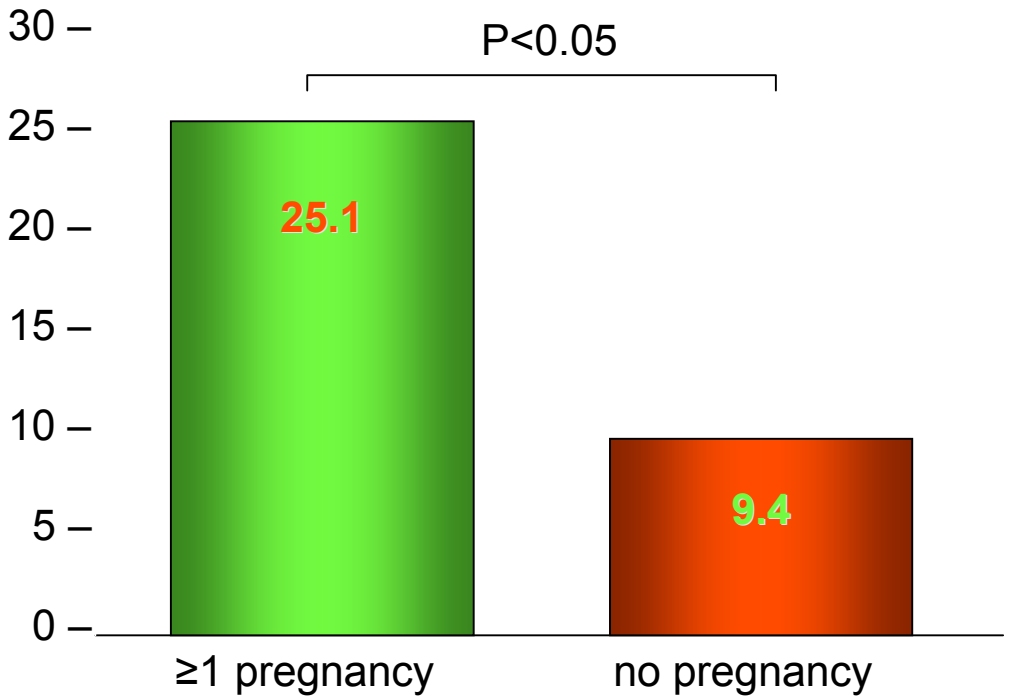




The mean thyroid volume increase during pregnancy is 18% at US evaluation

Rotondi M et al. JCEM, 2000, 85: 4534
Rasmussen NG et al. Am J Obstet Gynecol 1989; 160: 1216

Prevalence of thyroid nodules and pregnancy

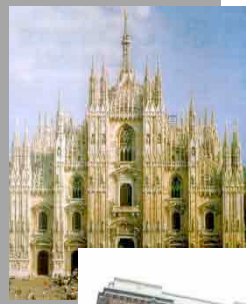


212 women in Kiel, a region with insufficient alimentary iodine supply

Struve CW et al. Thyroid, 1993; 3:7-9

Background

- Thyroid cancer during pregnancy causes considerable anxiety in both patient and physician due to uncertainty about the optimal timing of recommended treatments and concerns about maternal and neonatal morbidity
- Hormonal factors during pregnancy are supposed to accelerate the progression of thyroid cancer



Hod M et al. Obstet Gynecol Surv 1989; 44: 774-79
Choe W et al. Thyroid 1994; 4: 433-35

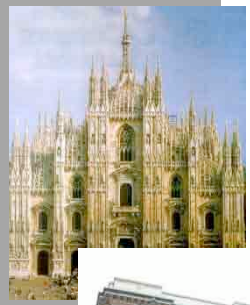
Differentiated thyroid cancer in pregnancy: epidemiology

- Thyroid cancer is the 2nd most common malignancy during pregnancy: **14** / 100.000 pregnancies.
- Papillary carcinoma is the most common hystological type during pregnancy.
- Up to **10%** of thyroid malignancies that occur during reproductive period are diagnosed during pregnancy or in the first year after delivery.

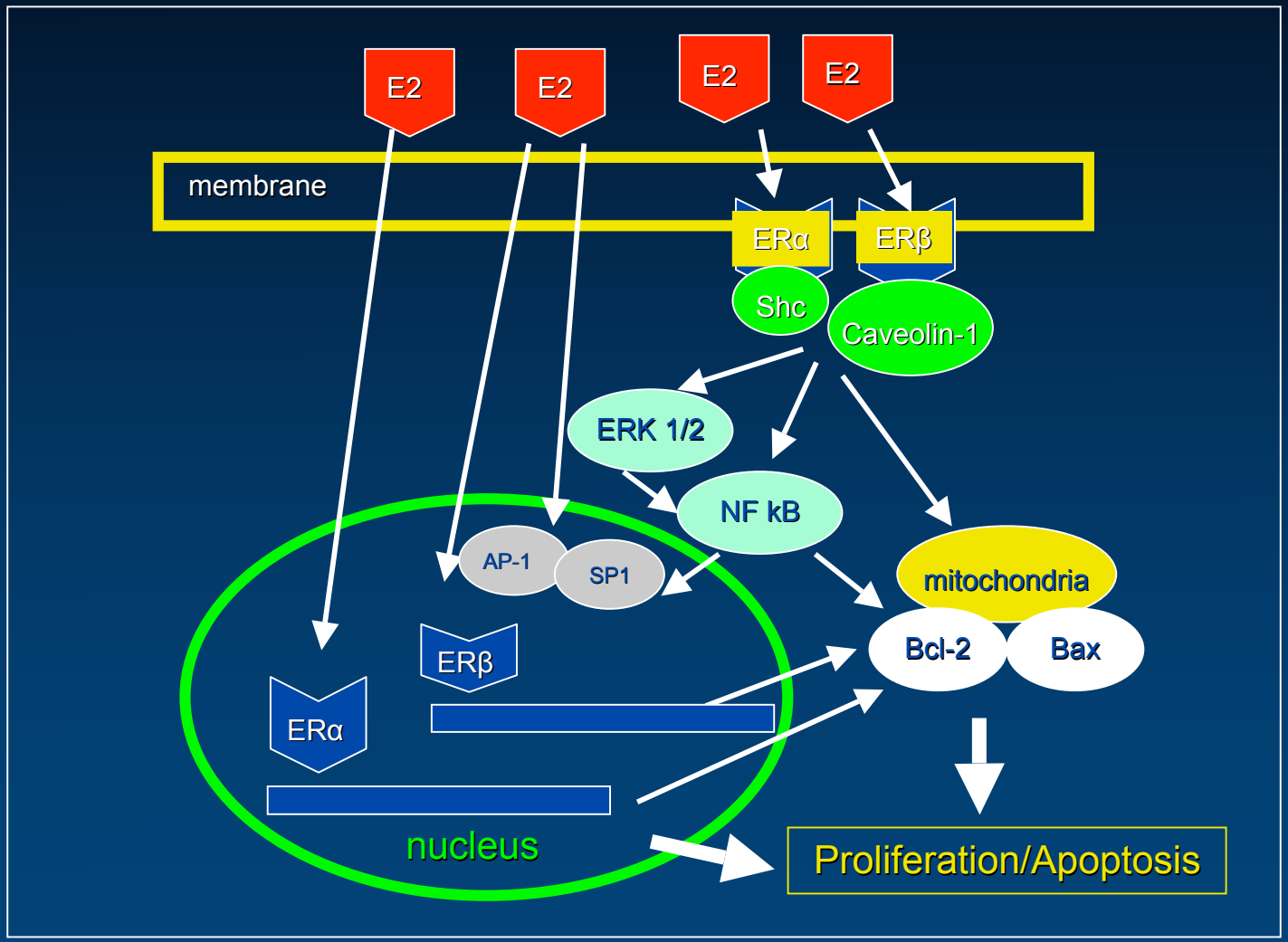
SEER cancer statistics review. National Cancer Institute 1975-2000; Smith LH. Am J Obstet Gynecol 2003; 189: 1128-35 ; Moosa M, Mazzaferri E, JCEM 1997, 82: 2862-6; Wémeau JL et al, Ann Endocrinol 2002, 63 (5): 438-442; Yasmeen S et al, Int J Gyn Obst 2005, 91: 15-20;

Items

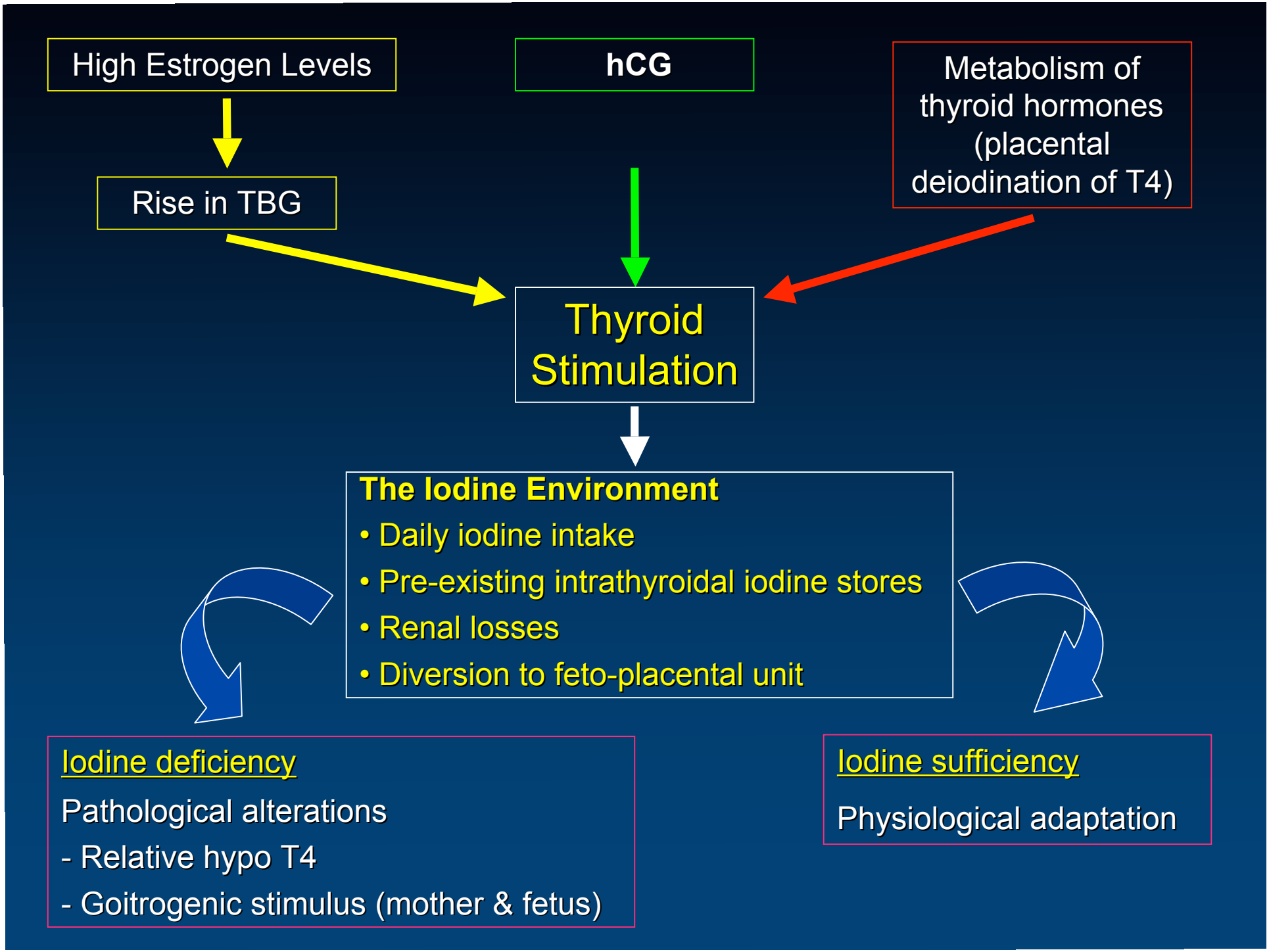
- Background
- **Thyroid Nodules Management:**
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- **Discussion**
- Differentiated Thyroid Cancer Management :
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- Discussion
- Conclusions



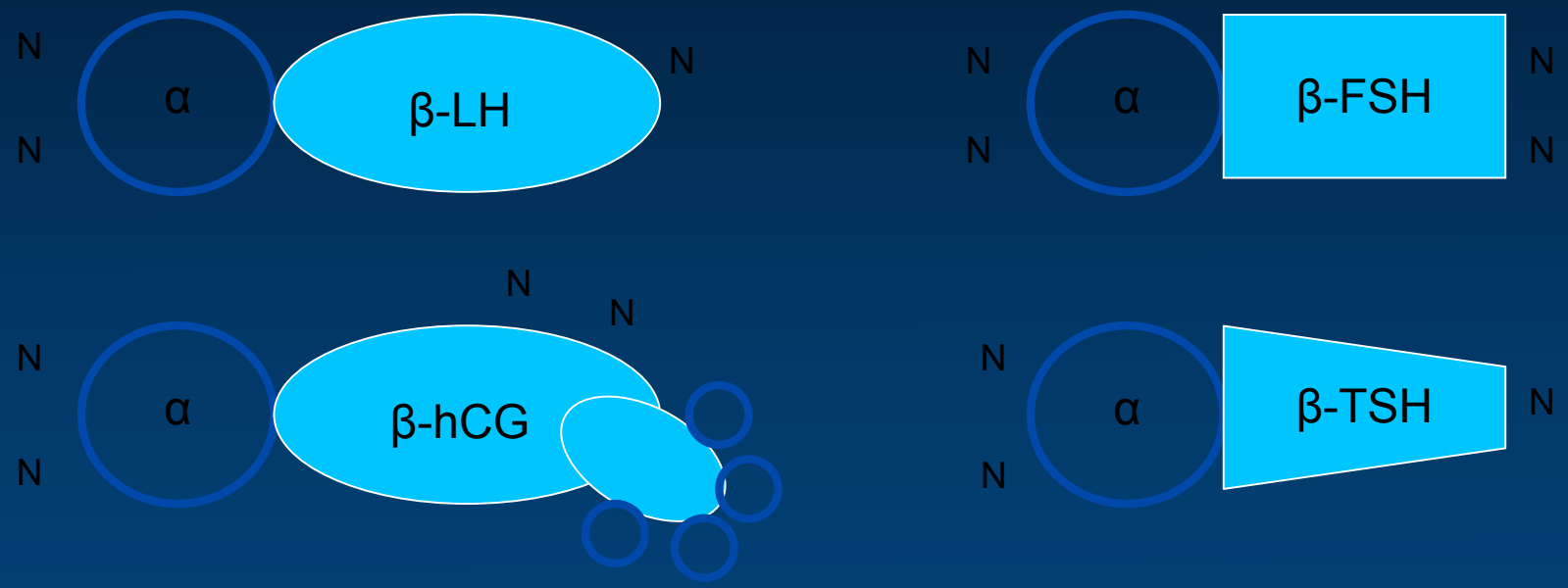
Effetti degli Estrogeni sulla Proliferazione dei Tireociti



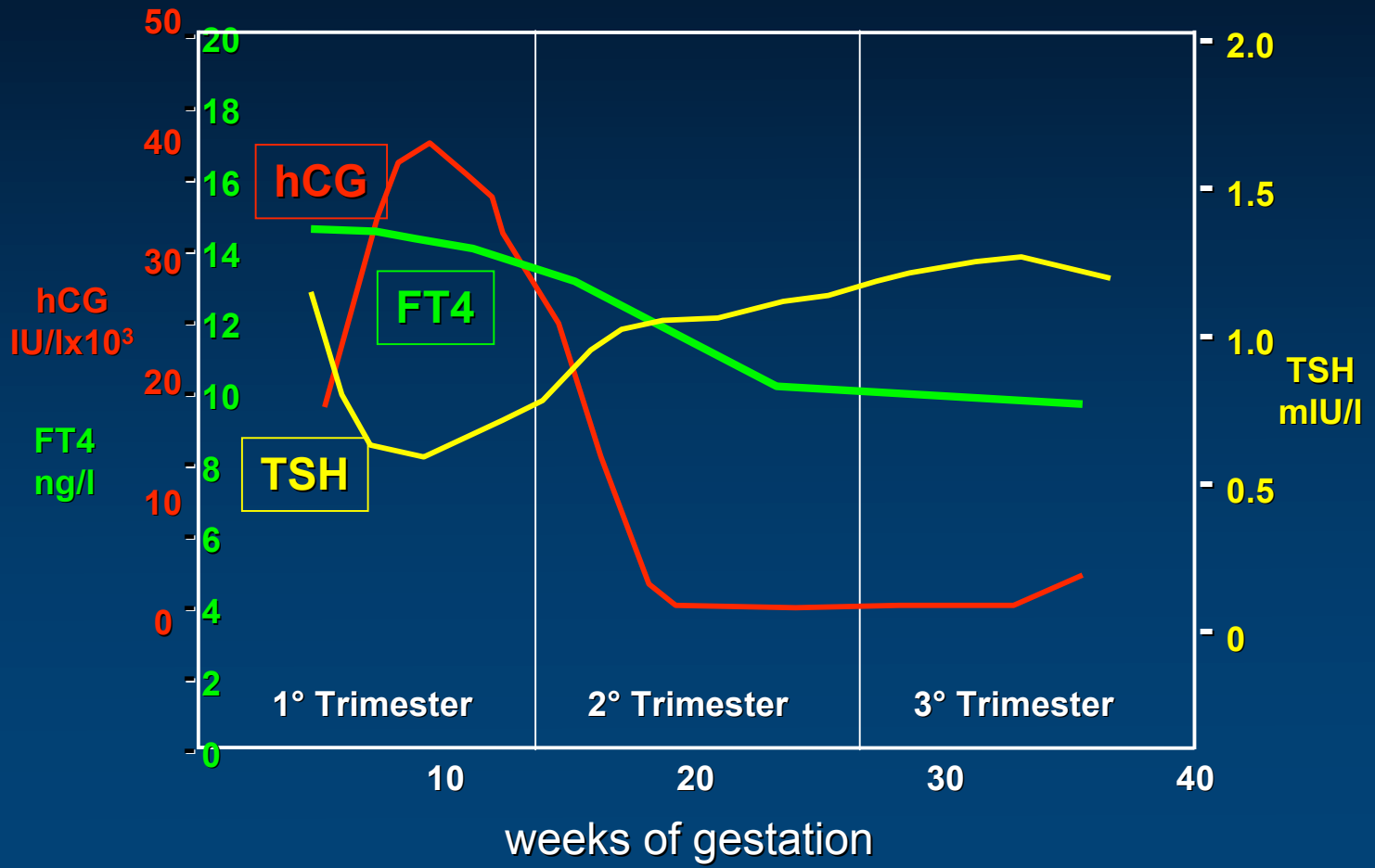
Chen GC. Curr Drugs Canc Targ 208; 8:367-77


High Estrogen Levels
hCG
Metabolism of thyroid hormones (placental deiodination of T4)
Rise in TBG
Thyroid Stimulation
The Iodine Environment
• Daily iodine intake
• Pre-existing intrathyroidal iodine stores
• Renal losses
• Diversion to feto-placental unit
Iodine deficiency
Pathological alterations
- Relative hypo T4
- Goitrogenic stimulus (mother & fetus)
Iodine sufficiency
Physiological adaptation

Omologie fra hCG e TSH

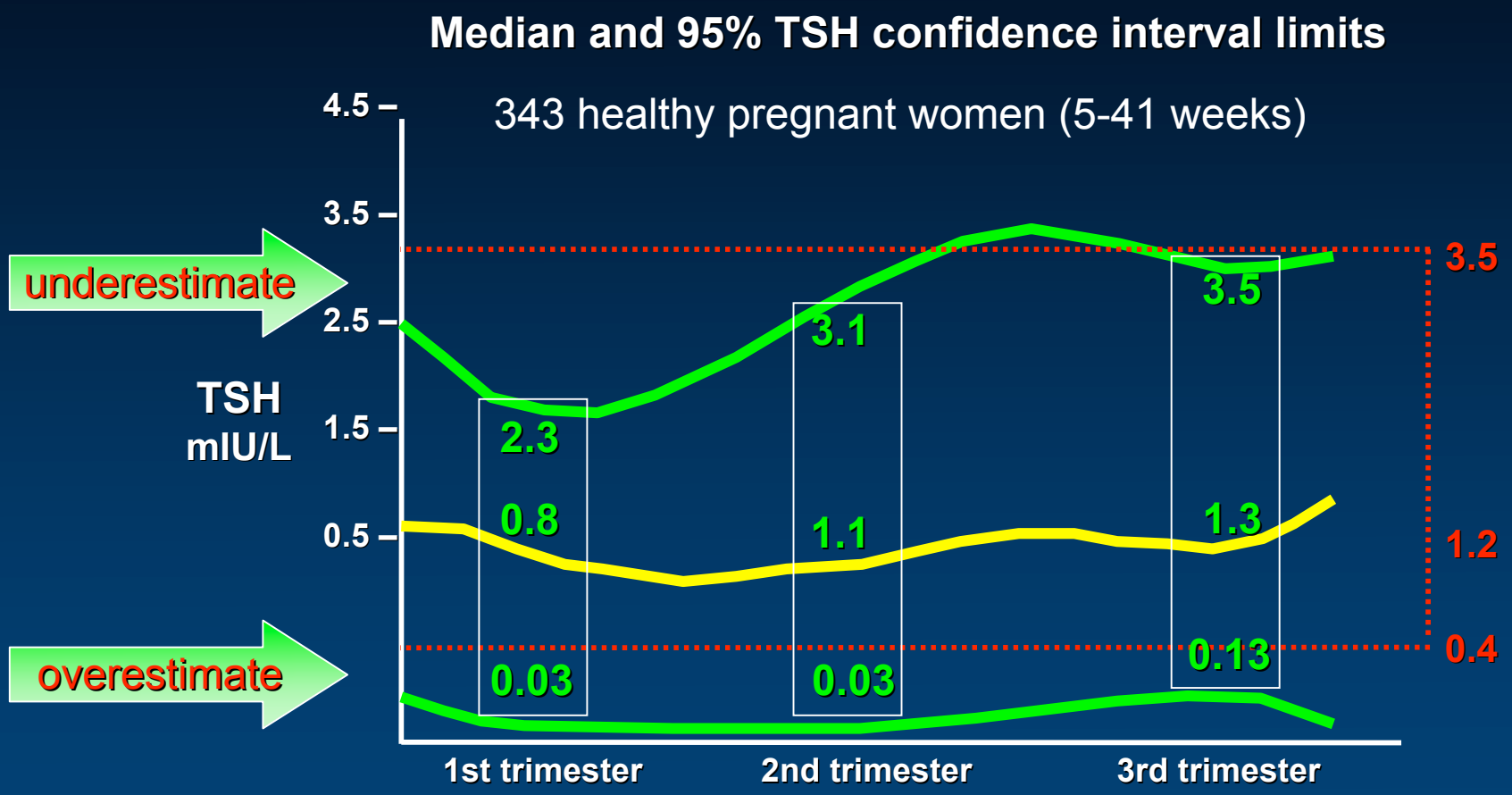


hCG, TSH e FT4: Variazioni in Gravidanza



Glinoer D et al. J Clin Endocrinol Metab 1990;71:276-87

Range di Riferimento Trimestre-Specifici in Gravidanza



Panesar NS. Ann Clin Biochem 2001; 38:329

Funzionalità Tiroidea in Gravidanza

- TSH
- FT4
- TPOAb

	I Trimestre	II Trimestre	IIITrimestre
2,5 centile	0,03	0,1	0,2
media	0,8	1,0-1,3	1,0-1,3
97,5 centile	2,5	3,0	3,0

TSH < 2.5th percentile: 2%

subclinical hyperthyroidism: 1.7%

overt hyperthyroidism: 0.3% (*Casey 2006)*

TSH < 0.03 mIU/l: 1.9%

subclinical hyperthyroidism: 1.2%

overt hyperthyroidism: 0.7% (*Vaidya 2007)*

Ipertiroidismo Subclinico ed Outcome Ostetrico

25,765 pregnant women

433 subclinical hyperthyroidism

Results

- Pregnancy outcomes: gestational hypertension was less frequent in subclinical hyperthyroid patients than in controls. Other pregnancy outcomes did not result significantly different
- Neonatal outcomes: did not result significantly different between subclinical hyper and controls

Casey BM. *Obstet Gynecol* 2006; 107:337-41

Radioiodine Treatment of Hyperthyroidism in a Pregnant Woman

Gertrud E.B. Berg, Ernst H. Nyström, Lars Jacobsson, Sture Lindberg, R. Göran Lindstedt, Sören Mattsson, C. Aimon Niklasson, A. Håkan Norén and Otto G.A. Westphal

- L'uso di radionuclidi sia a scopo diagnostico che terapeutico è controindicato in gravidanza

Berg GE. J Nucl Med 1998; 39:357-61

Valutazione Diagnostica del Nodulo Tiroideo in Gravidanza

- L'attenta valutazione dell'anamnesi della paziente, esame obiettivo, ed esame ecografico, rappresentano elementi necessari per valutare la necessità di eseguire FNA (Tan GH. 1995)
- Stratificare il rischio della paziente (familiarità per neoplasia tiroide, MEN 2, pregressa irradiazione) (Hegedus L. 2004)
- La presenza di almeno 2 caratteristiche di malignità identifica la maggior parte delle lesioni maligne (87-93% dei casi (Papini E. 2002)
- L'aumento di volume del nodulo tiroideo in gravidanza non sempre rappresenta caratteristica di malignità (Glinoer D.1991)

FNA in Gravidanza

- FNA è una procedura sicura, affidabile, e con un rischio molto basso di complicanze. Pertanto lo stato di gravidanza non rappresenta una controindicazione alla esecuzione di FNA
- (Belfiore A. 2001, Goellner JR 1987 , Atkinson BF C 1993, Solomon D 1993, Oertel YC 1996, Singer PA 1996)

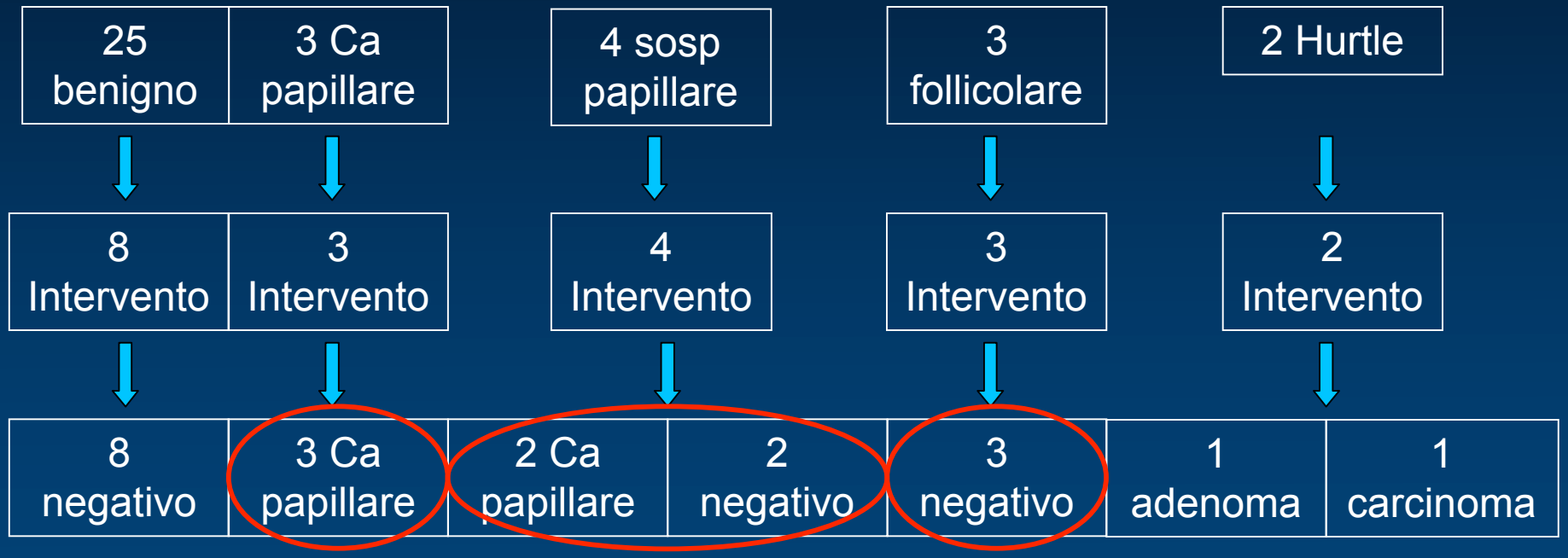
FNA in Gravidanza

- La fisiologica iperplasia tiroidea in gravidanza, complica l'interpretazione dell'esame citologico?

  L'esame istologico di 92 pazienti gravide ha evidenziato: "ampi follicoli con abbondante colloide e segni di ipertrofia cellulare"

Stoffer RP. Am J Obstet Gynecol 1957; 74:300-308

FNA in Gravidanza



Tan GH Arch Intern Med. 1996;156(20):2317-20

FNA di 57 noduli tiroidei in gravidanza e nel postpartum

- 38 (67%) benigno
- 12 (21%) Ca papillare
- 5 (9%) sospetto Ca papillare
- 2 (3%) follicolare

19

Citologico	Istologico
7 benigno	7 benigno
2 sosp Ca papillare	2 benigno
3 Ca papillare	3 Ca papillare
5 Ca pap/foll	2 benigno – 3 carcinoma
2 follicolare	1 benigno – 1 carcinoma

Marley EF. Diagn Cytopatol 1997; 16:122-5

Affidabilità dell'Esame Citologico in Gravidanza

- "We have not found any distinct cytologic features indicative of pregnancy or associated with pregnancy. We conclude that fine-needle aspirates of thyroid nodules from pregnant or postpartum patients should be evaluated by using established criteria. There is no cytologic evidence that these lesions differ. We urge pathologist not to be influenced by the anecdotal occurrence of "hyperplasia of pregnancy" (Marley EF. 1997)

Note: 1) Scarsità del campione (19 pazienti)

2) Disomogeneità nel timing di FNA

3) 12/19 (63%) maligno/sospetto con verifica istologica

Citologico	*Istologico*	*Maligni/Interventi (%)*
Benigno (15)	**Benigno (15)**	
Follicolare (5)	**Maligno (1)**	**13/24 (54.2%)**
Sospetto carcinoma (6)	**Maligno (2)**	
Carcinoma (11)	**Maligno (9)**	
Hurtle (2)	**Maligno (1)**	

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

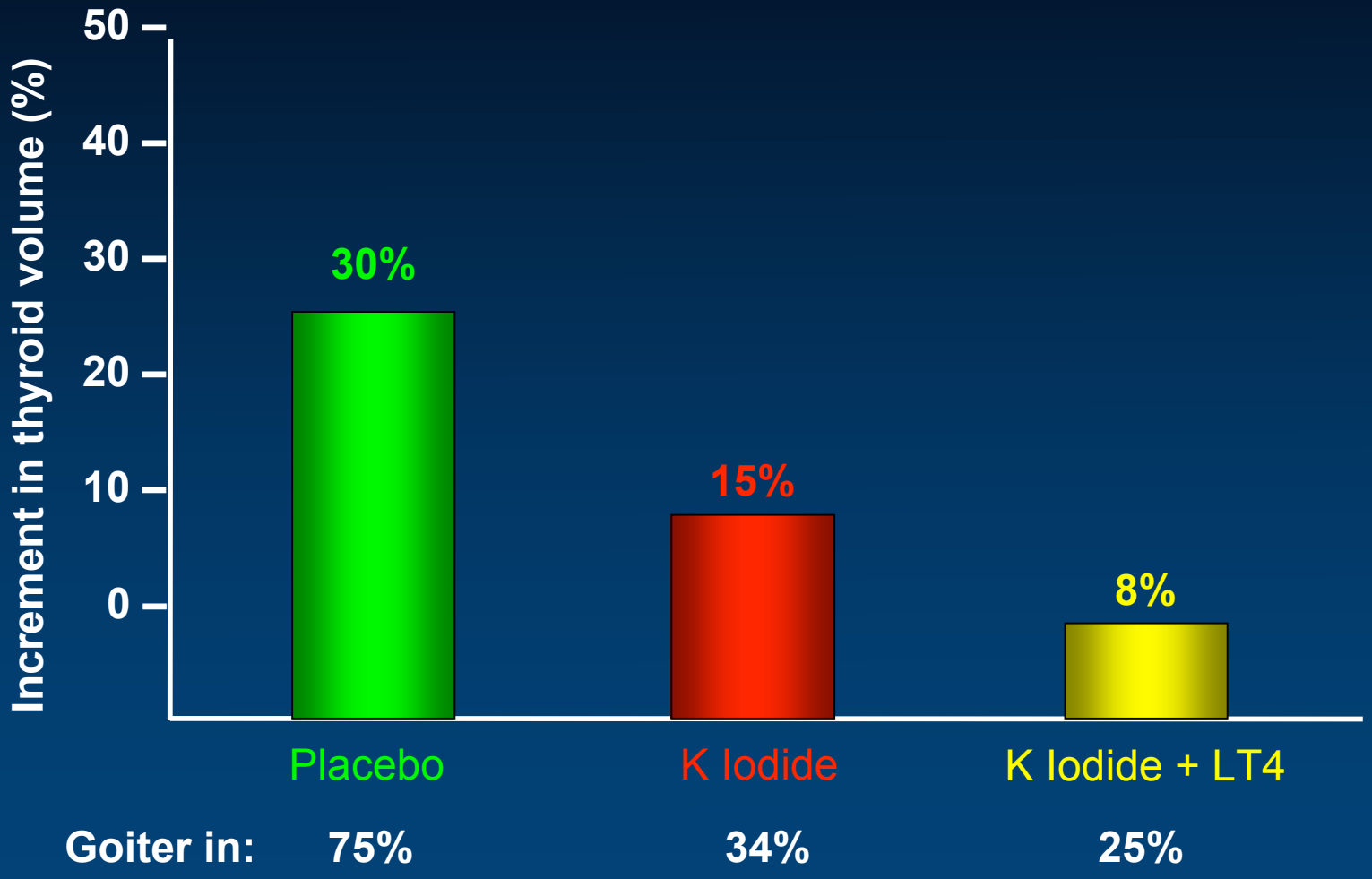
- "Although delay in the work-up of a nodule until after delivery causes no change in final prognosis as compared with surgical resection of a malignant lesion in the second trimester (Moosa M. 1997), knowing the diagnosis via FNA cytology is often helpful to the mother in planning the postpartum course, including decisions regarding breast-feeding and the potential need for adjunctive therapy with radiodiode after surgical removal of a cancer"

J Clin Endocrinol Metab 2007;92:S1-47

Terapia con LT4?

- Nessun trial ha valutato il trattamento con LT4 nei noduli tiroidei in gravidanza

Iodio, LT4 e Volume Tiroideo in Gravidanza

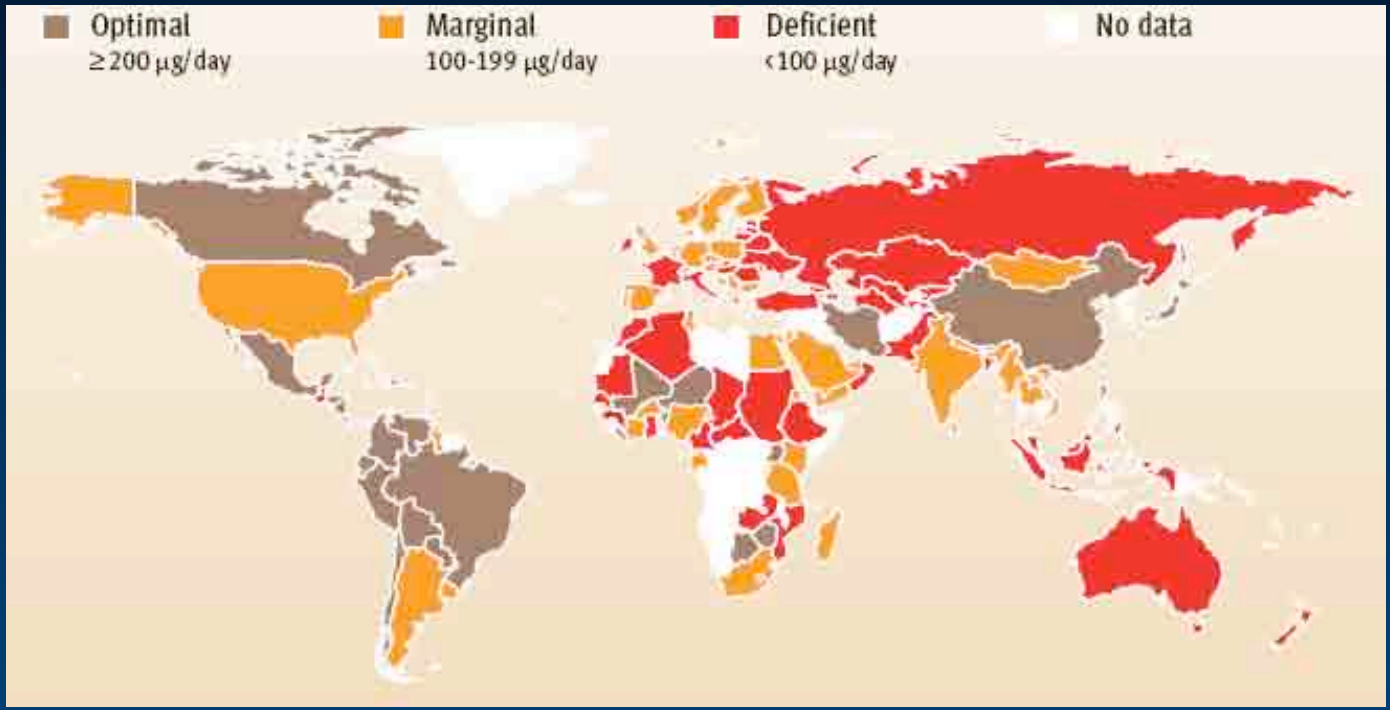


Glinoer D *et al.* 1995 *JCEM* 80:258

Terapia con LT4?

- Nessun trial ha valutato il trattamento con LT4 nei noduli tiroide in gravidanza
- Le evidenze disponibili non consentono di raccomandare nè a favore, nè contro la terapia con LT4

World Sources of Iodine



Utiger RD 2006 N Engl J Med

Deficit Iodico in Italia

- 10552 ragazzi dai 5 ai 13 anni (Campania).
- 32% <50 mcg/L
- 61% <100 mcg/L

Mazzarella C *et al.* 2009 Nutrition; 25-936-9

- 51 donne gravide I° Trimestre (Lazio)
- Mediana UIC: 74 mcg/L
- 92% <150 mcg/L

Marchioni E et al. 2008 Nutrition; 24:458-61

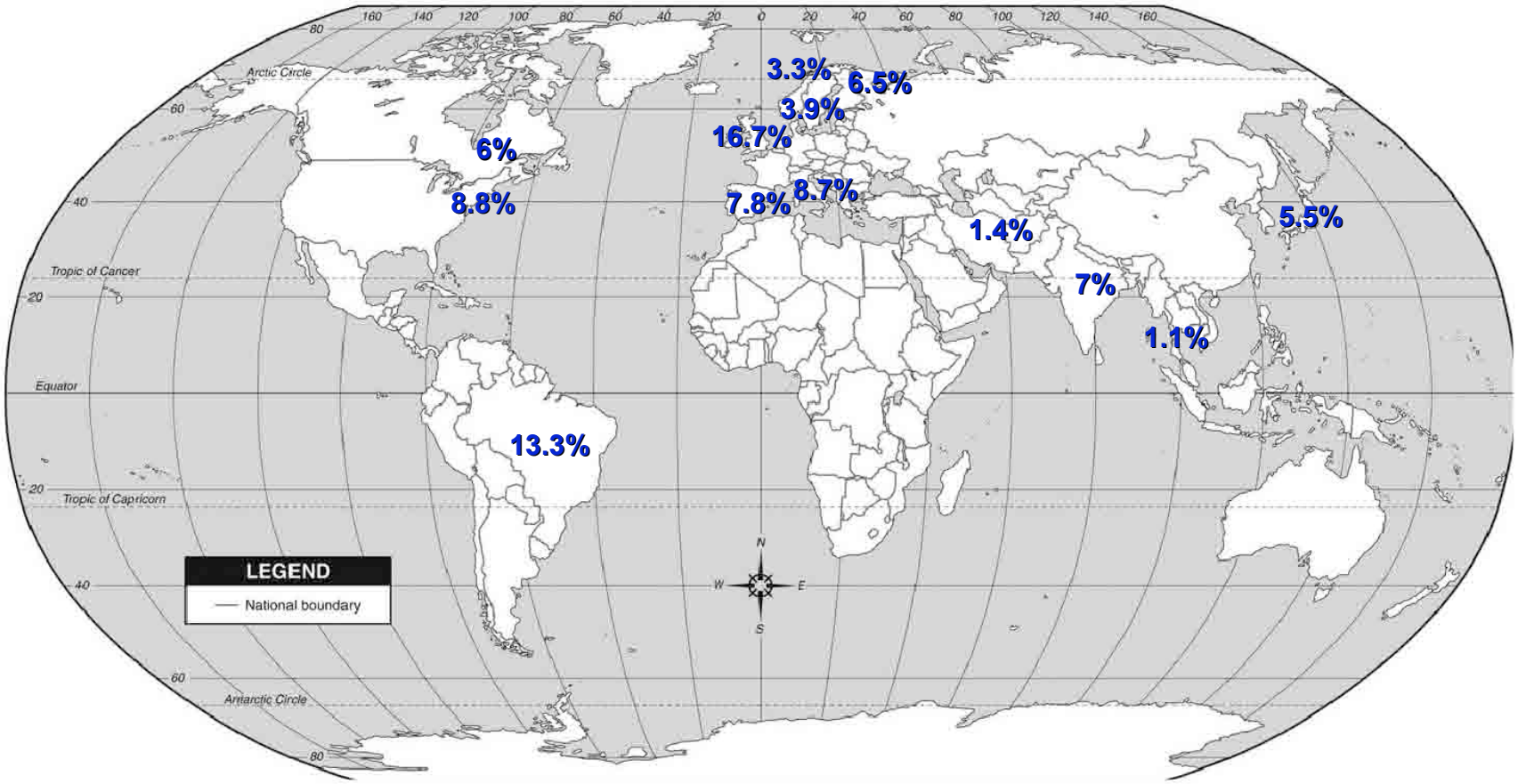
- 220 donne gravide I° Trimestre (Sicilia)
- Mediana UIC: 96 mcg/L

Moleti M et al. 2009 EJE 160:611-7

Terapia con LT4?

- Nessun trial ha valutato il trattamento con LT4 nei noduli tiroide in gravidanza
- Le evidenze disponibili non consentono di raccomandare nè a favore, nè contro la terapia con LT4
- Lo stato di gravidanza per se non rappresenta una controindicazione assoluta alla terapia semisoppressiva con LT4. Pertanto una paziente già in terapia, che inizi una gravidanza, non necessariamente deve interrompere la terapia stessa

Postpartum Thyroiditis: Prevalence



7.5-8%

Stagnaro-Green A. 2004

Nicholson WK 2006

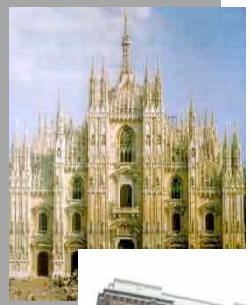
Terapia con LT4?

- Nessun trial ha valutato il trattamento con LT4 nei noduli tiroide in gravidanza
- Le evidenze disponibili non consentono di raccomandare nè a favore, nè contro la terapia con LT4
- Lo stato di gravidanza per se non rappresenta una controindicazione assoluta alla terapia semisoppressiva con LT4. Pertanto una paziente già in terapia, che inizi una gravidanza, non necessariamente deve interrompere la terapia stessa
- Circa 8% di tutte le gravide sviluppa tiroidite del post-partum, che talvolta si manifesta come tireotossicosi. Se la somministrazione di LT4 a scopo semisoppressivo, prosegue anche dopo il parto, è necessario considerare la possibilità di una tireotossicosi più severa

Thyroid Nodules.
Clinical Questions and Recommendations (1)

- **An US evaluation is advisable as a screening test in all pregnant women?**

  Screening of thyroid disease by ultrasonography (US) is not recommended in pregnant women. Test serum TSH and TPOAb and advise an increase in iodine intake (250 mcg/die) to avoid thyroid stimulation and a consequent volume enlargement



- **How should be managed a pregnant women found to have a thyroid nodule?**

  A pregnant women found to have a thyroid nodule should be reassured and evaluated in the same way as if she were not pregnant. Only thyroid radionuclide scanning is contraindicated.

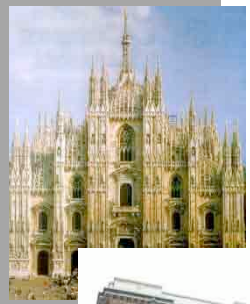
Thyroid Nodules
Clinical Questions and Recommendations (2)

- **When should be performed FNA assessment of a thyroid nodule in pregnancy?**

  Fine needle aspiration biopsy (FNA) under US guidance should be performed for thyroid nodules with suspicious clinical or US findings.

- **How should be managed thyroid nodules benign at FNA assessment?**

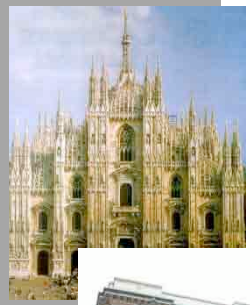
  Women with a benign nodule are followed-up without treatment, provided that thyroid function is within normal limits. Those whose nodules show a progressive growth or US features of malignancy should have a repeat FNA biopsy.



Thyroid Nodules
Clinical Questions and Recommendations (3)

- **What is the role of LT4 therapy for benign nodules and nodular goiters?**

  The available evidence does not allow to recommend for L-thyroxine therapy for benign nodules and goiters in pregnant women. However, in areas of mild to moderate iodine deficiency, due to the goitrogenic effect of pregnancy, a near-suppressive L-thyroxine treatment may be suggested



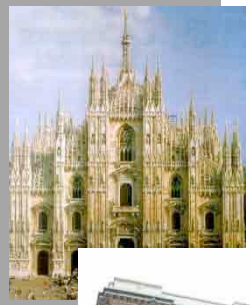
- **How should be managed nodular goiters with benign cytology that are cause of local pressure symptoms?**

  In nodular goiters with benign cytology and mild pressure symptoms surgery must be deferred until after postpartum period.

Thyroid Nodules
Clinical Questions and Recommendations (4)

- **How should be managed thyroid nodules with a "follicular lesion" at FNA?**

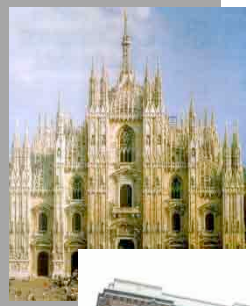
Women with a "follicular lesion" at FNA (Class 3*) should have a close clinical and US follow-up. In the absence of a rapid growth, worrisome cytological features or suspicious US findings, surgery may be deferred until after delivery.



* Thyroid Nodule SIAPEC-IAP Consensus 2007
AACE/AME/ETA Guidelines 2009

Items

- Background
- Thyroid Nodules Management:
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- Discussion
- **Differentiated Thyroid Cancer Management :**
  - **diagnosis before pregnancy**
  - **diagnosis in pregnancy**
  - **recommendations**
- **Discussion**
- Conclusions



Thyroid cancer in pregnancy: epidemiology

- Thyroid CA is the most common endocrine malignancy (from 3.6/100.000/ in 1973 to 8.7/100.000 in 2003)
- Thyroid CA is the 2nd most common malignancy during pregnancy: 14.4 / 100.000/ live birth
  - Prenatal = 3.3 / 100.000/ live birth
  - At delivery = 0.3 / 100.000/ live birth
  - Postnatal (within 1 year) = 10.8 / 100.000/ live birth
- Papillary CA is the most common hystotype in pregnancy
- About 10% of thyroid CA that occur during reproductive period are diagnosed during pregnancy or in the first year after delivery

Moosa & Mazzaferri JCEM 1997, Smith et al. 2003 ; Yasmeen et al Int J Gyn Obst 2005

Effect of pregnancy on preexistent DTC

Study	No of patients	Results
Rosvoll 1965	60 (38 disease free)	Disease free women (2-15 yr) had no recurrence during or after pregnancy. No progression in the 22 patients with disease
Hill 1996	70 pregnant and 109 non pregnant	Similar recurrence and survival rates between 70 women with pregnancy after DTC diagnosis and 109 women with DTC and no pregnancy
Pomorski 2000	23 disease - free	None relapsed before or during pregnancy
Rosario 2007	64 with remission criteria	No evidence of recurrent disease, as assessed by clinical exam, US of the neck and Tg measurement
Loh 2009	18	No evidence of recurrent disease in women who underwent pregnancy after being treated with total Tx with or without RI
Leboeuf 2007	36	Pregnancy is unlikely to cause recurrence in the early PP period in the absence of residual disease but can occasionally be associated with progression of known metastatic lesions

The effect of a subsequent pregnancy on preexistent DTC: Conclusions

- Pregnancy is a mild stimulus to thyroid cancer growth, as evidenced by minor disease progression in those patients with known structural disease before pregnancy
- This mild stimulation does not result in clinically evident recurrent disease in the immediate post-partum period in DTC patients carefully staged before pregnancy with negative neck US and undetectable or low level serum Tg
- There are no data that a subsequent pregnancy increases the risk for thyroid cancer recurrence

A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors

Clinical Endocrinology 2008

Anna M. Sawka*,†, Deepak C. Lakra‡, Jane Lea§, Bandar Alshehri¶, Richard W. Tsang**,††, James D. Brierley**,††, Sharon Straus‡‡,§§, Lehana Thabane¶¶,***, Amiram Gafni¶¶,†††, Shereen Ezzat†,‡‡‡,§§§,¶¶¶, Susan R. George*,† and David P. Goldstein****

- Systematic review of the literature
- 16 observational studies reporting data from:
  - 3023 women
  - 591 pregnancies
  - 496 live births
- Age at first RAI treatment: 8 - 50 years
- Cumulative activities of RAI administered: 30 to 1099 mCi

Apart from a transient absence of menstrual periods, which occurred in 8-27% women within the first year after RI administration, treatment with RI for DTC was generally not associated with a significantly increased risk of long term infertility, miscarriage, stillbirths, neonatal mortality and congenital malformations

Outcome of pregnancy and radioiodine exposure*

*induced abortion is excluded

Factor	N. of pregnancy	Miscarriage	Stillbirth
Before any treatment	1596	179 (11%)	27 (2%)
After surgery for DTC	272	53 (19%)	4 (1%)
Cumulative 131-I activity before conception			
0 MBq	66	13 (20%)	2 (4%)
< 370 MBq	97	19 (20%)	2 (3%)
370-3700 MBq	30	3 (10%)	0
> 3700 MBq	79	18 (23%)	0
131-I activity during the year before conception			
0 MBq	202	36 (18%)	4 (2%)
< 370 MBq	60	13 (22%)	0
> 370 MBq	10	4 (40%)	0

Schlumberger M, et al; J Nucl Med 1996; 37: 606-612

Therapeutic Administration of ^{131}I for Differentiated Thyroid Cancer: Radiation Dose to Ovaries and Outcome of Pregnancies

J Nucl Med 2008

Jérôme-Philippe Garsi[1–3], Martin Schlumberger[2], Carole Rubino[1–3], Marcel Ricard[2], Martine Labbé[1–3], Claudia Ceccarelli[4], Claire Schvartz[5], Michel Henri-Amar[6], Stéphane Bardet[6], and Florent de Vathaire[1–3]

- 2673 pregnancies, 483 of which occurred after RI treatment
- Data from 309 lived births to exposed women

RI treatment was not found to increase the miscarriage rate even in women treated during the year before conception and not even in women who had received high cumulative activities (> 3700 MBq)

The incidence of stillbirths, pre-term births, low-birth weight, congenital malformations, death during the first year of life, thyroid and not thyroid cancers in the offspring, were not significantly different before and after RI therapy

Medical therapy of DTC in pregnancy

Recurrence and survival among pregnant women with DTC do not significantly differ from that among age-matched non pregnant women with DTC

The appropriate level of TSH suppression to be achieved during pregnancy in patients previously treated for DTC depends both on pre-conception tumor risk and on evidence of residual or recurrent disease

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and DTC

RECOMMENDATION 49

a) In patients with persistent disease, the serum TSH should be maintained below 0.1 mU/L indefinitely in the absence of specific contraindications.
Recommendation rating: B

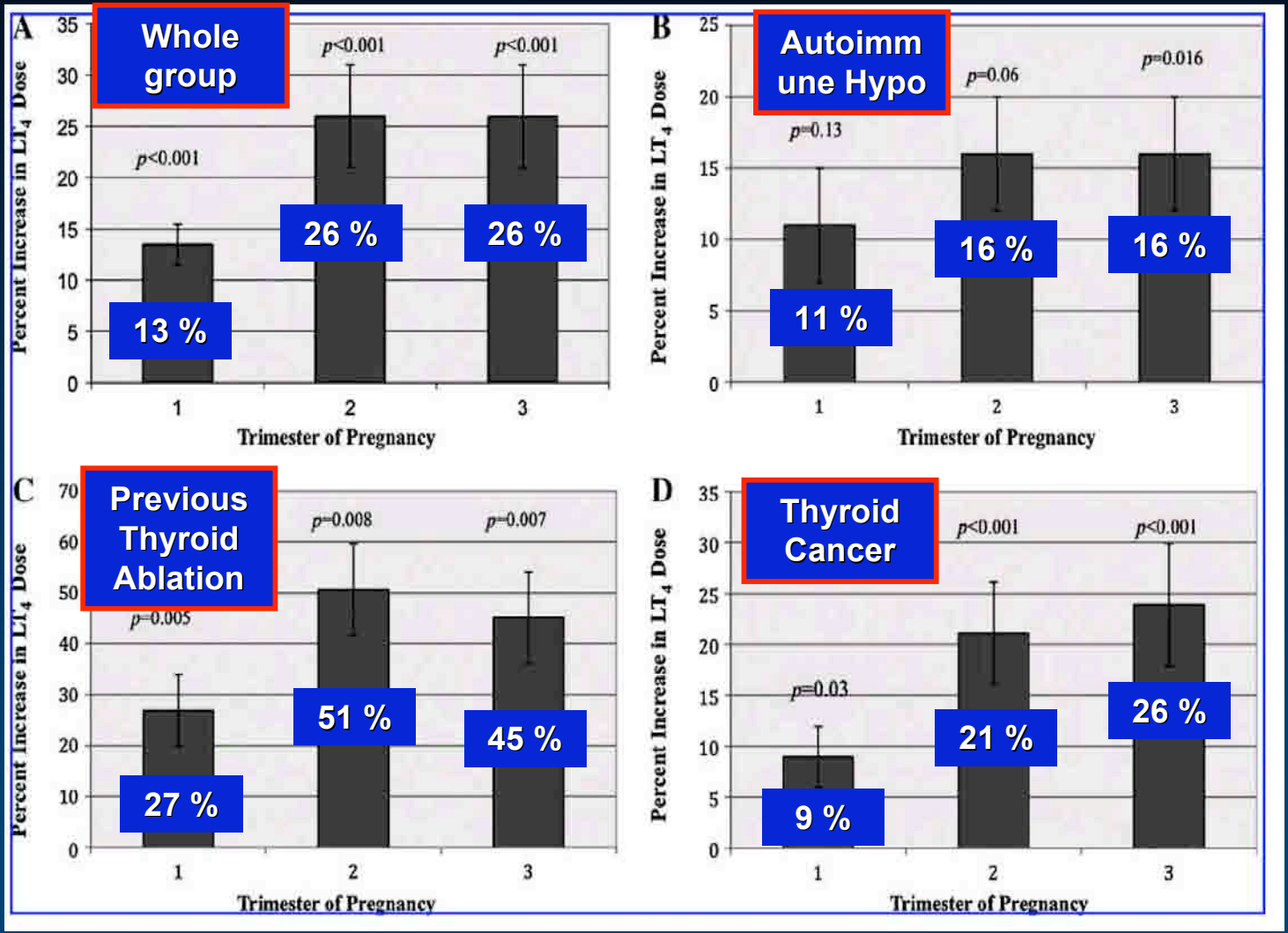
(b) In patients who are clinically and biochemically free of disease but who presented with high risk disease, consideration should be given to maintaining TSH suppressive therapy to achieve serum TSH levels of 0.1–0.5 mU/L for 5–10 years.
Recommendation rating: C

(c) In patients free of disease, especially those at low risk for recurrence, the serum TSH may be kept within the low normal range (0.3–2 mU/L).
Recommendation rating: B

(d) In patients who have not undergone remnant ablation who are clinically free of disease and have undetectable suppressed serum Tg and normal neck US, the serum TSH may be allowed to rise to the low normal range (0.3–2 mU/L). Recommendation rating: C

Cooper et al, Thyroid 2009

The Magnitude of Increased L-T4 Requirements in Hypothyroid Pregnant Women Depends upon the Etiology of Hypothyroidism



Loh et al. Thyroid 2009

20% of DTC women required LT4 dose adjustments in the first trimester, 65% in the second trimester and 20% in the third trimester

Medical Therapy of DTC in pregnancy Recommendations

- Immediately check thyroid function tests as soon as pregnancy is confirmed and monitor thereafter in order to perform individual adjustments of the LT4 dose throughout pregnancy
- Check serum TSH and free thyroid hormones levels at least at each trimester
- The adequacy of LT4 treatment should be checked four weeks after any LT4 dose change
- Probably, DTC patients with evidence of persistent disease would require a more aggressive monitoring during pregnancy, by checking thyroid status monthly

Prognosis of thyroid cancer discovered during pregnancy

Study	No of patients / controls	Results
Herzon 1994	22 / 464	No difference in the 12-years survival rate
Moosa, 1997	61 / 528	DTC in pregnancy is similar for recurrence and survival to that occurring in non-pregnant women of similar age
Vini, 1999	9	Good outcome for DTC in pregnant women
Monroy-Lozano, 2001	6 / 24	No statistical differences in prognostic score, recurrence, mortality (follow-up 20-25 yrs), no local recurrence. The greater prevalence of cervical nodes metastasis in pap CA diagnosed during pregnancy does not alter the final prognosis
Jasmeen, 2005	129 / 466	Women with DTC in pregnancy and age-matched non-pregnant DTC controls had NS difference in recurrence and survival rates
Nam, 2005	15	No local recurrence and no distant metastasis
Vannucchi 2009	15 / 61	Pregnancy has a negative impact on the outcome of DTC both in terms of persistence or relapse disease. The presence of ERα in the majority of tumors diagnosed during pregnancy indicates that the poorer outcome could be estrogen-related

Pregnancy and the outcome of DTC

Vannucchi et al, EJE 2009

	Group 1 n= 47 (%)	Group 2 n= 15 (%)*	Group 3 n= 61 (%)	P value
Age at diagnosis (mean ±SD)	36.1±5.3	32.3±6.4	34.1±6.2	0.08
Months of follow-up (mean±SD)	68.2±63.9	60.1±52.1	64.7±43.5	0.92
pTNM				
T1	18/47 (38.3)	5/15 (33.3)	20/61 (32.8)	0.97
T2	9/47 (19.1)	2/15 (13.3)	12/61 (19.7)	
T3	19/47 (40.4)	7/15 (46.6)	27/61 (44.3)	
T4	1/47 (2.1)	0/15 (0)	2/61 (3.3)	
NX	15/47 (31.9)	3/15 (20)	18/61 (29.5)	0.44
N0	12/47 (25.5)	2/15 (13.3)	18/61 (29.5)	
N1	20/47 (42.5)	10/15 (66.6)	25/61 (40.9)	
Papillary histotype**	46/47 (97.8)	12/15 (80)	60/61 (98.3)	**<0.0001[a]**
Radioiodine ablation	38/47 (80.8)	15/15 (100)	53/61 (86.9)	0.17
^{131}I MBq (mean±SD)	3826±2053	5602±5975	4912±3873	0.31
ERα tumor expression	5/16 (31)	7/8 (87.5)	0/14	**0.01[b]**
Persistence	2/47 (4.2)	9/15 (60)	8/61 (13.1)	**<0.0001[c]**

DTC diagnosed during pregnancy was associated with a poorer prognosis compared to tumors not developed in pregnancy (P<0.0001).

ERα expression significantly differed among tumors of the three groups

Outcome of pregnant women with thyroid cancer according to the time of surgery

Study	tx in pregnancy vs. post- partum (PP)	Results
Doherty 1995	4 vs. 3	No recurrence in PP tx
Moosa, 1997	14 vs. 47	No difference in local recurrence or distant metastasis
Nam, 2005	6 vs. 8	No difference for local recurrence or distal metastasis

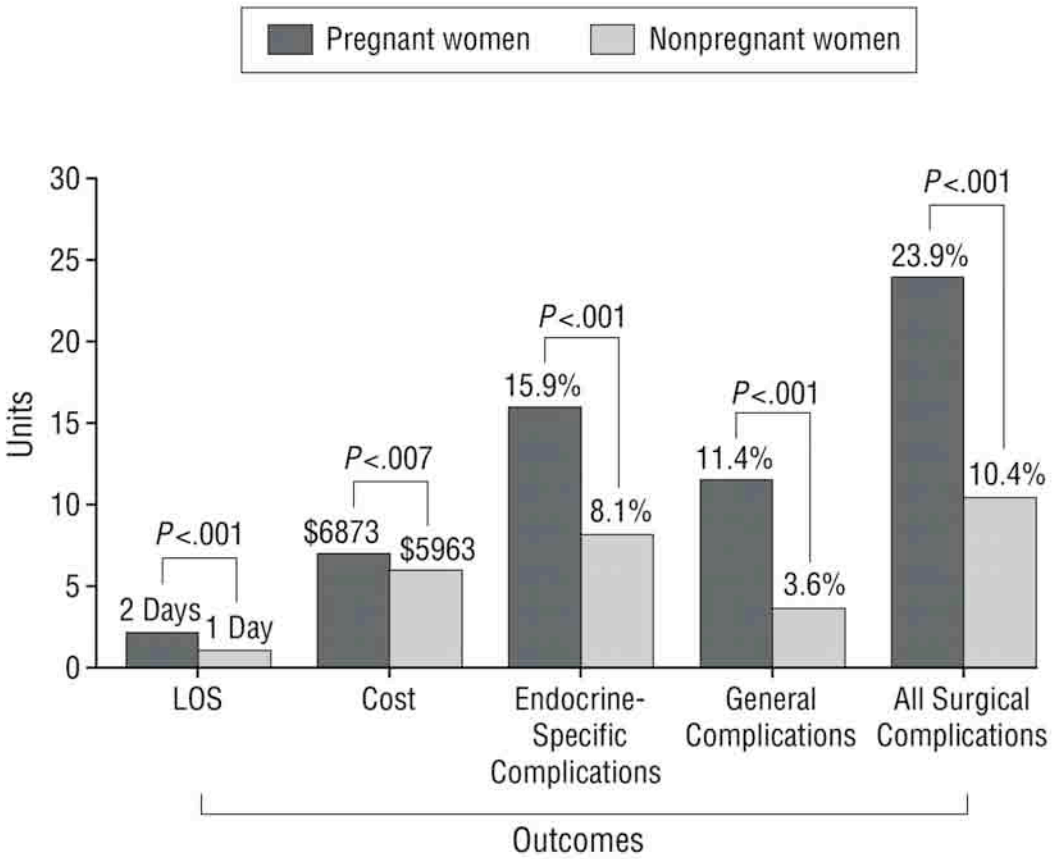
Side effects of surgery during pregnancy

Study	% patients operated during 2nd trimester	Side effects: mother	Side effects: fetus
Cunningham, 1970	-	-	3 / 5
Rosen, 1986	8	0 / 2	0 / 2
Herzon 1994	27	-	0 / 6
Doherty, 1995	36	0 / 4	0 / 4
Tan, 1996	33	0 / 4	0 / 4
Moosa, 1997	20	-	-
Vini 1999	11	0 / 1	0 / 1
Nam 2005	40	0 / 6	0 / 6
Jasmeen, 2005	78	0 / 96	0 / 96
Chong, 2007	-	0 / 2	0 / 2
Total		0 / 115	3 / 126

Outcomes Following Thyroid and Parathyroid Surgery in Pregnant Women

SreyRam Kuy, MD; Sanziana A. Roman, MD; Rani Desai, PhD; Julie Ann Sosa, MA, MD

Arch Surg. 2009;144(5):399-406



- The fetal and maternal complication rates were 5.5% and 4.5%, respectively.
- On multivariate regression analysis, pregnancy was an independent predictor of:
  - higher combined surgicalcomplications (OR, 2; P<.001)
  - longer adjusted length of stay (0.3 d. longer; P<.001)
  - higher adjusted hospital costs ($300; P<.001)
- Other independent predic tors of outcome were surgeon volume, patient race or eth-nicity, and insurance status.

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and DTC

RECOMMENDATION 20

(a) A nodule with cytology indicating PTC discovered early in pregnancy should be monitored sonographically and if it grows substantially (as defined above) by 24 weeks gestation, surgery should be performed at that point.
However, if it remains stable by midgestation or if it is diagnosed in the second half of pregnancy, surgery may be performed after delivery. In patients with more advanced disease, surgery in the second trimester is reasonable.

Recommendation rating: C

(b) In pregnant women with FNA that is suspicious for or diagnostic of PTC, consideration could be given to administration of LT4 therapy to keep the TSH in the range of 0.1–1mU/L.

Recommendation rating: C

Cooper et al, Thyroid 2009

The post-surgical medical treatment in pregnant women submitted to total thyroidectomy (tx) for DTC

1) Avoid maternal hypothyroidism

Maternal hypothyroidism, even subclinical, has serious adverse effects both on the fetus and on the outcome of gestation

LT4 treatment should be initiated immediately after total thyroidectomy
- dose raging from 100 mcg to 150 mcg thyroxine per day
- titrate the dose according to body weight (bw)

In non-pregnant women, the full replacement LT4 dose is 1.7–2.0 mcg/kg bw per day. During pregnancy, because of the increased requirements, the full replacement LT4 dose should be increased to **2.0 –2.4 mcg/kg bw per day**

Abalovich et al, JCEM 2007

2) Keep maternal serum TSH low

Being the second goal of LT4 treatment the **suppression** of serum TSH, the appropriate dose should be probably **closer to 2.4** than to 2.0 mcg/kg bw per day. Suppression of TSH to ≤ 0.1 mU/l is indicated during pregnancy while waiting for RI ablation of thyroid remnants, which must be postponed to the postpartum period.

3) correct post-surgical hypocalcemia , if present

during pregnancy → Increased calcitriol levels
Enhanced intestinal calcium absorption

Hypo-parathyroid pregnant women need a higher dose of calcitriol than the non-pregnant ones → Strict monitoring of serum calcium (ionized calcium) is mandatory

- Undertreatment: maternal hypocalcemia increases the risk of premature labor and of neonatal secondary hyperparathyroidism, skeletal demineralization, subperiosteal bone resorption, and osteitis fibrosa cistica.
- Overtreatment: maternal hypercalcemia and neonatal hypoparathyroidism

- **The use of calcium supplementation with calcitriol is recommended, along with monitoring of symptoms of hypocalcemia and of serum ionized calcium levels to titrate the calcitriol dose**
- **The requirements in calcitriol vary during the second half of pregnancy**
- **The use of active forms of vitamin D is strongly recommended during pregnancy (shorter half-life and lower risk of toxicity)**

Kovacs et al, Endoc Rev 1997, Landing et al, 1970, Friedman et al, 1969

^{131}I and BREAST-FEEDING WOMEN

RECOMMENDATION 74

a) Radioactive iodine should not be given to nursing women. Depending on the clinical situation, RAI therapy could be deferred until a time when lactating women have stopped breast-feeding for at least 6–8 weeks.

Recommendation rating: B

(b) Dopaminergic agents might be useful in decreasing breast exposure in recently lactating women, although caution should be exercised given the risk of serious side effects associated with their routine use to suppress postpartum lactation.

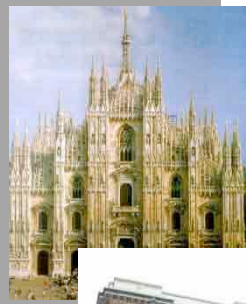
Recommendation rating: C

Cooper et al, Thyroid 2009

DTC in pregnancy. Clinical Questions and Recommendations (1)

- **What is the standard treatment for pregnant women diagnosed to have a DTC?**

  The standard treatment of differentiated thyroid cancer (DTC) in pregnancy is similar to that of nonpregnant women and involves total thyroidectomy followed, in patients at risk, by radioiodine ablation (RAI) of residual tissue and/or neoplasia



- **Pregnancy should be interrupted after diagnosis of DTC?**

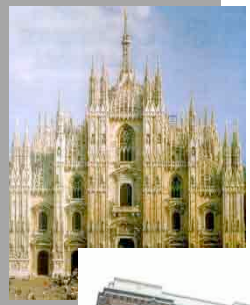
  If DTC is discovered in the 1st or the early 2nd trimester, pregnancy should never be interrupted and, in selected cases, surgery can be offered in the 2nd trimester.

DTC in pregnancy. Clinical Questions and Recommendations (2)

- **When should be performed surgery in a pregnant woman after the diagnosis of DTC?**

  If DTC is discovered in the late 2nd or 3rd trimester, surgery should be deferred to the post-partum period

  Women with DTC and no evidence of aggressive or advanced disease who elect to wait for surgery until post-partum period may be reassured that most DTC are slow growing and surgery soon after delivery is unlikely to change prognosis

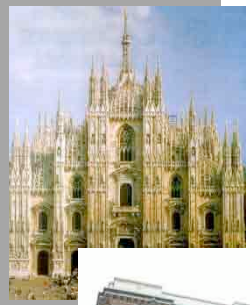


DTC in pregnancy. Clinical Questions and Recommendations (3)

- **When RAI Therapy should be performed?**

After surgery, RAI therapy should not be given to women with DTC who are still breast-feeding. Breast feeding should be stopped by at least 6-8 weeks before RAI. Dopaminergic agents may be useful

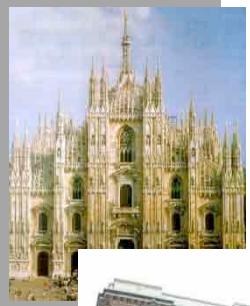
RAI treatment may be deferred until 12 months after surgery, unless in presence of aggressive or advanced disease.



DTC in pregnancy. Clinical Questions and Recommendations (4)

- **How long should pregnancy be avoided after a RAI treatment?**

A further pregnancy should be avoided for 6 months in women who receive therapeutic RAI doses to ensure stability of thyroid function, confirm remission of thyroid cancer and reduce the risk of a possible miscarriage.

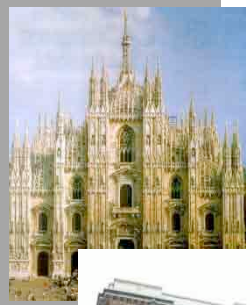


DTC in pregnancy. Clinical Questions and Recommendations (5)

- **How should levothyroxine therapy be tailored in a woman with a previously treated DTC who becomes pregnant?**

In pregnant women with a previously treated DTC, it is appropriate to increase the dose of thyroid hormone both to avoid maternal hypothyroidism and to maintain serum TSH at the same level of suppression recommended in the pre-conception period

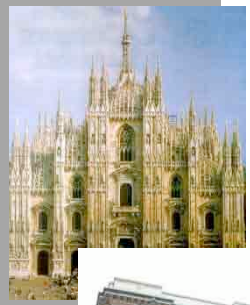
TSH suppression (TSH < 0.1 mU/l) is indicated in patients with biochemical and/or imaging evidence of disease



DTC in pregnancy. Clinical Questions and Recommendations (6)

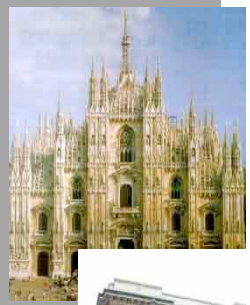
- **How should be tailored the treatment of a postsurgical hypoparathyroidism in a pregnant woman?**

Pregnant women with postsurgical hypo-parathyroidism need an increase of the dose of calcitriol and a close monitoring of serum calcium level.



Items

- Background
- Thyroid Nodules Management:
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- Discussion
- Differentiated Thyroid Cancer Management :
  - diagnosis before pregnancy
  - diagnosis in pregnancy
  - recommendations
- Discussion
- **Conclusions**



Grazie per l'attenzione