

Management of Thyroid Disorders

By

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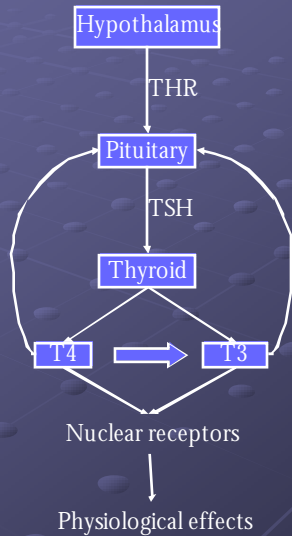
Overview

- Pathophysiology of thyroid hormones
- Thyrotoxicosis – causes and management
- Hypothyroidism
- Subclinical thyroid disorders + management in pregnancy
- The Thyroid nodule

Pathophysiology

- The thyroid gland actively transport iodide from circulatory blood into thyroid follicular cells.
- Iodide organified into thyroglobulin
- Proteolysis → release of T3 & T4

Hypothalamus Pituitary Thyroid Axis



Thyrotoxicosis

Causes & Management

Thyrotoxicosis: Refers to hypermetabolic clinical syndrome resulting from serum elevations in thyroid hormones levels. Free T4 and T3 or both.

Hyperthyroidism: Is a type of thyrotoxicosis in which there is accelerated thyroid hormone biosynthesis and secretion by the thyroid gland.

Clinical Features

• Symptoms

- Weight loss despite increase appetite
- Heat intolerance & sweating
- Tremor
- Irritability, frenetic activity, emotional lability, psychosis
- Oligomenorrhea

• Signs

- Tachycardia, AF
- Palmar Erythema, Hair thinning
- Eye Signs: Lid lag, Lid retraction, Exophthalmos
- Goitre, Bruit
- Pretibial Myxedema

Investigations

- TSH (suppressed)
- Free T4 ↑, Free T3 ↑
- Thyroid autoantibodies: TRAB, Anti TPO, Antithyroglobulin antibodies
- Mild normocytic anaemia, ESR ↑, LFTs ↑
- Isotope scan if cause is unclear

Causes

- Graves
- Lymphocytic thyroiditis
- Post-partum thyroiditis

- Toxic nodules
- Multinodular goitre

- Subacute thyroiditis

- Others: Drugs amiodrone
- TSHoma

Case History #1

A previously fit 32-year-old woman notices tremor and heat intolerance. She has lost one and a half stones (9.5kg) in weight over the past 6 months. You note signs of hyperthyroidism and a diffuse goitre. Her mother is treated for hypothyroidism. The patient smokes 20 cigarettes per day. She and her husband want to start a family in the foreseeable future.

How should she be investigated?

Does she require a thyroid scan?

What is the preferred first line of treatment?

If she has a child, how likely is the child to be affected by Graves' disease?



Graves Disease

- **Autoimmune disease caused by stimulatory TSH receptor antibodies (also react with orbital autoantigens)**
- **Commoner in females 9:1**
- **Homogeneous increase uptake on thyroid scintigraphy**

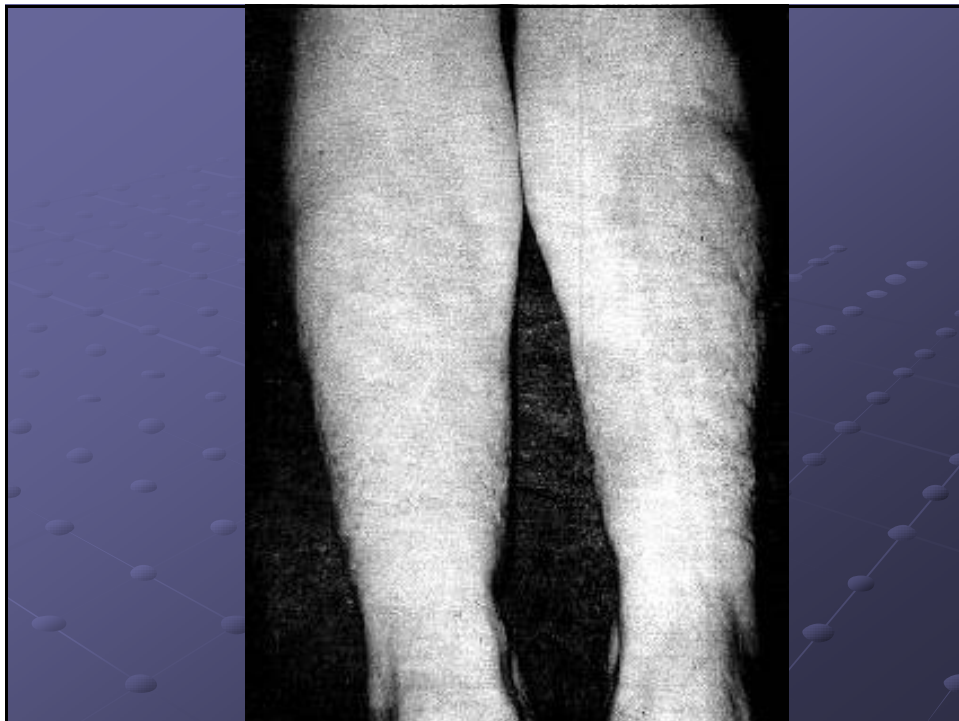
▪ **Treatment :**

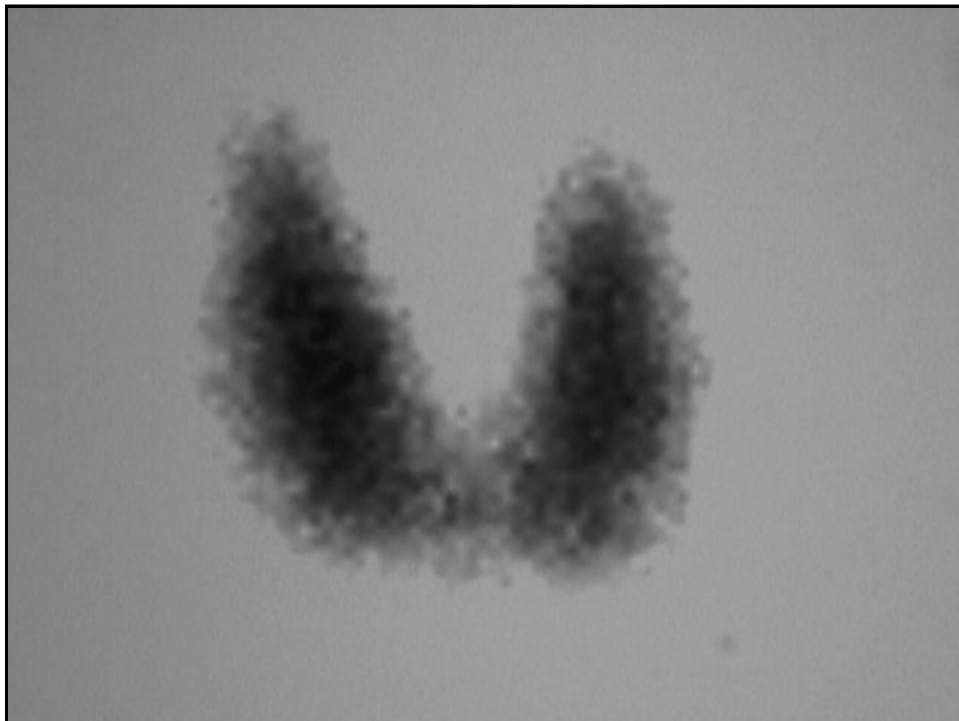
1. Medical Treatment -> antithyroid drugs, examples, carbimazole, PTU
 - beware side effects, example, Agranulocytosis
 - at least 6 months
 - Block and replace v/s titration – hypothesis: antithyroid drugs – immune modulatory & antioxidant properties – modify natural history of disease.
2. Radioactive Iodine treatment (I 131) – failure of medical treatment c/i pregnancy, breast-feeding, younger patient <15yr old, Graves ophthalmoplagia
3. Surgery – last resort for patient unwilling to have RAT or for cosmetic reasons

Case #1

1. Thyroid hormone, TSH, thyroid antibodies
2. Thyroid scanning not routinely warranted
3. Medical t/x 1st line
4. 1 in 3 chance of AITD if female

N.B. Nurses' Health Study – association with smoking





Case History #2

A 65-year-old man has noted a swelling in his neck, gradually increasing in size over the past 3 years. Although generally healthy, he has mild angina, which is stable at present. He is being treated with atenolol and isosorbide mononitrate, and uses sublingual nitrate only occasionally. Isotope scan shows 50g goitre with patchy uptake. His thyrotropin (TSH) is undetectable but his free T4 is only marginally elevated at 26 pmol/l (normal 12-25 pmol/l).

Should his hyperthyroidism be treated?

He is concerned about radioactive iodine therapy, can we reassure him?

Is long-term antithyroid drug treatment advisable?

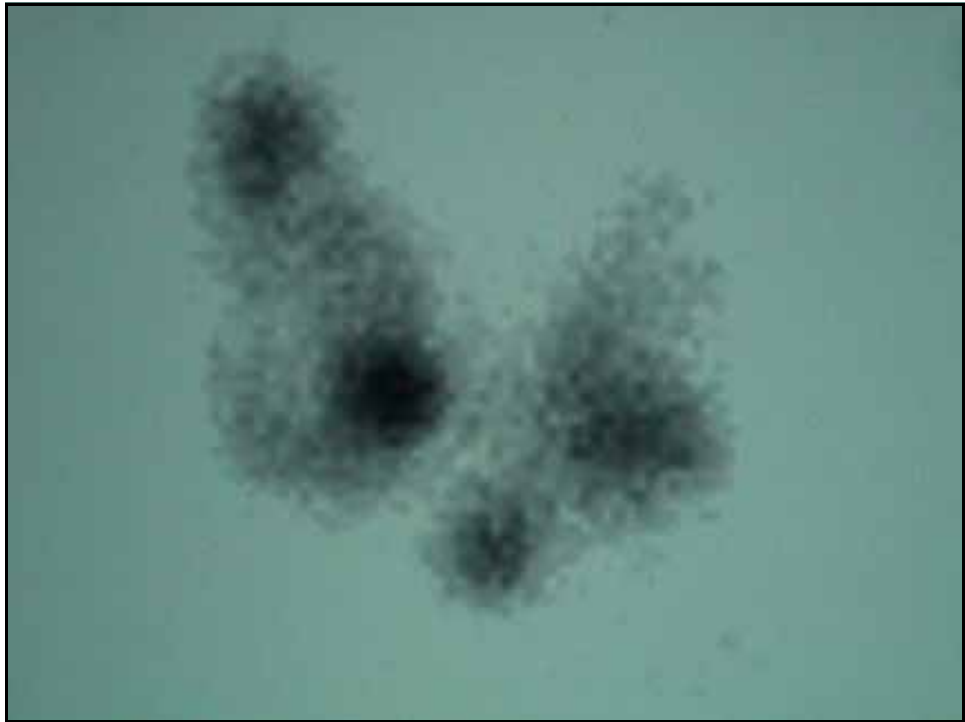
If he opts for surgery, should he have a subtotal or total thyroidectomy?

Toxic multinodular goitre

- End result of slow process
- Iodine uptake is normal or elevated and radionuclide scans demonstrate multiple nodules or heterogenous tracer

● Treatment

- Radioactive iodine (larger dose)
- Antithyroid medication (lifelong treatment)
- Surgery



Case #2

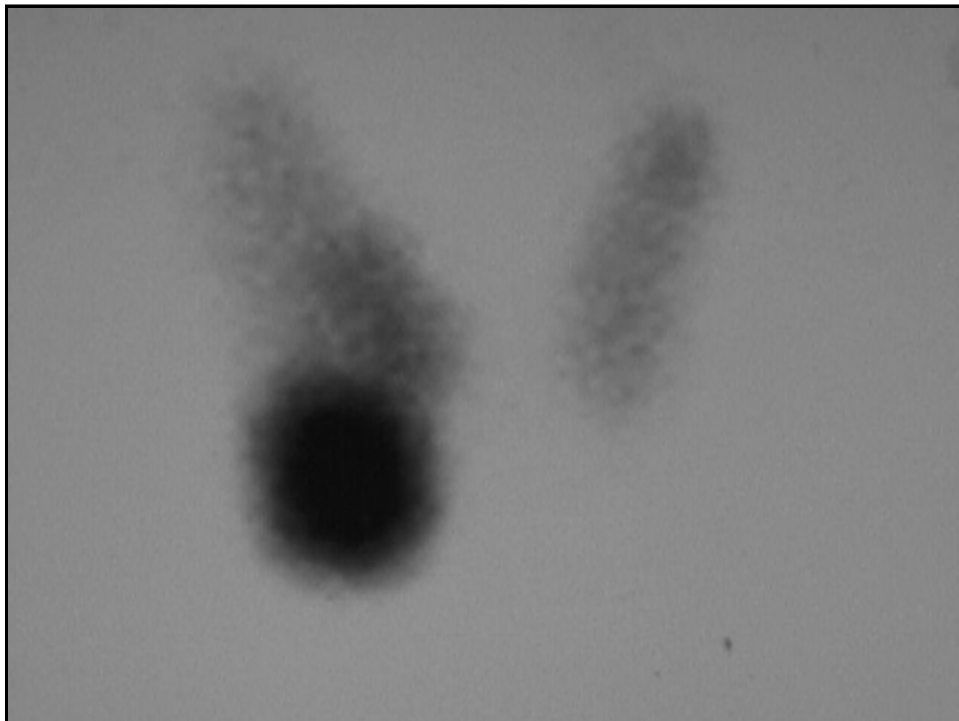
- Patient has 3 significant problems:
 1. Goitre
 2. Subclinical hyperthyroidism
 3. Angina
- Good evidence – hyperthyroidism should be treated
- Radioactive iodine 1st line safe & effective + shrink gland
- Surgery relatively contra-indicated

Toxic Nodules

- Thyroid scan reveals a hyperfunctional (i.e. hot nodule) with depressed tracer uptake in the remainder of the gland

● Treatment

- Radioactive iodine or surgery
- Medical treatment (lifelong)



Subacute Thyroiditis

- Viral infections as a precipitating factor
- Clinical signs & symptoms of \uparrow T4
- Substantial thyroid pain and tenderness
- Usually hyperthyroid phase may last 4-10 weeks, followed by hypothyroid phase
- Low radioiodine uptake (<3%)

● Treatment

- Symptom relief: β blocker, NSAID, occasionally steroids

Amiodarone & The Thyroid

- 37% Iodine by weight
- 2 types of Amiodarone Thyrotoxicosis

	Type 1	Type 2
Pre-existing thyroid disease	Graves or Multinodular goitre	No
Duration of amiodarone use	< 2 years	Usually longer
Goitre	Usually	Usually not
Autoantibodies	If Graves' disease	No
Thyrotoxicosis	Non transient	Transient
? Stop amiodarone	If possible	Not necessary
First line therapy	High dose antithyroid drugs	Prednisolone
Subsequent hypothyroidism	Unusual	Frequent but transient

Hypothyroidism

Common & easy to treat

● Causes

1. Autoimmune causes

- Primary atrophic hypothyroidism – female to male ratio 6:1
- Hashimoto's thyroiditis – goitre

2. Acquired causes

- Iodine deficiency
- Post thyroidectomy or radioiodine treatment
- Drug induced
- Subacute thyroiditis

Symptoms & Signs

- Tiredness
- Lethargy
- Depression
- Cold intolerance
- Menorrhagia
- Myalgia
- Hoarse voice
- Bradycardia
- Dry skin
- Non pitting oedema
- Slow relaxing reflexes
- Peripheral neuropathy
- Goitre
- Signs of pericardial effusion

Treatment

- Thyroxine replacement
- Start 25-50 mcg/day -> elderly/cardiac
50-100 mcg/day in younger patients
- Goal -> TSH between 0.5 – 2.5 mu/l

Pregnancy & Thyroid Dysfunction

Good evidence for the need of strict control of thyroid homeostasis particularly during organogenesis

Changes in thyroid function during pregnancy

- ↑ oestrogen & thyroid binding globulin causes increase in total T4.
Free T3 & free T4 also increase causing low TSH

- What is the normal thyroid level in pregnancy?
 - Lower limit OK
 - Upper limit
 - National Academy of Clinical Biochemistry Guidelines:
 - Ambulatory patients with serum TSH above 2.5 mIU/L maybe in the early stages of thyroid failure, specially if TPOAb is detected.

 - Association of Clinical Endocrinologists (ACE) Guidelines:
 - Proposed adoption of a TSH reference range of 0.3-3.0 mIU/L

Hyperthyroidism

- **Transient gestational thyrotoxicosis** a/w hyperemesis gravidarum
 - HCG structurally related to TSH, high level causes transient thyrotoxicosis
 - TRAB –ve -> may need short term ATD
- **Graves disease**
 - PTU – preferred lack of teratogenesis
 - Lowest dose PTU – keeping free T4 upper limit of normal
 - Fetal thyrotoxicosis – previous history of GD
 - TRAB checked early and at 36 weeks
 - Prediction of fetal hyperthyroidism as crosses placenta
 - May require Beta blocker & ATD

Hypothyroidism during pregnancy

- Common in women of child bearing age
- 2.5% of all pregnancy

Causes

- Primary atrophic hypothyroidism
- Post thyroidectomy or Radio Iodine treatment
- Subacute thyroiditis
- Iodine deficiency
- Pituitary failure

Consequences of hypothyroidism during pregnancy

- 1999 NEJM -> undetected and inadequately treated hypothyroidism was associated with IQ changes in the infants of the mothers
- Uncontrolled hypothyroidism in the mother can have neuro psychological effects on the development of the child

What can be done?

- **Borderline TSH**
 - Subclinical hypothyroidism and positive antibodies -> start thyroxine replacement
- **50% Increase of thyroxine requirement in 1st trimester**
 - Higher end of normal TSH < 1.0 mIU/L
- **Return to pre-pregnancy dose after delivery**

Miscarriage because of thyroid antibodies

(Eur J Endocrinal 2004 June)

- Meta analysis of all studies which have evaluated the relationship between thyroid autoimmunity and miscarriage. A clear association was found with an odds ratio of 2.73

Maternal TPO antibodies: Should they be treated?

- Low dose thyroxine if given early in euthyroid pregnant women with positive TPO antibodies is associated with lower rate of miscarriage and preterm delivery.
 - Negro R al. LEvothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease. *JCEM*, 2006;91:2587

Subclinical Thyroid Disease

- Hypothyroidism - TSH > 4.5, normal T3 & T4
 - Common
 - 5% return to normal
 - Treated pregnancy or anticipation of pregnancy or if symptomatic
 - Monitor annually if TPOAB +ve
- Hyperthyroidism
 - Exogenous LT4 therapy or endogenous disease
 - Elderly – treat aggressively – CV risk & ↓BMD



Management of the Thyroid nodule

Case History

- JC is a 48-yr-old man who has developed a swelling in the right side of his neck over the past 3 months. It is not painful, and he has no compressive symptoms. His health is generally good. You note a 2cm diameter swelling in relation to the right lobe of the thyroid. He is clinically euthyroid and thyroid function is normal.
- What is your differential diagnosis?
- How would you investigate the swelling further?
- He would like to know what the chances are that the lump is malignant.
- He is afraid of surgery and asks if it is safe to follow him up medically.

Background

- Thyroid nodules are extremely common
- 5% of the US population has a thyroid nodule
- Majority of them are benign (95%)
- What approach to adopt. Is it benign or malignant?

History

Factors suggesting malignancy:

- Age <20 or >70
- Male sex
- Associated symptoms of dysphagia or dysphonia
- History of neck irradiation or thyroid cancer
- Firm, hard or immobile nodules
- Cervical lymphadenopathy

Factors suggesting benign disease:

- Family history of autoimmune disease or benign nodules
- Thyroid dysfunction
- Pain or tenderness associated with nodules
- Soft, smooth and mobile nodule

Lab Evaluation

- TSH
- Free T4 and T3 if TSH is borderline
- Thyroid antibodies if family history of thyroid disorders

Imaging Studies

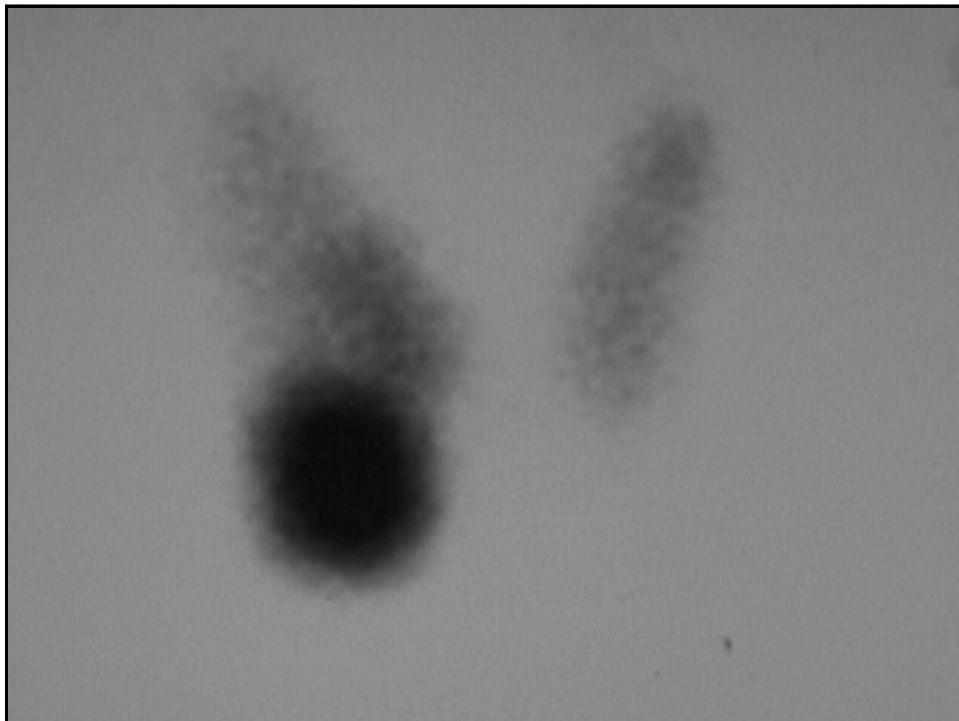
- Thyroid scintigraphy
- Ultrasound
- CT/MRI

CT/MRI

- Substernal lesions
- Not cost effective

Thyroid Scintigraphy

- Previously important imaging study
- Hot, warm or cold nodules
- Cold nodules -> 5-8% malignant
 - Not very useful as majority cold nodules (94%)
 - <1cm not detected



Ultrasonography

- Highly sensitive in determining size and number of thyroid nodules
- Cannot distinguish between benign and malignant
- High resolution sonography gives an idea of vascular characteristic of nodule
- Guidance to FNAC when nodule is not palpable

Fine-needle Aspiration Biopsy

- Most important step in the diagnosis and evaluation of thyroid nodule
- Dependant on skills of physician and histopathologist experience
- Highly cost effective

American Association of Clinical Endocrinologist

- No US-FNA nodule <10mm unless suspicious US findings or high risk history
- US FNA on all hypoechoic nodules >10mm with irregular margins, tall more than wide, microcalcification
- Complex thyroid nodule – US FNA solid component before fluid drainage
- Followup US 6 months - incidentiloma

- 10% are non diagnostic
- 75% are benign
- 5% show papillary, anaplastic, or medullary cell carcinomas
- 10% are follicular lesions of which 20% carcinomas

Category	Description
Thy 1	<i>Non-diagnostic</i> Action: Repeat (? With ultrasound guidance)
Thy 2	<i>Non-neoplastic</i> Action: Repeat at 3-6 months
Thy 3	<i>All follicular lesions</i> Action: Discuss with MDT, thyroid lobectomy
Thy 4	<i>Abnormal, suspicious of malignancy</i> Action: Discuss with MDT, thyroid lobectomy
Thy 5	<i>Diagnostic of malignancy</i> Action: Management by surgeon and oncologist

For patient JC

- Patient over 45, recent onset swelling, >2cm -> investigation with view of surgery
- Most important investigation is FNAC
- Low risk -> repeat biopsy at 3-6 months
- High risk -> surgery
- Early treatment of all high risk lesions is recommended

Summary

● History and examination

● TSH

suppressed -> endocrinologist -> RAI

normal -> FNAC + ultrasound

● FNAC

benign

repeat

surgery for cosmetic reasons

malignant

surgeons / oncologists

The Future

- We still do not understand thyroid autoimmunity completely
 - Eventual therapy of Graves & Hashimotos pharmacologically possible and maybe important in Graves orbitopathy
- Effects of Thyroid hormones in the developing brain – evidence maternal deficiency – impaired neurodevelopment – screening in early gestation?
- Gene therapy – in thyroid cancer

Final Words

- Think Thyroid
- Important to get diagnosis right in thyrotoxicosis
- Subclinical hypothyroidism important in pregnancy
- Beware of suspicious thyroid nodules