

Hypothyroidism in Pregnancy

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Outline

- Normal physiology
- Physiological changes in pregnancy
- Overt hypothyroidism
- Subclinical hypothyroidism
- Screening
- Treatment.

Control of Thyroid Function

Hypothalamus releases TRH →

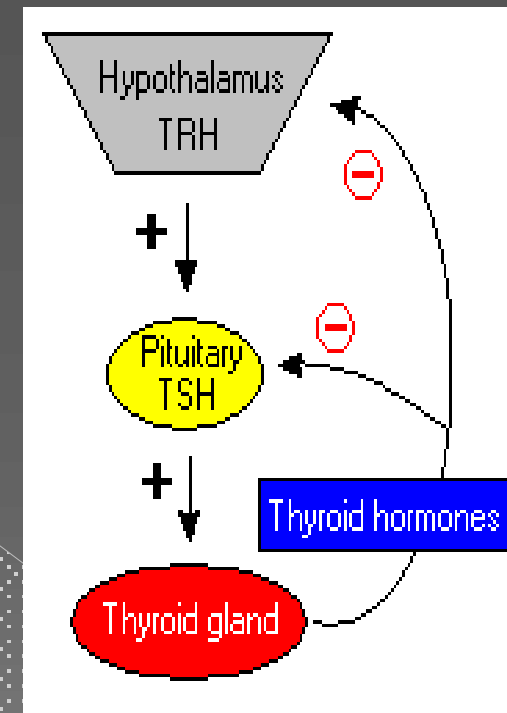
Act on the pituitary gland to release TSH →

TSH causes the thyroid gland to release the thyroid hormones (T_3 and T_4)

TRH and TSH concentrations are inversely related to T_3 and T_4 concentrations.

• 99% circulating T_3 and T_4 is bound to TBG.
1%

free form Biologically Active

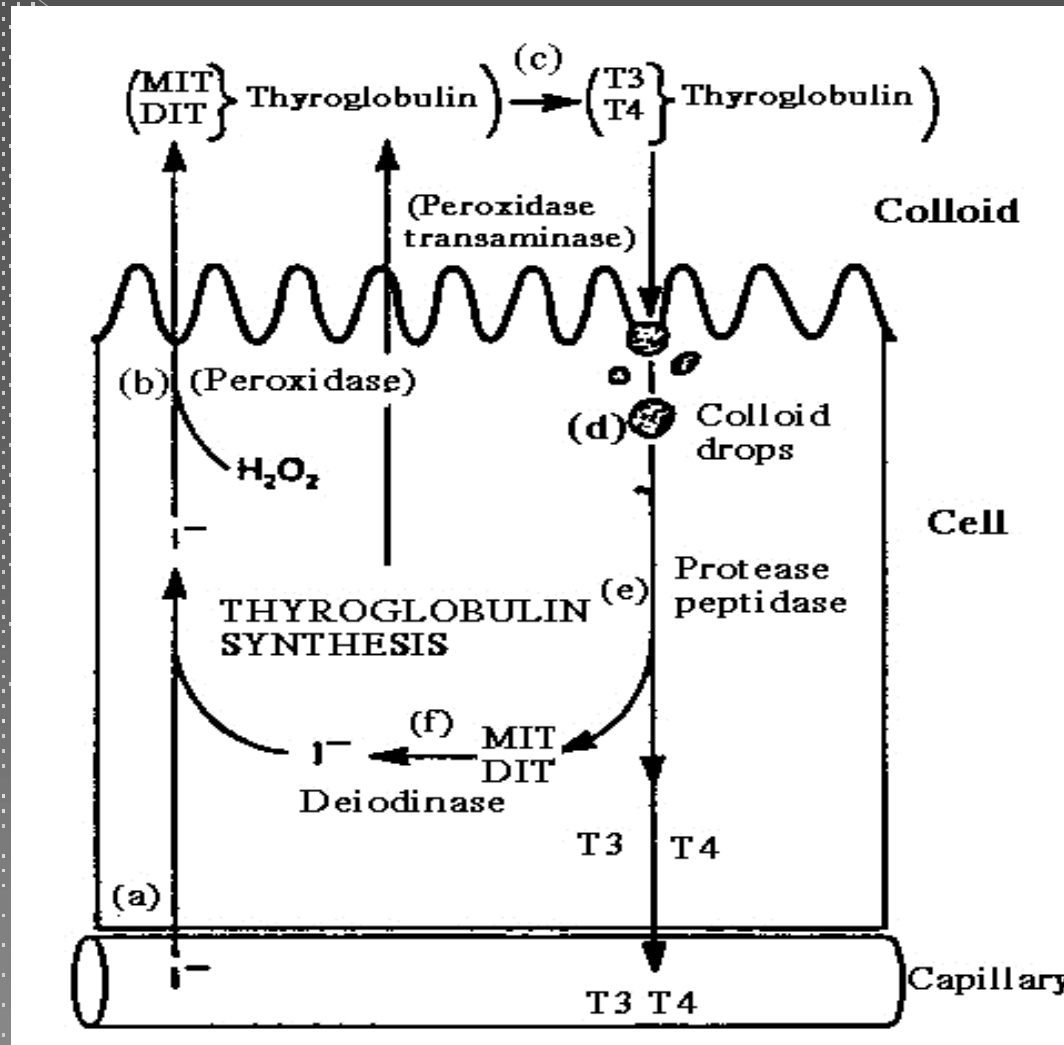


Aboubakr Elnashar

Steps involved in synthesis of thyroid hormones

- Iodide trapping
- Oxidation of iodide ion
- Organification
- Coupling of iodotyrosine residue
- Release of T3 and T4 into the blood.

Thyroid hormone synthesis



- T4 is produced in larger amount
- T3 is 4 times more potent than T4.
- Peripheral conversion of T4 to T3 occurs in certain tissues.
- 99% of circulating T3 and T4 is bound to THYROID BINDING GLOBULIN, only 1% is free form- biologically active.

PHYSIOLOGICAL CHANGES DURING PREGNANCY

- Moderate enlargement
- Glandular hyperplasia and increased vascularity.
- Thyroid volume increased from 12ml in the first trimester to 15ml at delivery.

Physiological changes contd...

- Fetal thyroid gland starts synthesising hormones by 10- 12 wks gestation.
- Maternal thyroxine is important for normal fetal brain development
- Especially prior to the function of fetal thyroid gland.

Physiological changes contd..

- Maternal thyroxine accounts for 30% of thyroxine in fetal serum at term.
- Through out the pregnancy maternal thyroxine is transferred to the fetus.

THYROID BINDING GLOBULIN

- Increase – hepatic synthesis is increased by estrogen stimulation.
- Reaches its peak at about 20 weeks.

TOTAL T4

- Increases sharply – 6 to 9 weeks.
- Reaches a plateau at about 20 weeks.

TOTAL T3

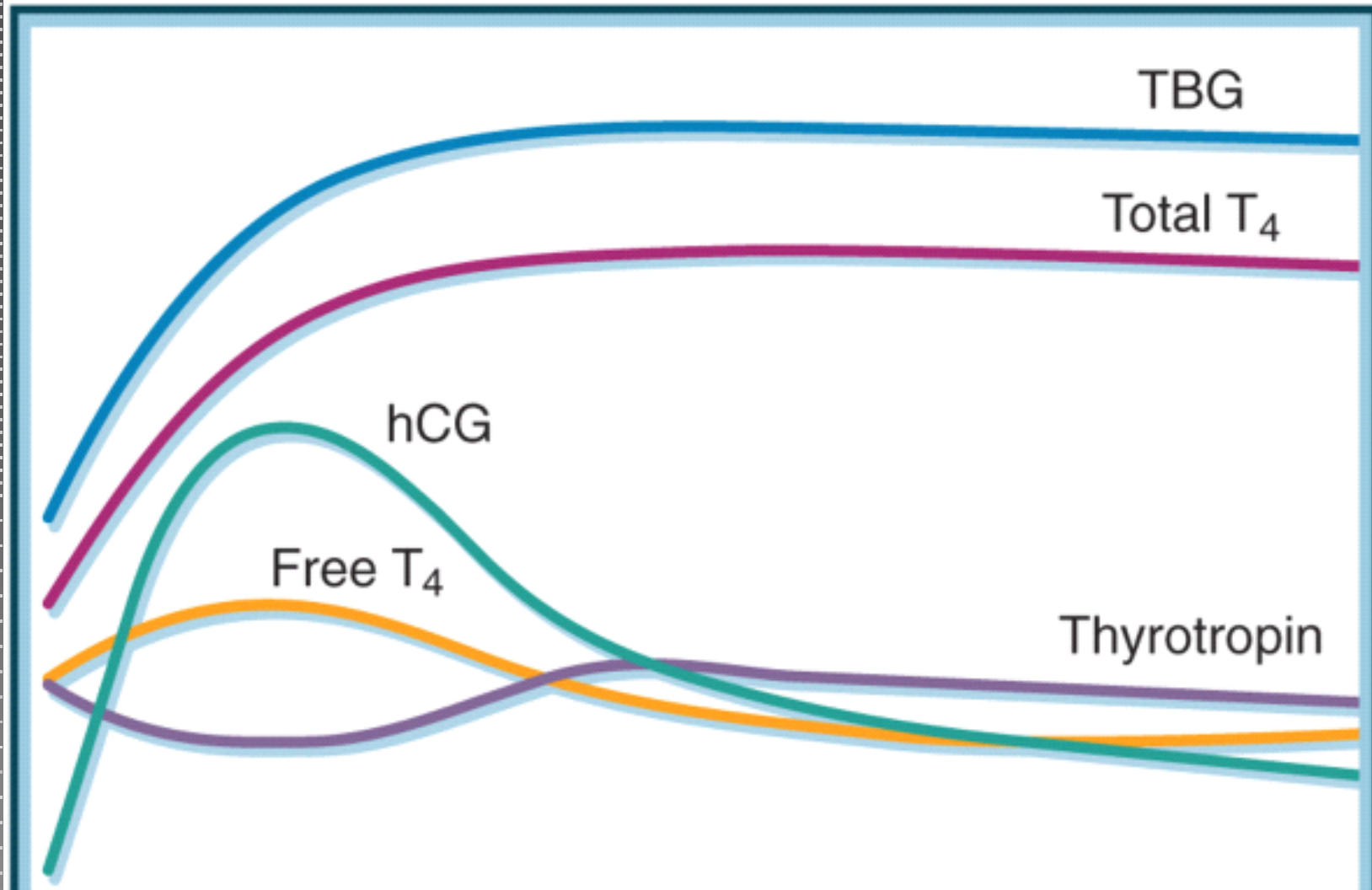
- Increases upto 18weeks thereafter plateaus.

FREE T4 & FREE T3

- Rises slightly and peaks along with hcg levels and then return to normal.
- But do fall little in the 2nd & 3rd trimesters.

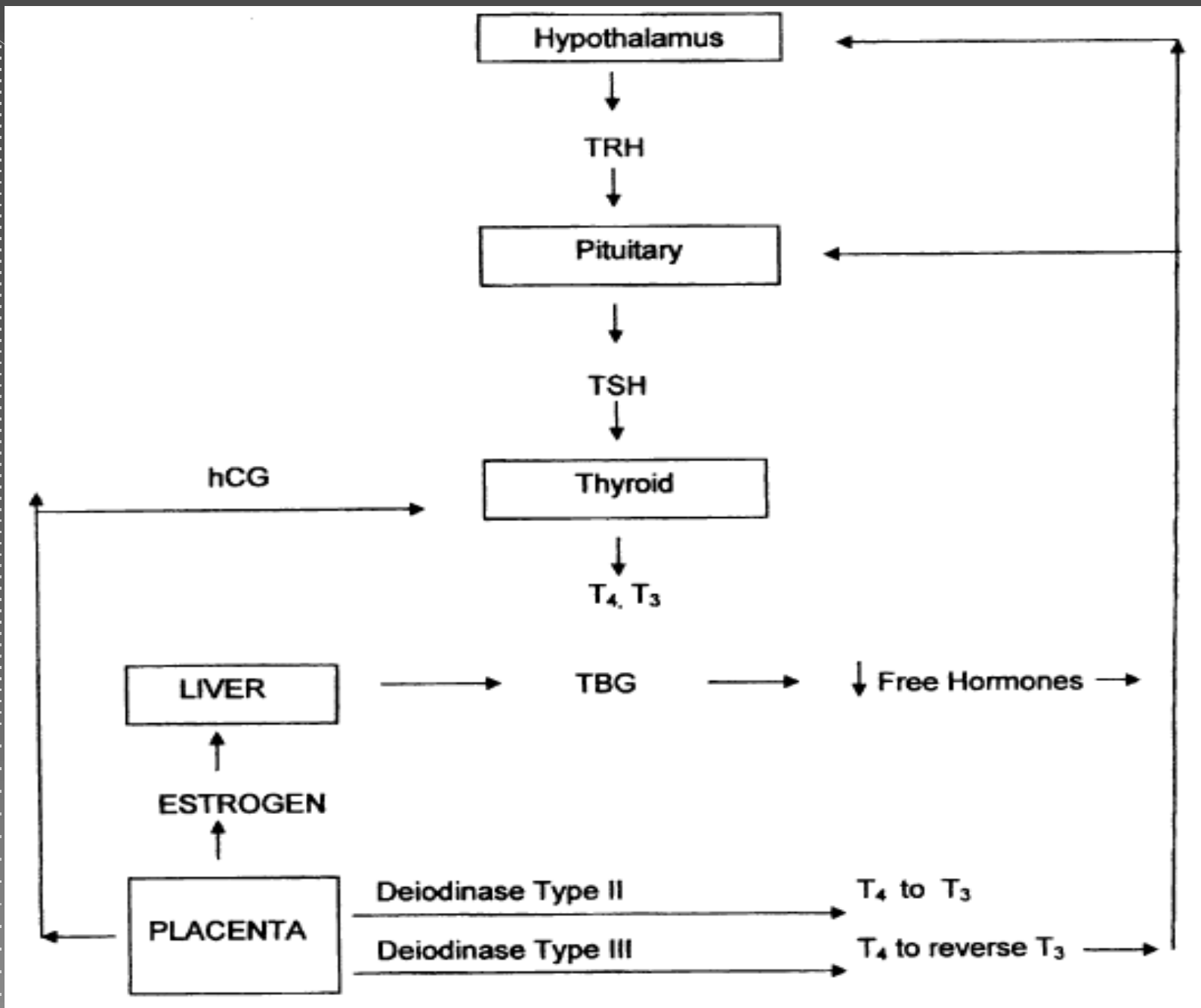
RELATIVE CHANGES IN MATERNAL THYROID FUNCTION DURING PREGNANCY

Mother



THYROID STIMULATING HORMONE:-

- ◉ Decreases in early pregnancy due to thyrotropic activity of alpha form of HCG.
- ◉ Which increases T3 and T4 thereby reduces the TSH by feedback.
- ◉ Increases in 2nd and 3rd trimester (increased TBG)
- ◉ TSH does not cross the placenta.



NORMAL LABORATORY VALUES IN UNCOMPLICATED PREGNANCY

	Non pregnant	1 st trimester	2 nd trimester	3 rd trimester
TSH(mIU/ml)	0.34-4.25	0.6-3.4	0.37-3.6	0.38-4.04
TBG(mg/dl)	1.3-3	1.8-3.2	2.8-4	2.6-4.2
Free T4(ng/dl)	0.8-1.7	0.8-1.2	0.6-1	0.5-0.8
Total T4(microgm/dl)	5.4-11.7	6.5-10.1	7.5-10.3	6.3-9.7
Free T3(pg/dl)	2.4-4.2	4.1-4.4	4-4.2	Not reported
Total T3(ng/dl)	77-135	97-149	117-169	123-162

Pregnancy is a state of relative iodine deficiency, because:

- Active transport to fetoplacental unit
- Increase iodine excretion in urine, 2

fold

(increased GFR & decreased renal tubular reabsorption)

- Thyroid gland increases its uptake from the blood

EFFECTS OF PREGNANCY ON THYROID PHYSIOLOGY

Physiologic Change	Thyroid-Related Consequences
↑ Serum thyroxine-binding globulin	↑ Total T ₄ and T ₃ ; ↑ T ₄ production
↑ Plasma volume	↑ T ₄ and T ₃ pool size; ↑ T ₄ production; ↑ cardiac output
First trimester ↑ in hCG	↑ Free T ₄ ; ↓ basal thyrotropin; ↑ T ₄ production
↑ Renal I ⁻ clearance	↑ Iodine requirements
↑ Oxygen consumption by fetoplacental unit, gravid uterus, and mother	↑ Basal metabolic rate; ↑ cardiac output

Clinical(Overt) / Subclinical Hypothyroidism

- Serum TSH level > 3.0 mIU/l
- Subclinical hypothyroidism \rightarrow elevated TSH with normal FT4, FT3.

	Clinical Hypothyroidism	Subclinical Hypothyroidism
TSH	High (>10)	High ($>3 - <10$)
Free T4	Low	Normal
Free T3	Normal or low	Normal

Clinical Hypothyroidism:

- Hashimoto thyroiditis
- Other causes:
 - Iodine deficiency
 - Previous treatment of graves disease by radio-ablation
 - Less common causes:
 - a) sub acute thyroiditis
 - b) drug induced hypothyroidism
 - c) isolated maternal hypothyroxinemia

Hashimoto's Thyroiditis

- Most common cause.
- An autoimmune disorder.
- Characterised by glandular destruction from autoantibodies.
- Anti-Thyroidperoxidase antibody
 - Anti-thyroglobulin antibody and
- Anti-TSH-receptor antibody.

Pathogenesis:

- T cells recognize the patient's own thyroid antigens as foreign.
- Stimulate B cells to make anti-thyroid antibodies.
- Almost 100% associated with anti-TPO antibody.
- May cause transient hyperthyroidism.

Pregnancy outcome with overt hypothyroidism

- Preeclampsia
- Placenta abruption
- Cardiac dysfunction
- Birth weight less than 2000g
- Stillbirths.
- Cognitive impairment of fetus
- Post partum thyroid dysfunction

But adequate hormone replacement during pregnancy minimises the risk of adverse outcomes.

Pregnancy outcome with overt hypothyroidism.

- Severe hypothyroidism with pregnancy is uncommon, because it is often associated with
 - infertility and
 - increased miscarriage rates.

Fetal and neonatal effects

- Maternal TSH- receptor-blocking antibodies - cross the placenta
 - fetal thyroid dysfunction.
- Anti-TPO antibodies and Anti-thyroglobulin antibodies } little or no effect
 - cross the placenta.

Iodine Deficiency

- Adequate iodine is required for fetal neurological development.
- Daily intake - pregnancy 220 $\mu\text{g}/\text{d}$
- lactation 290 $\mu\text{g}/\text{d}$

- There are varying degrees of preventable brain damage due to iodine deficiency.
- MILD- intellectual impairment.
- MODERATE- effects on intellectual and psychomotor function.
- SEVERE-endemic cretinism.

Drug induced hypothyroidism

- Interfere with thyroid hormone synthesis:
 - a) anti-thyroid drugs
 - b) iodine
 - c) lithium
- Increased thyroxine clearance:
 - a) carbamazepine
 - b) phenytoin
 - c) rifampin
- Decreased conversion T4 to T3:
 - a) amiodarone

Interfere with intestinal absorption:

Ferrous Sulfate

Sucralfate

Cholestyramine

Aluminium Hydroxide

Inhibit



GIT
Absorption
of thyroid
hormone.

Separated
by 4 hours

Subclinical Hypothyroidism

- Elevated TSH (> 3.0 mIU/l) with normal FT4, FT3.
- 31 % with anti-TPO antibody
- More common in women with autoimmune diseases
- The rate of progression to overt thyroid failure is impacted by
 - a) TSH level,
 - b) age
 - c) other disorders such as diabetes
 - d) Presence of antithyroid antibodies

Adverse pregnancy outcome:

- Subclinical hypothyroidism – adverse pregnancy outcomes-
 - Preterm birth
 - Preterm PROM
 - Placental abruption.

ISOLATED MATERNAL HYPOTHYROXINEMIA

- Women with low serum freeT4 and normal TSH .
- Low prevalence of anti-thyroid antibodies.
- No correlation between their TSH and freeT4.
- No increased adverse perinatal outcomes.

Post partum thyroiditis

- Transient auto-immune thyroiditis is consistently found in 5 to 10% of women during the first year after childbirth.
- Two recognised clinical phases:
 - ✓ Destruction induced thyrotoxicosis
 - ✓ Hypothyroidism.

Phases of postpartum thyroiditis

Factor	Thyrotoxicosis	Hypothyroidism
onset	1-4months	4-8months
Incidence	4%	2-5%
Mechanism	Destruction induced hormone release	Thyroid insufficiency
Symptoms	Painless goitre, fatigue, palpitations	Goitre, fatigue, inability to concentrate.
Treatment	Symptomatic therapy- β blockers.	Thyroxine for 6-12months
Sequale	2/3-euthyroid 1/3 -hypothyroid	1/3 permanently hypothyroid.

Overlapping Complaints

Symptoms	Hypothyroidism	Pregnancy
Fatigue	×	×
Constipation	×	×
Hair Loss	×	
Dry Skin	×	
Brittle Nail	×	
Weight Gain	×	×
Fluid Retention	×	×
Bradycardia		
Carpel Tunnel Syndrome	×	×



Screening and Its Importance

Indications for Screening

universal screening is not recommended according to ACOG

- ◉ Age >30 years
- ◉ Women on thyroid therapy
- ◉ Family Hx of autoimmune thyroid disease
- ◉ Presence of goiter or thyroid nodules
- ◉ Hx of thyroid surgery
- ◉ Infertility

- ◉ Previous Hx of

- neck radiation

- postpartum thyroid dysfunction

- previous birth of infant with thyroid problem

- ◉ Other autoimmune conditions: Type 1 DM

- ◉ Unexplained anemia

- ◉ Hypo natremia

- ◉ High cholesterol level

Pre-pregnancy assessment

- ◉ Women with known hypothyroidism should consult a physician before planning.
- ◉ Women with Type-1DM or other autoimmune diseases:
 - screening for TSH
 - Antithyroid antibodies.

Laboratory Workup

- Overt hypothyroidism:

 - symptomatic patient*

 - elevated TSH level(>10mIU/L)*

 - low levels of FreeT₄ and FreeT₃*

- Subclinical hypothyroidism:

 - asymptomatic patient*

 - elevated TSH(>3 TO <10mIU/L)*

 - normal FreeT₄ and FreeT₃*

Treatment

- Replacement with external thyroid hormone -- levothyroxine (Levothyroid, Levoxyl, Synthroid, and Unithroid).
- Levothyroxine (Synthroid) **pregnancy category A**
 - > A stereoisomer of physiologic thyroxine
 - > 1 to 2 $\mu\text{g}/\text{kg}$,
 - > usually about 50 to 100 mcg/day
 - > 30-60 minutes before eating breakfast.




- Overt hypothyroidism: Thyroxine initiated with $2\mu\text{g}/\text{kg}/\text{d}$.
- Titrated according to TSH levels.
- Subclinical hypothyroidism: initiated with $50\mu\text{g}/\text{day}$.

Treatment and Goals

- The American Association of Clinical Endocrinologists recommends keeping the thyroid-stimulating hormone (TSH) level between **0.5 and 2.5 mIU/L**.
- After readjustment of levothyroxine, observe 6-8 weeks
- Serum thyrotropin levels are measured every 4-6 weeks interval
- Thyroxine dose is adjusted by 25 to 50 μ g until normal TSH values 0.5 to 2.5 mIU/l reached.

- Safe in pregnancy and lactation
 - Very little thyroxine crosses the placenta
 - NO risk of thyrotoxicosis of fetus
- Patients who were on thyroxine therapy before pregnancy should increase the dose by 30% once pregnancy is confirmed.
- TSH should be monitored every trimester until delivery.

- Post natal management:
 - thyroxine requirement decreases
 - dosage to be readjusted.



THANK YOU