

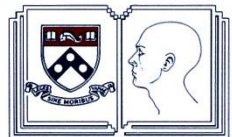
# Pediatric Thyroid Nodules

Ken Kazahaya, MD, MBA, FACS

Children's Hospital of Philadelphia

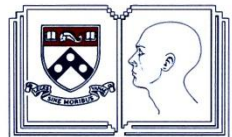
and

University of Pennsylvania School of Medicine



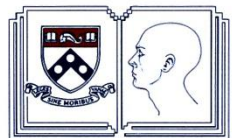
# Thyroid Nodules

- **Approx 275,000 new thyroid nodules detected annually (adults and children)**
- **Challenge to determine which nodules are malignant**
- **Typically asymptomatic**
- **Most pts - euthyroid**



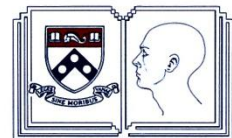
# Pediatric Thyroid Masses

- **Thyroid disorders affect about 4% of school-aged children**
- **Thyroid nodules relatively uncommon**
  - **3.7% in pediatric population**
  - **Majority of lesions present as solitary nodules**
  - **Significantly higher incidence of malignancy in nodules in children – 18% to 21%, some report even as high as 43%; mean of 26.4%**
  - **Predominant diagnosis – Follicular Adenoma**
- **Some advocate surgically removing any nodule in the pediatric population**



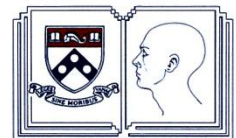
# Thyroid Nodules DDx

<b>Malignant</b>	<b>Benign</b>
Papillary Thyroid Carcinoma Follicular Thyroid Carcinoma Mixed Type Thyroid Carcinoma Medullary Thyroid Carcinoma Anaplastic Thyroid Carcinoma Undifferentiated Thyroid Ca Lymphoma Metastatic disease	Follicular Adenoma Thyroiditis Thyroglossal Cyst Colloid Nodule Branchial Anomaly



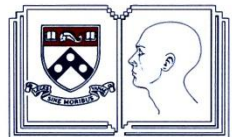
# Pediatric Thyroid Nodules

- **Comprehensive medical history**
- **Physical examination**
- **Lab studies**
- **Imaging**
- **Fine-needle aspiration biopsy (FNAB)**
- **Surgery**



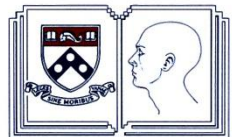
# Malignancy Risks

- **Previous head and neck radiation**
- **Younger age (<20 yrs)**
- **FHx of thyroid cancer or MEN**
- **Appearance or enlargement while on thyroid suppressive treatment**



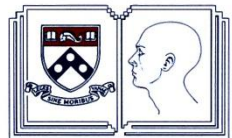
# Pediatric Thyroid Nodules

- **Physical examination**
  - **Thyroid findings**
    - **Size and consistency of thyroid gland**
    - **Size and location of nodule**
    - **Mobility of nodule**
  - **Hoarseness / VC paresis**
  - **Cervical adenopathy**



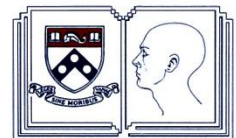
# Concerning Nodule Characteristics

- Nodule > 4cm
- Firm nodule
- Irregular shape
- Rapid growth
- Fixation to skin
- Fixation to adjacent structures
- Compressive sx's:
  - Dysphagia
  - Dysphonia
  - Hemoptysis
- Vocal cord paralysis
- Palpable ipsilateral adenopathy



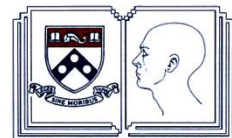
# Laboratory Examination

- **Thyrotropin – TSH**
- **T<sub>3</sub>, T<sub>4</sub>,**
- **Thyroglobulin**
- **Thyroglobulin antibodies**
- **ESR**
- **Thyroid peroxidase antibody**
- **Calcitonin**



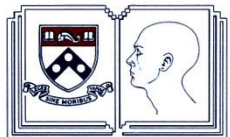
# Radioisotope Imaging

- Not as frequently utilized
- May be useful for a nodule w/ hyperthyroidism
- Technetium and iodine most commonly used
  - Technetium washes out rapidly from thyroid, better resolution
  - Iodine requires delay and longer scan time
- Nodules < 1 cm cannot be reliably detected
  
- 80-85% “cold” – 14% to 22% malignant
- 5% “hot” – 1% malignant
- 10%-15% “warm” – 10% to 36% malignant



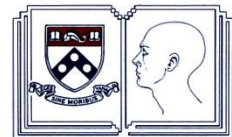
# CT and MRI

- **Limited role in initial management of solitary thyroid nodules.**
- **Prefer non-contrast CT – iodine-based contrast will delay any nuclear med scan for 4-8 weeks**



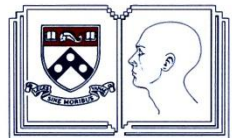
# Ultrasonography

- **Most widely used imaging modality**
- **Detects solid nodules > 3mm and cystic nodules > 2mm**
- **Concerning findings for malignancy**
  - **Size > 1cm**
  - **Microcalcifications**
  - **Hypoechoogenicity**
  - **Central intranodular vascular pattern**
  - **Heterogeneous echo structure**
  - **Absent or irregular “halo”**
  - **Irregular margin**
  - **Extraglandular extension**
  - **Lymph node alterations**



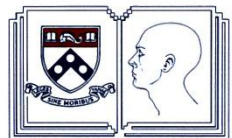
# Ultrasonography

- **Non-palpable or difficult to palpate nodules for US-guided FNA**
- **Follow-up imaging for solitary nodules managed conservatively**
- **Non-diagnostic FNA (not US-guided)**



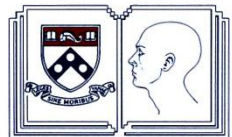
# Fine-Needle Aspiration Biopsy (FNAB)

- **“Gold Standard” for the evaluation of a thyroid nodule**
- **Quick safe procedure, few complications and does not require radiation exposure**
- **Decreases overall cost of care by about 25% by eliminating unnecessary surgeries and limiting the use of frozen sections intraoperatively**



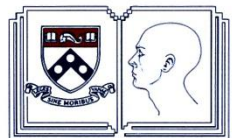
# FNAB

- **Can be difficult to perform on awake child**
  - Topical analgesia/anesthetic
  - Sedation
  - May require general anesthesia
- **Can use U/S for guidance and increase yield**
- **Best test to determine malignancy**
- **False negative - usually from sampling or interpretive errors**
- **False positive - rare**



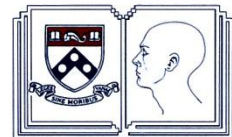
# Difficulties w/ Pediatric FNAB

- **Anatomical and physical limitations**
- **Patient discomfort or inability to tolerate the procedure, necessitating sedation or GA**
- **Need for an experience cytopathologist**
- **Need for experienced ultrasonographer**
- **Sampling errors**



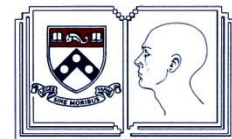
# FNA Complications

- Pain
- Hematoma
- Entry into trachea
- Transient thyroid swelling
- Cystic degeneration
- Transient bradycardia
- Transient VC paralysis
- Formation of calcifications
- Necrosis of nodule
- Capsule pseudoinvasion
- Fibrosis
- Transient thyrotoxicosis
- Elevation of thyroglobulin levels



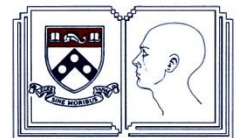
# Pediatric Thyroid FNAB

- **Results less accurate than in adults**
  - **Adult accuracy as high as 97%**
  - **Pediatric accuracy reported as high as 90%**
- **Useful for preoperative planning**
- **Predict more aggressive surgical approach**
- **Allows for more appropriate counseling of patient and family**



# Thyroid Nodule Evaluation

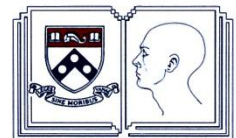
- **Hyperthyroid - Low TSH**
  - $^{123}\text{I}$  or  $^{99}\text{Tc}$  scan
    - **Hyperfunctioning**
      - Evaluate for hyperthyroidism
      - Consider thyroid suppression
    - **Non-functioning, “cold”**
      - Diagnostic U/S
      - Recommend FNAB



# Thyroid nodule – nl or ↑TSH

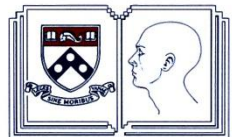
- **Diagnostic U/S**

- **No nodule and elevated TSH – eval for hypothyroidism**
- **Cystic → aspirate**
  - **Residual nodule → FNAB**
  - **Completely disappears**
    - **U/S in 4-6 weeks**
    - **If recurrent cyst – consider hemithyroidectomy**
- **Solid → FNAB**



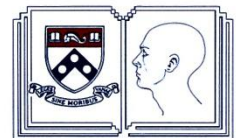
# FNAB

- **Benign**
- **Suspicious / follicular neoplasm**
  - Consider hemithyroidectomy
- **Equivocal / Non-diagnostic**
  - Repeat FNAB in about 3 months
  - If repeat FNAB still equivocal – consider hemithyroidectomy
- **Malignant → Total thyroidectomy neck dissection.**



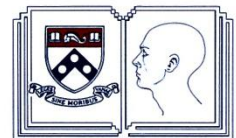
# FNAB - Benign

- **All benign nodules should be followed at least every 6 months**
  - **Serial examinations**
  - **Interval ultrasounds**
  - **If no significant change in size (<50% change in volume or <20% change in at least two dimensions), then can increase interval**
  - **If change in size > 50% of volume or >20% change in at least two dimensions, with a minimum of 2mm increase in solid nodules, then FNA should be repeated or can consider surgical excision**

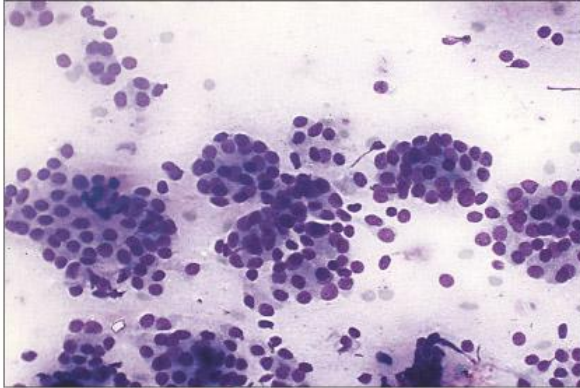


# **FNAB – Indeterminant/Suspicious**

- **“Follicular neoplasm” “Hürthle cell neoplasm”**
- **20-30% end up being malignant**
- **Molecular markers – BRAF, RAS, RET, Pax8-PPAR, galectin-3**
- **Consider  $^{99m}\text{Tc}$  or  $^{123}\text{I}$  scanning – “hot” nodule would reduce suspicion for malignancy**
- **Lobectomy/Hemithyroidectomy**
- **Consider total thyroidectomy if risk factors present**

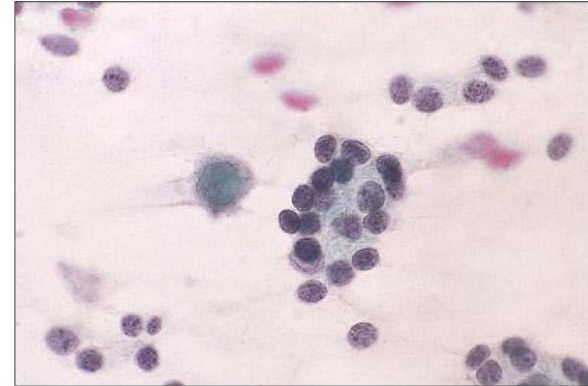


# FNA – Adenoma v. FTC



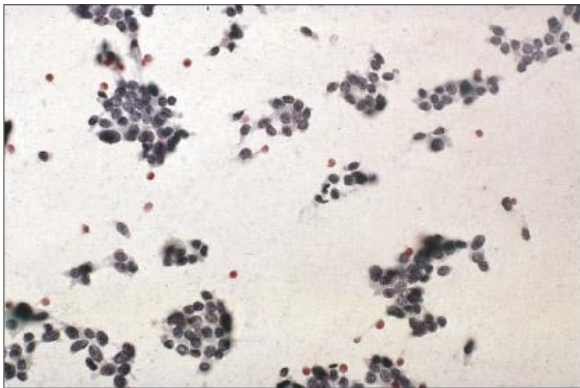
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**Typically more cellular**



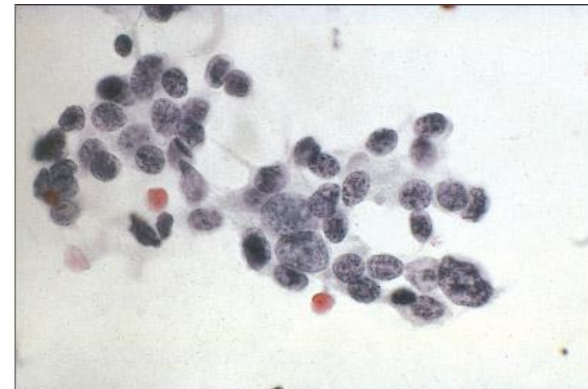
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**Syncytial grouping of the cells**



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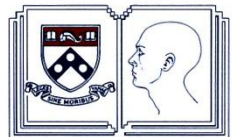
**FTC – cellular, absence of colloid, enlarged, monomorphic cells, coarse chromatin, indistinct cell margin**



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# Completion thyroidectomy

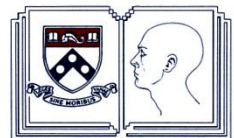
- **Can schedule a few weeks after the hemithyroidectomy**
- **Staged procedure report fewer complications**
  - Hypocalcemia
  - Hoarseness
- **Interval delay should not increase metastatic risk**



# **FNAB – Benign or Non-diagnostic**

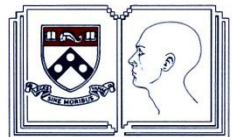
## **Consider total thyroidectomy in certain cases**

- **Large nodule > 4cm**
- **Extremely young**
- **Strong FHx thyroid Ca**
- **Previous radiation to neck**
- **Compressive/invasive features**
- **Rapid growth of nodule**
- **MEN or FMTC**
- **Cervical metastasis**
- **Painful/tender nodule**
- **Growth despite suppression**
- **Nodules with Hashimoto's thyroiditis**
- **Nodules with Grave's dz**

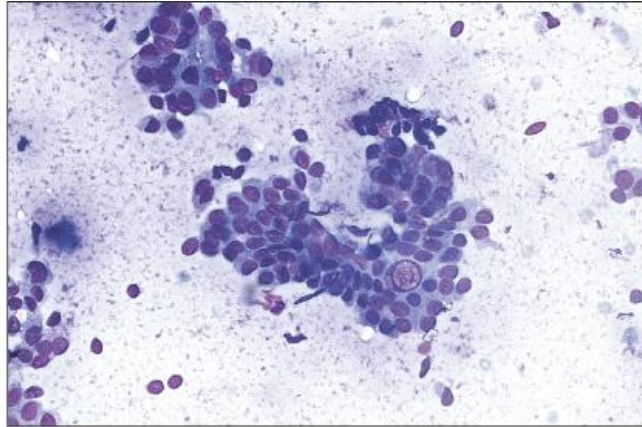


# Malignant FNAB

- **Total thyroidectomy preferred – 85.5%**
  - More extensive disease
  - Unknown multifocality
  - Higher rate of spread
  - Reduces risk of cancer recurrence
- **Increased need for repeat surgery when less than total thyroidectomy performed**
- **Management of lymph node debated**
  - Central compartment dissection
  - Modified radical lymphadenectomy

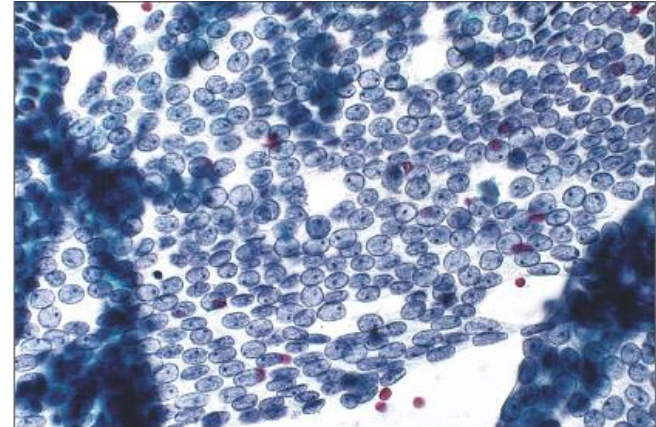


# FNAB - PTC



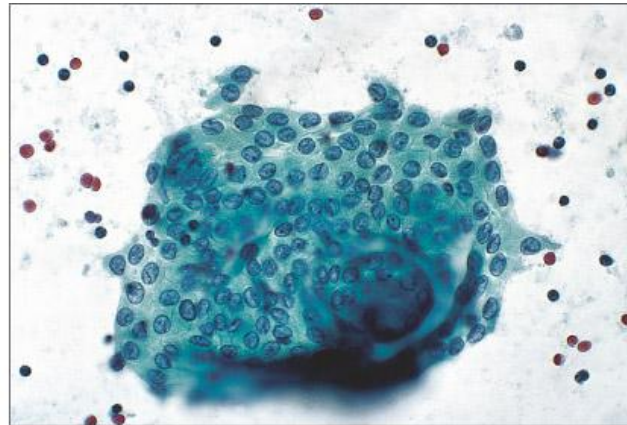
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**Nuclear crowding,  
intranuclear inclusions**



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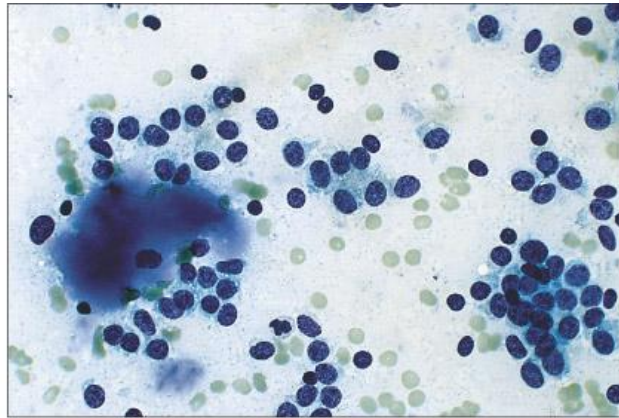
**Fine, evenly distributed  
chromatin with margination –  
makes nuclei appear clear, watery**



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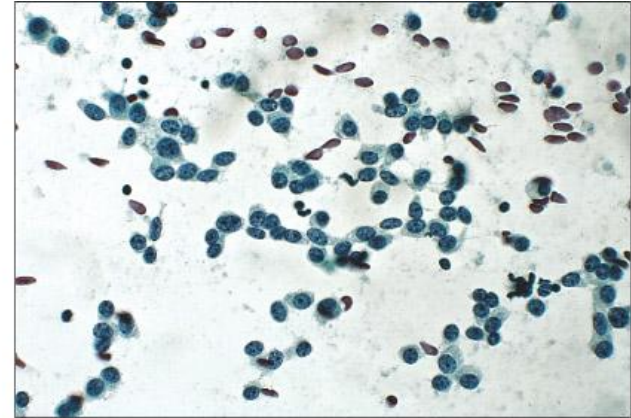
**Refractile psammoma body**

# FNAB - MTC



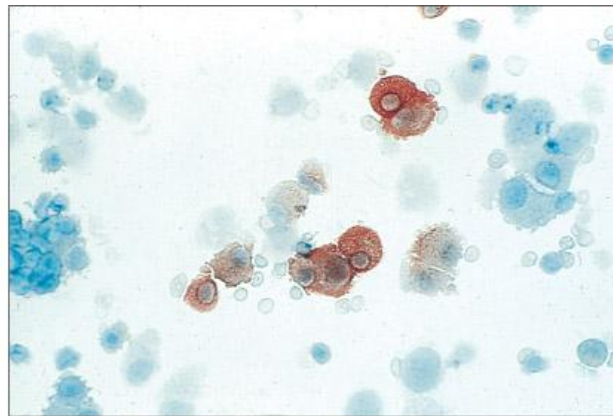
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**Amyloid; coarse chromatin,  
loose groups of cells**



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**Coarse 'salt and pepper' chromatin  
typical of a neuroendocrine neoplasm**

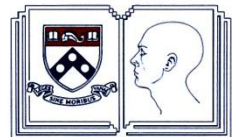


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**Calcitonin**

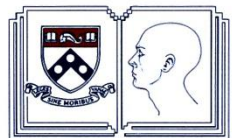
# Ped Thyroid Cancer

- **Disease limited to thyroid – 42%**
- **Increased propensity for regional and distant disease than adults**
  - **Regional nodal involvement – 40%-80%**
  - **Distant metastases – 7% to 25%**
    - **Lung – most common**
    - **Bone or Liver – rare**
- **Higher recurrence rate**
- **Longer overall survival**



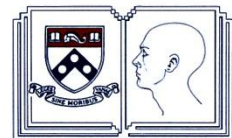
# Pediatric Thyroid Cancer

- **Thyroid carcinoma – 1.5% to 2%**
- **2:1 Female-to-Male preponderance**
- **Papillary thyroid carcinoma – 85%-90%**
- **Medullary thyroid carcinoma – 5%**
- **95% greater than 10 years of age**



# Management of thyroid malignancy

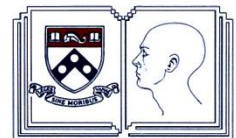
- **Total or near-total thyroidectomy**
- **Central neck dissection**
- **Pediatric pts frequently present with advanced disease**
  - **Nodal disease on physical examination or ultrasonography → Neck Dissection**
  - **Distant metastasis → Recommend CXR**
- **Consider post-op radioablation –  $^{131}\text{I}$**



# Thyroidectomy Risks

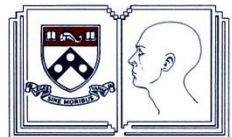
- **16% - 21% complication rate**
  - Majority – temporary hypocalcemia
  - Lobectomy with fewer complications
  - Higher complication rates in younger patients

**(estimated 17% complication rate in adults)**
- **2% - Permanent hypoparathyroidism**
- **1% - Permanent recurrent laryngeal nerve palsy**



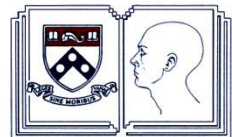
# Hypoparathyroidism

- **Primarily due to incidental stunning**
- **Devascularization of glands**
- **Removal of the parathyroid glands**
- **Number of viable parathyroid glands required is debated**
  - **One to 3 glands**
  - **Some recommend at least one gland be autotransplanted into the ipsilateral SCM**
- **Total/subtotal thyroidectomy has no significant correlation to increased incidental parathyroid removal or permanent hypocalcemia**
- **Incidental gland removal about 20%**



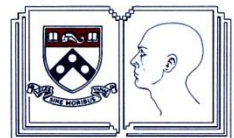
# Remnant Radioablation (RAI)

- **Surgery +  $^{131}\text{I}$  ablation**
  - 86% remained recurrence free
  - 14% locoregional recurrence
    - 28% thyroid bed
    - 63% lymphatic
- **Increased risks for recurrence**
  - Less than total thyroidectomy
  - Lack of  $^{131}\text{I}$  remnant ablation
  - Incomplete primary lymphadenectomy



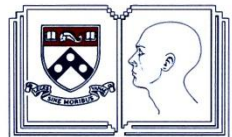
# RAI concerns

- **Secondary neoplasm – salivary gland, stomach, breast, bone marrow**
- **Rubino 2003 – Secondary neoplasm with RAI doses > 500mCi**
- **No evidence of secondary neoplasms with typical post-surgical RAI of 30 – 100 mCi.**
- **ATA recommends minimum activity of I<sup>131</sup> (30 to 100 mCi) necessary to achieve successful remnant ablation should be used**



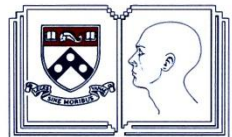
# RAI recommendations

- **Known distant metastases**
- **Gross extrathyroidal extension**
- **Primary tumor size > 4 cm**
- **Higher risk features – e.g. histology**



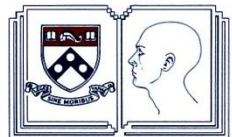
# RAI recommendations

- **NOT recommended**
  - **Unifocal cancer < 1cm without higher risk features**
  - **Multifocal cancer**
    - **All foci < 1cm**
    - **Absence of other higher risk features**



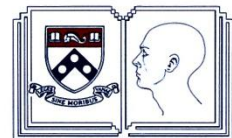
# Post-operative management

- **Levothyroxine suppression of TSH**
  - Reduce stimulation for follicular growth
  - Association between thyroid hormone suppression and reduction of adverse clinical events
- **ATA recommendations for TSH levels**
  - Below 0.1 mU/L – persistent disease, high-risk pt
  - 0.2 – 0.5 mU/L – clinically and biochemically free of disease, low-risk pt, or pt who have not had RAI
  - Normal range - 0.3 – 2 mU/L - in patients free of disease and of low risk



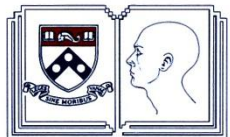
# Follow-up Evaluations

- **Post-surgery – 3-4 weeks**
- **Body scan and RAI - about 6 weeks**
- **6-12 months – U/S, serum Thyroglobulin(Tg) and anti-Tg antibodies (TgAb)**
  - **FNA – suspicious lesions or nodes > 5-8mm**
  - **Tg produced by normal or malignant follicular cells**
  - **Serial Tg levels - 80% predictive value**
  - **rhTSH-stimulated Tg < 1µg/L in absence of TgAB – 98-99.5% completely tumor free.**
- **Routine serial evaluations**



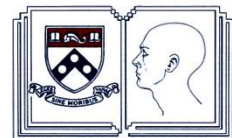
# Survival

- **Papillary Carcinoma**
  - 98% - 5 yr
  - 97% - 15 yr
  - 91% - 30 yr
- **Follicular Carcinoma**
  - 96% - 5 yr
  - 95% - 15 yr
  - 92% - 30 yr
- **Medullary Carcinoma**
  - 96% - 5 yr
  - 86% - 15 yr
  - 15% - 30 yr

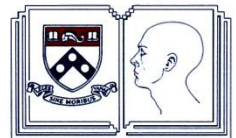


# Survival

- **Overall mean survival time – 30.5 yrs**
  - Female- 40 yrs
  - Male – 20.4 yrs
- **Survival dependent on histology**
- **Distant metastases at time of presentation – significantly worse outcome**
- **Pts with surgery had longer survival**

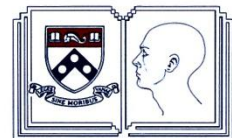


# QUESTIONS?



# American Thyroid Association

- **Recent Thyroid Guidelines**
  - Revised Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer
  - Management of medullary thyroid carcinoma
  - Consensus Statement on Neck Surgery to Treat Thyroid Cancer
- **[www.thyroid.org](http://www.thyroid.org)**



# Thank You

