


HIPERTIROID DALAM KEHAMILAN

MASITA FUJIKO

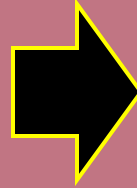
**Divisi Fetomaternal, Departemen Obgin FK UNHAS/
RS Dr.Wahidin Sudirohusodo
Makassar**



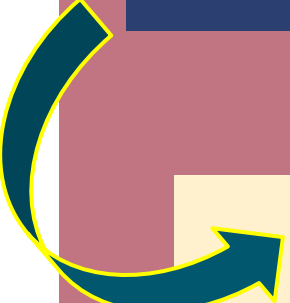
- Hipertiroid adalah kondisi klinik dan biokimiawi yang menunjukkan meningkatnya kadar hormon Tiroid
- Hiperaktivitas kelenjar tiroid
- Ditemukan 0,1 -0,4% dalam kehamilan dan banyak disebabkan oleh penyakit Grave (85%)



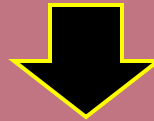
Kehamilan akan menyebabkan perubahan struktur dan fungsi kelenjar tiroid ibu



Perubahan fisiologis peningkatan hormon tiroid 40-100% untuk keperluan ibu dan janin

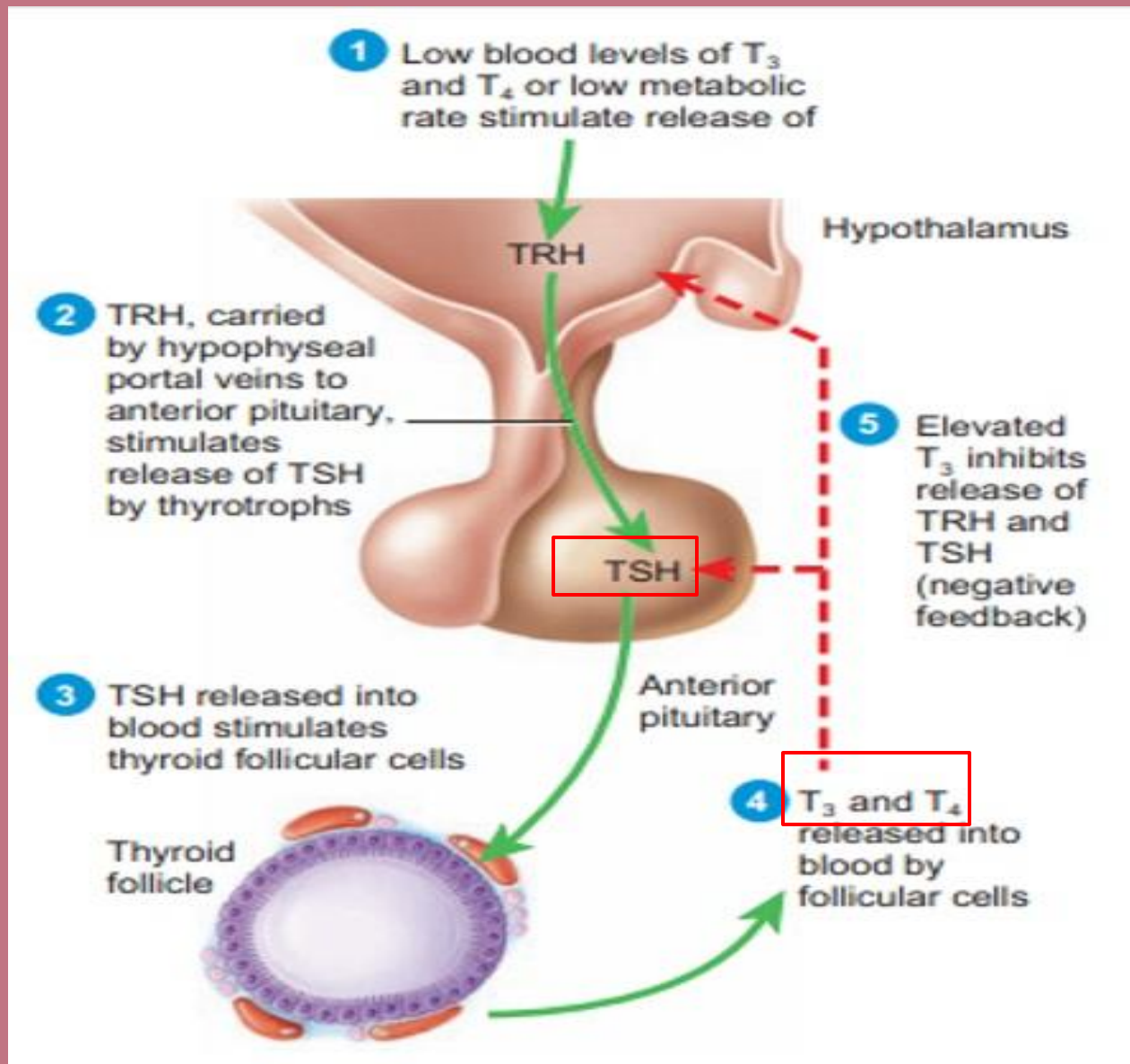


Menyulitkan penegakan diagnosis penyakit atau menentukan adanya kelainan tiroid



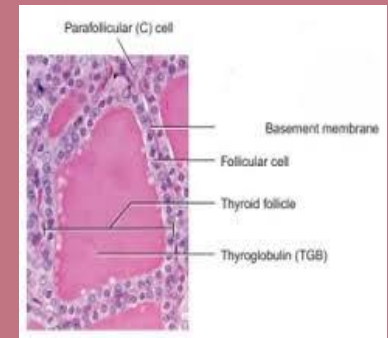
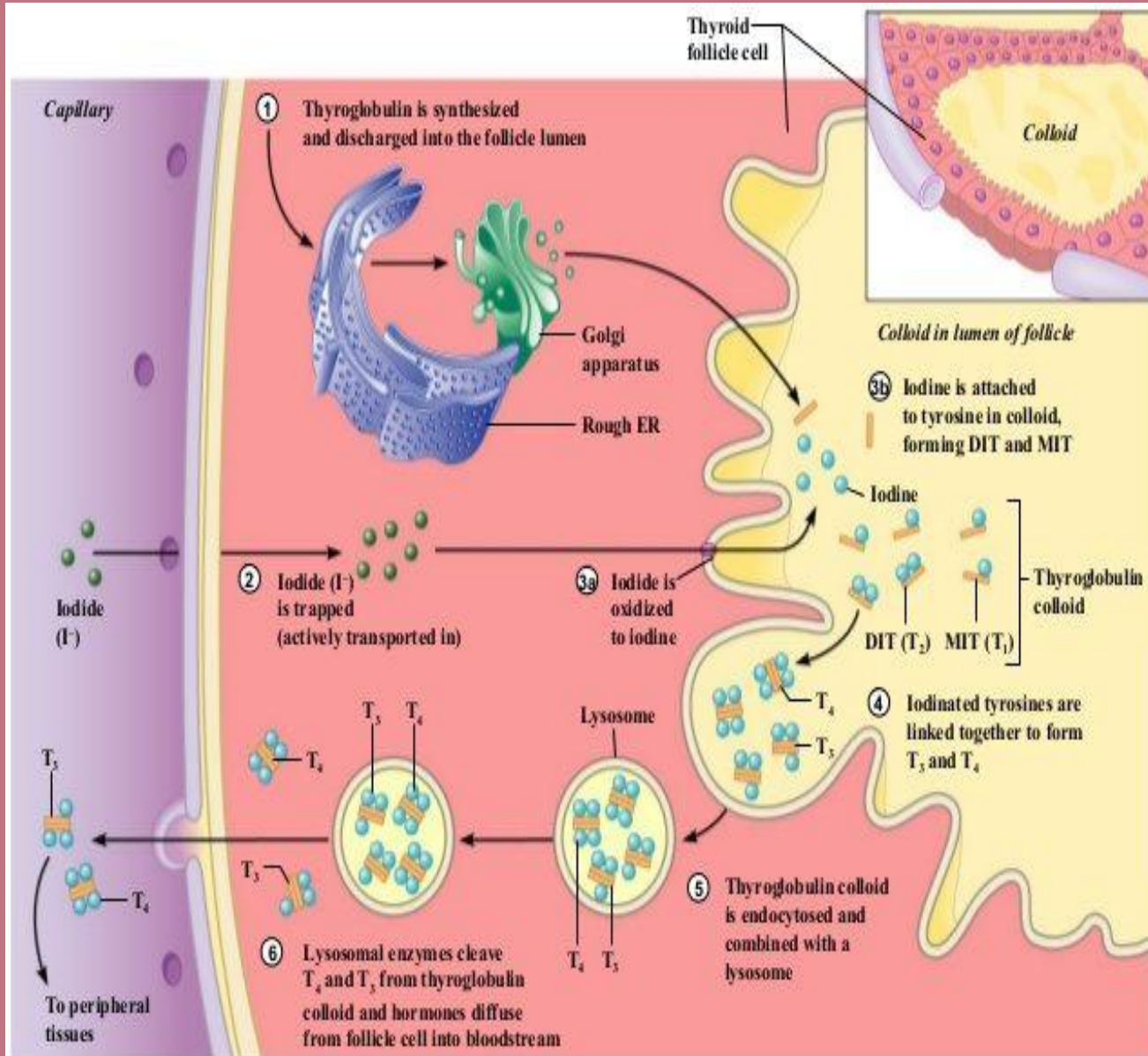
Gejala seperti cemas, berkeringat, dispneu, takikardi, murmur sistole pada jantung juga sering ditemukan pada kehamilan normal

- **Hipertiroid yang tidak terdeteksi dan diberi penanganan maksimal** → Meningkatkan risiko keguguran, solusio plasenta, persalinan prematur
- Pada ibu komplikasi aritmia jantung, gagal jantung kongestif dapat terjadi
- **Badai tiroid** → dalam kasus yang memburuk → morbiditas dan mortalitas

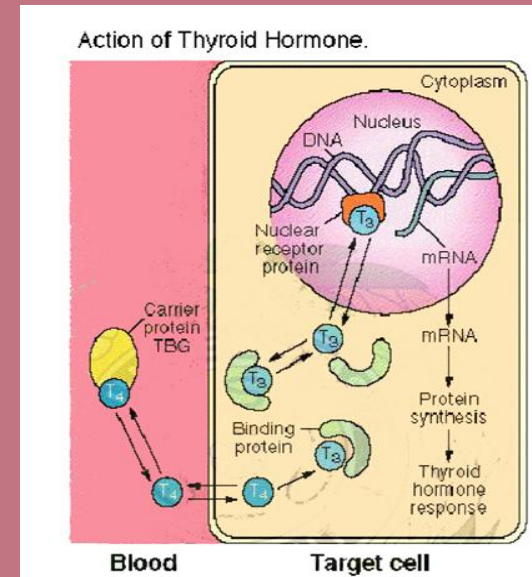
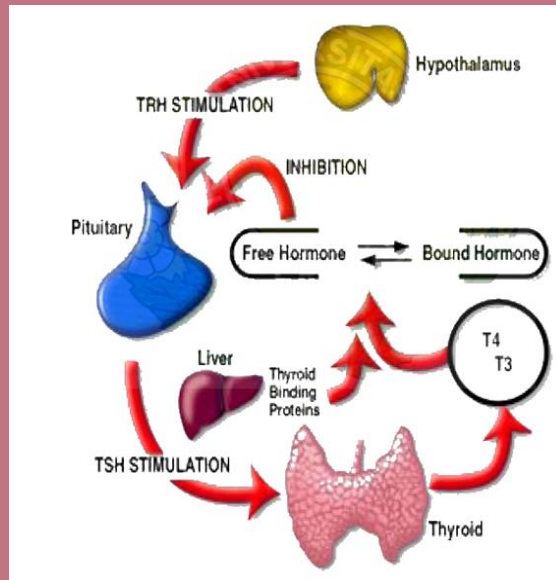


Poros hipotalamus hipofise organ target kelenjar tiroid

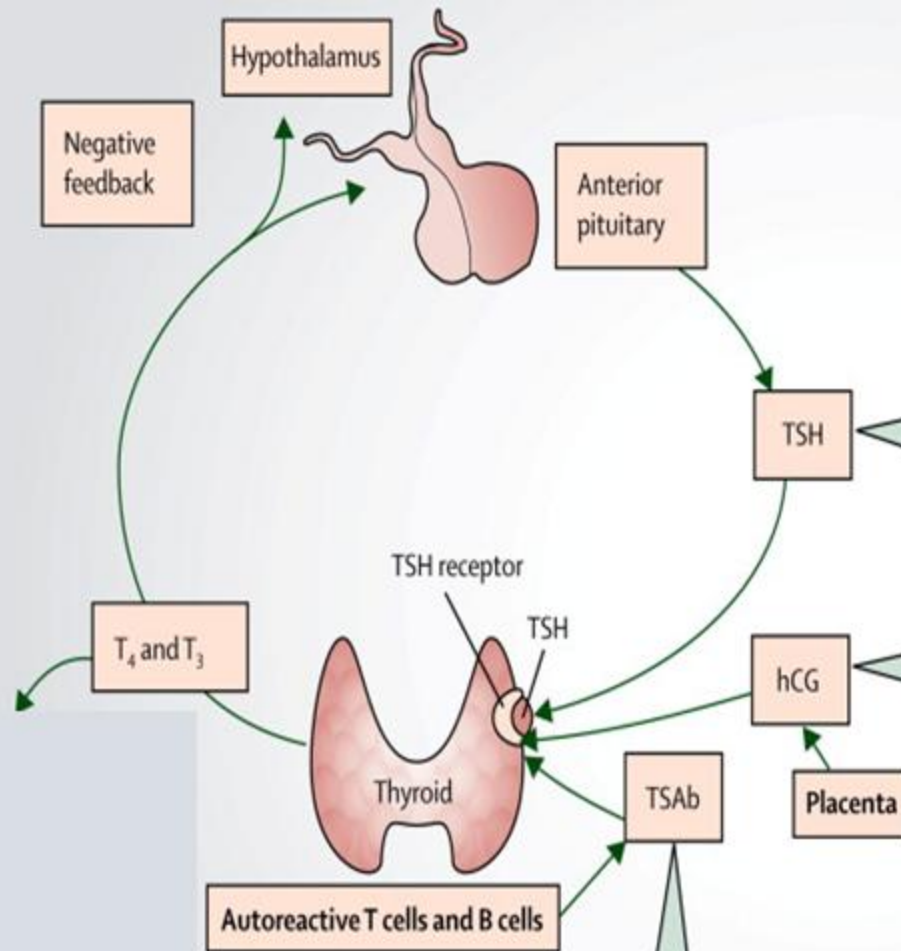
BIOSINTESIS HORMON TIROID



- Didalam sirkulasi jumlah T₄ yang berikatan dengan globulin (TBG) di hepar lebih banyak dibandingkan T₃
- T₃ bentuk yang paling aktif
- T₄ TBG → T₃
- T₃ dan T₄ yang bekerja pada sel organ target



Hypothalamic-pituitary-thyroid axis



Normal
TSH stimulates the thyroid to produce thyroid hormones, T₄ and T₃. Serum concentrations of TSH are slightly less than the reference range for non-pregnant women, especially in the first trimester due to the stimulatory effects of hCG on the thyroid gland

Hyperthyroidism
TSH secretion is suppressed because of the negative feedback of raised circulating thyroid hormones concentrations

Normal
hCG synthesised in the placenta stimulates the TSH receptor causing a mild increase in FT4 concentrations and a reciprocal decline in serum TSH

Hyperthyroidism

- Gestational hyperthyroidism is seen in women with very high hCG concentrations during normal pregnancy or in more pathological states like molar pregnancy or choriocarcinoma,
- In Graves' disease, hCG's stimulation of the TSH receptor is overshadowed by the stimulatory effects of TSAb

Normal
Not present in healthy women

Hyperthyroidism

- In Graves' disease, TSAb activate the TSH receptor to cause hyperthyroidism
- TSAb pass the placenta and can cause fetal and neonatal Graves' disease

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 Wiersinga¹¹

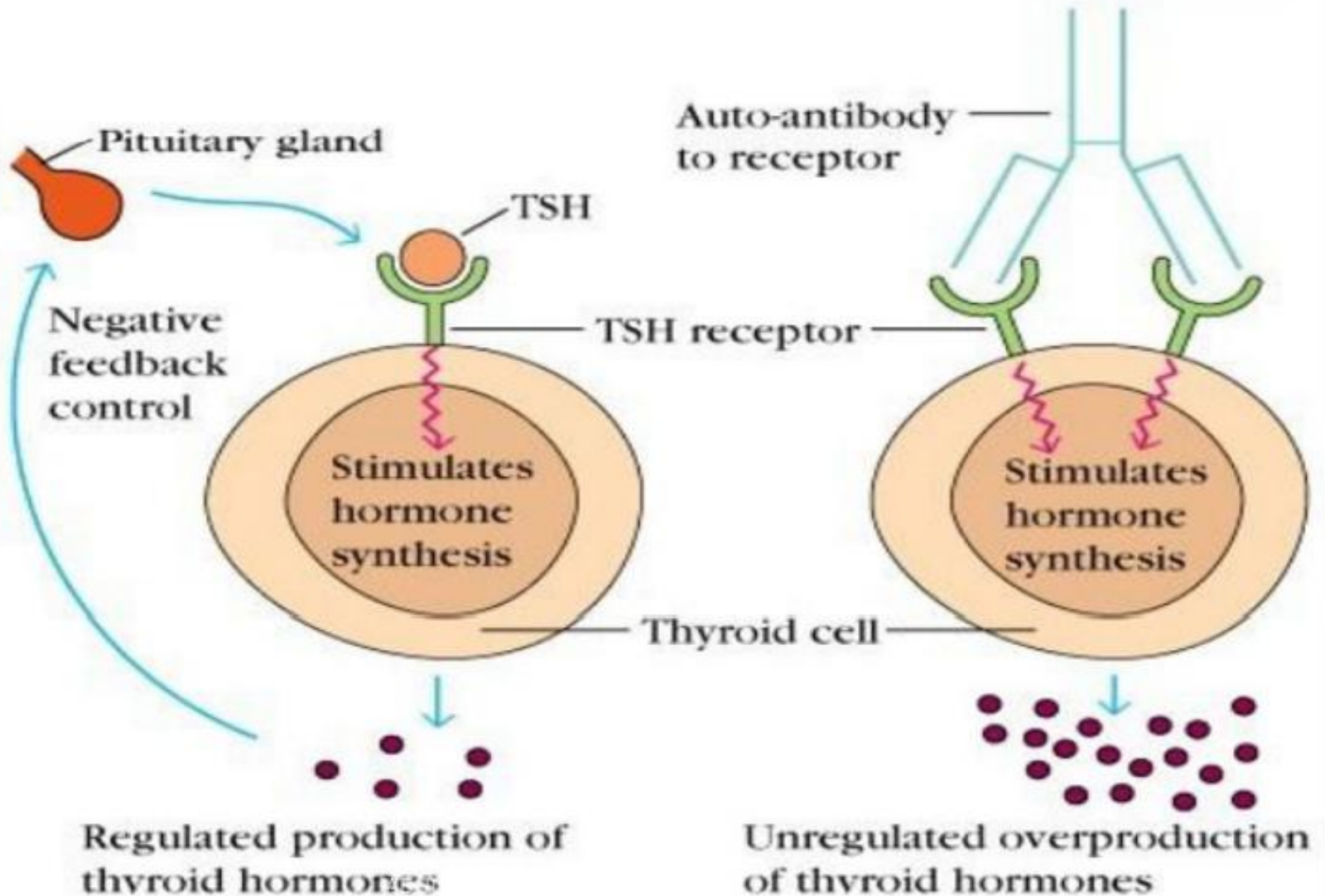



- Pada kehamilan dengan gemelli peningkatan HCG dapat semakin tinggi → Hipertiroid
- Studi pada 63 women with hCG concentrations >200,000 IU/L, TSH (0.2 mIU/L) dan 67% dari 100% jika konsentrasi hCG >400,000 IU/L

Faktor pencetus hipertiroid dalam kehamilan

- Hipertiroid dalam kehamilan pada umumnya disebabkan oleh **penyakit autoimun Grave**. Penyebab yang lainnya, adalah struma multinodular, adenoma toksik, tiroiditis
- Grave' disease → proses **autoimun** → antibody tiroid → menempel dan mengaktivasi reseptor TSH → hiper fungsi dari kelenjar tiroid
- Episode kekambuhan → riwayat hipertiroid

STIMULATING AUTO-ANTIBODIES (Graves' disease)



- 
- **Transien hipertiroidisme** didiagnosis pada sekitar 3-5 % dari kehamilan dan termasuk wanita dengan hiperemesis gravidarum , kehamilan kembar dan mola hidatidosa
 - B HCG meningkat pada trimester pertama puncaknya pada minggu 10-12 kehamilan
 - TSH menurun dan FT₄ normal

Sistem organ	Gejala	Tanda
Neuropsikiatrik	Kecemasan, Kebingungan, Koma	<i>Muscle wasting</i> Hiperfleksia, tremor
Gastrointestinal	Hiperdefekasi, diare	
Kelernjar tiroid	<i>Neckfullness, tenderness</i>	Penyebaran pembesaran, bruit
Kardiorespirasi	Palpitasi, dyspnea, nyeri dada	Fibrilasi atrium, takikardia, gagal jantung kongestif
Dermatologis	Rambut rontok	Pretibial mixedema, kulit hangat dan lembab, palmar eritema
Oftalmologis	Diplopia, iritasi mata	Exophthalmus, ophthalmoplegia

DIAGNOSIS

- Pada kasus yang jelas diagnosis klinis kehamilan dengan hipertiroid mudah ditegakkan
- Sebaliknya pada kasus yang ringan secara klinis maupun laboratorium sulit untuk membuat diagnosis
- Diagnosis hipertiroidisme harus selalu dikonfirmasi oleh pengukuran FT₄ dan TSH
- TSH < 2.5 mIU/L (trimester pertama) setelah < 3.0 mIU/L
- Hipertiroidisme, TSH < 0,1 mIU/L

ACOG Guidelines at a Glance Thyroid Disease in Pregnancy

July 01, 2015

By Sarah J. Kilpatrick, MD, PhD

TSH	FT ₄	FT ₃	TT ₄	TT ₃	
No change	No change	↑	↑	↑	Pregnancy
↓	↑	↑	↑	↑	Hyperthyroidism
↓	No change	No change	No change	No change	Subclinical hyperthyroidism

PRINSIP PENATALAKSANAAN

Implementasi bertujuan memberikan perawatan terbaik untuk ibu hamil dan mencegah efek buruk pada ibu , janin dan neonatus



1.Observasi

2.Obat anti tiroid

3.β Blocker

4.Operatif
(Tiroidektomi)

Review Article

Management of Hyperthyroidism in Pregnancy: Comparison of Recommendations of American Thyroid Association and Endocrine Society

Shahram Alamdari, Fereidoun Azizi, Hossein Delshad, Farzaneh Sarvghadi, Atieh Amouzegar, and Ladan Mehran

Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Science, Tehran 19395-4763, Iran

Correspondence should be addressed to Shahram Alamdari; alamdari@endocrine.ac.ir

Received 8 December 2012; Accepted 31 March 2013

International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Aggarwal R et al. Int J Reprod Contracept Obstet Gynecol. 2016 Jan;5(1):1-5
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20151598>

Review Article

Management of hyperthyroidism in pregnancy

Rashmi Aggarwal*, Pradeep Chugh

Department of Thyroid and Endocrine Research Institute of Nuclear Medicine and Allies Sciences, Timarpur, Delhi, India

**PENATALAKSANAAN
INTENSIF
OBSTETRI**

UDIN SABARUDIN
ANITA DEBORAH ANWAR
JOHANES C. MOSE

2015

100 evidence-based

TABLE I: Comparison of recommendations of American Thyroid Association and Endocrine Society on the management of hyperthyroidism before pregnancy and on the diagnosis of hyperthyroidism and pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	Endocrine Society (2012)
Management before pregnancy	Same (R and T)	For overt hyperthyroidism due to Graves' disease or thyroid nodules, antithyroid drug (ATD) therapy should be either initiated (before pregnancy if possible, and for those with new diagnoses) or adjusted (for those with a prior history) to maintain the maternal thyroid hormone levels for free T4 at or just above the upper limit of the nonpregnant reference range, or to maintain total T4 at 1.5 times the upper limit of the normal reference range or the free T4 index in the upper limit of the normal reference range.
Thyroid function tests	In the presence of a suppressed serum TSH in the first trimester (TSH < 0.1 mIU/L), a history and physical examination are indicated. FT4 measurements should be obtained in all patients. Measurement of TT3 and TRAb may be helpful in establishing a diagnosis of hyperthyroidism.	Same (R)
Ultrasonography	There is not enough evidence to recommend for or against the use of thyroid ultrasound in differentiating the cause of hyperthyroidism in pregnancy.	None
Scanning and uptake	Radioactive iodine (RAI) scanning or radioiodine uptake determination should not be performed in pregnancy.	None
Differentiation of Graves disease and gestational thyrotoxicosis	Same (T)	Differentiation of Graves' from gestational thyrotoxicosis is supported by the presence of clinical evidence of autoimmunity, typical goiter, and presence of TSH receptor antibodies (TRAb). TPO-Ab may be present in either case.

TABLE 2: Comparison of recommendations of American Thyroid Association and Endocrine Society on the treatment of hyperthyroidism in pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	Endocrine Society (2012)
Antithyroid (ATD) treatment	PTU is preferred for the treatment of hyperthyroidism in the first trimester, and patients on MMI should be switched to PTU if pregnancy is confirmed in the first trimester. Following the first trimester, consideration should be given to switching to MMI.	Propylthiouracil (PTU), if available, is recommended as the first-line drug for treatment of hyperthyroidism during the first trimester of pregnancy because of the possible association of methimazole (MMI) with specific congenital abnormalities that occur during first trimester organogenesis, and MMI may also be prescribed if PTU is not available or if a patient cannot tolerate or has an adverse response to PTU. Practitioners should use their clinical judgment in choosing the ATD therapy, including the potential difficulties involved in switching patients from one drug to another. If switching from PTU to MMI, thyroid function should be assessed after 2 weeks and then at 2- to 4-week intervals.
Combination of LT4 and ATD	A combination regimen of T4 and an ATD should not be used in pregnancy, except in the rare situation of fetal hyperthyroidism.	None
Monitoring liver function in women on PTU	None	Although liver toxicity may appear abruptly, it is reasonable to monitor liver function in pregnant women on PTU every 3-4 weeks and to encourage patients to promptly report any new symptoms.
Monitoring of thyroid function	In women being treated with ATDs in pregnancy, FT4 and TSH should be monitored approximately every 2-6 weeks. The primary goal is a serum FT4 at or moderately above the normal reference range.	Same (T)
Surgery	Same (R and T)	Subtotal thyroidectomy may be indicated during pregnancy as therapy for maternal Graves' disease if (1) a patient has a severe adverse reaction to ATD therapy (2) persistently high doses of ATD are required (over 30 mg/d of MMI or 450 mg/d of PTU) or (3) a patient is nonadherent to ATD therapy and has uncontrolled hyperthyroidism. The optimal timing of surgery is in the second trimester.

TABLE 3: Comparison of recommendations of American Thyroid Association and Endocrine Society on the fetal aspects of hyperthyroidism in pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	Endocrine Society (2012)
Thyroid receptor antibodies (TRAb)	If the patient has a past or present history of Graves' disease, a maternal serum determination of TRAb should be obtained at 20–24 weeks gestation.	TRAb should be measured by 22-week gestational age in mothers with (1) current Graves' disease; or (2) a history of Graves' disease and treatment with 131I or thyroidectomy before pregnancy; (3) a previous neonate with Graves' disease; or (4) previously elevated TRAb
Fetal Surveillance	Fetal surveillance with serial ultrasounds should be performed in women who have uncontrolled hyperthyroidism and/or women with high TRAb levels (greater than three times the upper limit of normal). A consultation with an experienced obstetrician or maternal-fetal medicine specialist is optimal. Such monitoring may include ultrasound for heart rate, growth, amniotic fluid volume, and fetal goiter.	In women with TRAb or thyroid-stimulating Ig elevated at least 2- to 3-fold the normal level and in women treated with ATD, maternal free T ₄ and fetal thyroid dysfunction should be screened for during the fetal anatomy ultrasound done in the 18th–22nd week and repeated every 4–6 weeks or as clinically indicated. Evidence of fetal thyroid dysfunction could include thyroid enlargement, growth restriction, hydrops, presence of goiter, advanced bone age, tachycardia, or cardiac failure, if fetal hyperthyroidism is diagnosed and thought to endanger the pregnancy, treatment using MMI or PTU should be given with frequent clinical, laboratory, and ultrasound monitoring.
Umbilical blood sampling	Cordocentesis should be used in extremely rare circumstances and performed in an appropriate setting. It may occasionally be of use when fetal goiter is detected in women taking ATDs to help determine whether the fetus is hyperthyroid or hypothyroid.	Same (R)
Evaluation of newborn	Same (T)	All newborns of mothers with Graves' disease (except those with negative TRAb and not requiring ATD) should be evaluated by a medical care provider for thyroid dysfunction and treated if necessary.

TABLE 4: Comparison of recommendations of American Thyroid Association and Endocrine Society on other aspects of hyperthyroidism in pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	Endocrine Society (2012)
Management of gestational hyperthyroidism	<p>The appropriate management of women with gestational hyperthyroidism and hyperemesis gravidarum includes supportive therapy, management of dehydration, and hospitalization if needed.</p> <p>ATDs are not recommended for the management of gestational hyperthyroidism.</p> <p>Same (T)</p>	<p>Most women with hyperemesis gravidarum, clinical hyperthyroidism, suppressed TSH, and elevated free T4 do not require ATD treatment. Clinical judgment should be followed in women who appear significantly thyrotoxic or who have in addition serum total T3 values above the reference range for pregnancy. Beta blockers such as metoprolol may be helpful and may be used with obstetrical agreement. Women with hyperemesis gravidarum and diagnosed to have Graves' hyperthyroidism (free T4 above the reference range or total T4 > 150% of top normal pregnancy value, TSH < 0.01 mIU/liter, and presence of TRAb) will require ATD treatment, as clinically necessary.</p>
Subclinical hypothyroidism	<p>Same (T)</p>	<p>There is no evidence that treatment of subclinical hyperthyroidism improves pregnancy outcome, and treatment could potentially adversely affect fetal outcome.</p>

KONSEKUENSI PENGGUNAAN OBAT ANTI TIROID

EFEK SAMPING OAT

EFEK TERATOGENIK OAT

RESIKO HIPOTIROID BAYI

PTU Vs Methimazol

- Methimazole (MMI) dan propylthiouracil (PTU) adalah standar OAT pengobatan hipertiroidisme pada kehamilan
- PTU menghambat sintesis T₄ dan T₃ di kelenjar tiroid dan menghambat konversi T₄ menjadi T₃ di perifer sedang Metimazol menghambat proses Oksidasi Iodida di kel tiroid
- Efek teratogenik dari MMI dan PTU masih banyak kontroversi. (MMI > PTU). PTU lebih dianjurkan pada trimester pertama dan dapat dilanjutkan dengan MMI setelah trimester ke dua
- Penggunaan PTU pertimbangkan efek hepatotoksik

- Dosis obat tergantung pada keadaan hipertiroid dan minggu gestasi
- Pada awal kehamilan sebelum terbentuknya plasenta, diberikan dengan dosis 3 sampai 4 kali 100 mg sehari, sedangkan MMI 3 kali 10 mg sehari
- Setelah keadaan eutiroid tercapai maka dosis dapat diturunkan
- Target TSH 0,1 -2,5 trimester pertama dan 0,3-3,0 trimester kedua dan tiga
- *fT₄ serum (rujukan 10-26 pmol/l), fT₃ (rujukan 3 – 7 pmol/l)*
- Kasus Graves disease pengobatan sampai 1-2 tahun. (TSH, T₃, T₄ N 6 bulan prognosis baik)
- Pada umumnya dengan dosis PTU 100-200 mg/hari dan MMI 10-15 mg/hari selama hamil tidak akan memberikan efek hipotiroid pada anak

Pertimbangan pemberian Beta-blocker dalam kehamilan

International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Aggarwal R et al. *Int J Reprod Contracept Obstet Gynecol.* 2016 Jan;5(1):1-5
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

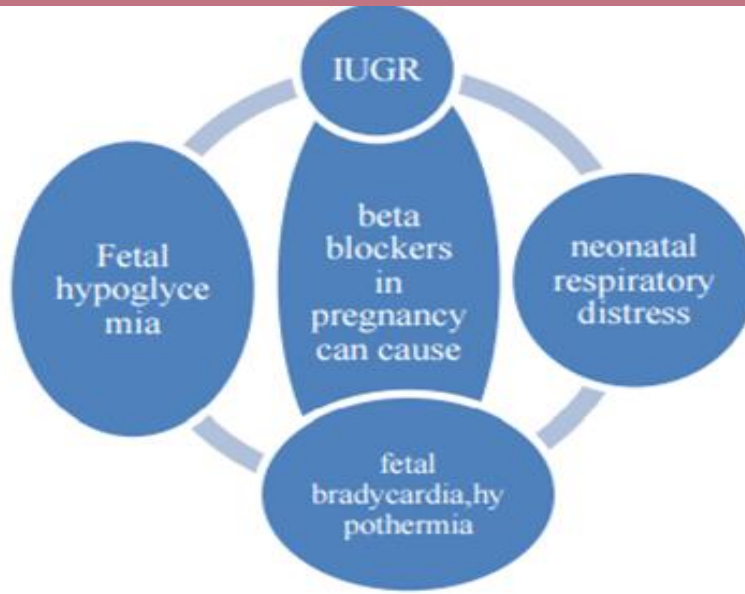
DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20151598>

Review Article

Management of hyperthyroidism in pregnancy

Rashmi Aggarwal*, Pradeep Chugh

Department of Thyroid and Endocrine Research Institute of Nuclear Medicine and Allies Sciences, Timarpur, Delhi, India



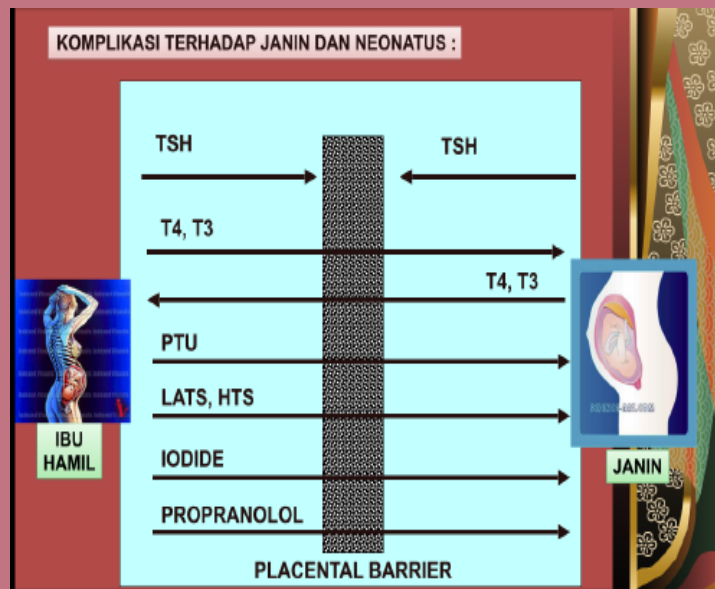
Mengontrol gejala hypermetabolik (takikardi, tremor dsb)

Dosis aman digunakan 40 mg selama 3 minggu tidak berbahaya terhadap bayi

Effects of beta-blockers in pregnancy.

Konsekwensi pemberian OAT pada janin

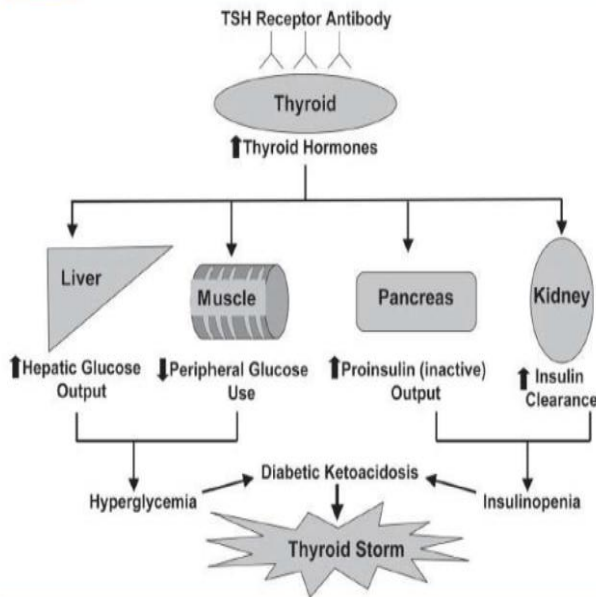
- Dosis tinggi OAT dapat menyebabkan hipotoroid
- Karbimasol → scalp defect (aplasia kutis)
- Dosis PTU dibawah 150 mg/hari dan karbimasol 15 mg/hari umumnya tidak menyebabkan masalah pada fetus



KRISIS TIROID DAN PELAKSANAANNYA

Kejadian akut atau eksaserbasi akut dari hipertiroid

Medscape



Source: Endocr Pract © 2009 American Association of Clinical Endocrinologists

GEJALA KRISIS TIROID DAN PENATALAKSANAANNYA

GEJALA KRISIS TIROID

- Hipermetabolisme, demam, berkeringat
- Gangguan Kardiovaskulern: takikardia, fibrilasi atrial/ventrikel, gagal jantung
- SSP : iritabilitas, agitasi, tremor, gangguan mental (delirium, koma, psikosis)
- Gangguan GI tractus : vimitus, diare, jaundice
- Laboratorium : Leukositosis, gangguan hepar, TSH rendah, FT4 dan FT3 tinggi

PRESIPITASI KRISIS TIROID

Tindakan operasi emergensi	Resisten obat anti tiroid
Induksi anestesia	Infark miokard
Diabetes Ketosidosis	Infeksi
Emboli pulmonal	Hipertensi/ preeklampsia
	Anemia Gravis

Pasien dirawat *obstetric ICU* (konsultasi : Dept IPD, Endokrinologi, Divisi Fetomaternal dan Dep Neurologi)

- Pemeriksaan Laboratorium : darah komplit, elektrolit, Faal hati, ginjal dan kadar gula darah,
- Pemasangan infus dan oksigen (Monitoring Kesejahteraan janin KTG, pemberian cairan elektrolit, monitoring CV, pemberian obat simptomatis, Pemasangan NGT

Pemberian obat anti hipertiroid PTU dan Jodium untuk menekan T4 (Naj atau Lugol)

1. PTU melalui selang nasogastrik 300-600 mg dosis awal dilanjutkan 150-300 mg diulang 6 jam
2. 1 jam setelah pemberian PTU a. Naj, 500 mg 8-12 jam
b. Lar Lugol 30-60 tts/perhari. c. Naj dihentikan setelah ada perbaikan

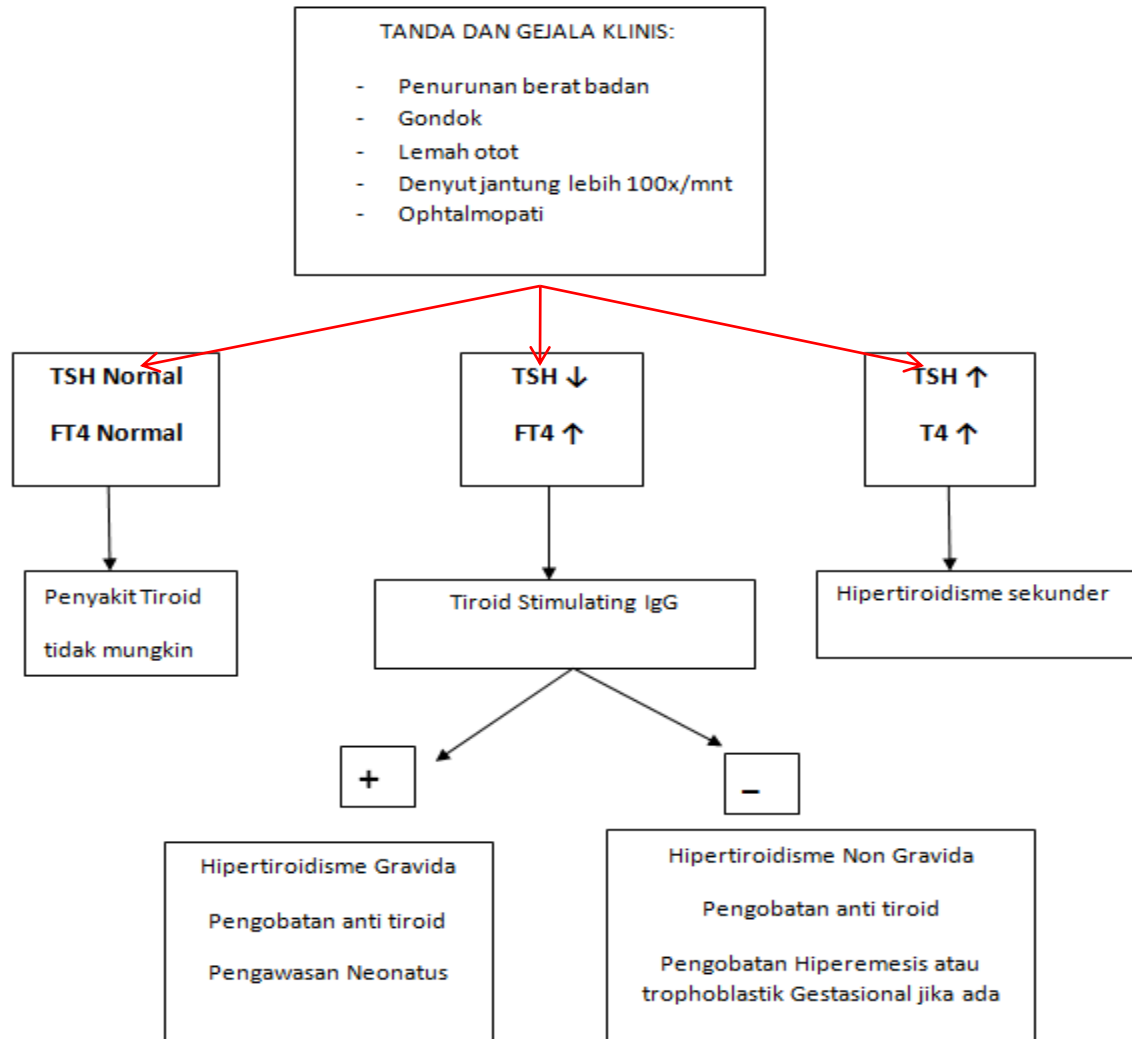
Pemberian obat anti takikardia ibu : 1. Propranolol 1-2 mg/min i.v atau dosis yg cukup menurunkan nadi 90 bpm atau 40-80 mg p.o diulang 4-6 jam 2. Bila perlu dipasang kateter arteri pulmonalis

Pemberian obat adrenal Glucocorticoid utk mencegah konversi T4-T3 disirkulasi perifer. Pilihan obat : 1. Hidrokortison 100 mg i.v/8jam 2. Prednison 60 mg p.o setiap hari 3. Deksametason 2 mg/ i.v im /6 jam dihentikan bila ada perbaikan

Bila secara konvensional tidak berhasil, plasmaforesisi atau dialisis peritoneal utk menghilangkan hormon tiroid perifer

Bila tidak berhasil dilakukan subtotal tiroidektomi pada trimester kedua atau pemberian preparat radioaktif pascasalin

ALGORITME EVALUASI HIPERTIROIDISME SELAMA KEHAMILAN



**PENATALAKSANAAN
INTENSIF
OBSTETRI**


UDIN SABARUDIN
ANITA DEBORAH ANWAR
JOHANES C. MOSE

What's new in thyroid disease in pregnancy in 2015?

Rekomendasi tingkat A

1. Rekomendasi pertama (tidak melakukan screening universal untuk penyakit tiroid pada kehamilan).
2. TSH adalah tes skrining lini pertama untuk menilai status tiroid pada kehamilan.
3. TSH dan FT₄ harus diukur untuk mendiagnosis penyakit tiroid pada kehamilan.
4. Wanita hamil dengan hipertiroidisme yang jelas harus ditangani dengan thioamide untuk meminimalkan hasil yang merugikan risiko.
5. FT₄ harus dipantau pada wanita hamil dengan hipertiroidisme dan thioamide dosis disesuaikan.

ACOG Guidelines at a Glance Thyroid Disease in Pregnancy

- 
- Mempertahankan euthyroidism di pasien ini adalah sangat penting.
 - beberapa studi telah menunjukkan bahwa penatalaksanaan maksimal pasien hipertiroid dalam kehamilan akan meningkatkan ***outcome ibu dan bayi.***

TERIMA KASIH

جَزَاكُمُ اللَّهُ خَيْرًا

