MANAGEMENT OF THYROID NODULES

DR. A. ABU-BAKARE

Conflict of Interest Declaration: Nothing to Disclose

Presenter: **Dr. A. Abu-Bakare**

Title of Presentation: **Management of Thyroid Nodules**

I have no financial or personal relationship related to this presentation to disclose.

OBJECTIVES

- Recognize characteristics of thyroid nodules requiring further investigation
- Gain understanding of relevant investigations or tests
- Understand the implications of test results
- Know what nodules should be referred further
- Understand follow up pathway for different nodules

Thyroid Nodule

A discrete lesion within the thyroid gland

Radiologically distinct from the surrounding thyroid parenchyma

May be palpable or non palpable

Epidemiology

- In the general population,
  thyroid nodules are discovered by palpation in 3% to 7%,
  and by US in 20% to 76%
- More common in women than men
- Prevalence increases linearly with age, exposure to ionizing radiation, and iodine deficiency
- Some data suggest 2% cancer and 98% benign
- Other data suggests 5-10% cancer (rates with bias)

Prior to FNA 14% of resected nodules were malignant
Now (2007) 56% of nodules resected are malignant

Etiologies of Thyroid nodules

- **Benign**
  - Benign thyroid cysts (degenerated nodules)
  - Colloid nodules
  - Multinodular goiter
- **Malignant**
  - Papillary carcinoma
  - Follicular carcinoma
  - Hurthle cell tumor
  - Medullary Thyroid Carcinoma
  - Anaplastic Carcinoma
  - Lymphoma of thyroid

CASE 1

55 year-old lady seen two years ago with a left thyroid nodule and ?Hyperthyroidism.

She complained of hot flashes, insomnia and episodes of palpitations. She had no weight loss, visual disturbances, dysphagia or diarrhea. She had dysesthesias over her hands. She had no history of exposure to irradiation or family history of Thyroid disease. She did not smoke. She was on Clonidine and Propranolol.

History

Symptoms

The most common presentation of a thyroid nodule, benign or malignant, is a painless mass in the region of the thyroid gland.

Symptoms consistent with malignancy

- Pain
- Dysphagia
- Stridor
- Hemoptysis
- Rapid enlargement
- Hoarseness

History (continued...)

Risk factors

- Thyroid exposure to irradiation
  - low or high dose external irradiation
  - Especially in childhood for:
    - large thymus, acne, enlarged tonsils, cervical adenitis, sinusitis, and malignancies
  - 30%-50% chance of a thyroid nodule to be malignant
  - Schneider and co-workers (1986) studied, with long term F/U, 3000 patients who underwent childhood irradiation.
    - 1145 had thyroid nodules
    - 318/1145 had thyroid cancer (mostly papillary)

History (continued...)

Risk factors (continued…)

Age and Sex

Benign nodules occur most frequently in women

20-40 years

5%-10% of these are malignant

Men have a higher risk of a nodule being malignant

Belfiore and co-workers found that:

- the odds of cancer in men quadrupled by the age of 64
- a thyroid nodule in a man older than 70 years had a 50% chance of being malignant

History (continued…)

Family History

- History of family member with medullary thyroid carcinoma
- History of family member with other endocrine abnormalities (parathyroid, adrenals)
- History of familial polyposis (Gardner’s syndrome)

Evaluation of the thyroid Nodule *(Physical Exam)*

Examination of the thyroid nodule:

- consistency - hard *vs.* soft
- size - < 4.0 cm
- Multinodular *vs.* solitary nodule
  - multi nodular - 3% chance of malignancy (Goldman, 1996)
  - solitary nodule - 5%-12% chance of malignancy (Goldman, 1996)
- Mobility with swallowing
- Mobility with respect to surrounding tissues
- Well circumscribed *vs.* ill defined borders

CASE 1 contd

Her BMI was 24.2kg/m2, BP 130, Pulse 76 bpm. She a palpable goiter L>R with no bruit moved with deglutition. It was firm and nontender. She had no lymphadenopathy. No orbitopathy. She had no lid lag and no tremor. Her DTRs were normal

Dx Toxic Goiter

Her FMD had ordered an FNA, it was negative.

Evaluation of the Thyroid Nodule
(Lab. Tests)

Thyroid function tests

- FT4
- FT3
- TSH
- Antithyroid Antibodies

?Serum Calcium, PTH

?Thyroglobulin (TG)

?Calcitonin

Evaluation of the Thyroid Nodule (Thyroid-Stimulating Hormone Suppression)

Mechanism/Rationale

- Exogenous thyroid hormone feeds back to the pituitary to decrease the production of TSH
- Cancer is autonomous and does not require TSH for growth whereas benign processes do
- Thyroid masses that shrink with suppression therapy are more likely to be benign
- Thyroid masses that continue to enlarge are likely to be malignant.

Limitations:

- 16% of malignant nodules are suppressible
- Only 21% of benign nodules are suppressible
- Provides little use in distinguishing benign from malignant nodules

CASE 1 contd

Labs:

Her TSH was 0.01mIU/L, FT4 15 pmol/l and FT3 5.2, ESR 5 mm/hr, TSH 0.01mIU/L, FT4 16.0 pmol/L and FT3 5.6 pmol/L.

Negative antithyroid antibodies.

Evaluation of the Thyroid Nodule *(Radioimaging)*

- Radioimaging usually not used in initial work-up of a thyroid nodule
- Ultrasounography
- Radioiodine scan
- Chest radiograph
- Computed tomography
- Magnetic resonance imaging
- PET scanning

Evaluation of the Thyroid Nodule *(Ultrasonography)*

Advantages

- Most sensitive procedure for identifying lesions in the thyroid (2-3mm)
- 90% accuracy in categorizing nodules as solid, cystic or mixed)
- Best method of determining the volume of a nodule
- Can detect the presence of lymph node enlargement and calcifications
- Noninvasive and inexpensive

CASE 1 contd

Ultrasound: Right nodule 4.2 x 1.7 x 1.1 cm, Left 4.8 x 2.4 x 2.0 cm with a solid lesion 3.0 x 2.0cm with demarcated margins and no increased vascularity.

Ultrasonography

When to use Ultrasonography:

Long term follow-up for the following:

- to evaluate the involution of a multinodular gland or a solitary benign nodule under suppression therapy
- monitor for re accumulation of a benign cystic lesion
- follow thyroid nodules enlargement or other changes

Evaluation of a thyroid nodule:

- help localize a lesion and direct a needle biopsy when a nodule is difficult to palpate or is deep-seated
- Determine if a benign lesion is solid or cystic

Disadvantages

- Cannot accurately distinguish benign from malignant nodules

Evaluation of the Thyroid Nodule *(Radioisotope Scanning)*

Prior to FNA, was the initial diagnostic procedure of choice

Performed with: technetium 99m pertechnetate or radioactive iodine

Technetium 99m pertechnetate

- cost-effective
- readily available
- short half-life
- trapped but not organified by the thyroid - cannot determine functionality of a nodule

Radioactive iodine

- radioactive iodine (I-131, I-125, I-123)
- is trapped and organified
- can determine functionality of a thyroid nodule

CASE 1 contd

Thyroid scan showed a hyperfuntioning left nodule, uptake 15% at 4 hours and 29.4% at 24 hours

Radioisotope Scanning *(continued...)*

Limitations:

- Not as sensitive or specific as fine needle aspiration in distinguishing benign from malignant nodule

- 90%-95% of thyroid nodules are hypofunctioning, 10%-20% being malignant

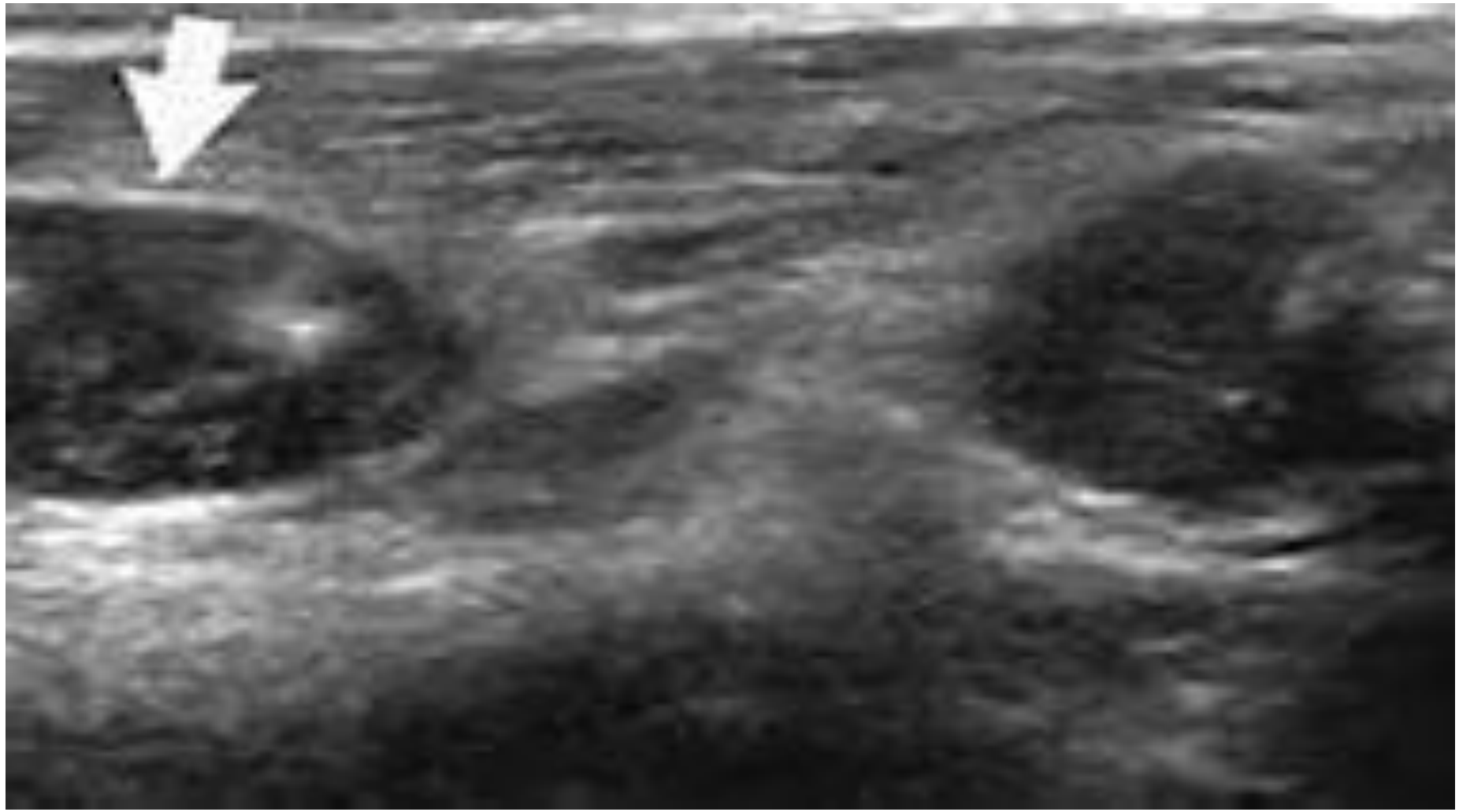
Campbell and Pillsbury (1989) performed a meta-analysis of 10 studies correlating the results of radionuclide scans in patients with solitary thyroid nodules with the pathology reports following surgery and found:

- 17% of cold nodules, 13% of warm or cool nodules, and 4% of hot nodules to be malignant

FACTORS SUGGESTING BENIGN LESION

- F.Hx of autoimmune disease (Hashimoto's thyroiditis)
- F.Hx of benign thyroid nodule or goiter
- Presense of thyroid hormone dysfunction, hypothyroid or hyperthyroid
- Pain or tenderness associated with nodule
- Soft, smooth, mobile
- MNG without a predominant nodule
- Warm nodule on thyroid scan
- Simple cyst on US

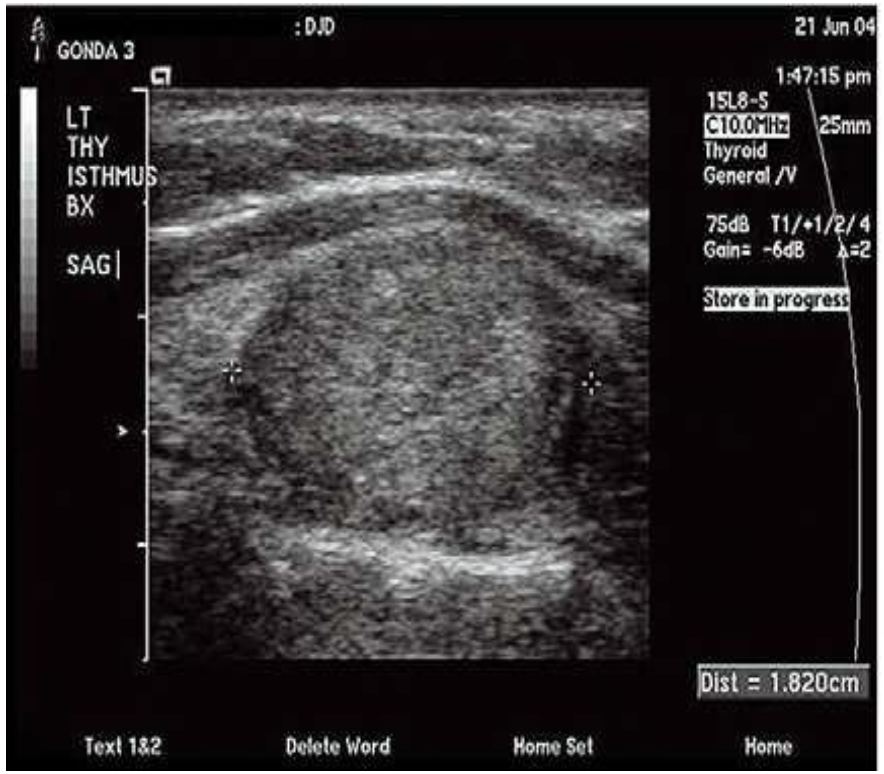
BENIGN

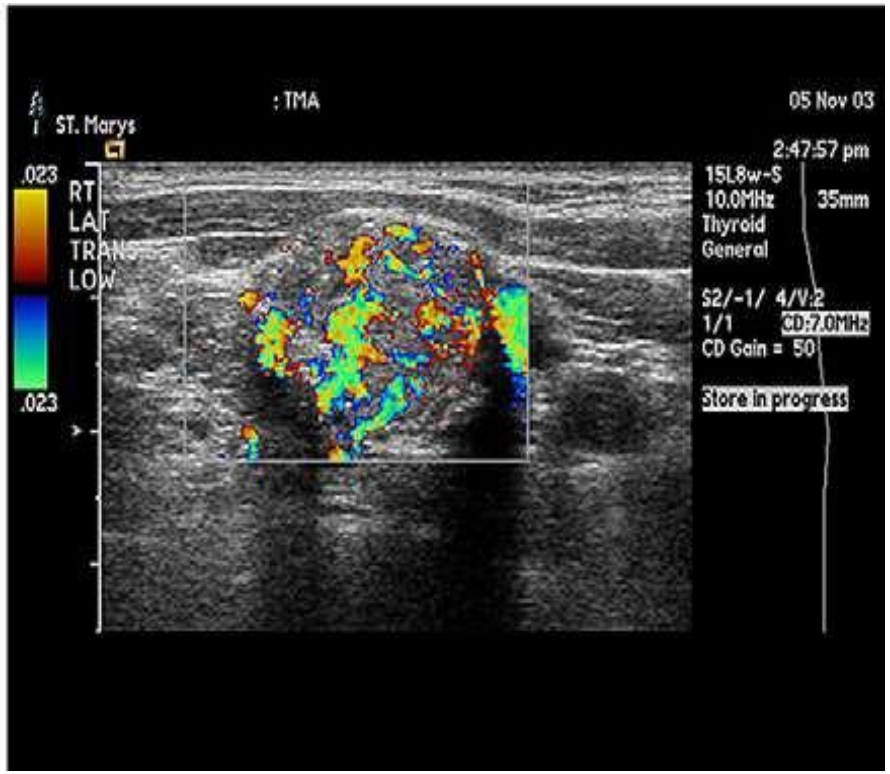


Septated cyst

Worrisome Features on Ultrasound

- **Microcalcifications**
- Hypoechoic
- Solid
- **Abnormal lymph nodes**
- **Extrathyroidal extension**
- Large
- **Central Vascularity**
- **Irregular Margins**
- Tall > Wide
- Coarse calcifications
- Absence of Halo
- ?Solitary





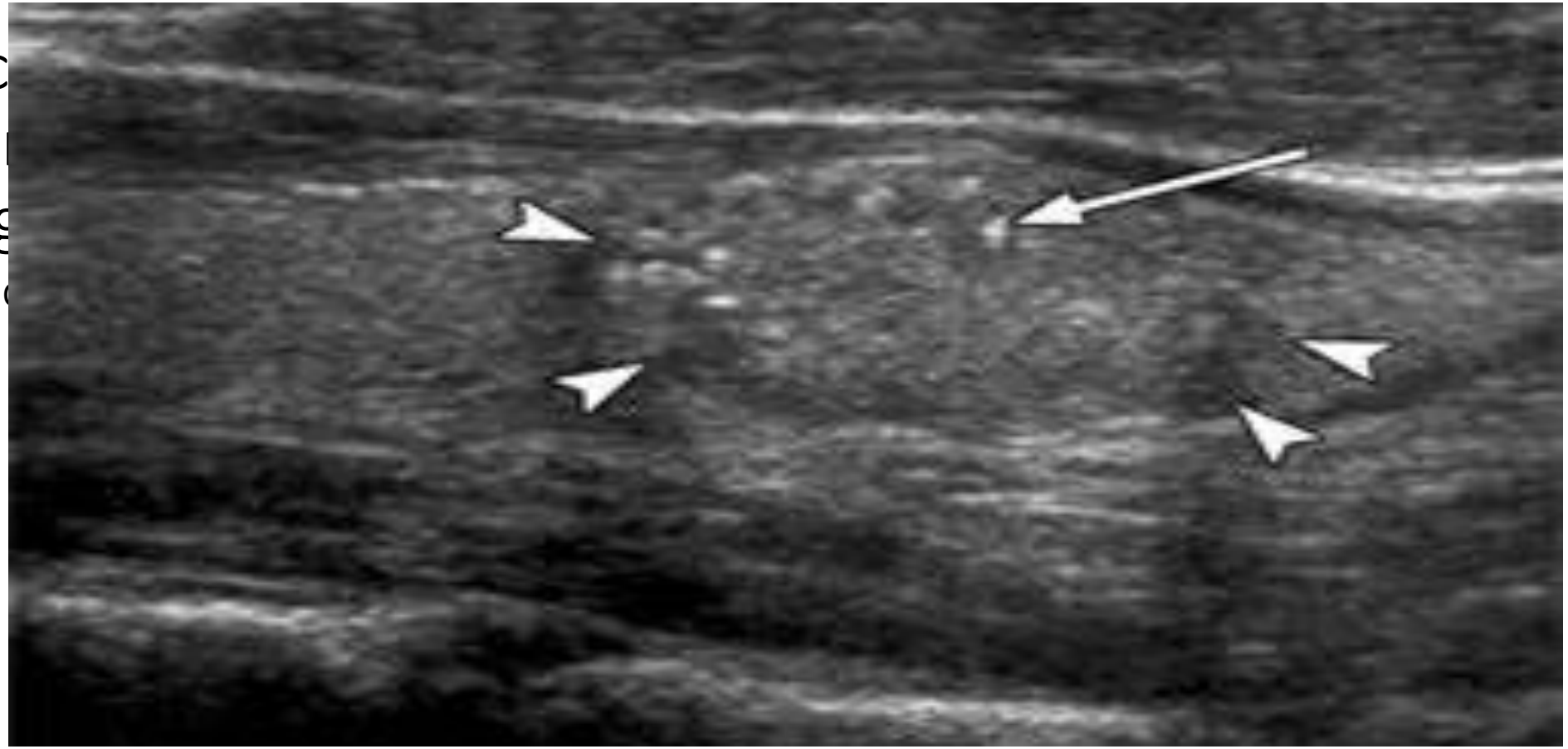
US images of a left lobe thyroid nodule. (Lt) The 1.7 1.4-cm solid left lobe thyroid nodule was hypoechoic. (Rt) Color Doppler flow imaging shows hypervascularity. FNA biopsy showed papillary thyroid carcinoma, which was confirmed at surgery.

Calc

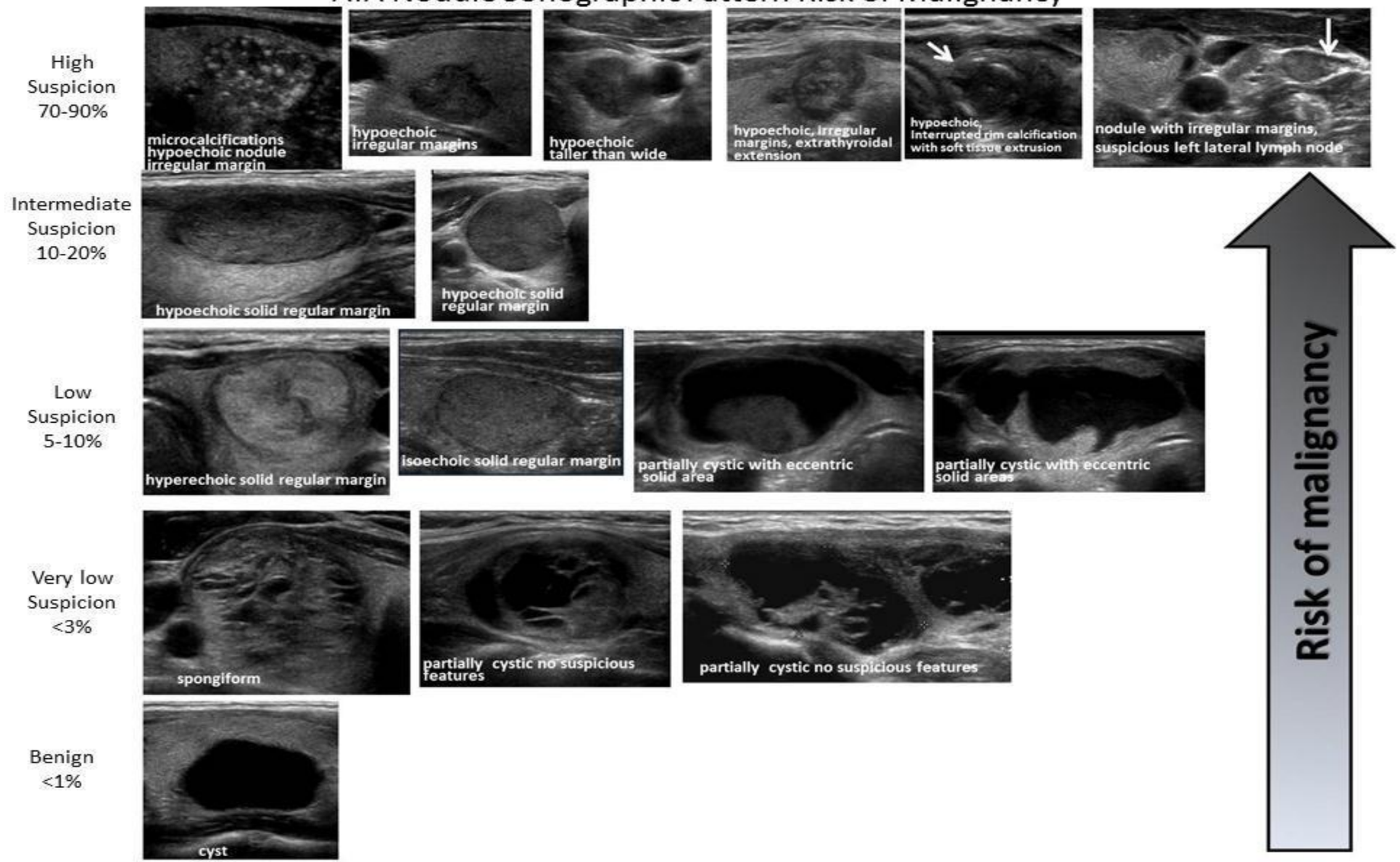
Poo

irreg

SUSPICI



ATA Nodule Sonographic Pattern Risk of Malignancy



Evaluation of the Thyroid Nodule *(Fine-Needle Aspiration)*

Currently considered to be the best first-line diagnostic procedure in the evaluation of a thyroid nodule:

Advantages:

- Safe Cost-effective
- Minimally invasive
- Leads to better selection of patients for surgery than any other test.

FNA halved the number of patients requiring thyroidectomy (Mazzaferri, 1993)

FNA has double the yield of cancer in those who do undergo thyroidectomy (Mazzaferri, 1993)

Fine-Needle Aspiration *(continued…)*

Limitations:

Skill of the aspirator

- Sampling error in lesions <1cm, >4cm, multinodular lesions, and hemorrhagic lesions
- Error can be diminished using ultrasound guidance
- Expertise of the cytologist
  difficulty in distinguishing some benign cellular adenomas from their malignant counterparts (follicular and Hurthle cell

False negative results = 1%-6% (Mazzeferri, 1993)

False positive results = 3%-6% (Rojeski, 1985, Mazzeferri, 1993, Hall, 1989)

Ultrasound Features, Risk of malignacy and FNA guidance

Sonographic pattern	Ultrasound features	Risk of malignancy	Consider FNA
High suspicion	Solid hypoechoic or solid hypoechoic component of a cystic lesion with one or more of following irregular margins, microcalcifications, taller than wide, extranodal extensions	>70 to 90%	FNA at >1cm
Intermediate suspicion	Hypoechoic solid nodule with smooth margins, no microcalcifications, extranodal ext. or taller than wide in shape	10 to 20%	Recommend FNA >1cm
Low suspicion	Isoechoic or hyperechoic soiid nodule or partially cysticwith eccentric solid areas with no microcalcifications, irregular margins, extranodal ext. or taller than wide	5 to 10%	FNA at >1.5 cm
Very low suspicion	Spongiform or patially cystic without any features as above	<3%	FNA at>2cm or obsevation
Benign	Purely cystic nodule	<1%	No biopsy

Diagnostic Category	Risk of Malignancy (%)	Usual management
Nondiagnostic or Unsatisfactory		Repeat FNA with ultrasound guidance
Benign	0-3	Clinical Follow up with ultrasound 6 months
Atypia of Undetermined significance or Follicular lesion of Undetermined significance(AUS/FUS)	5-15	Repeat FNA 3 months; if same, then lobectomy
Follicular Neoplasm or suspicious for Follicular neoplasm	15-30	Surgical Lobectomy
Suspicious for Malignancy	60-75	Near total thyroidectomy or surgical lobectomy
Malignant	97-99	Near total thyroidectomy

Classification of Malignant Thyroid Neoplasms

- Papillary carcinoma
  - Follicular variant
  - Tall cell
  - Diffuse sclerosing
  - Encapsulated
- Follicular carcinoma
  - Overtly invasive
  - Minimally invasive
- Hurthle cell carcinoma
- Anaplastic carcinoma
  - Giant cell
  - Small cell
- Medullary Carcinoma
- Miscellaneous
  - Sarcoma
  - Lymphoma
  - Squamous cell carcinoma
  - Mucoepidermoid carcinoma
  - Clear cell tumors
  - Pasma cell tumors
  - Metastatic
    - Direct extention
    - Kidney
    - Colon
    - Melanoma

CASE 1 contd

She appeared about 2 years after with complaints of night sweats and insomnia. She was seeing a Gynaecologist. She admitted to high anxiety. She was now on Gabapentin, Meloxicam and ? Clonidine. Her weight was stable. She continued to have palpitations but no chest pains.

Labs: FT4 12 pmol/l, and TSH <0.01mIU/L

Px: BMI 24.1 kg/m2, BP 150/60 and pulse 72bpm. Her thyroid was same. She had no orbitopathy, no bruits but had? tremor of her left outstretched hand. Her DTRs were normal.

CASE 1 contd

- Her repeat nuclear scan showed a 4 hour uptake of 16.2% and 24 hours 30.9% with her toxic nodule persisting.
- She was offered Surgery or ablative therapy but chose Surgery.

- Although her initially pathology was a Follicular lesion, favour Hyperplastic nodule, the Expert”s read it as Follicular carcinoma with a capsular invasion.

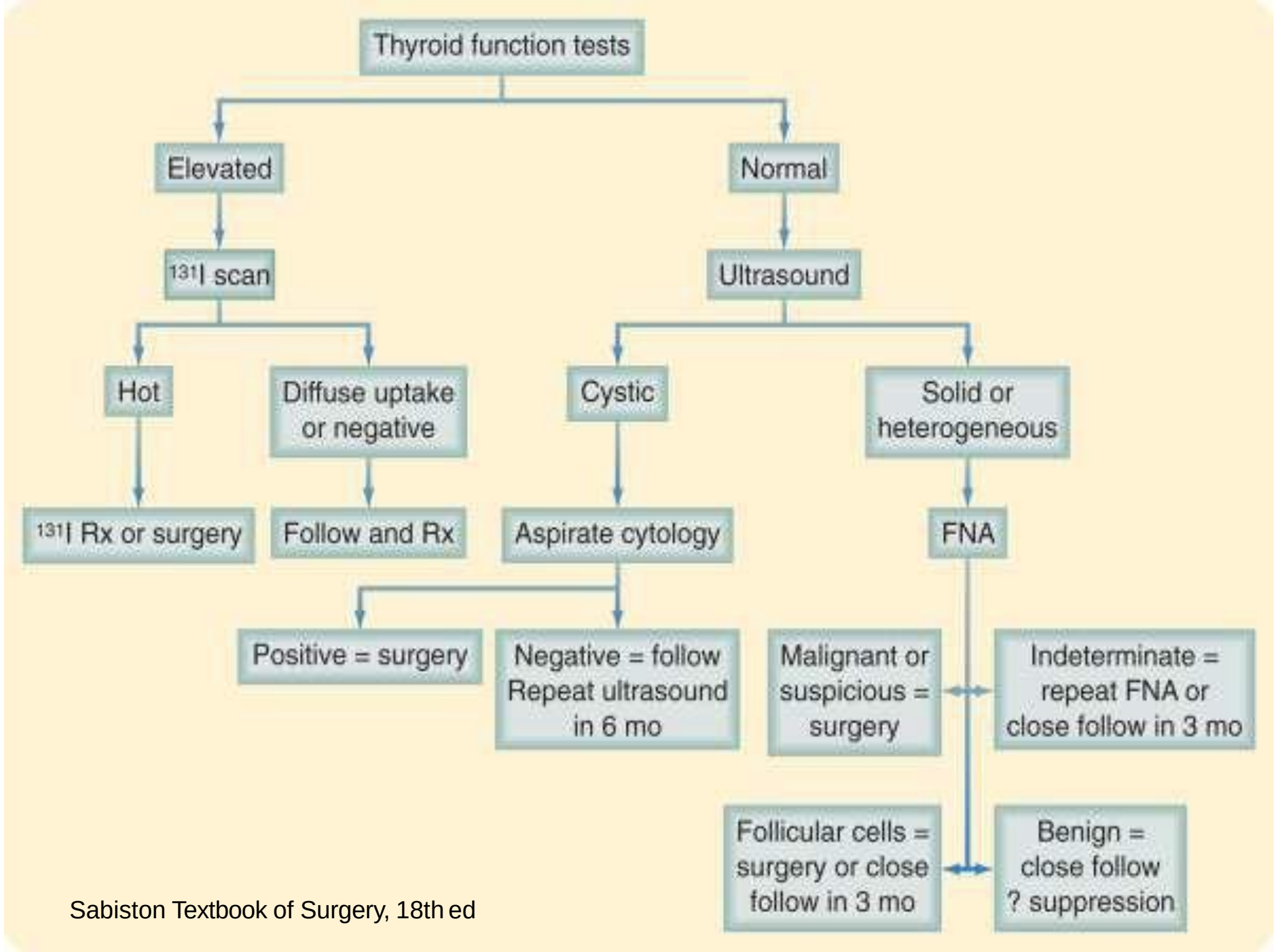
Interpreting the Biopsy Report

What you get:

- benign (low probability)
- indeterminate
- suspicious (high probability)
- inadequate specimen

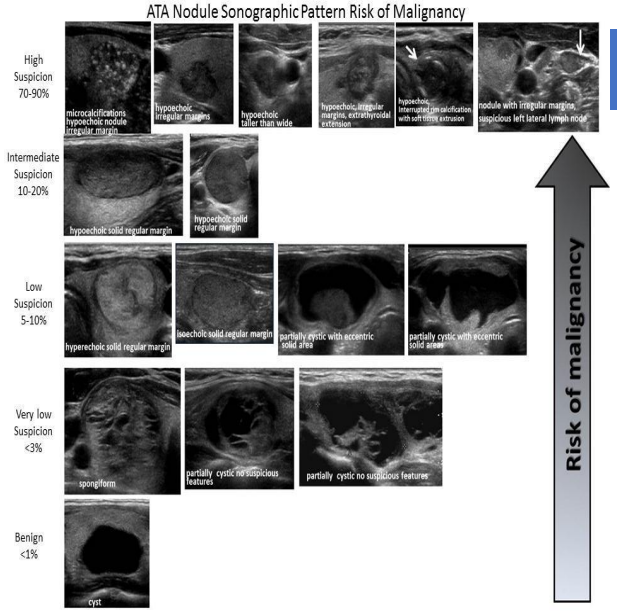
What it means:

- benign - 90-95% likelihood it is benign
- indeterminate- who knows?
- suspicious- it’s malignant.
- inadequate specimen - do it again (and again)



Sabiston Textbook of Surgery, 18th ed

ATA Guidelines for Thyroid Nodule



Haugen et al, Thyroid, 2015

Nodule TSH normal or high

US

Pure cyst or benign pattern
No FNA

High suspicion

Intermediate pattern

Low suspicion

Very low suspicion

FNA >1 cm

FNA >1.5 cm

FNA >2 cm

Take Home Point

1. **Do not routinely order [*or perform]* a thyroid ultrasound in patients with abnormal thyroid function tests if there is no palpable abnormality of the thyroid gland.**
2. **Do not routinely perform a thyroid scan in patients with nodule(s) but with normal thyroid function tests.**
3. **Do not routinely refer patients with thyroid nodules to Surgery**

THANK YOU
ANY QUESTIONS OR COMMENTS