Case Scenario Approach to Thyroid Disorders (Part 1)

HYPER & HYPOTHYROIDISM

zoom WEBINAR

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Case Scenario Approach to Thyroid Disorders (Hyperthyroidism)

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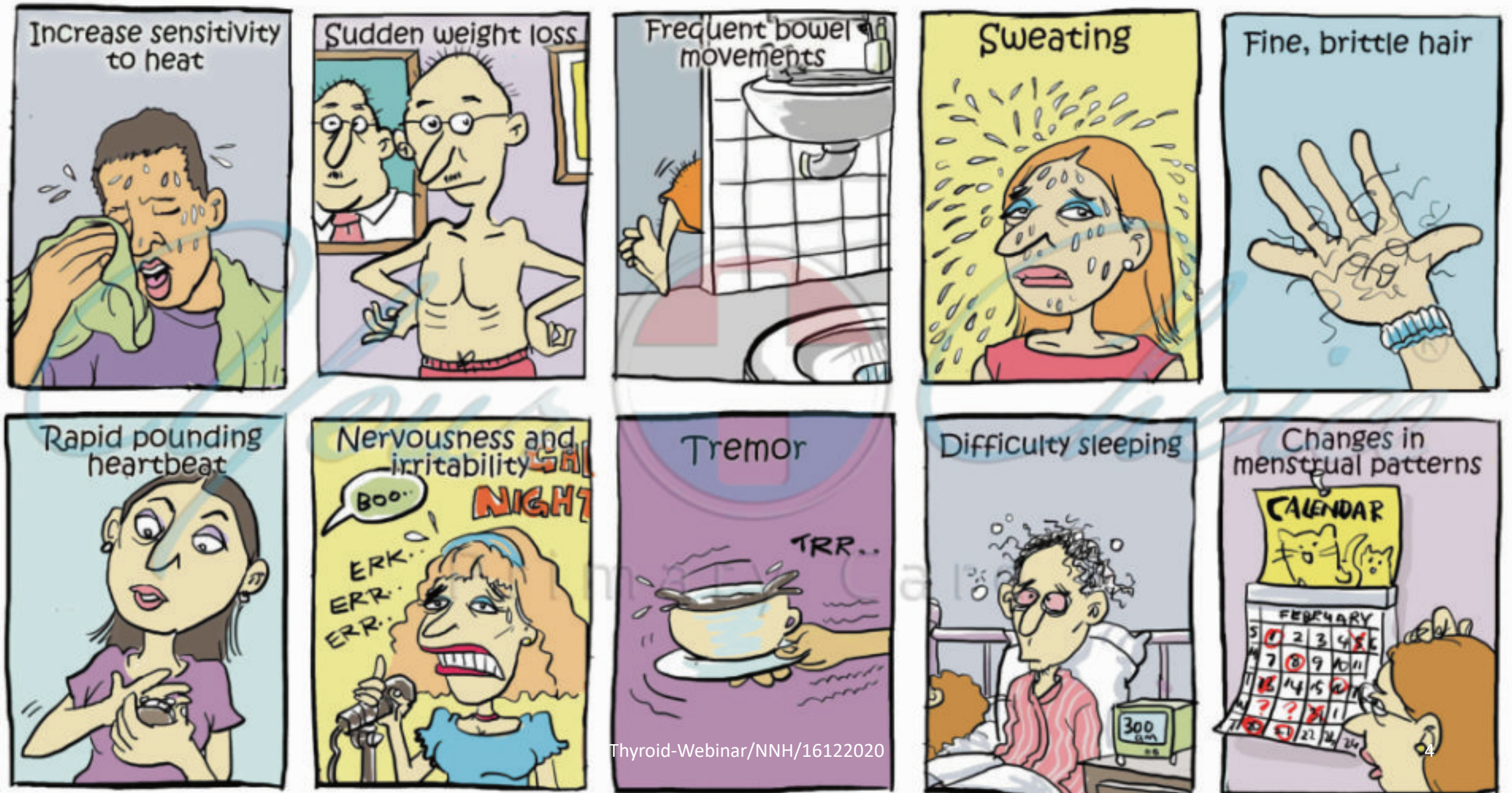
Scenario - 1

- ***35-year-old lady***
- **C/O**
  - Palpitation * 1 month
  - Shaky hands
- **O/E**
  - Diffuse Thyroid swelling
  - Tremor of outstretched hands
  - Tachycardia

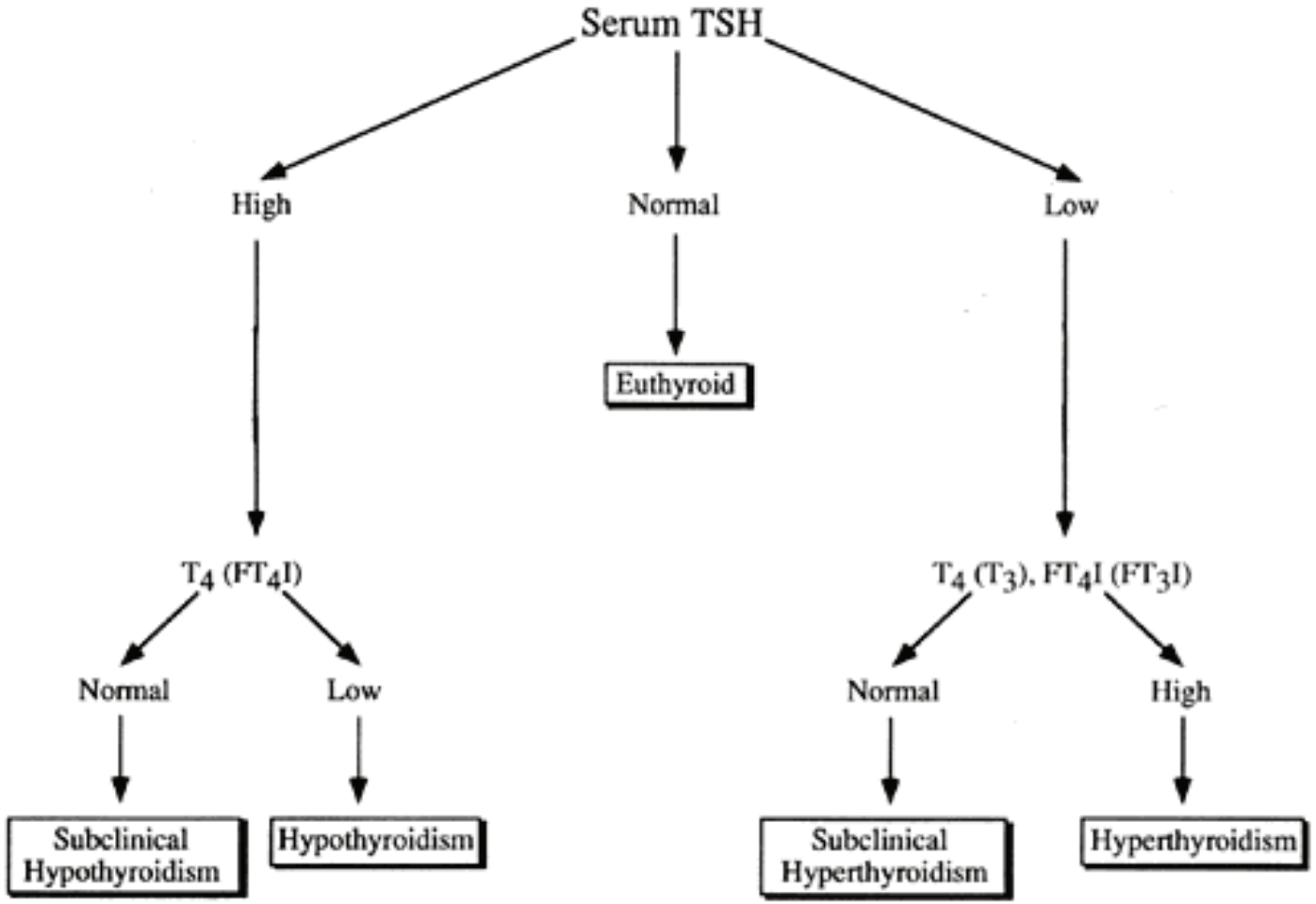
HYPERTHYROIDISM



‘‘Thyrotoxicosis’’ or ‘‘Hyperthyroidism’’

- ‘‘**Thyrotoxicosis**’’ refers to
  - a clinical state that results from *inappropriately high thyroid hormone action in tissues* generally due to inappropriately high tissue thyroid hormone levels.

- ‘‘**Hyperthyroidism**’’
  - is a form of thyrotoxicosis due to *inappropriately high synthesis and secretion of thyroid hormone(s) by the thyroid.*


Serum TSH
High
Normal
Low
Euthyroid
T4 (FT4I)
T4 (T3), FT4I (FT3I)
Normal
Low
Normal
High
Subclinical Hypothyroidism
Hypothyroidism
Subclinical Hyperthyroidism
Hyperthyroidism


Thyroid Function Tests

Scenario – 1 (Continued)

Test	Result	Ref. value
TSH	0.005	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	35	12-22 pmol/L
TT3	5.6	1.2- 3.4 nmol/L

Diagnosis:

Thyrotoxicosis

Cause ???

Table 1. Causes of Thyrotoxicosis

Thyrotoxicosis associated with a normal or elevated radioactive iodine (RAI) uptake over the neck[a]
▪ GD ▪ TA or TMNG ▪ Trophoblastic disease ▪ Thyroid-stimulating hormone (TSH)-producing pituitary adenomas ▪ Resistance to thyroid hormone (T_3 receptor β mutation [THRB])[b]
Thyrotoxicosis associated with a near-absent RAI uptake over the neck
▪ Painless (silent) thyroiditis ▪ Amiodarone-induced thyroiditis ▪ Subacute (granulomatous, de Quervain's) thyroiditis ▪ Palpation thyroiditis ▪ Iatrogenic thyrotoxicosis ▪ Factitious ingestion of thyroid hormone ▪ Struma ovarii ▪ Acute thyroiditis ▪ Extensive metastases from follicular thyroid cancer

[a] In iodine-induced or iodine-exposed hyperthyroidism (including amiodarone type 1), the uptake may be low.

[b] Patients are not uniformly clinically hyperthyroid.

Table 1. Causes of Thyrotoxicosis

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[a] In iodine-induced or iodine-exposed hyperthyroidism (including amiodarone type 1), the uptake may be low.

[b] Patients are not uniformly clinically hyperthyroid.

- the most common causes
  - ✓ Graves' disease (GD),
  - ✓ toxic multinodular goiter (TMNG),
  - ✓ toxic adenoma (TA)

To find out the etiology of thyrotoxicosis

- TRAb,
- ^{123}I or ^{99m}Tc pertechnetate uptake scan (when clinically suggests TA or TMNG)
- thyroidal blood flow on USG.

Scenario – 1 (Continued)

Test	Result	Ref. value
Anti-TSHR (TRAb)	3.80	<= 1.75 IU/L

Diagnosis:

Grave's Disease

Treatment ???

Symptomatic management (Beta-adrenergic blockade)

- recommended in all with symptomatic thyrotoxicosis, especially
  - ✓Elderly
  - ✓Resting HR > 90/minute or
  - ✓Coexistent cardiovascular disease.

Table 2. Beta-Adrenergic Receptor Blockade in the Treatment of Thyrotoxicosis

Drug	Dosage	Frequency	Considerations
Propanolol[a]	10–40 mg	*tid – qid*	• Nonselective β-adrenergic receptor blockade • Longest experience • May block T_4 to T_3 conversion at high doses
Atenolol	25–100 mg	*qd* or *bid*	• Relative β-1 selectivity • Increased compliance • Avoid during pregnancy
Metoprolol[b]	25–50 mg	*bid – tid*	• Relative β-1 selectivity
Nadolol	40–160 mg	*qd*	• Nonselective β-adrenergic receptor blockade • Once daily • Least experience to date • May block T_4 to T_3 conversion at high doses
Esmolol	IV pump 50–100 μg/kg/min		• In intensive care unit setting of severe thyrotoxicosis or storm

Quiescent asthma ,

Mild COPD or

Symptomatic Raynaud's

✓a relative β-1 selective agent cautiously

Not tolerate or

Severe asthma

✓CCB

(verapamil or diltiazem)

Table 3. Clinical Situations That Favor a Particular Modality as Treatment for Graves' Hyperthyroidism

Clinical situations	RAI	ATD	Surgery
Pregnancy[a]	X	P !	A !
Comorbities w/ increased surgical risk and/or limited life expectancy	P	A	X
Inactive Graves' orbitopathy (GO)	A	A	A
Active GO	[b]	P	P
Liver disease	P	!	A
Major adverse reactions to ATDs	P	X	A
Patients with previously operated or externally irradiated necks	P	A	!
Lack of access to a high-volume thyroid surgeon	P	A	!
Patients with high likelihood of remission (especially women, with mild disease, small goiters, and negative or low-titer thyrotropin receptor antibodies [TRAb])	A	P	A
Patients with periodic paralysis	P	A	P
Patients with right pulmonary hypertension, or congestive heart failure	P	A	!
Elderly with comorbidities	A	A	!
Thyroid malignancy confirmed or suspected	X	–	P
Large thyroid nodule (s)	–	A	P
Coexisting primary hyperparathyroidism requiring surgery	–	–	P

P, preferred therapy; **A**, acceptable therapy; **!**, cautious use; **–**, not first line therapy but may be acceptable depending on the clinical circumstances; **X**, contraindication.

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Choice of ATD and regimen and starting dose

- MMI in virtually every patient who chooses ATD for GD, except
  - ❑ first trimester of pregnancy
  - ❑ thyroid storm
  - ❑ minor reactions to MMI who refuse RAI or surgery
- Benefit of OD administration and reduced major S/E
- Higher doses ATD continuously + L-thyroxine in doses to maintain euthyroid levels (so-called block and replace therapy)
  - ❑ Not generally recommended because of higher S/E.
- Potassium iodide (38 mg of KI) as a beneficial adjunct to ATD therapy

Choice of ATD and regimen and starting dose

- 10 mg of carbimazole is metabolized to approximately 6 mg of MMI
- Rough guide to initial MMI daily dosing: If FT_4
  - ✓ 1–1.5 times ULN ⟶ 5–10 mg
  - ✓ 1.5–2 times ULN ⟶ 10–20 mg
  - ✓ 2–3 times ULN ⟶ 30–40 mg
- When rapid biochemical control needed, initial split dose of MMI
- PTU has shorter duration of action, starting with 50–150 mg TID, with maintenance dose of 50 mg BD/TID

Scenario – 1 (Continued)

- Carbimazole 30 mg OD started
- Propranolol 20 mg TID till FT4 normalized

Precaution ???

Follow up plan ???

Duration of treatment ???

Precaution afte
(Preferably, this

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- ✓
-

Table 3. Adverse events of antithyroid drugs

Common (1.0–5.0%)
- Skin rash
- Urticaria
- Arthralgia, polyarthritis
- Fever
- Transient mild leukopenia

Rare (0.2–1.0%)
- Gastrointestinal
- Abnormalities of taste and smell
- Agranulocytosis

Very rare (<0.1%)
- Aplastic anemia (PTU, CBZ)
- Thrombocytopenia (PTU, CBZ)
- Vasculitis, lupus-like, ANCA+ (PTU)
- Hepatitis (PTU)
- Hypoglycemia (anti-insulin Abs; PTU)
- Cholestatic jaundice (CBZ/MMI)

e,

Precaution after starting ATD

- **Minor cutaneous reactions** - concurrent antihistamine therapy without stopping the ATD.
- **Persistent symptomatic minor side effects** - cessation of the medication and changing to RAI or surgery or switching to the other ATD when RAI or surgery are not options.
- **Serious allergic reaction** - alternative drug is not recommended.

Follow up after ATD

- **MMI initial dose** 10–30 mg OD, titrated down to maintenance level
- FT4 and TT3, 2–6 weeks after initiation (TSH -suppressed several months)
- **Once euthyroid**,
  - ✓MMI decreased by 30%–50% , biochemical testing 4–6 weeks.
- **Once euthyroid with minimal dose** (5–10 mg daily),
  - ✓clinical and laboratory evaluation 2–3 monthly.
- **On long-term MMI** (>18 months),
  - ✓this interval can be increased to 6 months
  - ✓TRAb every 1–2 years, with consideration of MMI discontinuation

Follow up after ATD

- **12–18 months** (Remission 50–55%) , discontinued if TSH & TRAb normal
- **Relapse**
  - ✓most likely within 6–12 months but may occur years later
  - ✓severe hyperthyroidism, large goiters, persistent high TRAb
  - ✓followed closely for relapse in first year and then at least annually
  - ✓definitive treatment (RAI or thyroidectomy) or long-term low-dose MMI

Scenario – 1 (Continued)

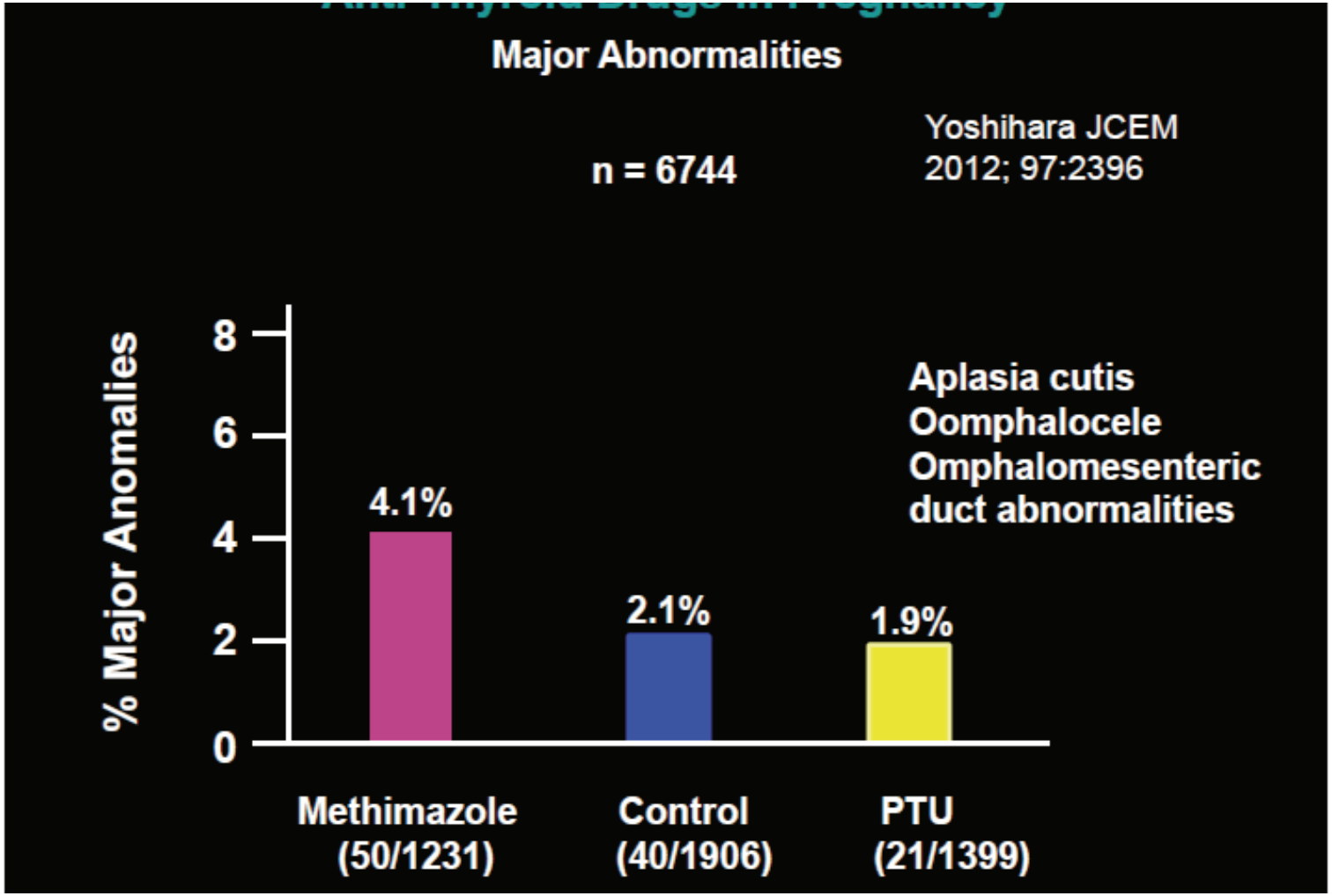
Test	Result	Ref. value
TSH	12	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	4.5	12-22 pmol/L
TT3	0.8	1.2- 3.4 nmol/L

- Missed follow up but continue same dose of Carbimazole
- Come back after 3 months with the TFT result.
- What will you do next?

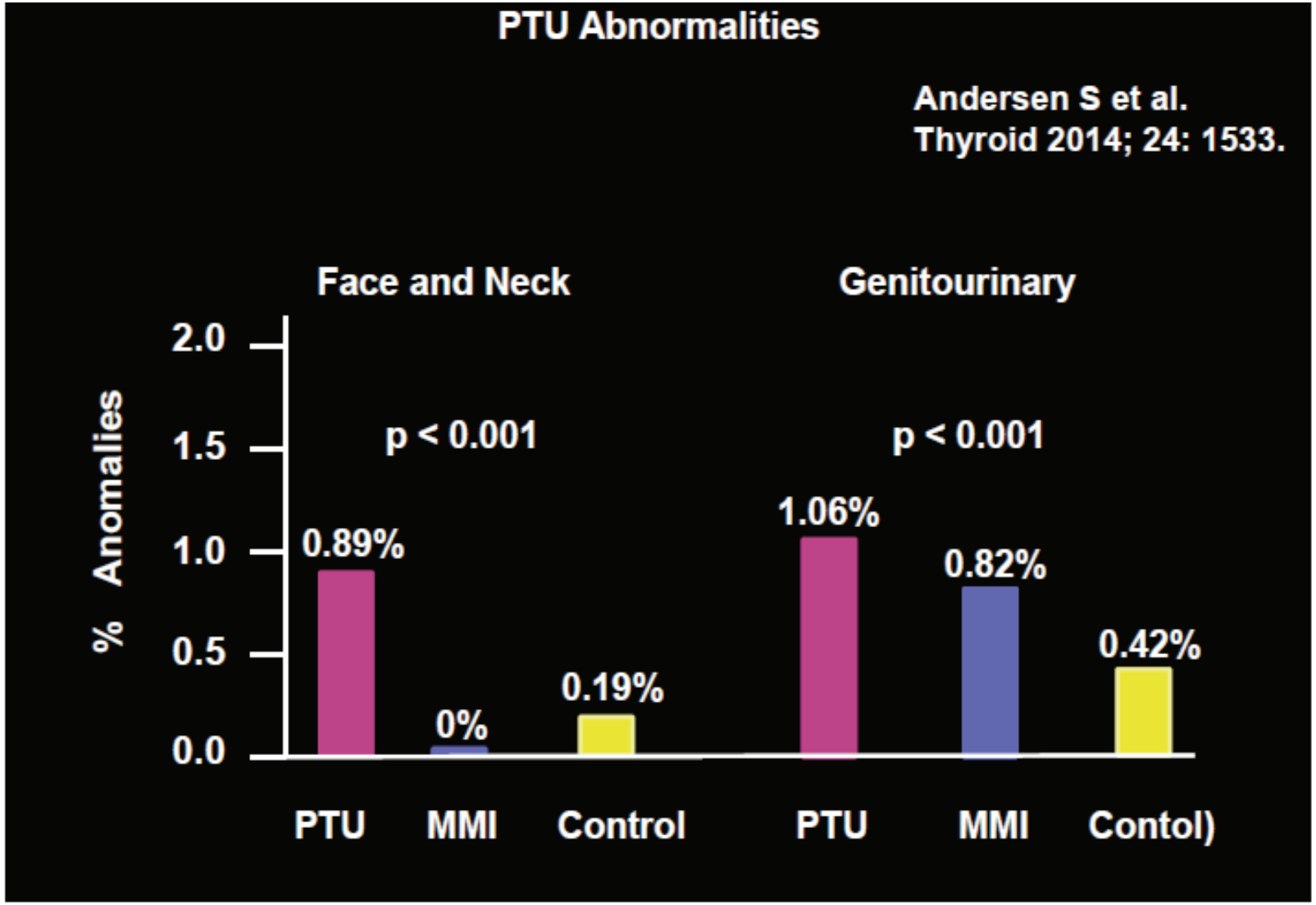
Scenario – 1 (Continued)

Test	Result	Ref. value
TSH	0.05	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	44	12-22 pmol/L

- Missed the follow up again, failed to resume Carbimazole
- Come back after 2 months with the TFT result.
- Recently tested positive for UCG. LMP 2 months ago.
- What will you do next?



ATD in pregnancy



PTU in pregnancy

MMI

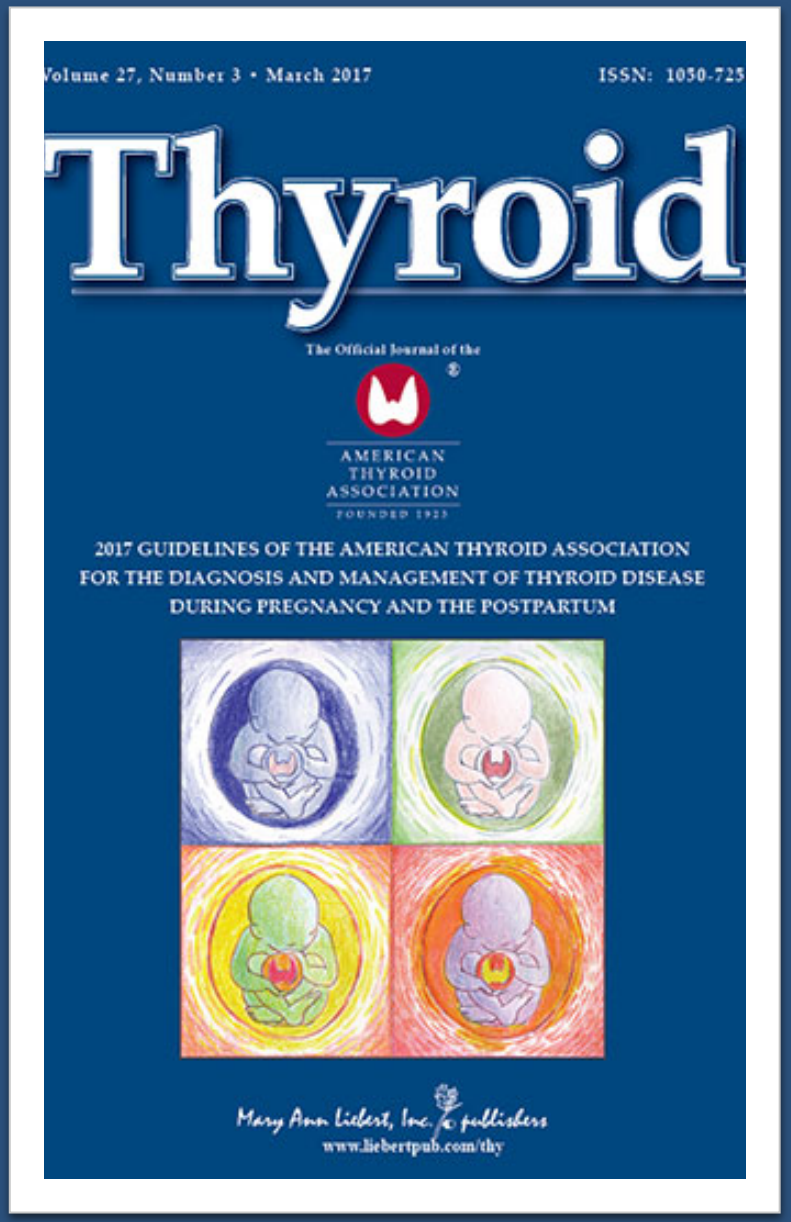
- aplasia cutis,
- choanal atresia, esophageal and other types of gut atresias,
- abdominal wall abnormalities omphalocale, eye, heart, and urinary tract malformations

PTU

- these defects tended to be less severe than with MMI
- included preauricular sinuses and cysts and urinary tract abnormalities

- 2–4% of children who have been exposed to MMI develop birth defect
- The prevalence of birth defects is the same with PTU, but the spectrum of defects is less severe, primarily consisting of face and neck cysts and urinary tract abnormalities in males

highest risk for birth defects from ATDs is gestational weeks 6-10



Continue antithyroid medication

- ***Factors predicting high clinical risk***
  1. currently hyperthyroid, or
  2. requirement of > 5-10 mg/day MMI or > 100-200 mg/day PTU

In such cases: continue ATD with lowest effective dose

a. PTU through 16 weeks of pregnancy.

b. switched to PTU as early as possible

c. When switching ,dose ratio of ~ 1:20 (e.g., MMI 10 mg daily = PTU 100 mg twice daily).

d. Block and replace Rx should not be used, except in the rare situation of isolated fetal hyperthyroidism.

Thyroidectomy

Indication for surgery (optimal time – 2nd trimester)

- allergies/ contraindications to both ATDs,
- Not compliant with drug,
- Euthyroidism cannot be achieved even on large doses of ATDs

- If maternal TRAb high (> 3x upper reference)
  - ➢Carefully monitored for fetal hyperthyroidism throughout pregnancy, even if the mother is euthyroid post-thyroidectomy.

Scenario – 1 (Continued)

- PTU 100 mg TID started with plan to change to MMI after first trimester
- Propranolol 20 mg TID till FT4 normalized

Follow up plan ???

Monitoring

a. If treated with ATD in pregnancy,
   - ✓FT4/TT4 and TSH every 4 weeks.
   - ✓targeting maternal serum FT4/TT4 at or moderately above the reference range.

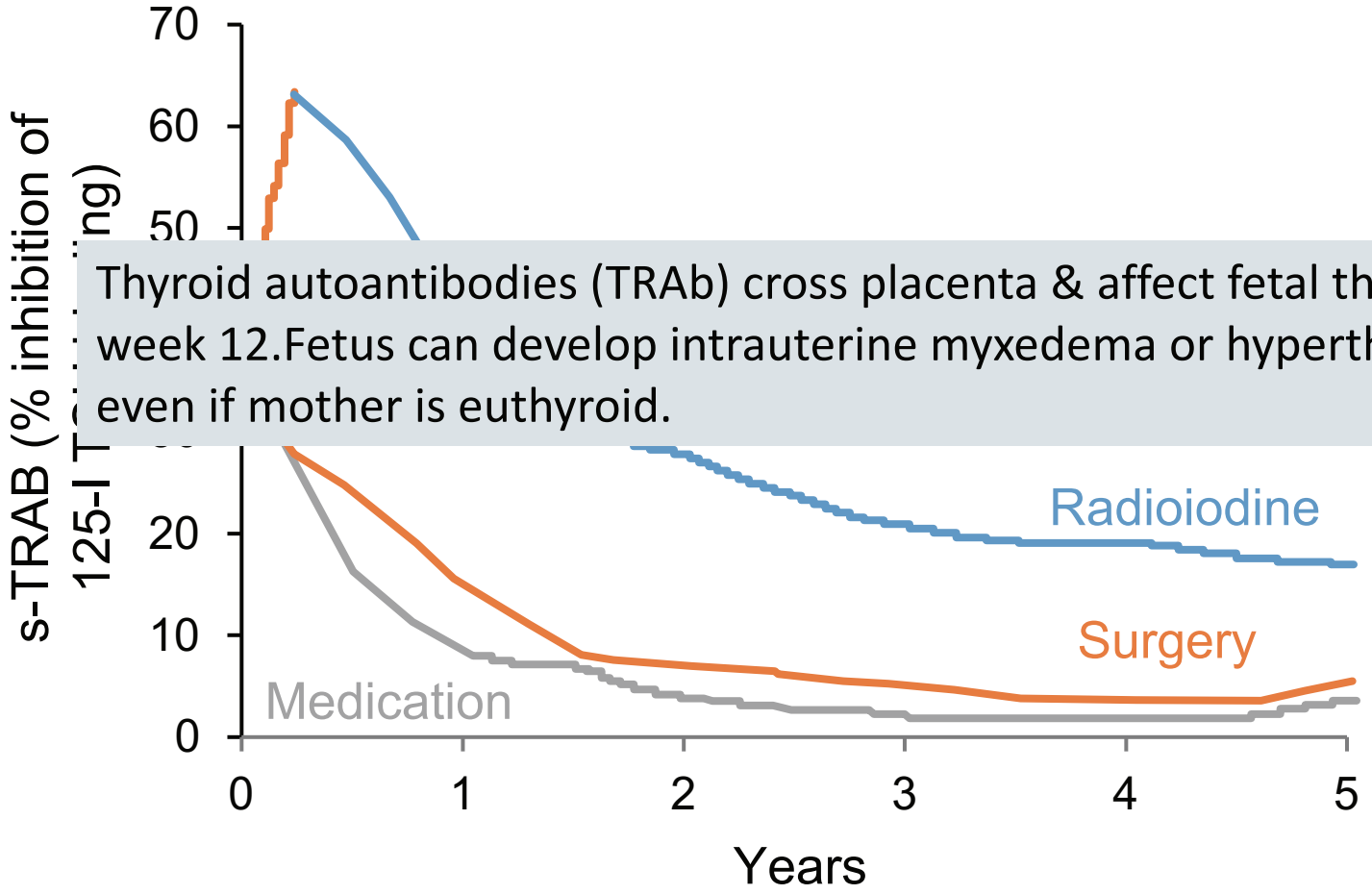
b. Determination of TRAb

c. If the maternal TSH-R-Ab concentration remains >3 times the cut-off,
   - ✓monitoring of the fetus for thyroid dysfunction throughout pregnancy is recommended

Determination of TRAb

- ***Prior GD treated with RAI/thyroidectomy***
  - ➢TRAb during the first trimester
    - ✓if elevated, again at 18–22 weeks
- ***Patients on ATD for GD when becoming pregnant or found GD during pregnancy***
  - ➢TRAb at initial pregnancy visit or at diagnosis
    - ✓if elevated, again at 18–22 weeks
- ***Patients with elevated TRAb levels at 18–22 weeks***
  - ✓TRAb at weeks 30–34 to guide decisions regarding neonatal monitoring.
  - ✓An exception is a woman with an intact thyroid who is no longer in need of ATD therapy.

TSH Receptor Antibodies (TRAb) After Various Types of Treatment for Graves' Disease



Thyroid autoantibodies (TRAb) cross placenta & affect fetal thyroid after week 12.Fetus can develop intrauterine myxedema or hyperthyroidism even if mother is euthyroid.

Scenario – 1 (Continued)

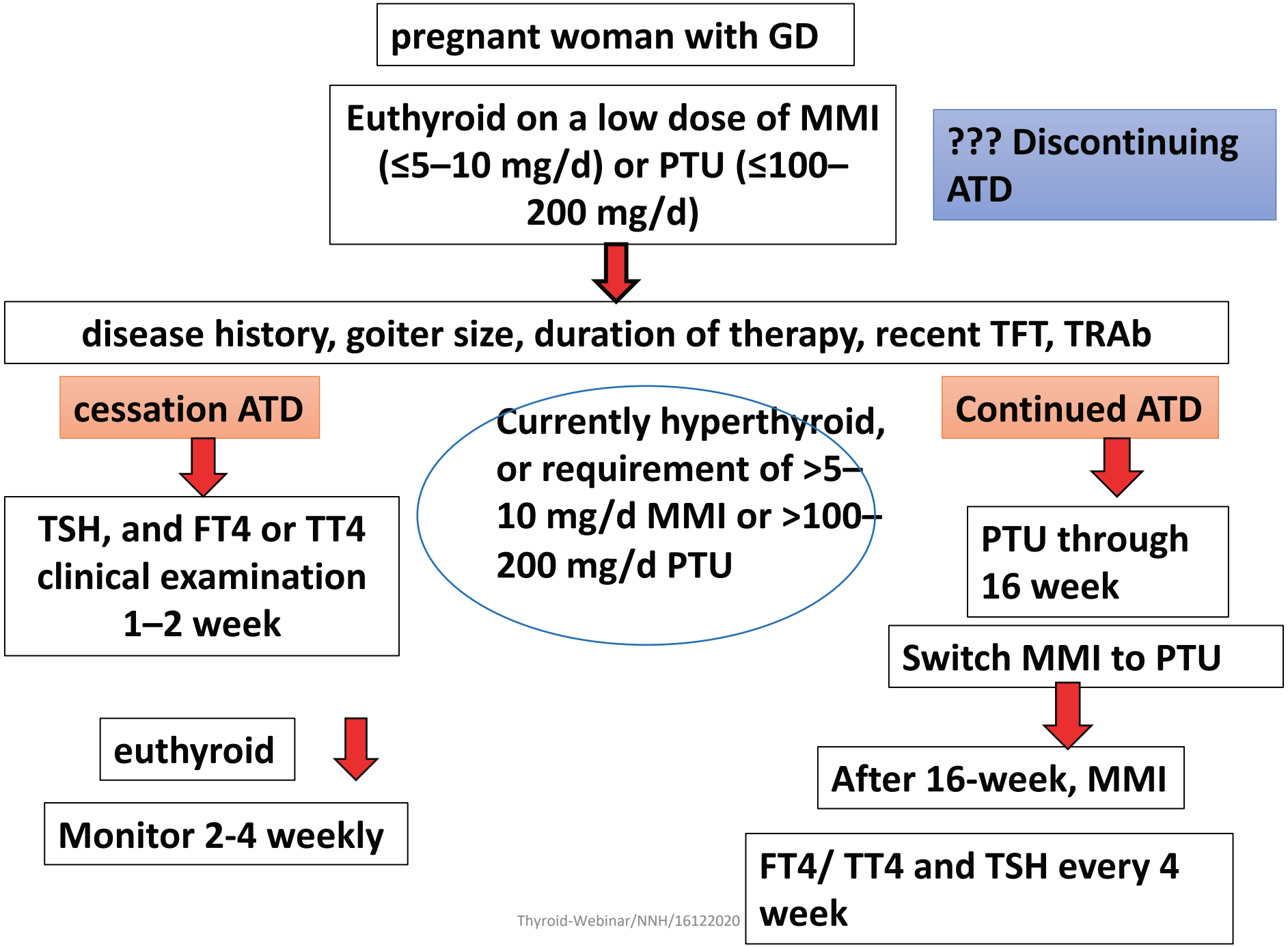
Gestation	Test	Result	Ref. value
10 weeks	Anti-TSHR (TRAb)	3. 5	<= 1.75 IU/L
21 weeks		2.8	
34 weeks		2.5	

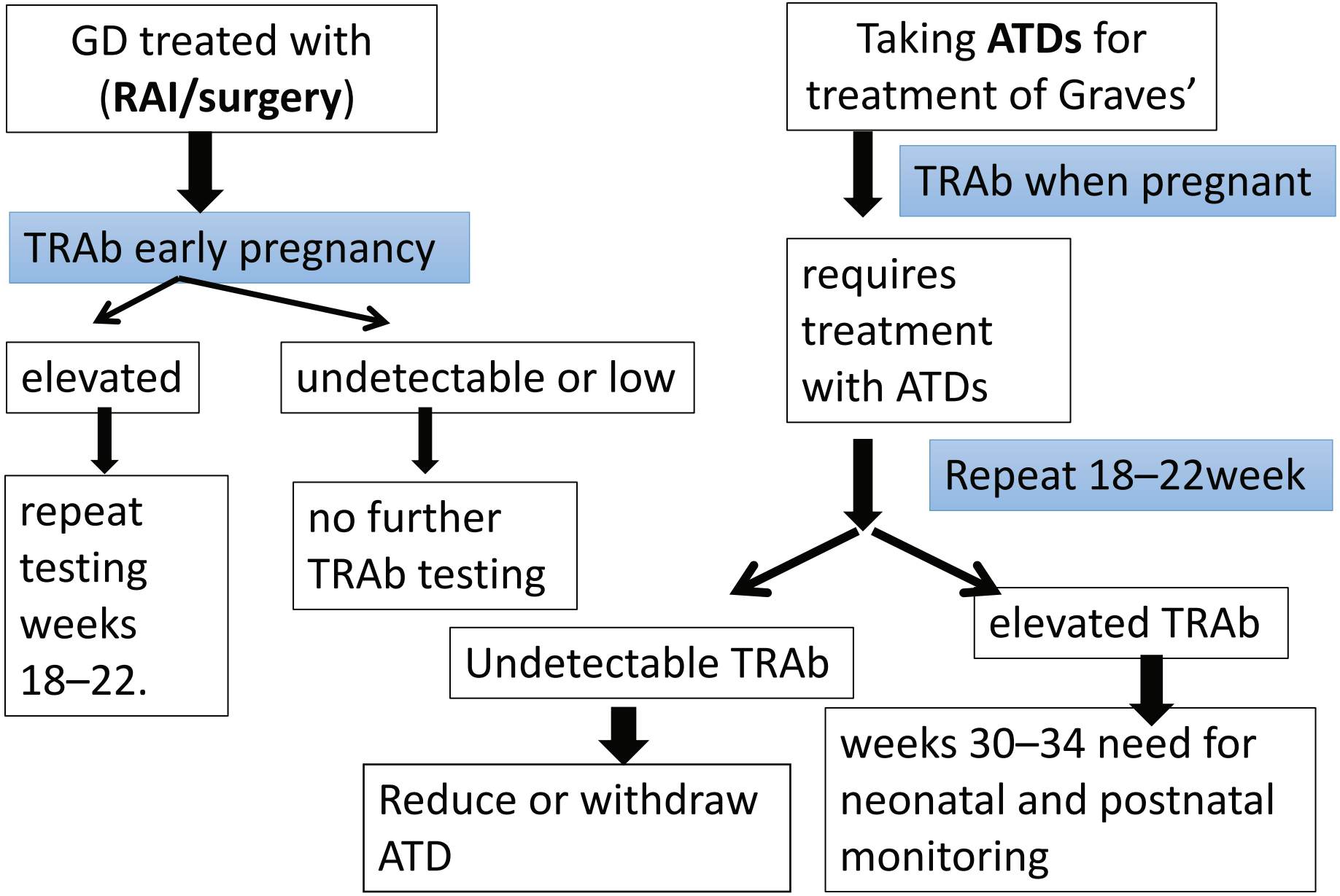
Deliver the baby at term

Postpartum Treatment ???

Postpartum phase

- GD recurrence was highest 7–9 months postpartum (RR 3.8) in studies in Denmark and Japan .
- Same treatments in lactating & non-lactating.
- Only small amounts of ATD enter breast milk, & Low doses of PTU (<250 mg) & MMI (<20 mg) safe for mother and child.
- MMI is recommended during lactation, with concerns about PTU-mediated hepatotoxicity.
- ATD should be taken after having breastfed and in divided doses


pregnant woman with GD
Euthyroid on a low dose of MMI (≤5–10 mg/d) or PTU (≤100–200 mg/d)
??? Discontinuing ATD
disease history, goiter size, duration of therapy, recent TFT, TRAb
cessation ATD
TSH, and FT4 or TT4
clinical examination
1–2 week
euthyroid
Monitor 2-4 weekly
Currently hyperthyroid, or requirement of >5–10 mg/d MMI or >100–200 mg/d PTU
Continued ATD
PTU through 16 week
Switch MMI to PTU
After 16-week, MMI
FT4/ TT4 and TSH every 4 week


GD treated with (**RAI/surgery**)
TRAb early pregnancy
elevated
undetectable or low
repeat testing weeks 18–22.
no further TRAb testing
Taking **ATDs** for treatment of Graves'
TRAb when pregnant
requires treatment with ATDs
Repeat 18–22week
Undetectable TRAb
elevated TRAb
Reduce or withdraw ATD
weeks 30–34 need for neonatal and postnatal monitoring

Scenario – 1 (Continued)

Test	Result	Ref. value
TSH	<0.005	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	99	12-22 pmol/L
TT3	9.6	1.2- 3.4 nmol/L
TRAb	7.5 IU/L	<= 1.75 IU/L

- ***Loss follow up after delivery of baby, stop ATD and admitted urgently after 6 months***
- **C/O**
  - High fever with cough * 4 days
  - Aggressive * 1 day
- **O/E**
  - T' 104 F, Agitated
  - Tremor of outstretched hands
  - HR – 140/min

Thyroid storm (Life-threatening thyrotoxicosis)

- Rare disorder characterized by multisystem involvement
- Mortality rates in the range of 8%–25% in modern series
- Dx made clinically in severely thyrotoxic patient + systemic decompensation.
- Require aggressive therapy
  - ✓Burch–Wartofsky Point Scale (BWPS) of ≥ 45 or
  - ✓Japanese Thyroid Association (JTA) categories of thyroid storm 1 (TS1) or thyroid storm 2 (TS2) with evidence of systemic decompensation
- BWPS of 25–44
  - ✓The decision to use aggressive therapy based on clinical judgment.

Table 4. Point Scale for the Diagnosis of Thyroid Storm

Criteria	Points
Thermoregulatory dysfunction	
Temperature °F (°C)	
99.0–99.9 (37.2–37.7)	5
100.0–100.9 (37.8–38.3)	10
101.0–101.9 (38.3–38.8)	15
102.0–102.9 (38.9–39.4)	20
103.0–103.9 (39.4–39.9)	25
≥ 104.0 (>40)	30
Cardiovascular	
Tachycardia (beats per minute)	
100–109	5
110–119	10
120–129	15
130–139	20
≥ 140	25
Atrial fibrillation	
Absent	0
Present	10

Criteria	Points
Gastrointestinal-hepatic dysfunction	
Manifestation	
Absent	0
Moderate (diarrhea, abdominal pain, nausea/vomiting)	10
Severe (jaundice)	20
Central nervous system disturbance	
Manifestation	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, extreme lethargy)	20
Severe (seizure, coma)	30

Burch–Wartofsky Point Scale (BWPS)

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Congestive heart failure	
Absent	0
Mild	5
Moderate	10
Severe	20

Precipitant history	
Status	
Positive	10
Negative	0

Scores Totaled	
>45	Thyroid storm
25–44	Impending storm
<25	Storm unlikely

Burch and Wartofsky, *Endocrinol Metab Clin North Am.* 1993;22:263-277. Printed with permission.

TABLE 9. FINAL CRITERIA FOR THE DIAGNOSIS OF THYROID STORM

Grade of TS	*Combinations of features*	*Requirements for diagnosis*
TS1	First combination	Thyrotoxicosis and at least one CNS manifestation and **one of the following: fever, tachycardia, CHF, or GI/hepatic manifestations**
TS1	Alternate combination	Thyrotoxicosis and at least three combinations of fever, or tachycardia, or CHF, or GI/hepatic manifestations
TS2	First combination	Thyrotoxicosis and a combination of two of the following: fever or tachycardia or CHF or GI/hepatic manifestations
TS2	Alternate combination	Patients who meet the diagnostic criteria for TS1 except that serum FT3 or FT4 values are not available but whose data before or after the episode suggest that they are thyrotoxic at the time of TS.

Definitions

Thyrotoxicosis: Elevated FT3 or FT4.

CNS manifestations: Restlessness, delirium, mental aberration/psychosis, somnolence/lethargy, convulsion, coma including a score of 1 or higher on the Japan Coma Scale (JCS) or 14 or lower on the Glasgow Coma Scale (GCS).

Fever: 38°C or higher.

Tachycardia: ≥130 beats/min (arrhythmias such as atrial fibrillation are evaluated by measuring the heart rate).

CHF: The patient presents with severe symptoms such as pulmonary edema, moist rales for more than half the lung field, or cardiogenic shock. The patient's CHF is categorized as Class IV by the NYHA classification or Class III or higher by the Killip classification.

GI/hepatic manifestations: The patient presents with nausea, vomiting, diarrhea, or a bilirubin of >3 mg/dL.

Exclusions and Provisos

Cases are excluded if other underlying diseases are clearly causing any of the following symptoms: fever (e.g., pneumonia and malignant hyperthermia), impaired consciousness (e.g., psychiatric disorders and cerebrovascular disorders), heart failure (e.g., acute myocardial infarction), and liver disorders (e.g., viral hepatitis and acute liver failure). However, some of these disorders trigger thyroid storm. Therefore, it is difficult to determine whether the symptom is caused by thyroid storm or is simply a symptom of an underlying disease that is possibly triggered by thyroid storm; the symptom should be regarded as being due to a thyroid storm that is caused by these precipitating factors. Clinical judgment in this matter is required.

Table 5. Thyroid Storm: Drugs and Doses

Drug	Dosage	Comment
Propylthiouracil[a]	500–1000 mg load, then 250 mg every 4 hours	▪ Blocks new hormone synthesis ▪ Blocks T_4-to-T_3 conversion
Methimazole	60–80 mg/day	▪ Blocks new hormone synthesis
Propranolol	60–80 mg every 4 hours	▪ Consider invasive monitoring in congestive heart failure patients ▪ Blocks T_4-to-T_3 conversion in high doses ▪ Alternate drug: esmolol infusion
Iodine (saturated solution of potassium iodide)	5 drops (0.25 mL or 250 mg) orally every 6 hours	▪ Do not start until 1 hour after antithyroid drugs ▪ Blocks new hormone synthesis ▪ Blocks thyroid hormone release ▪ Alternative drug: Lugol's solution
Hydrocortisone	300 mg intravenous load, then 100 mg every 8 hours	▪ May block T_4-to-T_3 conversion ▪ Prophylaxis against relative adrenal insufficiency ▪ Alternative drug: dexamethasone

[a] May be given intravenously.

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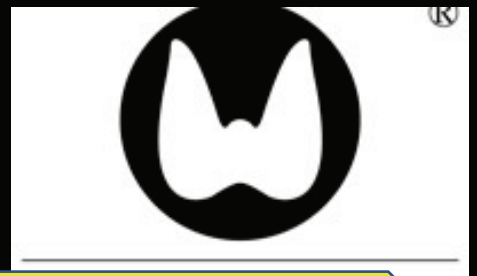


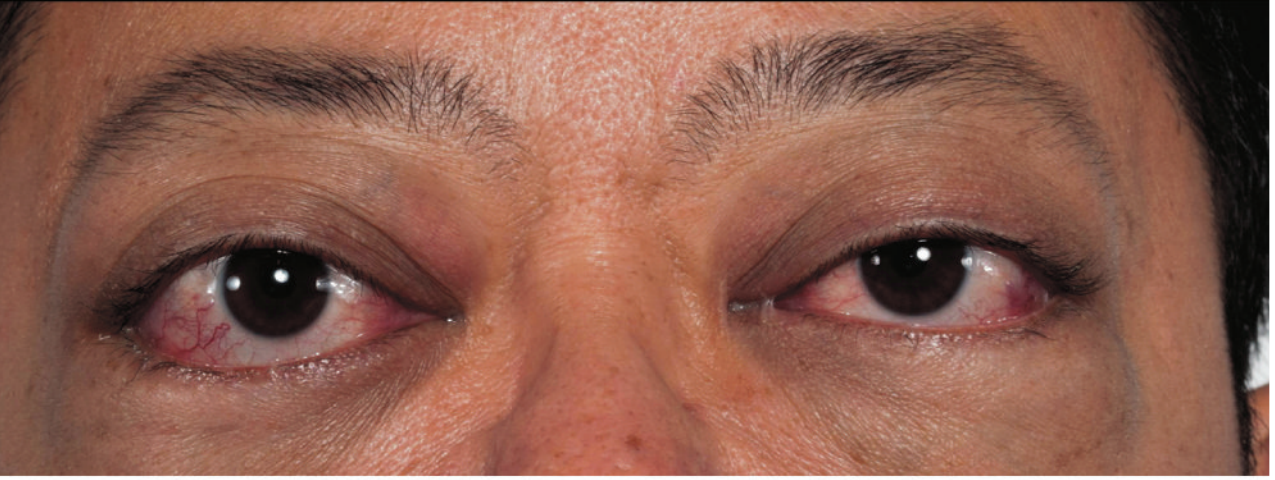
- A multimodality treatment approach
- cooling with acetaminophen and cooling blankets,
- volume resuscitation, nutritional support, and respiratory care
- monitoring in an intensive care unit

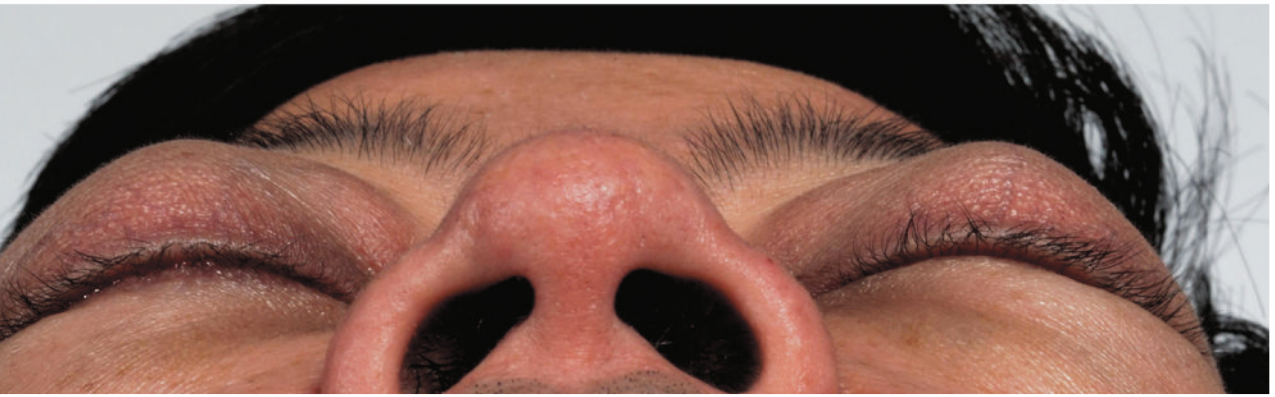
Scenario – 1 (Continued)

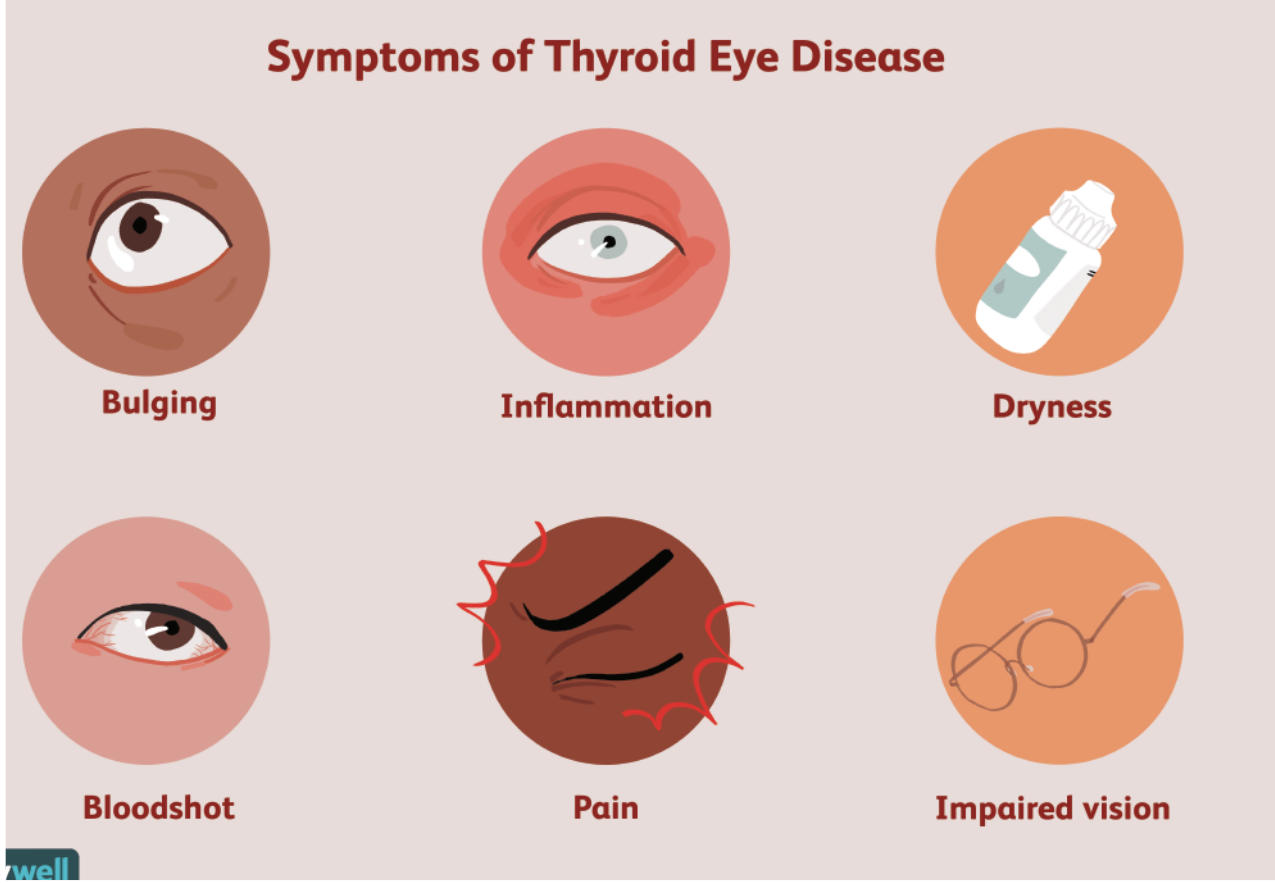
- Discharged with ATD and plan for definitive therapy once TFT normalized.
- Total thyroidectomy
- Now stable with Thyroxine 100 mcg OD, with reinforcement for drug compliance.

Scenario - 2

- ***48-year-old gentleman***
- **C/O**
  - Palpitation * 1 month
  - Shaky hands
  - Red eyes
- **O/E**
  - Diffuse Thyroid swelling
  - Tremor of outstretched hands
  - Tachycardia
  - Exopthalmos







Grave's Opthalmopathy (GO)

Scenario – 2 (Continued)

Test	Result	Ref. value
TSH	<0.005	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	75	12-22 pmol/L
TT3	8.6	1.2- 3.4 nmol/L
TRAb	9.5 IU/L	<= 1.75 IU/L

Diagnosis:

Grave's disease with GO

Treatment ???

Table 9. Risk Factors for Graves' Orbitopathy

Risk factor	Amenable to intervention	Comments
Age	No	Advanced age – risk for more severe GO.
Sex	No	GO is more frequent in women (as GD is); more severe in men.
Genetics/ Ancestry	No	Highest prevalence of GO in Caucasians, lowest in Asians. Immunomodulatory genes likely involved.
Mechanical factors	No	Noted wider lateral wall orbital angle in GO.
TSH receptor antibody	No[a]	Predicts GO risk and GO therapy response.
Smoking	Yes	Increases GO progression and decreases therapy efficacy. Smoking-cessation clinics favored for intervention.
Thyroid dysfunction	Yes	Need for expeditious control of hyperthyroidism then prevention of hypothyroidism post GD therapy.
RAI therapy	Yes	Risk is additive to smoking; increased with preexistent and active GO; preventable by glucocorticoids 6–12 weeks post RAI.

[a] Decreased TRAb noted with methimazole therapy yet available data is unable to separate that change from the natural history of GO with improving TRAb.

Table 6. Assessment of GO: Clinical Activity Score Elements

Elements[a]	Each visit	Comparison with previous visit	Score
Painful feeling behind the globe over last 4 weeks	X		1
Pain with eye movement during last 4 weeks	X		1
Redness of the eyelids	X		1
Redness of the conjunctiva	X		1
Swelling of the eyelids	X		1
Chemosis (edema of the conjunctiva)	X		1
Swollen caruncle (flesh body at medial angle of eye)	X		1
Increase in proptosis ≥2 mm		X	1
Decreased eye movements ≥5° any direction		X	1
Decreased visual acuity ≥1 line on Snellen chart		X	1

[a] A 7-point scale (excluding the last three elements) is used when no previous assessment is available. GO is considered active in patients with a CAS ≥3.

Sources: Adapted from Mourits et al. *Br J Ophthalmol*. 1989;73:639-644. and Mourits et al. *Clin Endocrinol. (Oxf)*1997;47:9-14.

Table 7. GO Severity Assessment

Grade[a]	Lid retraction	Soft tissues	Proptosis[b]	Diplopia	Corneal exposure	Optic nerve status
Mild	<2 mm	Mild involvement	<3 mm	Transient or absent	Absent	Normal
Moderate	≥2mm	Moderate involvement	≥3mm	Inconstant	Mild	Normal
Severe	≥2mm	Severe involvement	≥3mm	Constant	Mild	Normal
Sight threatening					Severe	Compression
Upper limits of normal						
African American		F/M = 23/24 mm				
White		F/M = 19/21 mm				
Asian		F/M = 16/17 mm (Thai) or 18.6 mm (Chinese)				

[a] **Mild GO:** patients whose features of GO have only a minor impact on daily life, generally insufficient to justify immunosuppressive or surgical treatment.
Moderate-to-severe GO: patients without sight-threatening GO whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive).
Sight-threatening GO: patients with dysthyroid optic neuropathy and/or corneal breakdown. This category warrants immediate intervention.

[b] Proptosis refers to the variation compared to the upper limit of normal for each race/sex or the patient's baseline, if available.

Sources: Adapted from de Juan et al. Arch Intern Med. 1980;140:1230-1231, Sarinnapakorn et al. *J Med Assoc. Thai* 2007;90:679-683, Tsai et al. Eye (Lond) 2006;20:569-573 and Bartalena et al. *Thyroid* 2008;18:333-346.

Table 8. Use of Oral Glucocorticoids for Prevention of Graves' Orbitopathy Development or Progression When Radioactive Iodine is Used to Treat Graves' Hyperthyroidism[a]

	Recommendation	RAI without glucocorticoids	RAI with oral glucocorticoids
No GO (nonsmoker)	39	Recommend	Recommend against
No GO (smoker)	41	Insufficient data to recommend for or against	
GO present-active and mild (risk factors absent)	43	Acceptable[b]	Acceptable[b]
GO present-active and mild (risk factors present)	44	Recommend against	Recommend
GO present-active and moderate-to-severe or sight-threatening	45	Recommend against	Recommend against
GO present-inactive	46	Recommend	Recommend against

[a] ATDs or thyroidectomy are also recommended treatment options in each of these scenarios, and they are the preferred choice of therapy in patients with active and moderate-to-severe or sight-threatening GO.

[b] The decision regarding use of concurrent glucocorticoids should be made in light of the

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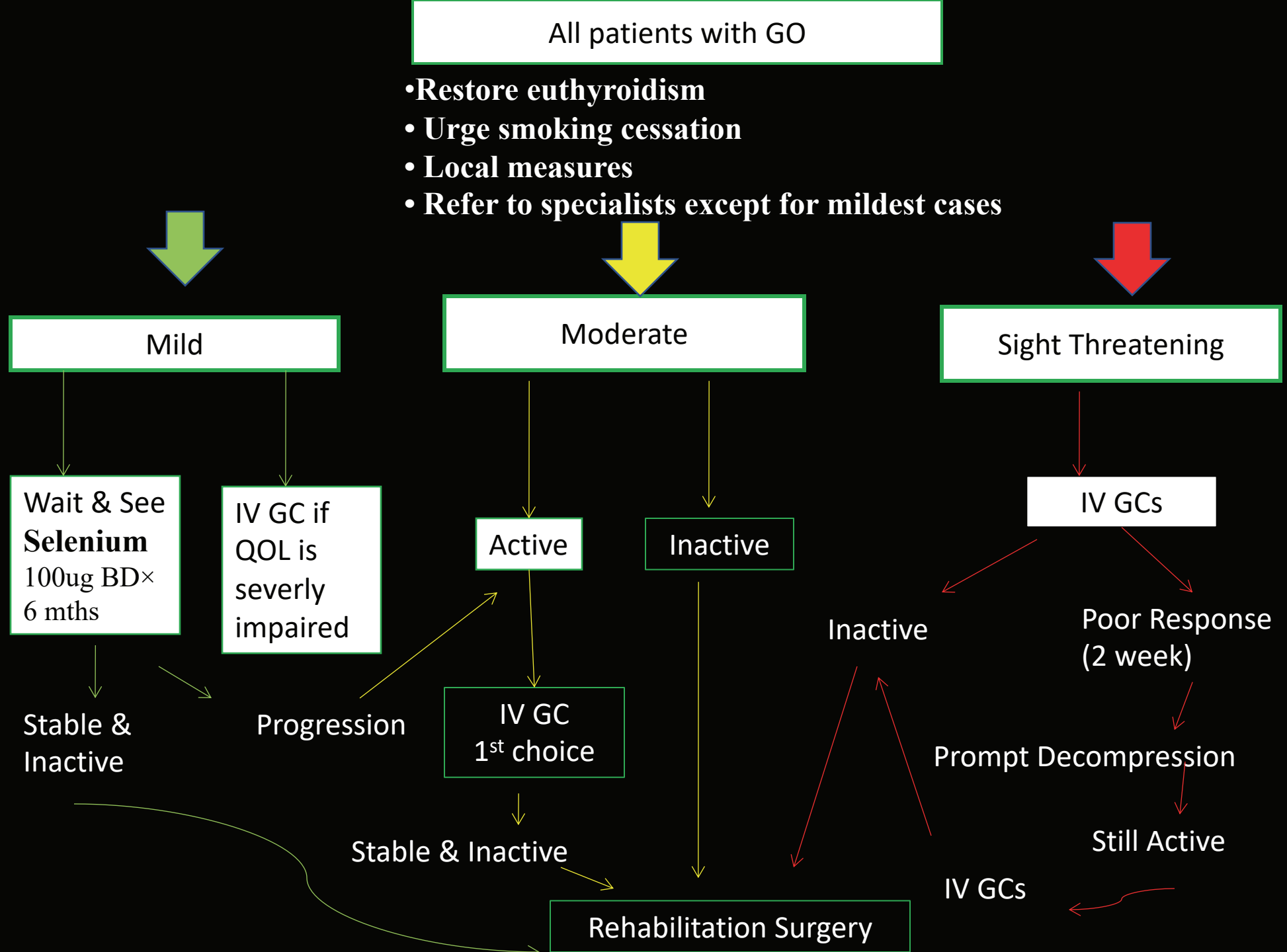
[b] The decision regarding use of concurrent glucocorticoids should be made in light of the

- Euthyroidism should be expeditiously achieved and maintained in hyperthyroid patients with GO or risk factors for the development of orbitopathy.
- to stop firsthand and secondhand smoking


All patients with GO
•Restore euthyroidism
• Urge smoking cessation
• Local measures
• Refer to specialists except for mildest cases
Mild
Moderate
Sight Threatening
Wait & See
Selenium
100ug BD×
6 mths
IV GC if
QOL is
severly
impaired
Active
Inactive
IV GCs
Inactive
Poor Response
(2 week)
Stable &
Inactive
Progression
IV GC
1st choice
Prompt Decompression
Still Active
Stable & Inactive
IV GCs
Rehabilitation Surgery

Scenario – 2 (Continued)

- Carbimazole 20 mg BD started
- Propranolol 40 mg TID till FT4 normalized
- Quit smoking
- Local measures

Clinical Activity Score – 3

(Active and mild GO)

Scenario - 3

- ***65-year-old lady***
- **C/O**
  - Palpitation * 1 month
  - Shaky hands
- **O/E**
  - MNG
  - Tremor of outstretched hands
  - Tachycardia

Scenario – 3 (Continued)

Test	Result	Ref. value
TSH	0.05	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	30	12-22 pmol/L
TT3	3.9	1.2- 3.4 nmol/L

Diagnosis:

? TMN

How will you confirm the Dx and manage ???

Toxic Multinodular Goiter

- Thyroid gland has a diffuse or focal nodular enlargement
- Nodules grow and begin to autonomously produce excess amounts of thyroid hormones
- Occurs in equal frequency in men and women and generally over the age of 40 years
- Nodules are benign adenomas and do not increase the risk of thyroid cancer
- Patients have symptoms of hyperthyroidism
- Diagnosis: History; Thyroid examination revealing a nodular thyroid; & Lab showing high T3/T4 and low TSH
- Confirmation: Radionuclide scanning of thyroid shows areas of increased uptake that correlate to overactive or "hot" nodules, as well as areas of absent uptake that correspond to suppressed normal thyroid tissue

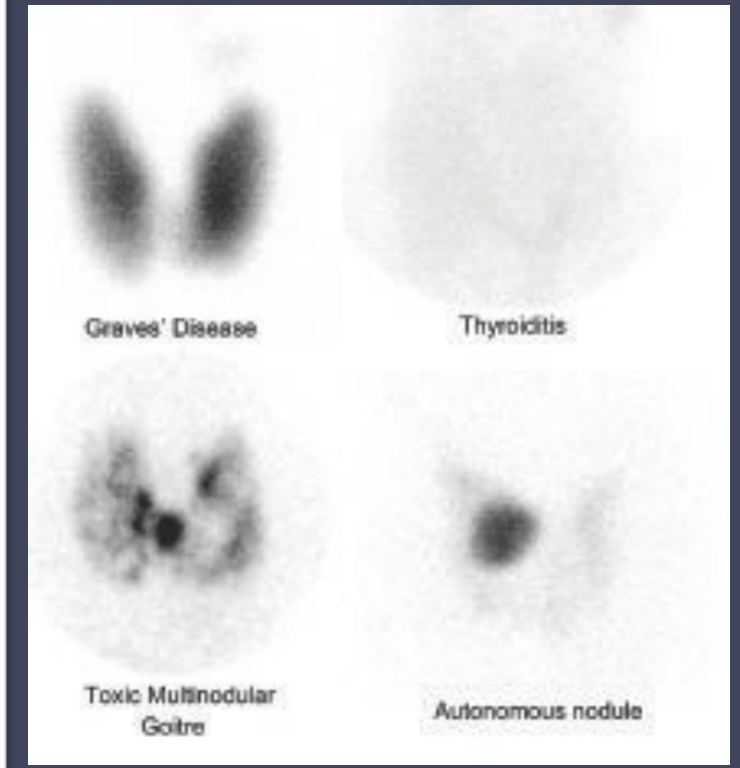


Table 10. Clinical Situations That Favor a Particular Modality as Treatment for TMNG or TA

Clinical situations	RAI	ATD	Surgery
Pregnancy[a]	X	P !	A !
Advanced age, comorbities w/ increased surgical risk and/or limited life expectancy	P	A	X
Patients with previously operated or externally irradiated necks	P	A	!
Lack of access to a high-volume thyroid surgeon	P	A	!
Symptoms or signs of compression within the neck	A	–	P
Thyroid malignancy confirmed or suspected	X	–	P
Large goiter / nodule	A	–	P
Goiter/nodule with substernal or retrosternal extension	A	–	P
Coexisting hyperparathyroidism requiring surgery	–	–	P

P, preferred therapy; **A**, acceptable therapy; **!**, cautious use; **–**, not first line therapy but may be acceptable depending on the clinical circumstances; **X**, contraindication.

[a] For women considering a pregnancy within 6 months, see discussion under Pregnancy.

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Patients with previously operated or externally irradiated necks	P	A	!
Lack of access to a high-volume thyroid surgeon	P	A	!
Symptoms or signs of compression within the neck	A	–	P
Thyroid malignancy confirmed or suspected	X	–	P

- Overtly TMNG or TA treated with ***RAI therapy*** or ***thyroidectomy***.
- On occasion, ***long-term, low-dose MMI*** may be appropriate.

RAI treatment of TMNG or TA

- Transient exacerbation of hyperthyroidism,
- Elderly & patients with comorbidities
  - ✓b-adrenergic blockade even in asymptomatic
  - ✓pretreatment with MMI (discontinued 2–3 days prior)
  - ✓resuming ATDs 3–7 days after RAI
- Sufficient activity of RAI in a single application
- The activity of RAI - 150–200 µCi (5.55–7.4 MBq) /g of tissue, higer than for GD [10–15 mCi (370–555 MBq)]
- Pre-treatment MMI or off-label use of rhTSH
  - ✓ reduce the total activity of RAI needed
  - ✓increase the risk of hypothyroidism

INSTRUCTIONS TO REDUCE EXPOSURE TO OTHERS AFTER I-131 RAI TREATMENT

ACTION	DURATION (DAYS)
Sleep in a separate bed (~6 feet of separation) from another adult	1-11*
Delay return to work	1-5*
Maximize distance from children and pregnant women (6 feet)	1-5*
Limit time in public places	1-3*
Do not travel by airplane or public transportation	1-3*
Do not travel on a prolonged automobile trip with others	2-3
Maintain prudent distances from others (~6 feet)	2-3
Drink plenty of fluids	2-3
Do not prepare food for others	2-3
Do not share utensils with others	2-3
Sit to urinate and flush the toilet 2-3 times after use	2-3
Sleep in a separate bed (~6 feet of separation) from pregnant partner, child or infant	6-23*

*duration depends on dose of I-131 given

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Scenario – 3 (Continued)

Test	Result	Ref. value
TSH	0.01	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	35	12-22 pmol/L

4 weeks after RAI, come back with TFT

How will you manage ???

Follow up plan ???

Follow up after RAI

- Within the first 1–2 months after RAI - free T4, total T3, and TSH.

- **Biochemical monitoring**
  - ✓4- to 6-week intervals for 6 months, or
  - ✓until the patient becomes hypothyroid and is stable on thyroid hormone replacement.

- **Retreatment with RAI**
  - ✓If hyperthyroidism persists beyond 6 months following RAI
  - ✓In selected patients with minimal response 3 months after therapy

Scenario - 4

- *65-year-old gentleman*
- **Refer to endocrine clinic because of abnormal TFT on routine clinical check up**
- **Asymptomatic and clinical examination NAD.**

Scenario – 4 (Continued)

Test	Result	Ref. value
TSH	0.05	0.27– 4.2 $\mathcal{M}$IU/ml
FT4	18	12-22 pmol/L
TT3	3.0	1.2- 3.4 nmol/L

- What will you do next?

Subclinical hyperthyroidism

- *The natural history*
  - ✓annualized rates of 0.5%–7% progression
  - ✓5%–12% reversion
- *More likely to spontaneously remit*
  - ✓Patients with GD rather than a TMNG (commonest cause)
- 24% increased risk of overall mortality (Meta-analysis)
- *With high risk of complications*
  - ✓TSH and FT_4 repeated within 2–6 weeks.
- *For all other patients*
  - ✓TSH at 3–6 months, prior to initiating therapy.

Subclinical hyperthyroidism

- *The natural history*
  - ✓annualized rates of 0.5%–7% progression
- ***TSH levels <0.1 mIU/L, increased risk of***
  - ✓ coronary heart disease mortality,
  - ✓ incident atrial fibrillation, heart failure,
  - ✓ fractures, and
  - ✓ excess mortality
- *With high risk of complications*
  - ✓TSH and FT_4 repeated within 2–6 weeks.
- *For all other patients*
  - ✓TSH at 3–6 months, prior to initiating therapy.

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Table 11. Subclinical Hyperthyroidism: When to Treat

Factor	TSH (<0.1 mU/L)	TSH (0.1–0.4 mU/L [a]
Age >65	Yes	Consider treating
Age <65 with comorbidities		
Heart disease	Yes	Consider treating
Osteoporosis	Yes	Consider treating
Menopausal, not on estrogens or bisphosphonates	Yes	Consider treating
Hyperthyroid symptoms	Yes	Consider treating
Age <65, asymptomatic	Consider treating	Observe

[a] Where 0.4 mU/L is the lower limit of the normal range.

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Table 11. Subclinical Hyperthyroidism: When to Treat

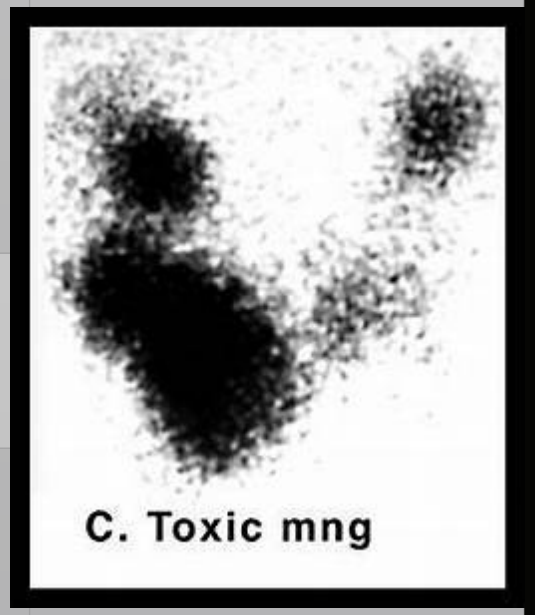
Factor	TSH (<0.1 mU/L)	TSH (0.1–0.4 mU/L [a])
Menopausal, not on estrogens or bisphosphonates	Yes	Consider treating
Hyperthyroid symptoms	Yes	Consider treating
Age <65, asymptomatic	Consider treating	Observe

[a] Where 0.4 mU/L is the lower limit of the normal range.

- If SH is to be treated,
  - ✓ Treatment based on the etiology of thyroid dysfunction
  - ✓ Follow same principles as outlined for overt hyperthyroidism

Scenario – 4 (Continued)

Test	Result	Ref. value
TSH	0.005	
FT4	20	
TT3	3.0	



- Repeat TFT after 3 months shows persistence of abnormality
- Thyroid uptake scan – Toxic MNG
- Refer for RAI

Take home message

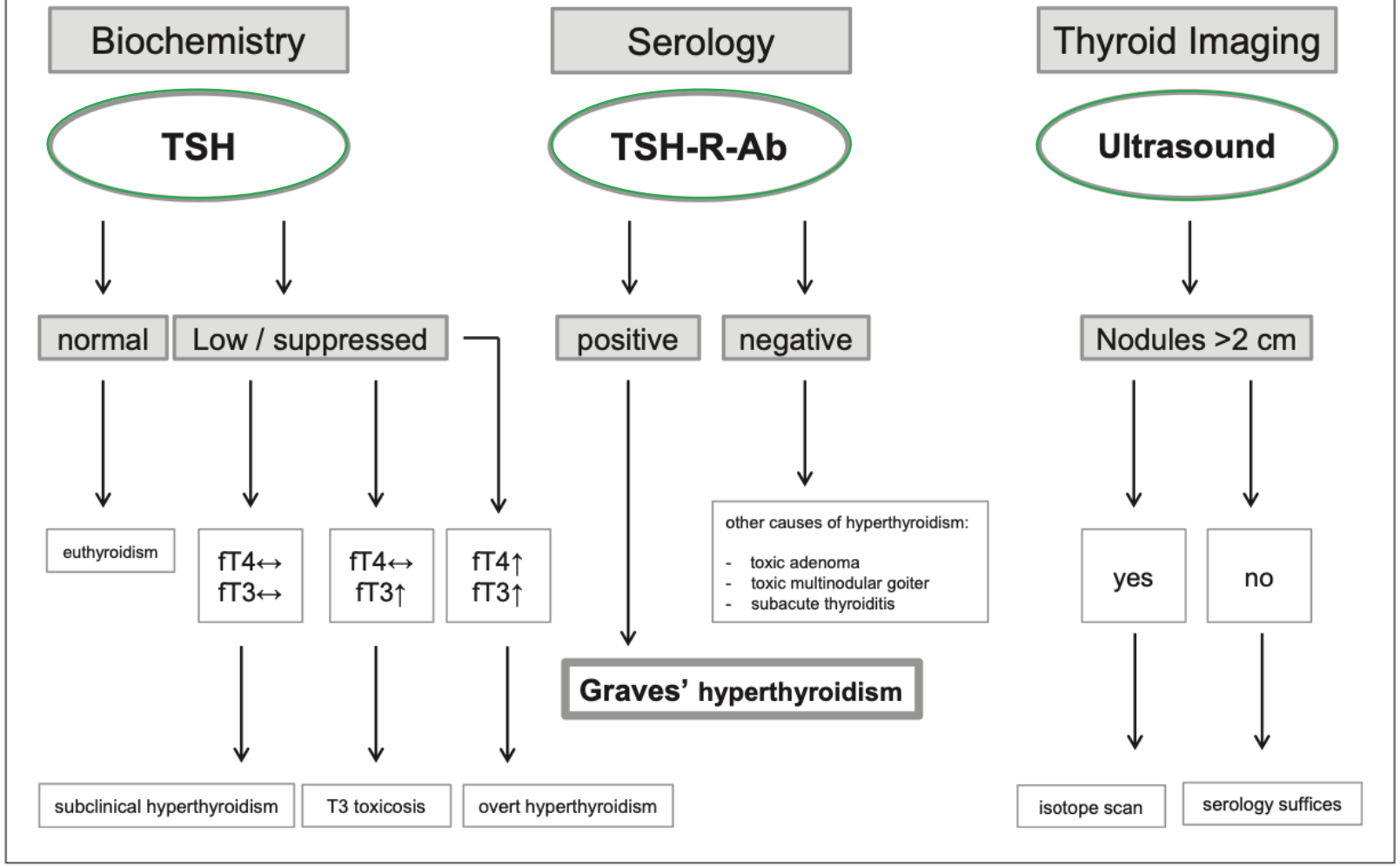


Fig. 1. Algorithm for investigating a patient with suspected Graves' hyperthyroidism.

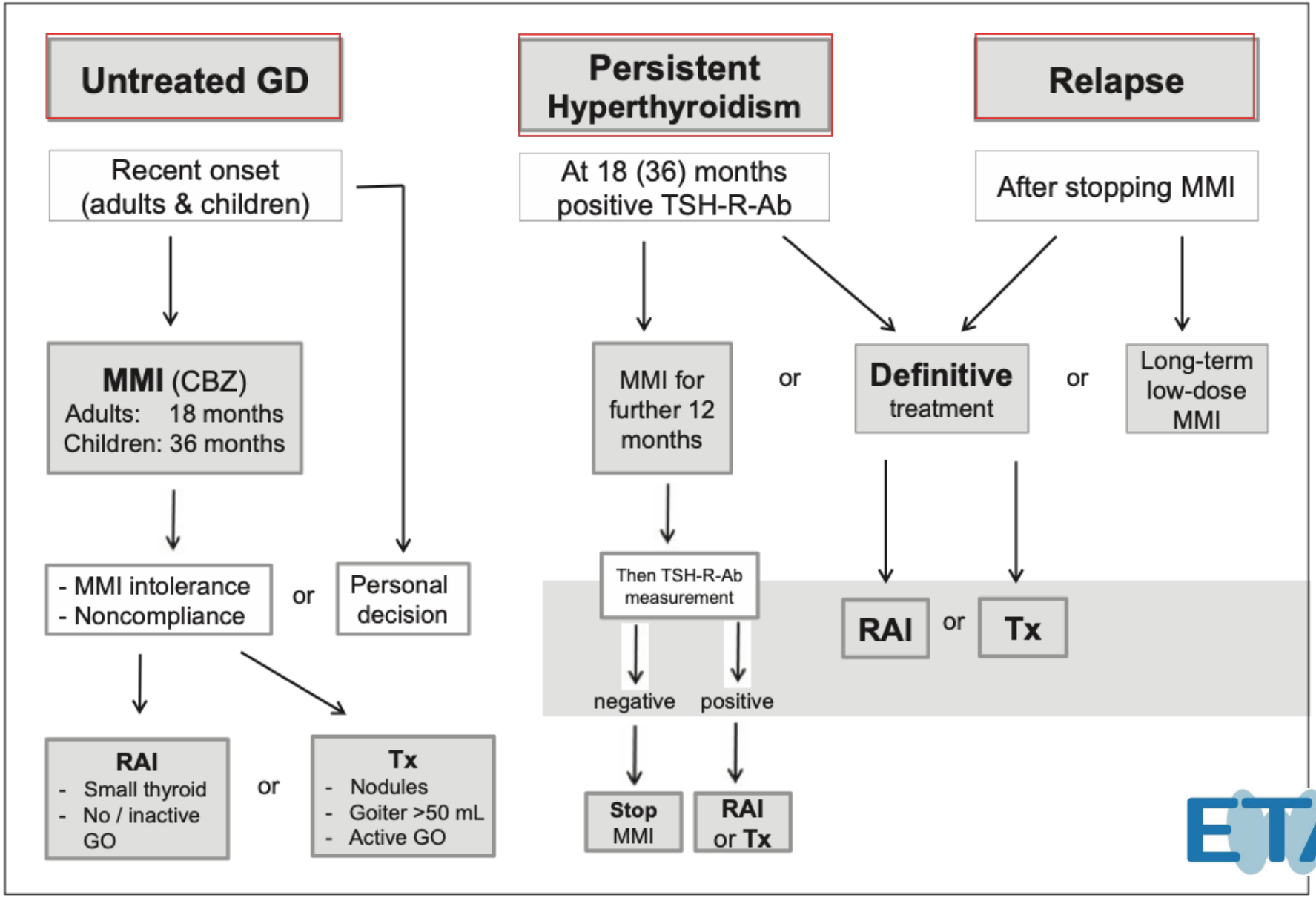


Fig. 2. Algorithm for the management of a patient with Graves' hyperthyroidism. GD, Graves' disease; MMI, methimazole; CBZ, carbimazole; GO, Graves' orbitopathy; RAI, radioactive iodine; Tx, total thyroidectomy.

THANK YOU!