Weill Cornell-Qatar
Qatar University

Thyroid disorders
(part 1: hypothyroidism)

Mohsen Eledrisi, MD, FACE, FACP
Department of Medicine
Hamad Medical Corporation
Doha, Qatar
www.eledrisi.com

CASE 1

- A 42-year-old lady presents with fatigue, joint pains and weight gain for 3 months
- Exam: normal vitals, weight 65 kg, dry skin small thyroid
- TSH done 2 months ago: 18 (normal: 0.4-4.5)
- Today TSH: 22.2, Free T_4 9 (11-19)
- **How to approach?**

Interpretation of thyroid function tests

- High TSH:
  - Indicates **primary hypothyroidism**
  - Defect in thyroid (mostly autoimmune)
  - Repeat in 6-8 weeks to confirm
  - Can add Free T4 to confirm
- Normal (or low) TSH and low Free T4:
  - Indicates **secondary hypothyroidism**
  - Rare

American Thyroid Association. Thyroid 2014;24:1670

Symptoms of hypothyroidism

- Fatigue
- Dry skin, hair loss
- Weight gain, cold intolerance
- Constipation, muscle cramps, voice changes
- Abnormal menses (heavy bleeding, delayed periods)
- Abnormal sleep pattern, anxiety

Garber J, et al. Thyroid 2012;22:1200

Physical examination in hypothyroidism

Non-pitting edema

Periorbital edema

CASE 1: assessment & plan

- Assessment:
  - High TSH
  - Confirmed on a repeat test
  - Diagnosis:
    - Primary hypothyroidism
- Plan:
  - Start levothyroxine

Levothyroxine dose

- **How much?**
  - 1.6 micrograms/kg/day
- **How to start?**

  A) Full dose at start for:

  – Age <65 years

American Thyroid Association. Thyroid 2014;24:1670

Levothyroxine dose

B) Low dose for:

1) Patients with coronary artery disease

2) People >65 years without heart disease

(expert opinion)

- Start with (25-50 mcg/d), increase gradually

American Thyroid Association. Thyroid 2014;24:1670.

Education on thyroxine

- When to take it?
  - Take 30-60 minutes before breakfast
  - Can take it at bedtime (≥3 hours after the last meal)
- Timing of improvement of symptoms?
  - May take few weeks to months
- Pregnancy?
  - Do not stop it
  - Follow up soon

American Thyroid Association. Thyroid 2014;24:1670.

CASE 1: PLAN

- Weight is 65 kg
- Start Levothyroxine 100 mcg/day
- Follow up?
  - After 6-8 weeks
  - What labs?
    - TSH only

Follow up after starting thyroxine

- Symptoms alone are not sensitive
- What is the target TSH?
  - Within normal
- Increment of dose change: (12.5-25 mcg/day)
- Some patients have symptoms when TSH is on the higher side of normal
  - **Consider target TSH < 2.5**

CASE 1: follow up

- After 2 months:
  - TSH 6.1 (0.4-4.5)
- Action?
  - Increase dose to 125 mcg/day
- F/U in 2 months
- TSH 2.5
  - Great !!

Hypothyroidism: long term f/u plan

- TSH every 3 months till 2 normal levels
- Then once a year
- **Come back earlier if:**
  - Planning pregnancy
  - Pregnancy
  - New symptoms
  - Let us know if you start taking new medications

CASE 2

- A 32-year-old lady with hypothyroidism for 5 years
- On Levothyroxine 125 mcg qd
- TSH has been normal for the last 3 years
- Last was 12 months ago: 3.2
- Today TSH 7.1 (0.4-4.5)
- **How to approach?**

CASE 2: questions

- Is the patient adherent to thyroxine daily ?
- On other medications? (can change requirement)
- Pregnancy? (increases requirement)
- Weight change? (weight gain increases requirement)

What medications can affect thyroid gland or thyroid medication?

Medications and thyroid

Interfere with absorption

- Calcium salts
- Ferrous sulfate
- PPI
- Bile acid sequestrants
- Sevelamer
- Orlistat

American Thyroid Association. Thyroid 2014;24:1670

Interfere with thyroid hormone production or secretion

- Amiodarone
- Lithium
- Interferon alfa
- Monoclonal antibody therapy
  - (e.g Alemtuzumab)
- Cancer therapy
  - (e.g. tyrosine kinase inhibitors)

Burch H. N Engl J Med 2019;381:749.

Increase clearance or affect binding of thyroid hormones

- **Increase requirement for thyroxine:**

  - Estrogen, Carbamazepine, Rifampin

    Phenobarbital, Phenytoin, Sertraline

- **Decrease requirement for thyroxine:**

  - Androgens

Managing medications with thyroxine

- Those affecting absorption:
  - Separate them from thyroxine (at least 4 hours)
- Other medications:
  - Monitor TSH
  - Adjust thyroxine dose if needed

American Thyroid Association. Thyroid 2014;24:1670

CASE 3

- A 34-year-old lady with hypothyroidism for 4 years
- On levothyroxine 100 mcg qd
- No complaints
- Pregnancy test was positive last week
- TSH 3.5 (0.4-4.5)
- Free T_4 14 (10-19)
- **How to approach?**

Hypothyroidism in pregnancy

- Levothyroxine dose usually needs an increase:
  - Generally, 25-50% (variable from 10 to 80%)
- Target TSH:
  - **<2.5: if planning pregnancy**
  - **≤2.5: in 1st trimester**
  - **≤3: in 2nd & 3rd trimesters**

American Thyroid Association. Thyroid 2017;21:2011

Management of hypothyroidism in pregnancy

- Advise the patient to increase levothyroxine dose if missed period or positive home pregnancy test
- One way is to take 9 doses/week
- Monitor TSH every 4 weeks during 1st trimester
- After delivery: return to pre-pregnancy levothyroxine dose and monitor TSH

American Thyroid Association. Thyroid 2017;21:2011

CASE 4

- A 56-year-old lady with type 2 diabetes, hypertension
- No complaints
- TSH 7.2 (0.4-4.5)
- Free T_4 15 (10-19)
- **How to approach?**

Subclinical hypothyroidism

- High TSH & normal FT4
- Most have TSH <10
- Affects 4-15% of the population
- Likely over-estimated as elderly have higher TSH
- Most have no symptoms
- Difficult to attribute symptoms (if present) to it

Biondi B, et al. JAMA 2019;322:153.
American Thyroid Association/AACE. Thyroid 2012;22:1200

Management of subclinical hypothyroidism

- First: **REPEAT TEST** after 2-3 months
- About 60% of TSH levels <10 will normalize within five years
- Progression to overt hypothyroidism: 2-4%/year
- Some recommend checking TPO antibodies
- No benefit from treating people age ≥65

European Thyroid Association. Eur Thyroid J 2013;2(4):215
American Thyroid Association/AACE. Thyroid 2012;22:1200
TRUST trial. N Engl J Med 2017; 376:2534

When to treat subclinical hypothyroidism?

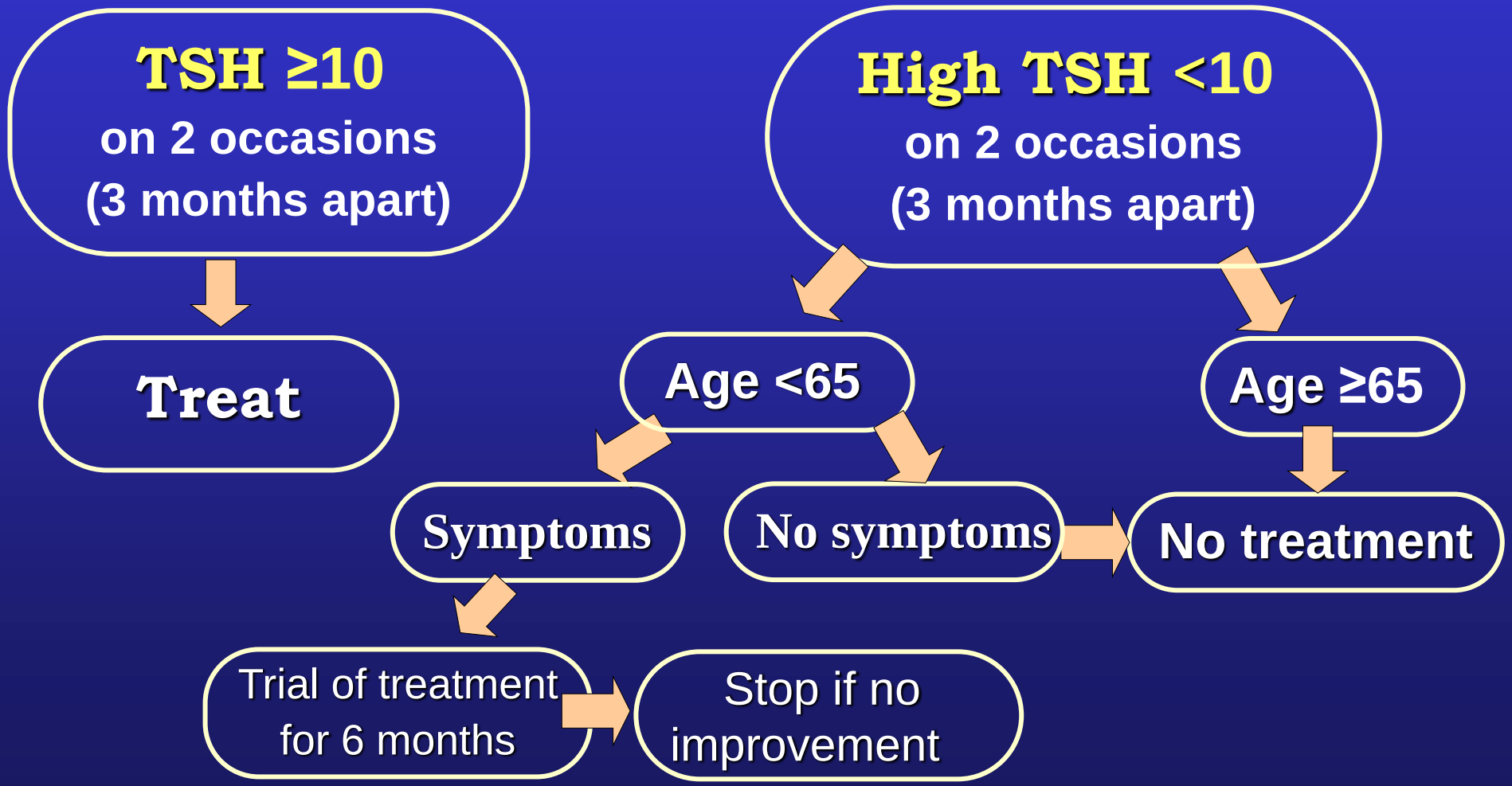
1) Pregnancy

2) Planning pregnancy

3) Infertility

NICE guidelines 2019.

Management of subclinical hypothyroidism



NICE guidelines 2019.

Follow up of subclinical hypothyroidism

- If treatment if indicated:
  - Starting dose of levothyroxine: 25-50 mcg qd
  - Target is normal TSH (some suggest <2.5)
  - Target in pregnancy, planning pregnancy, infertility: <2.5
- If no treatment is given:
  - TSH every 6 months for 2 years then yearly

European Thyroid Association. Eur Thyroid J 2013;2(4):215
American Thyroid Association/AACE. Thyroid 2012;22:1200

Summary

- TSH to screen for thyroid disease
- Provide education for patients on thyroxine
- Review medications that may affect thyroid function
- Thyroxine dose usually requires ↑ during pregnancy
- Target TSH in pregnancy or planning for pregnancy is lower
- Identify and manage subclinical hypothyroidism

Thyroid disorders
(part 2: hyperthyroidism/ thyroid nodules)

CASE 1

- A 29-year-old lady presents with palpitations & sweating for 2 months
- Exam: pulse 120/min
- Hand tremors, proptosis, enlarged thyroid
- TSH <0.01 (0.4-4.5), Free T_4 28 (10-19)
- **How to approach?**

Thyrotoxicosis or Hyperthyroidism ?

Thyrotoxicosis = “excess thyroid hormones”

Hyperthyroidism = “overactive thyroid gland”

Thyrotoxicosis includes hyperthyroidism

Symptoms of thyrotoxicosis

- Palpitations, tremors
- Anxiety
- Heat intolerance
- Weight loss (with normal or increased appetite)
- Increased frequency of bowel movements
- Eye symptoms (in Graves' disease):
  - Eye pain or itching, blurry vision, diplopia

Physical examination in hyperthyroidism

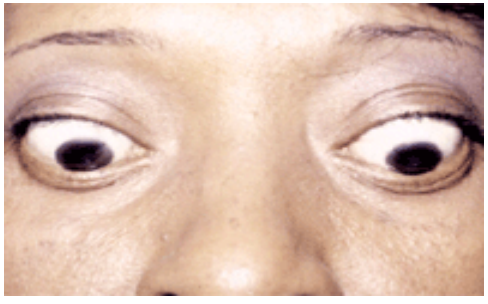
Pretibial myxedema

Goiter

Eye disease in hyperthyroidism

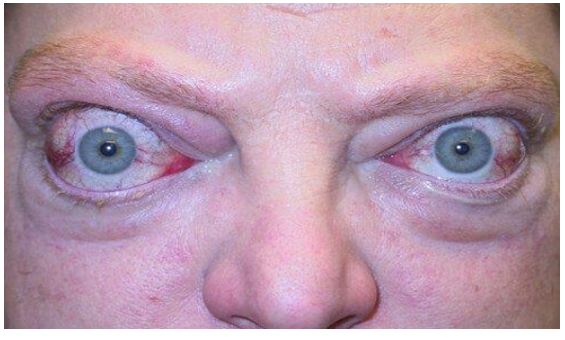
Stare

Lid lag



Ophthalmopathy

(Exophthalmos, conjunctival edema, impaired EOM)



Labs in thyrotoxicosis

- Low TSH (suppressed <0.01 Um/L)
- High Free T_4
- Rarely free T_4 is normal
- T_3 toxicosis (high T_3 with normal FT_4)
  - Can order total T3 (Free T3 is more expensive)

Causes of thyrotoxicosis

- Graves' disease (most common)
- Toxic adenoma
- Toxic Multinodular goiter
- Thyroiditis
- Pituitary tumor
- Trophoblastic disease
- Amiodarone-induced
- Iatrogenic
- Factitious
- Struma ovarii

Clinical picture of thyrotoxicosis

+

Goiter

+

Ophthalmopathy

=

Graves' disease

Approach to thyrotoxicosis

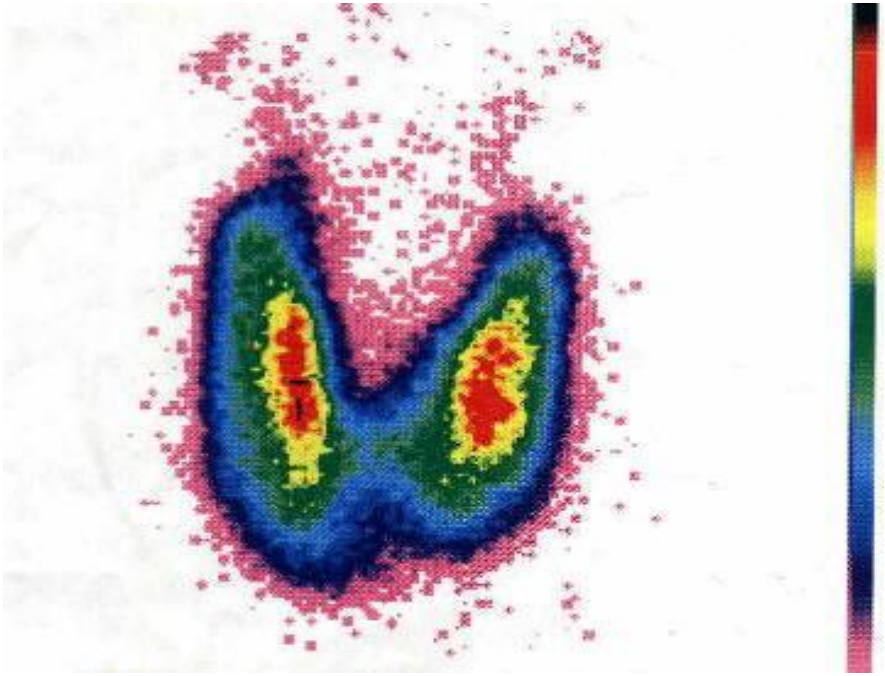
- If clinical picture is not clear, obtain TSH receptor antibodies
- TSH receptor antibodies (TRAb):
  - Present: Graves' disease
  - Absent: Graves' or other causes
- If TRAb negative, do thyroid scan:
  - Evaluates the size of the thyroid
  - Gives the percent uptake

Interpretation of thyroid scan

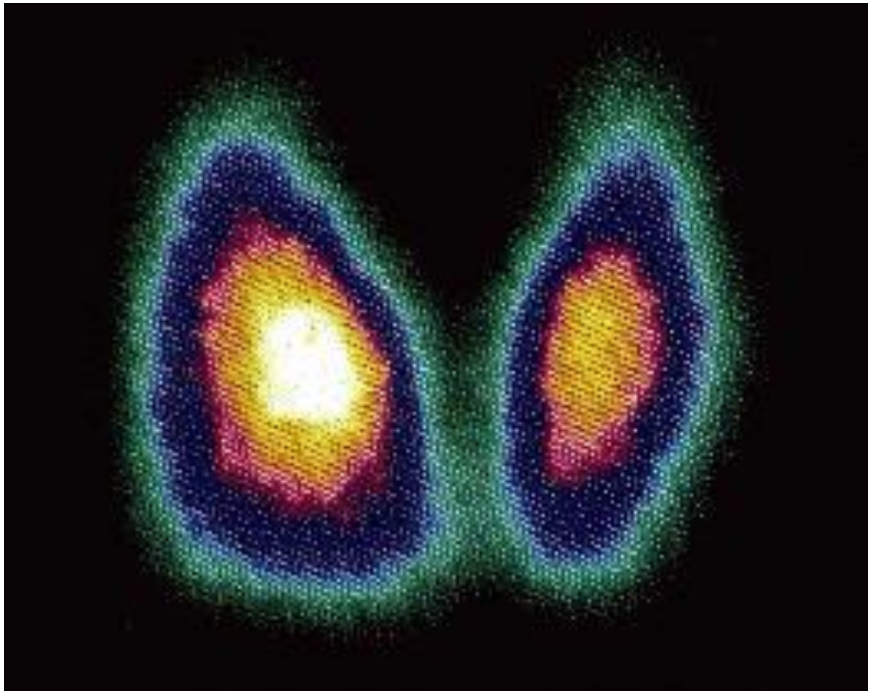
- **Normal or high uptake :**
  - Graves' disease
  - Toxic adenoma
  - Toxic multinodular goiter
  - TSH-producing pituitary adenoma

Interpretation of thyroid scan

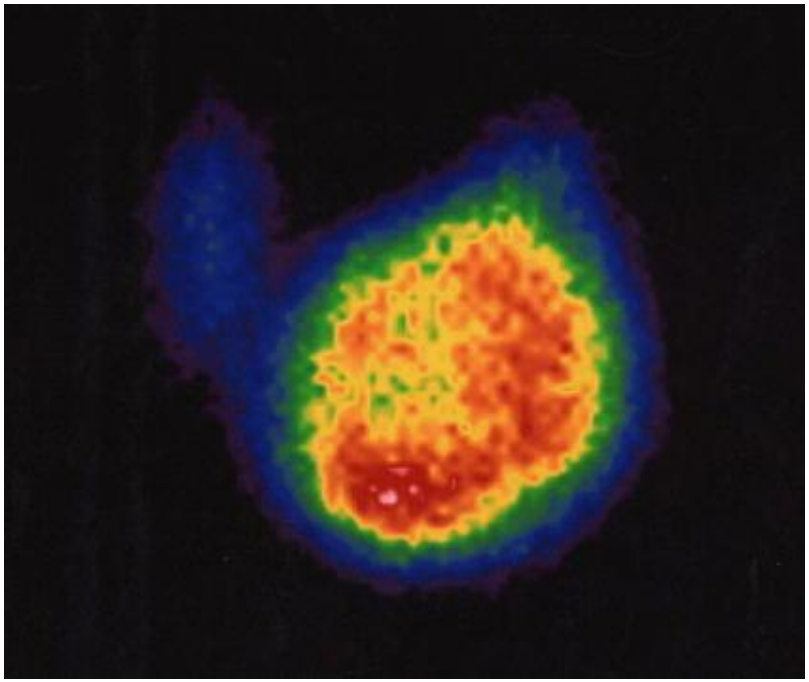
- **Low uptake :**
  - Thyroiditis
  - Factitious ingestion of thyroid hormone
  - Struma ovarii



Normal thyroid scan



Graves’ disease



Toxic adenoma

CASE 2

- A 33-year-old lady presents with sweating, fatigue, and palpitations
- Exam: pulse 108/min, enlarged thyroid
- TSH <0.01 (0.4-4.5), Free T_4 32 (11-19)
- TSH receptor antibodies (TRAb): high
- **How to approach?**

Management of Graves' disease

1) Symptomatic treatment: (all patients)

- Beta-blockers:

A) Propranolol

LA form (qd) available

- Non-selective, most experience

- Preferred for nursing and pregnant mothers

B) Atenolol

(better adherence, avoid in pregnancy)

C) Metoprolol

Management of Graves' disease

1) Symptomatic treatment:

- If Beta-blockers are contraindicated or not tolerated:

can use Verapamil or Diltiazem

Management of Graves' disease

2) Definitive treatment:

- Options of therapy:

A) Anti-thyroid drugs (ATD)

B) Radioactive iodine therapy

C) Surgery

Which modality should be offered?

- Depends on:
  - Clinical features
  - Patient preference
  - Availability

Anti-thyroid drugs (ATD): clinical considerations

- Mild disease with mild goiter
- Planning pregnancy in the next 4-6 months
- Pregnancy
- Moderate to severe ophthalmopathy

American Thyroid Association. Thyroid 2016;26:1343

ATD: available agents

- Methimazole (MMI) or Carbimazole
- Propylthiouracil (PTU)

Choice of ATD

- MMI (or carbimazole) is preferred due to less risk of liver toxicity
- Risk of liver toxicity: 0.4% with MMI; 2.7% with PTU
- Exceptions (when to use PTU):
  - During the first trimester of pregnancy
  - Thyroid storm
  - Minor reactions to MMI if the patient refused RAI therapy or surgery

Radioactive Iodine (RAI) therapy

- Can be considered as 1st option
- Can be used if medications are not effective or not tolerated
- Safe, usually one-time therapy
- Avoid pregnancy for 6 months after treatment
- Antithyroid drugs before treatment only if severe symptoms or elderly with comorbidities (as heart failure)
- May develop hypothyroidism (>80%)

Surgery

- **Consider if:**
  - Compressive symptoms or very large goiters
  - Failure of antithyroid drugs and RAI is not available
  - Moderate to severe Graves' ophthalmopathy
  - Planning pregnancy in next 6 months

American Thyroid Association. Thyroid 2016;26:1343

Case 3

- A 29-year-old lady presents with sweating, nervousness and palpitations for 4 weeks
- She delivered a baby 2 months ago
- She is not taking any medications
- Exam: pulse 104/min. Thyroid: normal
- TSH <0.01 (0.4-4.5), Free T_4 22 (10-19)
- **How to approach?**

Case approach

- She has a picture of thyrotoxicosis
- Thyroid scan to define the cause
- Can do TRAb (not helpful if negative)
- Thyroid scan:
  - Normal size
  - Low uptake
- This is suggestive of thyroiditis

Management of thyroiditis

1) **Symptomatic treatment:**
   - Beta blockers
   - NSAID for pain
   - Steroids if severe symptoms
2) **Follow up:**
   - Is important as there is increased risk of hypothyroidism

CASE 4

- A 30-year old lady presents with swelling of the neck for 3 months
- Exam: thyroid mass
- **How to approach?**

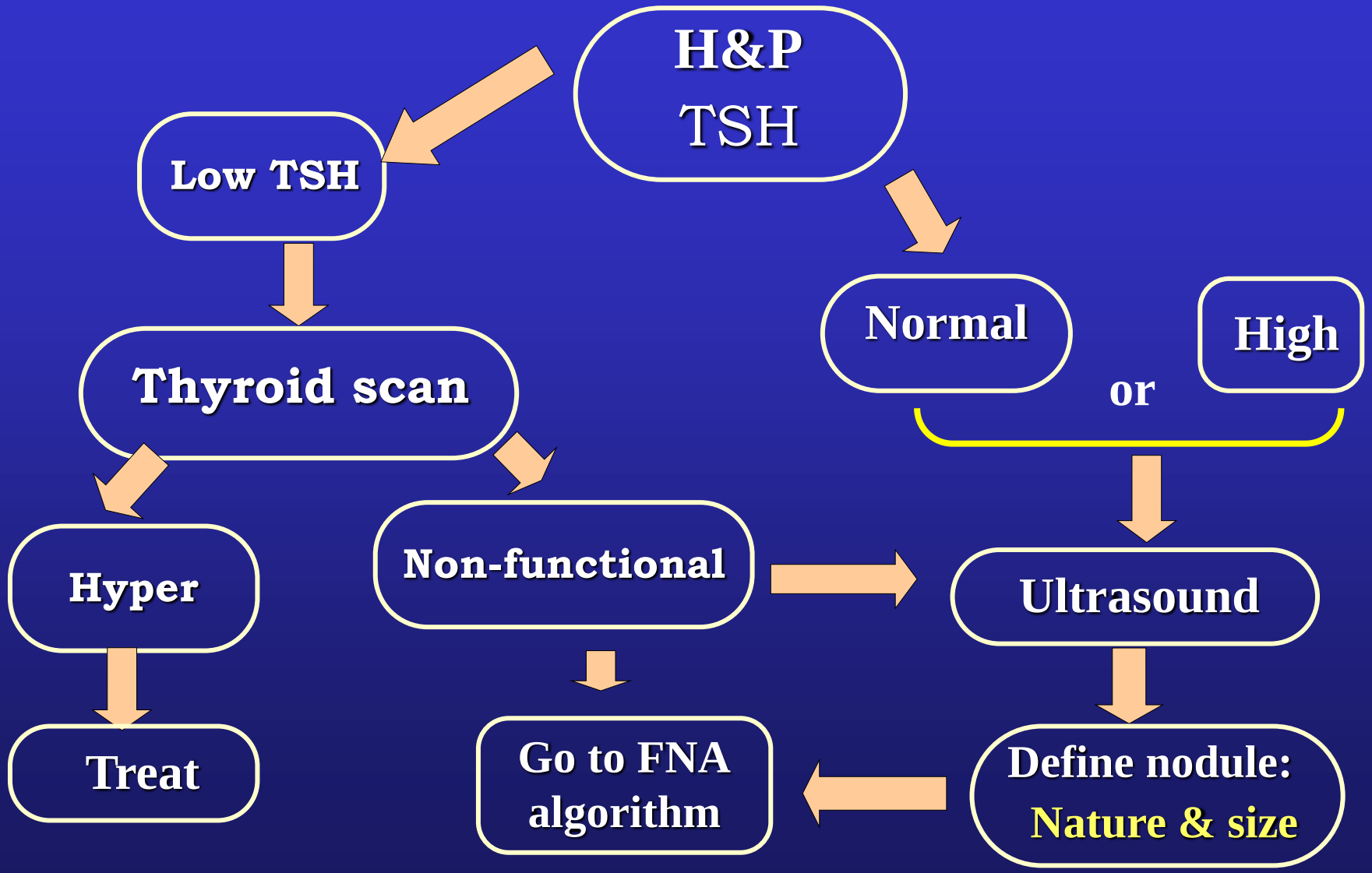
Thyroid nodule: history

- SOB, dysphagia, dysphonia, choking with position
- Rate of growth
- History of head/neck irradiation
- Symptoms of hyperthyroidism or hypothyroidism
- Family history of thyroid cancer

CASE 4: Exam

- A 2 × 2 cm mass in the lower right part of the neck
- Soft, moves with swallowing
- No lymph nodes were palpable
- Rest of exam: normal
- **How to approach?**

Evaluation of thyroid nodule



American Thyroid Association. Thyroid 2016;26;1.

Thyroid ultrasound

- Confirms the presence of nodules
- Detects non-palpable nodules
- Size and nature of nodules and risk of malignancy
- Follow up of nodules
- FNA-biopsy (U/S-guided)

Thyroid nodules: ↑ risk of malignancy

- History of head and neck irradiation
- Age <30 years
- Family history of thyroid carcinoma
- MEN type 2
- Growing nodule
- Compressive symptoms
- Hard nodule
- Fixed nodule
- Cervical lymphadenopathy

High suspicious features on ultrasound

- Solid hypoechoic or solid hypoechoic component of a partially cystic nodule with any of the following:
  - Irregular margins
  - Microcalcifications
  - Rim calcifications
  - Taller than wide shape
  - Extrathyroidal extension
  - Suspicious lymph node

Intermediate suspicious features on ultrasound

Hypoechoic solid

with regular margin

Low suspicious features on ultrasound

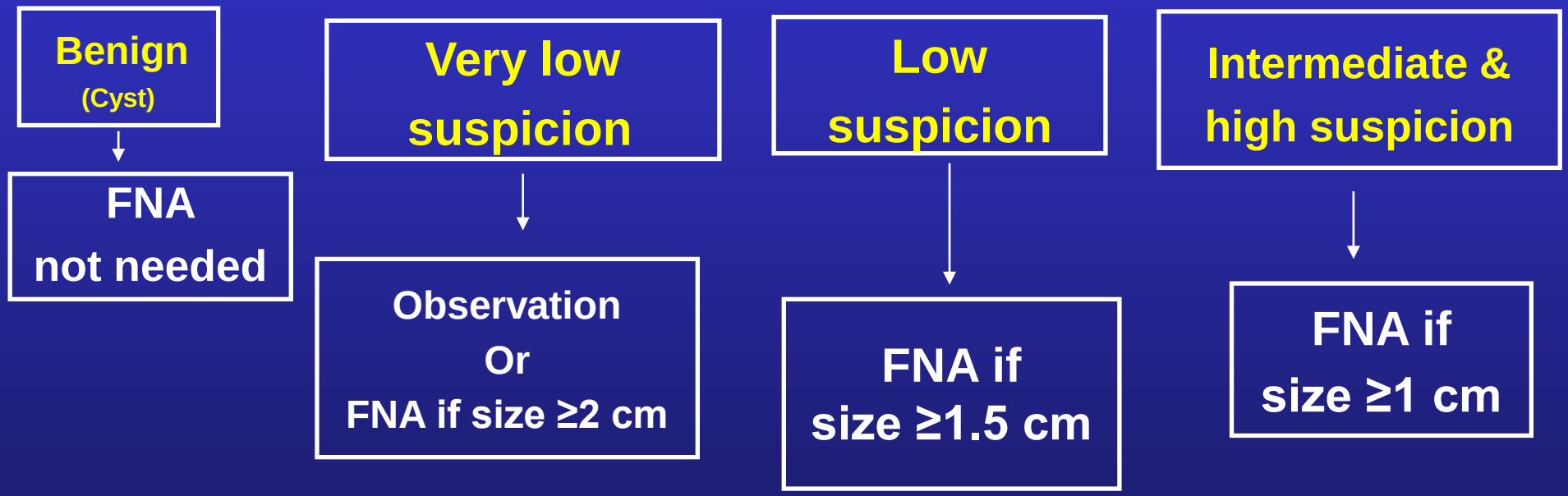
- Hyperechoic solid with regular margin
- Isoechoic solid with regular margin
- Partially cystic nodule with solid areas

Very low suspicious features on ultrasound

- Spongiform
- Partially cystic nodule

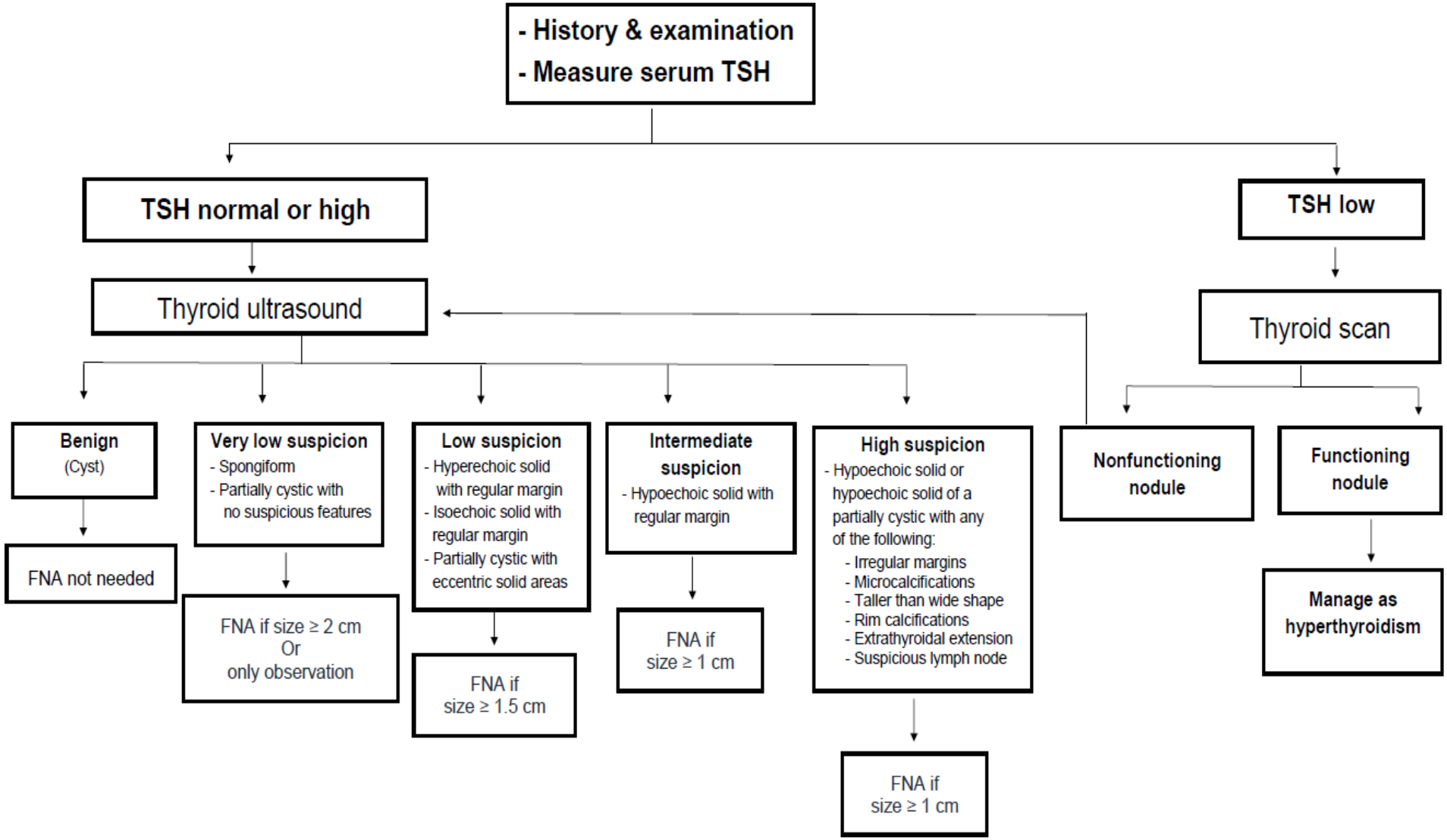
Cyst → **is usually benign**

Thyroid nodule FNA algorithm

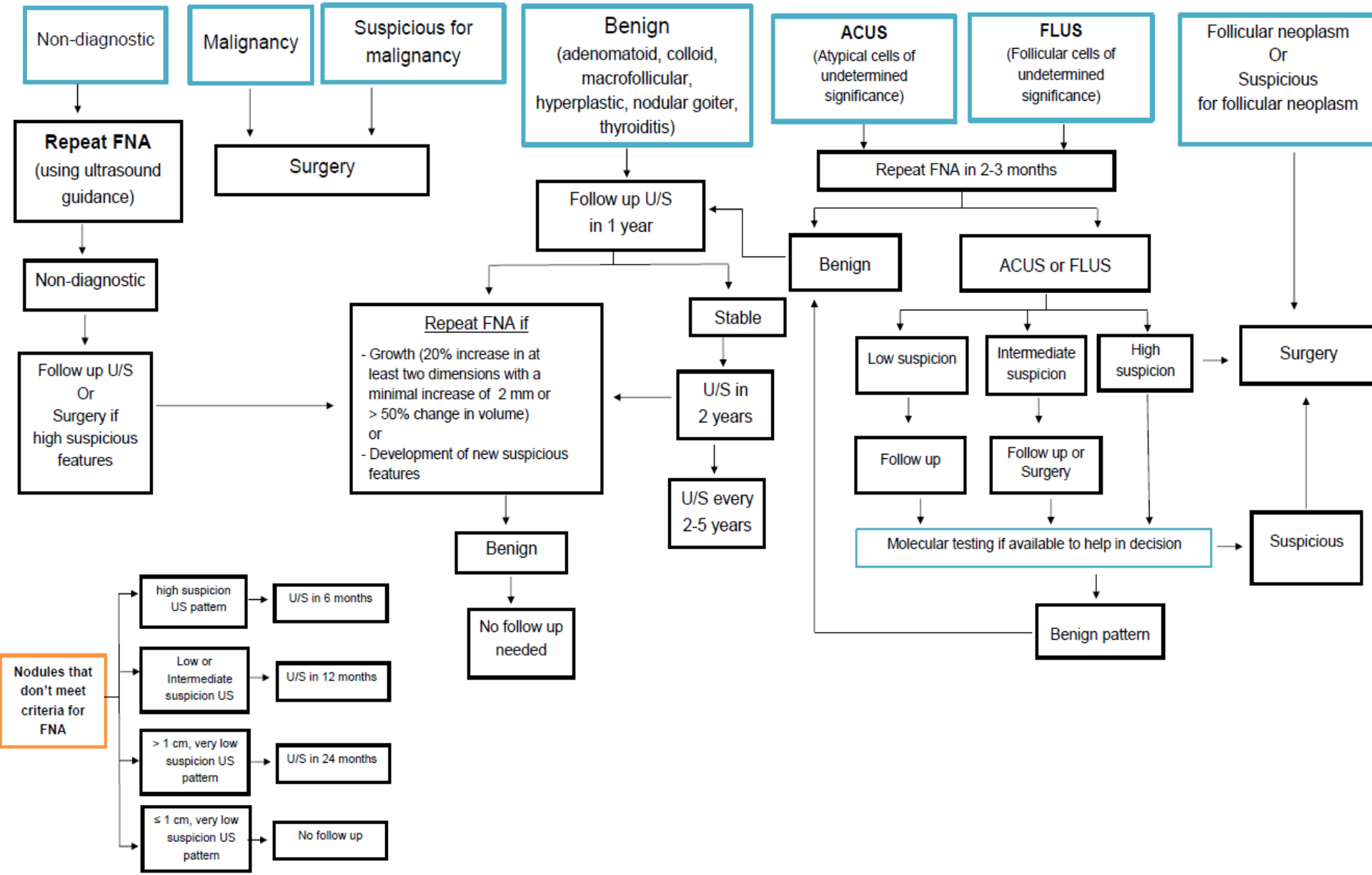


American Thyroid Association. Thyroid 2016;26;1.

Approach to thyroid nodule



Management of thyroid FNA results



Thyroid nodules: when to do surgery ?

- Malignancy
- Suspicious for malignancy
- Indeterminate cytology + high risk
- Repeat non-diagnostic + high risk
- Follicular neoplasm (FN) or suspicious for FN

American Thyroid Association. Thyroid 2016;26;1.

CASE 5

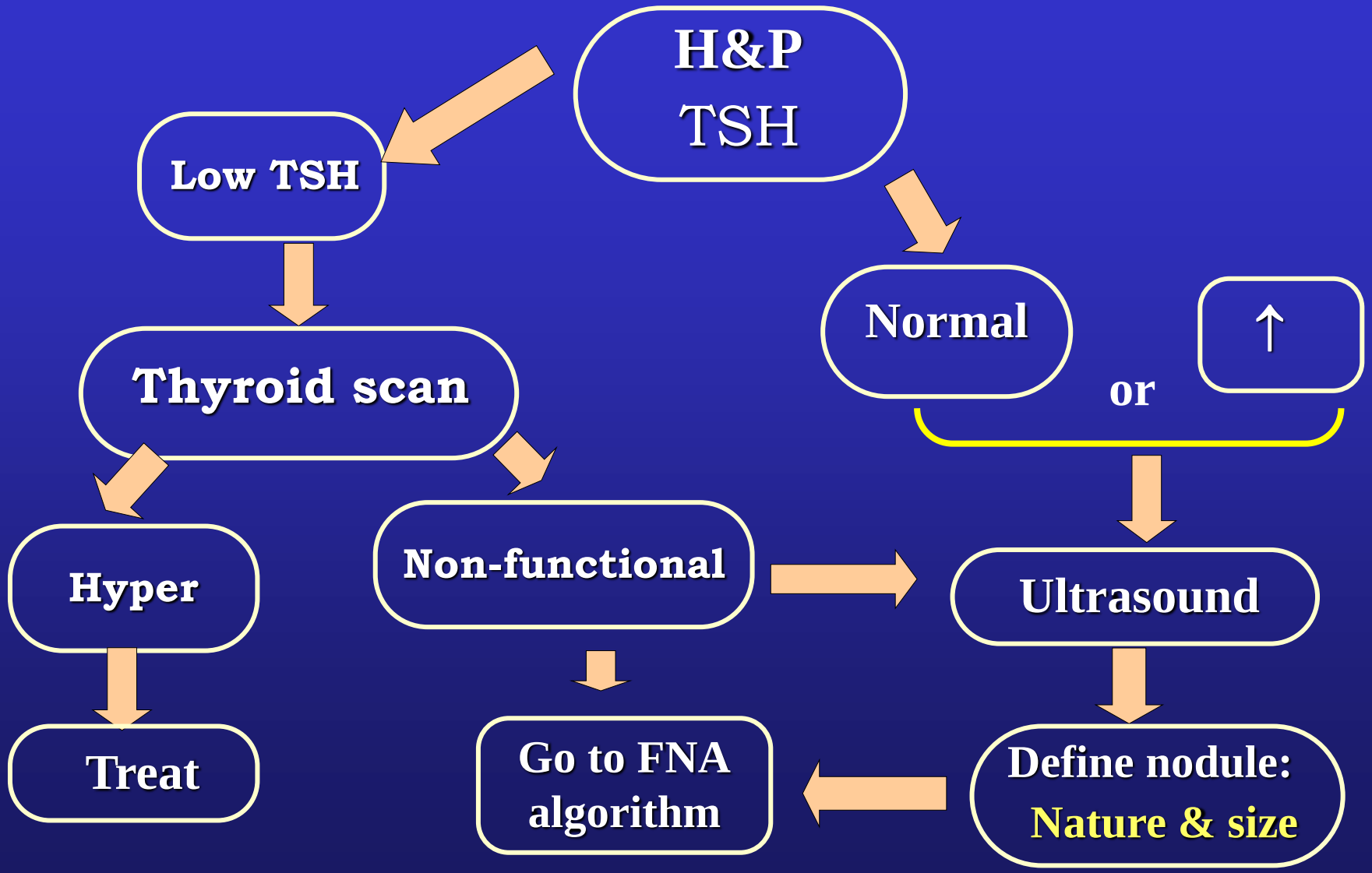
- A 66-year-old lady had a recent acute minor ischemic stroke
- Doppler ultrasound of the carotid arteries:
  - Showed 2 thyroid nodules
- She has no complaints
- Physical exam including the thyroid was normal.
- **How would you approach?**

Incidentally-discovered thyroid nodule (Thyroid incidentaloma)

- Non-palpable thyroid nodules that are detected during other imaging procedures
- Same approach as thyroid nodule
- History and physical
- Check TSH
- Thyroid ultrasound

American Thyroid Association/AACE. Thyroid 2012;22:1200

Evaluation of thyroid nodule



American Thyroid Association. Thyroid 2016;26;1.

Summary

- TRAb or thyroid scan for the cause of thyrotoxicosis
- Treatment options for GD: drugs, RAI, surgery
- Choice depend on clinical features & patient value
- MMI preferred. PTU in 1st trimester and thyroid storm
- Thyroiditis: analgesia PRN. f/u risk of hypothyroidism
- Thyroid nodule: H & P, check TSH
- If normal or ↑ TSH, do ultrasound; assess need FNA