Why is there a lump in my neck and do I need to worry?

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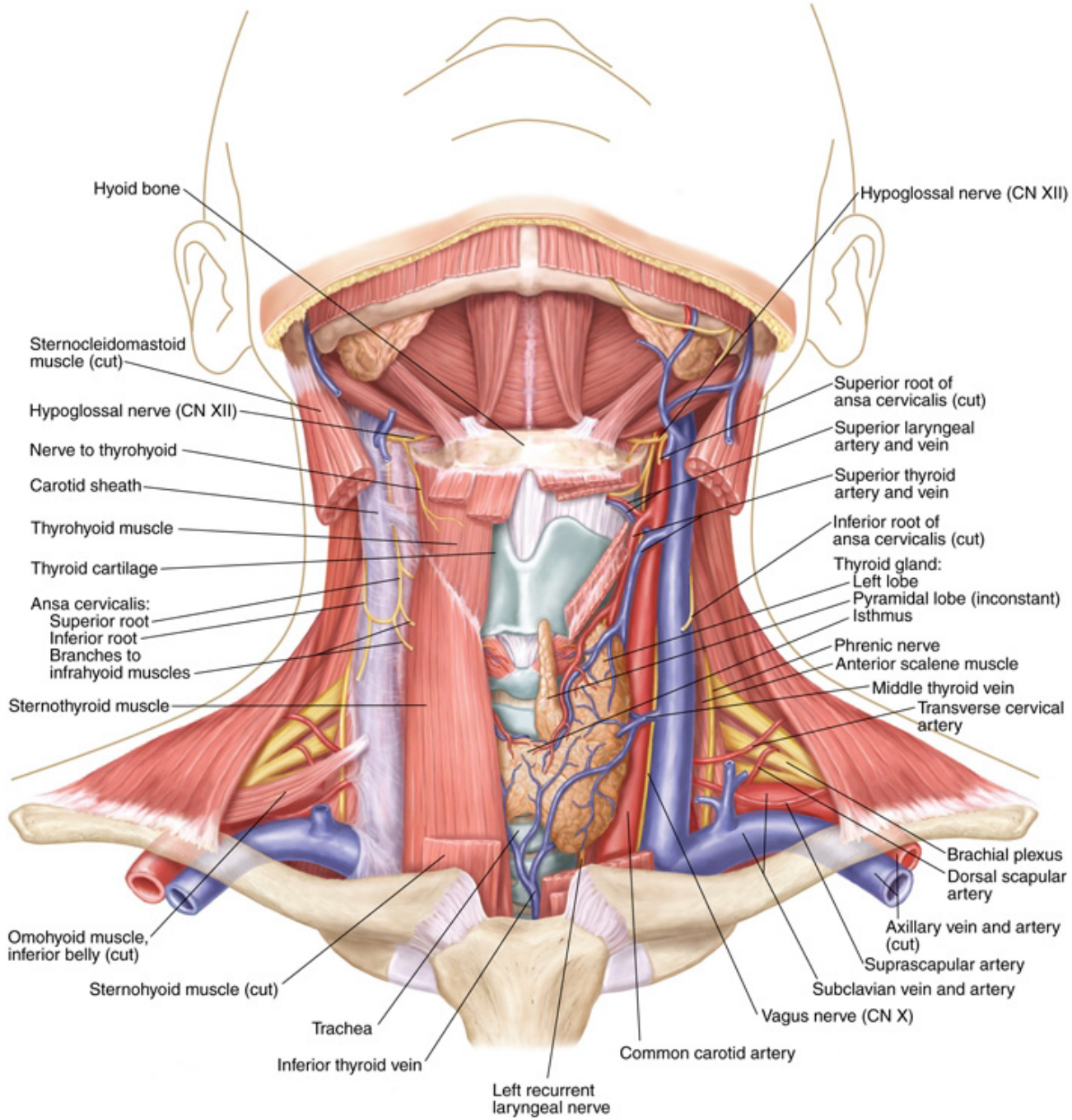
Osher Mini-Medical School Lecture
November 27, 2018

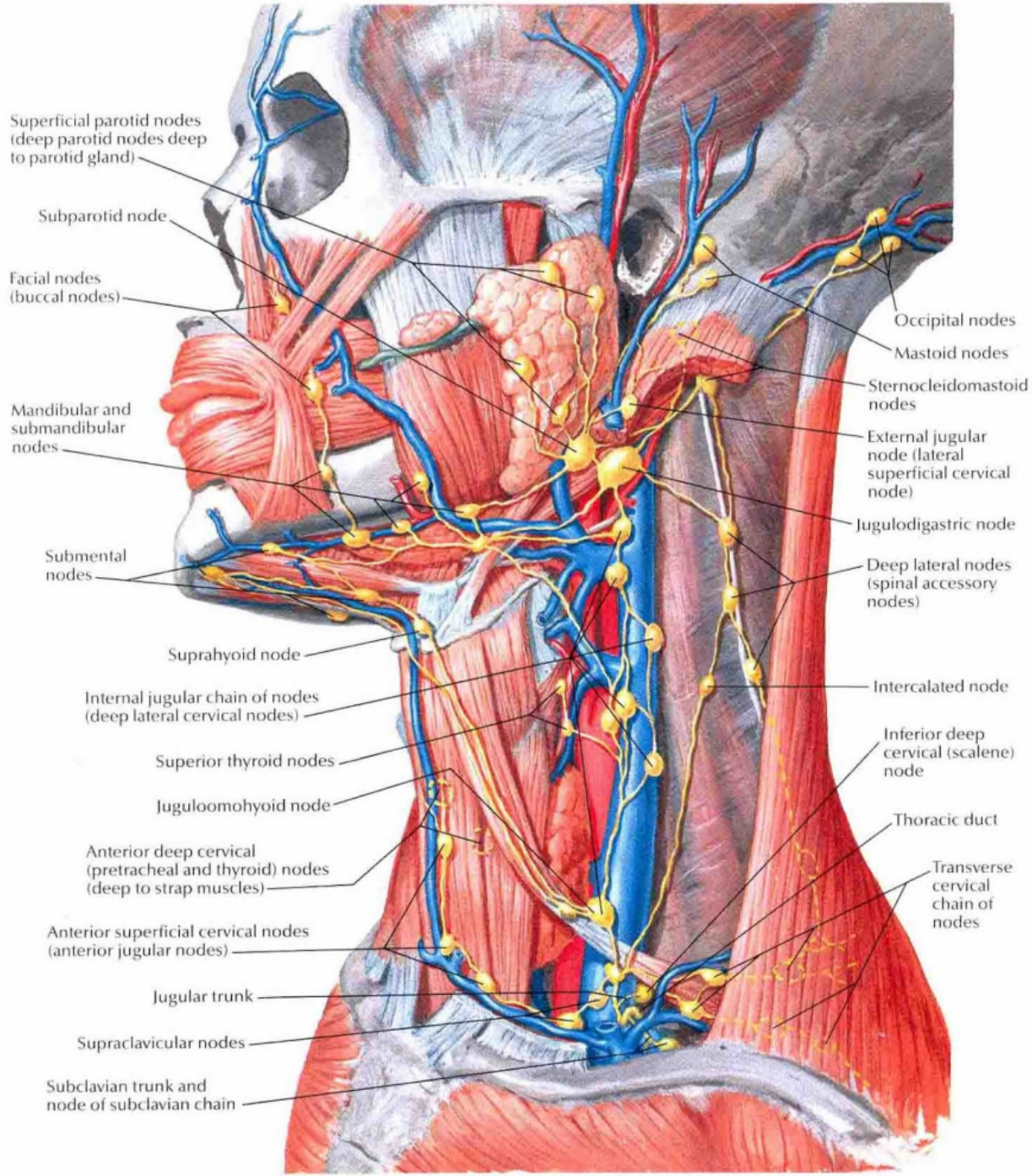
Disclosures

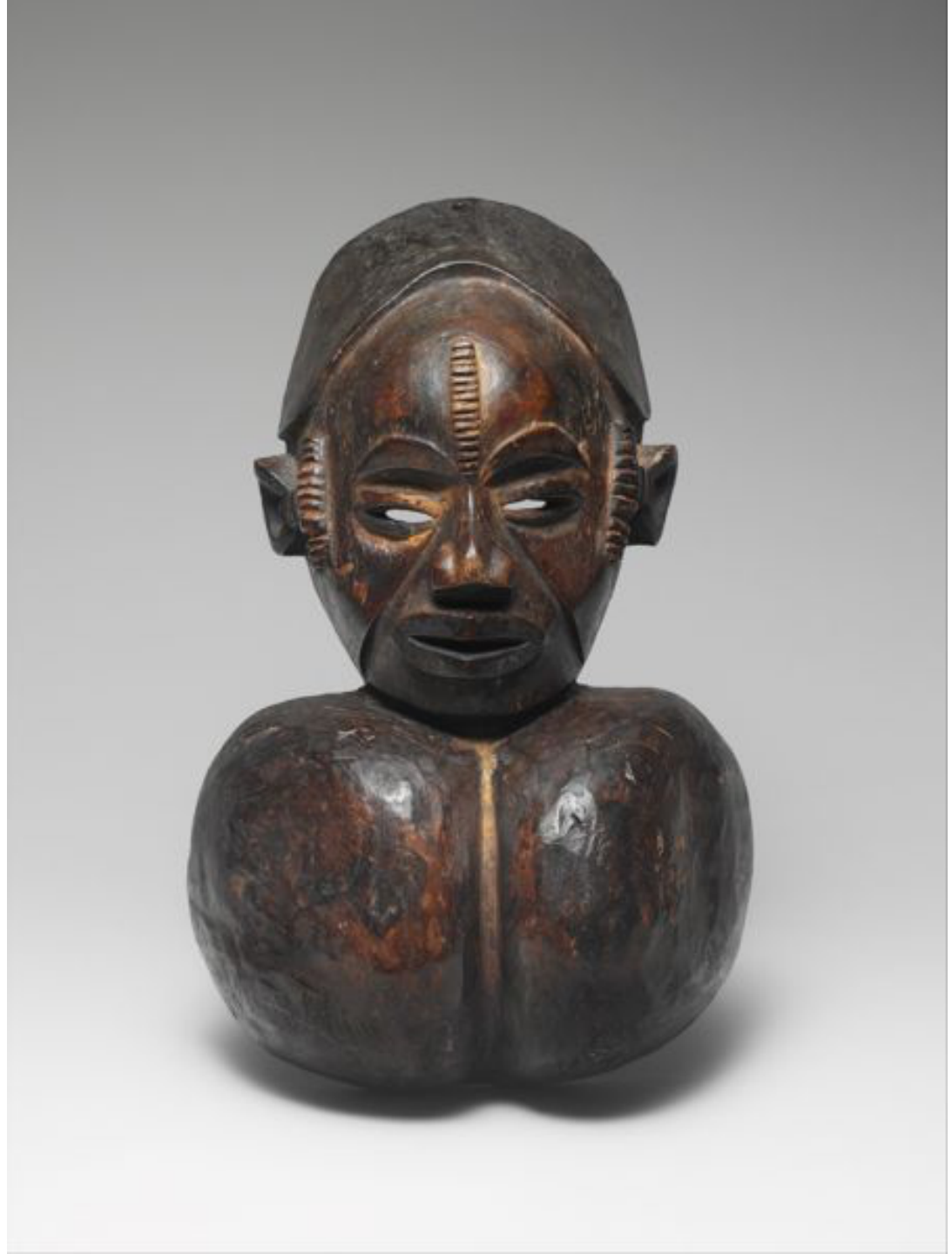
- No disclosures

Outline

- An introduction to the neck
- Anatomy of the neck
- Common types of neck masses
- What to do when you find a neck mass?
- Some thoughts on thyroid nodules/thyroid cancer/overdiagnosis and overtreatment



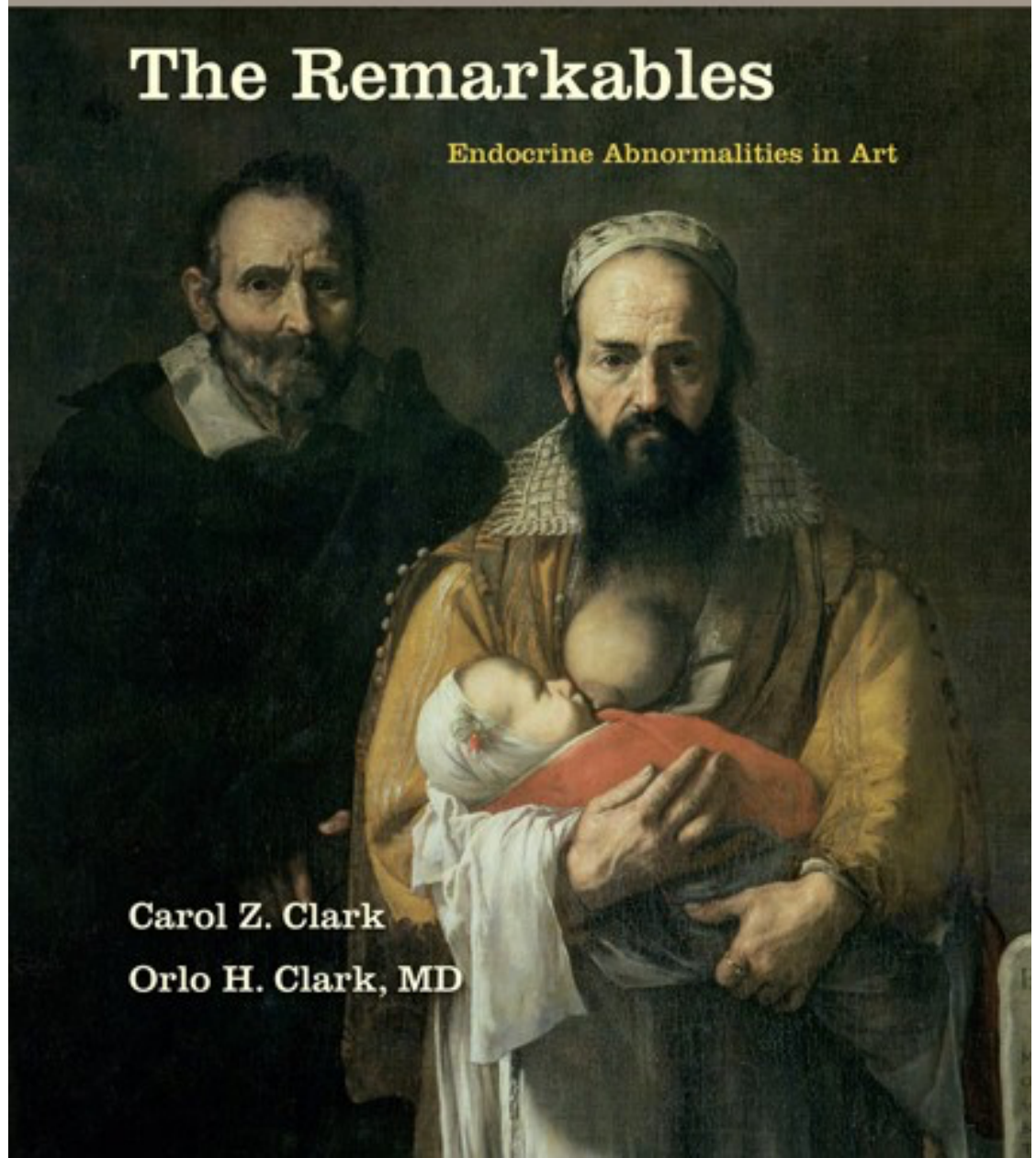

Superficial parotid nodes (deep parotid nodes deep to parotid gland)
Subparotid node
Facial nodes (buccal nodes)
Mandibular and submandibular nodes
Submental nodes
Suprahyoid node
Internal jugular chain of nodes (deep lateral cervical nodes)
Superior thyroid nodes
Juguloomohyoid node
Anterior deep cervical (pretracheal and thyroid) nodes (deep to strap muscles)
Anterior superficial cervical nodes (anterior jugular nodes)
Jugular trunk
Supraclavicular nodes
Subclavian trunk and node of subclavian chain
Occipital nodes
Mastoid nodes
Sternocleidomastoid nodes
External jugular node (lateral superficial cervical node)
Jugulodigastric node
Deep lateral nodes (spinal accessory nodes)
Intercalated node
Inferior deep cervical (scalene) node
Thoracic duct
Transverse cervical chain of nodes



Perspectives in Medical Humanities

The Remarkables

Endocrine Abnormalities in Art



Carol Z. Clark

Orlo H. Clark, MD

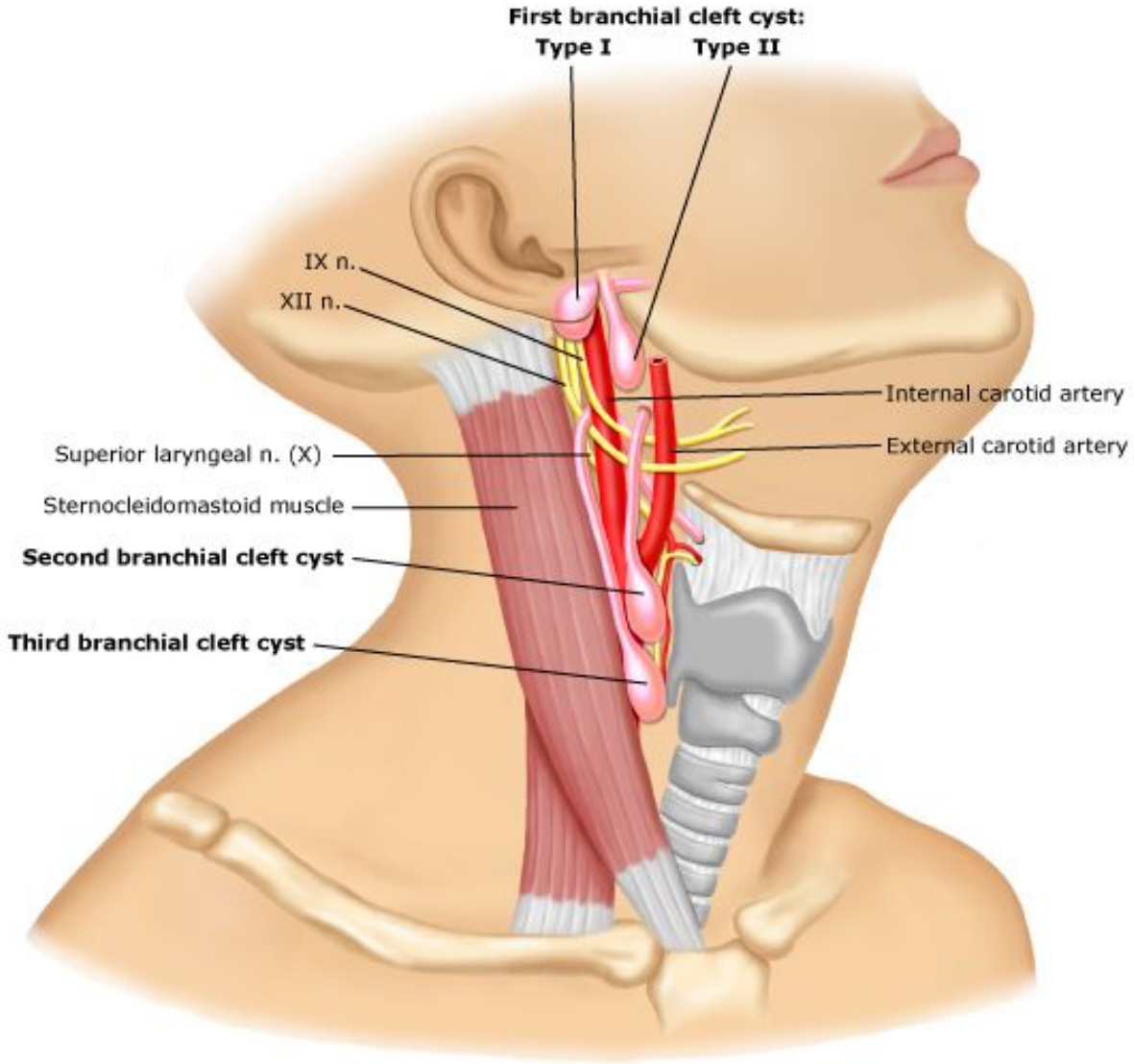
The Big Picture – How to classify neck masses?

- Congenital
- Infectious/Inflammatory
- Neoplastic

Common neck masses: congenital

Branchial cleft cyst

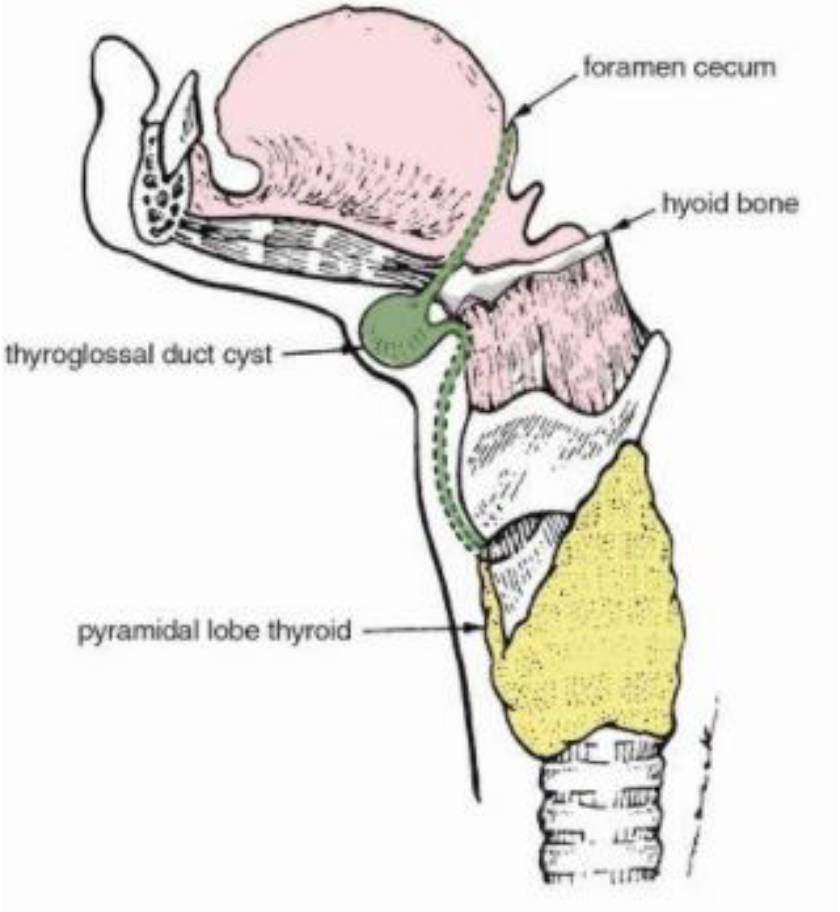
Branchial cleft cyst



Common neck masses: congenital

Thyroglossal duct cyst

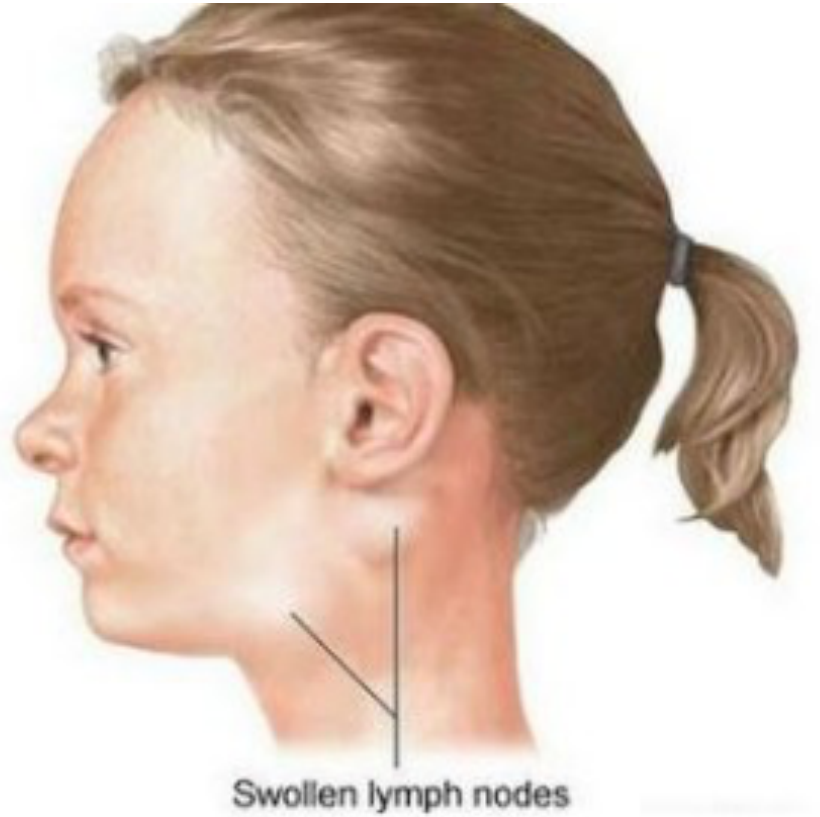
Thyroglossal duct cyst



Common neck masses: infectious/ inflammatory

Reactive lymph node

Common neck masses: infectious/ inflammatory



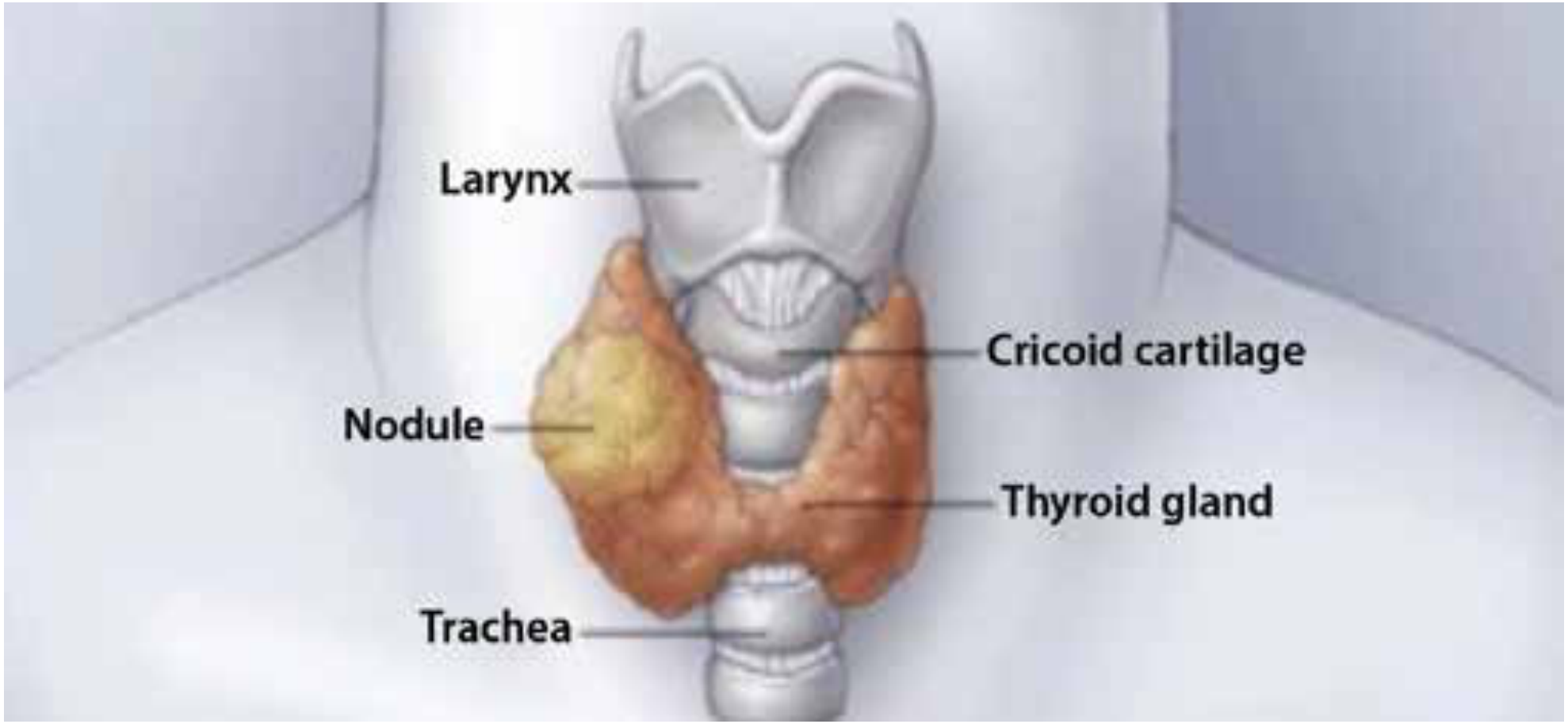
- Mononucleosis with swollen cervical nodes

Mononucleosis with swollen nodes

What are some common neck masses?

Right thyroid nodule

Right thyroid nodule



Numerous other possibilities!

Table 1
"KITTENS" mnemonic for the differential diagnosis of the adult neck mass

K	**Congenital/developmental anomalies**
	Thyroglossal duct cyst
	Branchial cleft cyst
	Dermoid cyst
	Vascular malformation, ie, "lymphangioma," "lymphovenous malformation," etc
I	**Infectious/inflammatory**
	Lymphadenitis/cervical adenopathy
	Viral (EBV)
	Bacterial (cat scratch disease, mycobacteria, atypical mycobacteria)
T	**Trauma**
	Hematoma
	Pseudoaneurysm
	Laryngocele
T	**Toxic**
	Thyroid toxicosis
E	**Endocrine**
	Thyroid neoplasms
	Parathyroid neoplasms
N	**Neoplasms**
	Salivary gland
	Parapharyngeal space—salivary tumors, glomus tumors, neurogenic tumors
	Lipoma
	Lymphoma
S	**Systemic disease**
	Sarcoidosis
	Sjögren syndrome
	Kimura disease
	Castleman disease

Data from Pasha R. Otolaryngology: head and neck surgery clinical reference guide. 2nd edition. San Diego: Plural Publishing, Inc; 2006. p. 79, 207.

Numerous other possibilities!

Space or Anatomic region	Differential Diagnosis
Superficial Fascia	Teratoma, Vascular Malformations, lipoma, plexiform Neurofibroma, fibromatosis colli of SCM (in neonates)
Danger Sp.	Cellulitis/Abscess
Masticator Sp.	Venous/lymphatic Malf., rhabdomyosarcoma, cellulitis/abscess
Parotid Sp.	Infection, Lymphatic malf., RMV thrombosis
Carotid Sp.	IJV thrombosis, lymphadenopathy, abscess, neuroblastoma
Retropharyngeal Sp.	Cellulitis/Abscess, extension of tumours or goiter
Perivertebral Sp.	Neuroenteric cyst, Cellulitis/Abscess, Spondylodiskitis
Posterior Cervical Sp.	Lymphatic malf., lymphadenopathy, lymphoma
Submandibular/Subling ual Sp.	Thyroglossal cyst, venous/lymphatic Malf, dermoid cyst, ranula, sublingual gland disease
Pharyngeal and Parapharyngeal Sp.	Lymphangioma, paraganglioma, rhabdomyosarcoma, abscess, Lymphoma

Infantile Hemangioma : can occur in any space!

How to evaluate a neck mass?

- Helpful information:
  - Age
  - Duration of time (>2-4 weeks?)
  - Recent infections?
  - Risk factors?
  - How does it feel (hard, fixed)?

Younger age

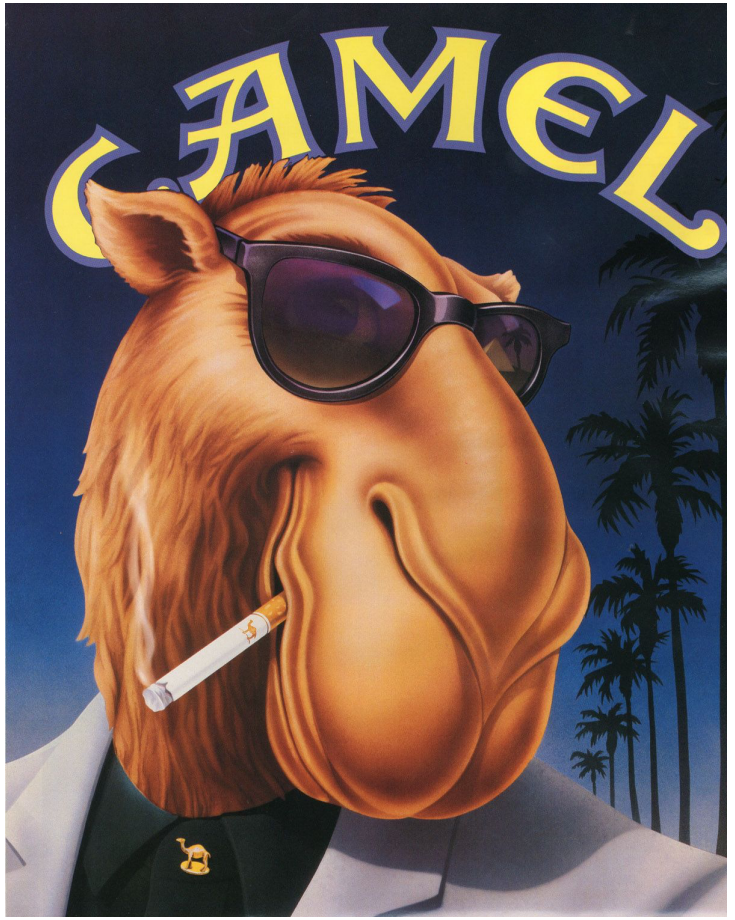
- More likely congenital or infectious/inflammatory
- Less likely malignant but still requires evaluation

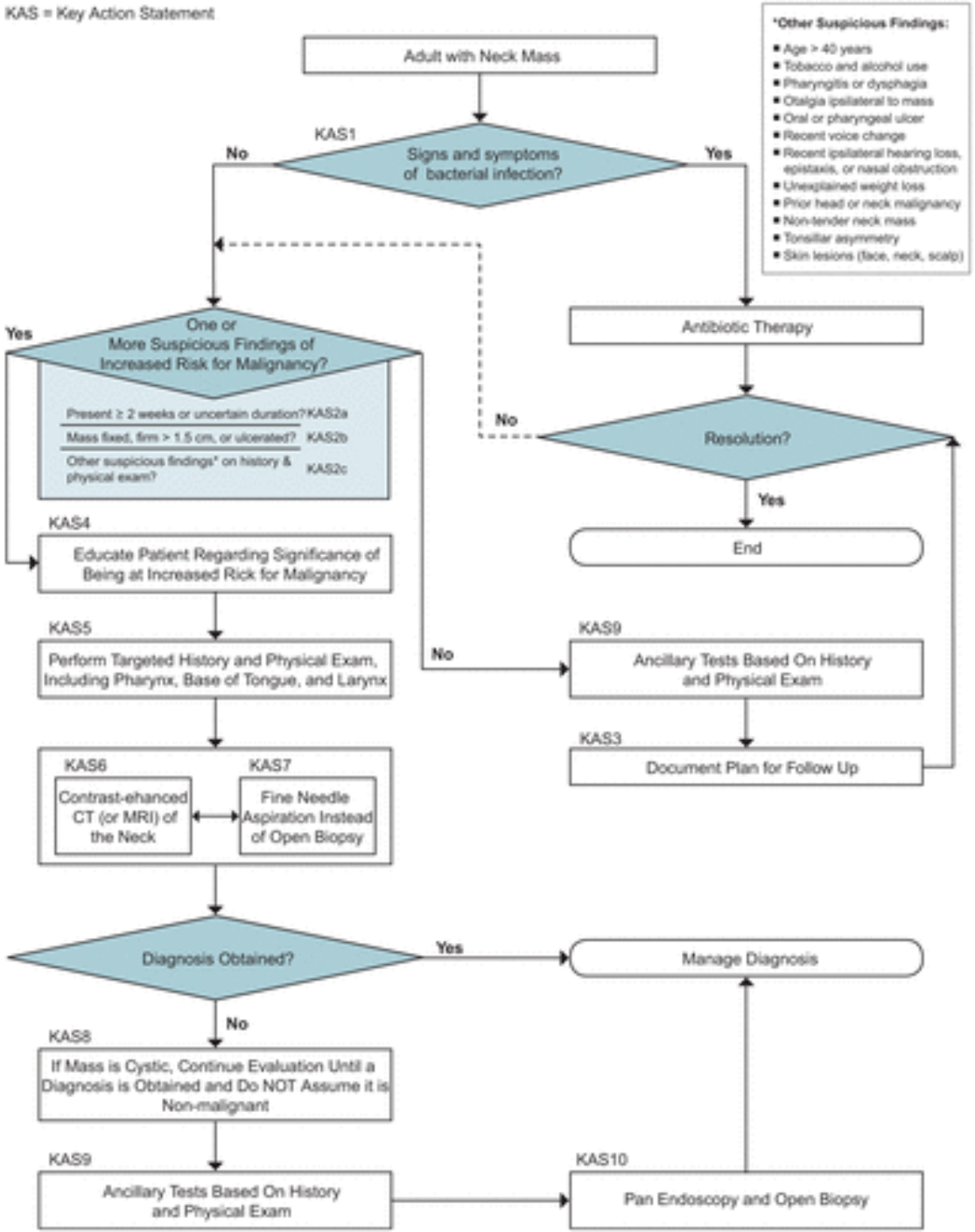
Older age (>40)

- Increased overall risk of malignant cause, should definitely be evaluated

Risk factors

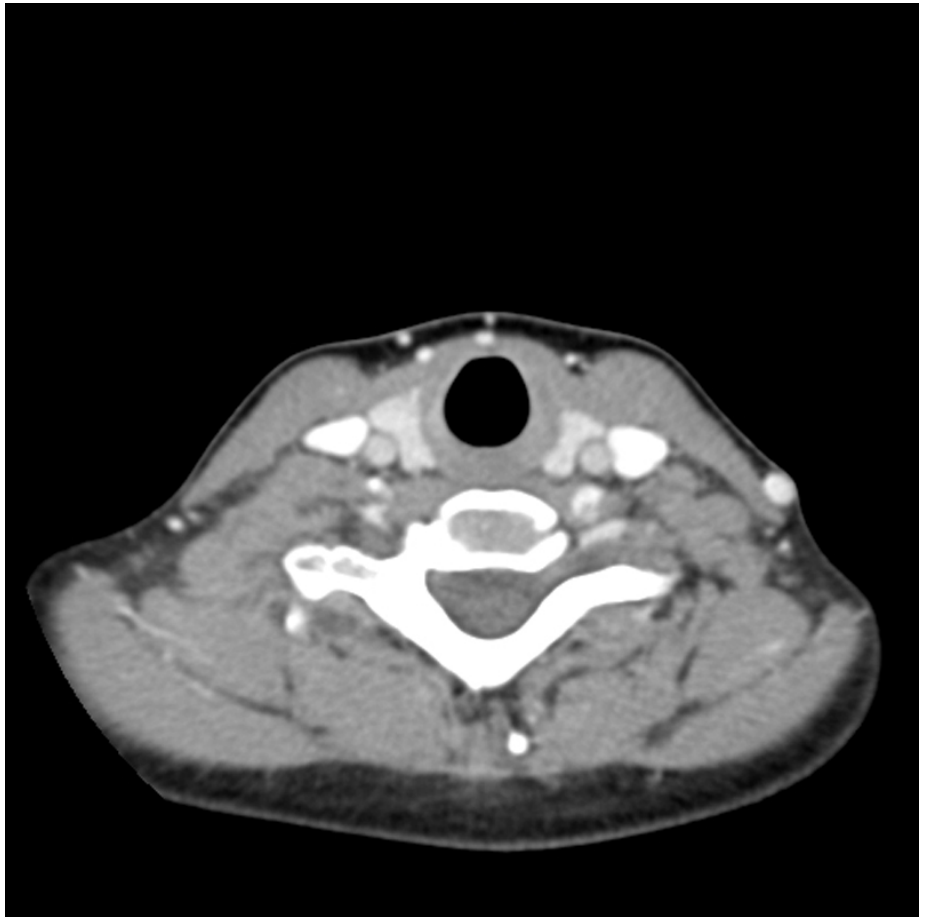
- Tobacco use
- Alcohol abuse
- HPV status
- Immunocompromised





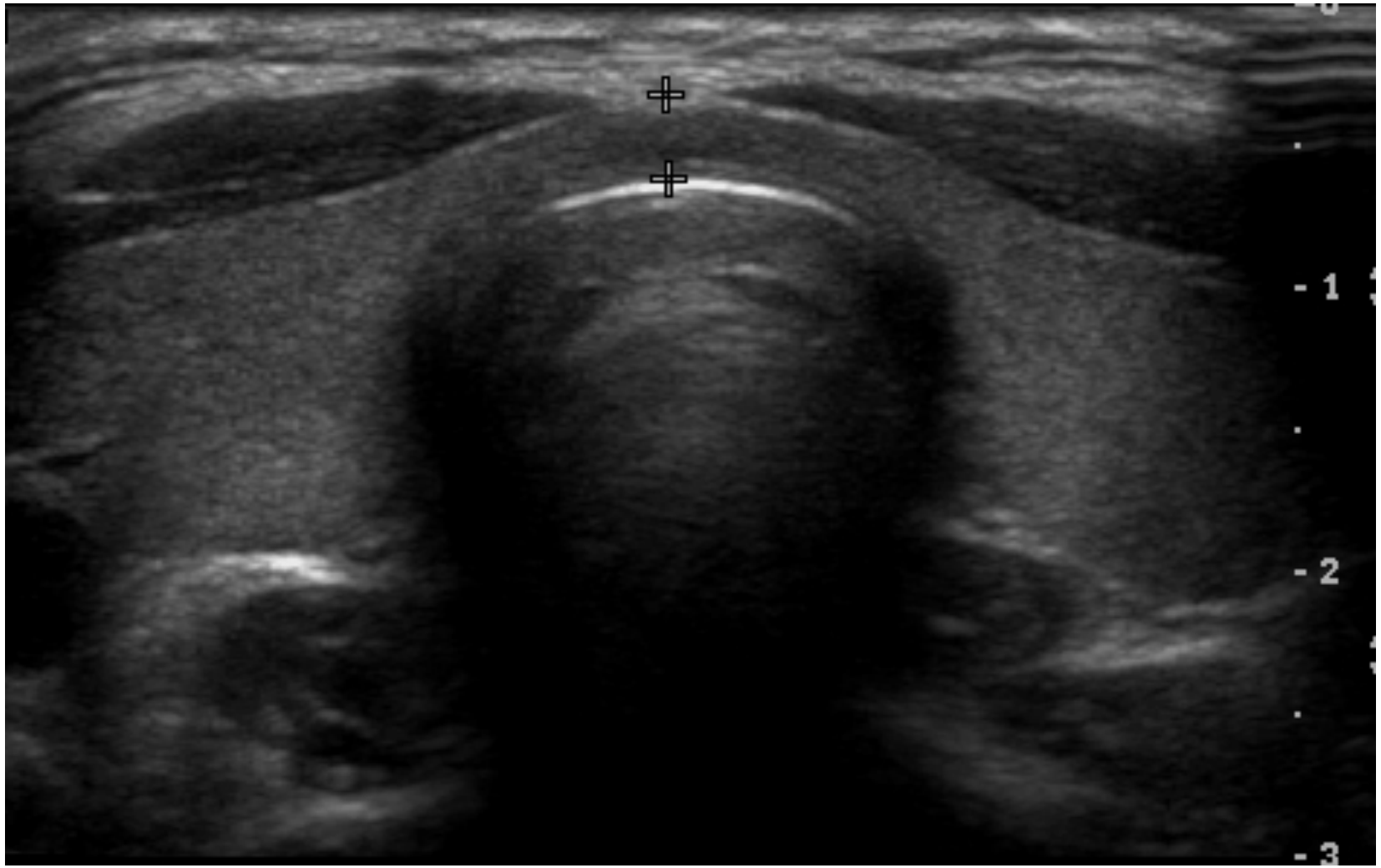
2017 Clinical Practice Guidelines
AAO/Head and Neck Surgery Foundation

Imaging studies



- CT scan and ultrasound are the most commonly used and useful imaging studies of the neck

Neck ultrasound

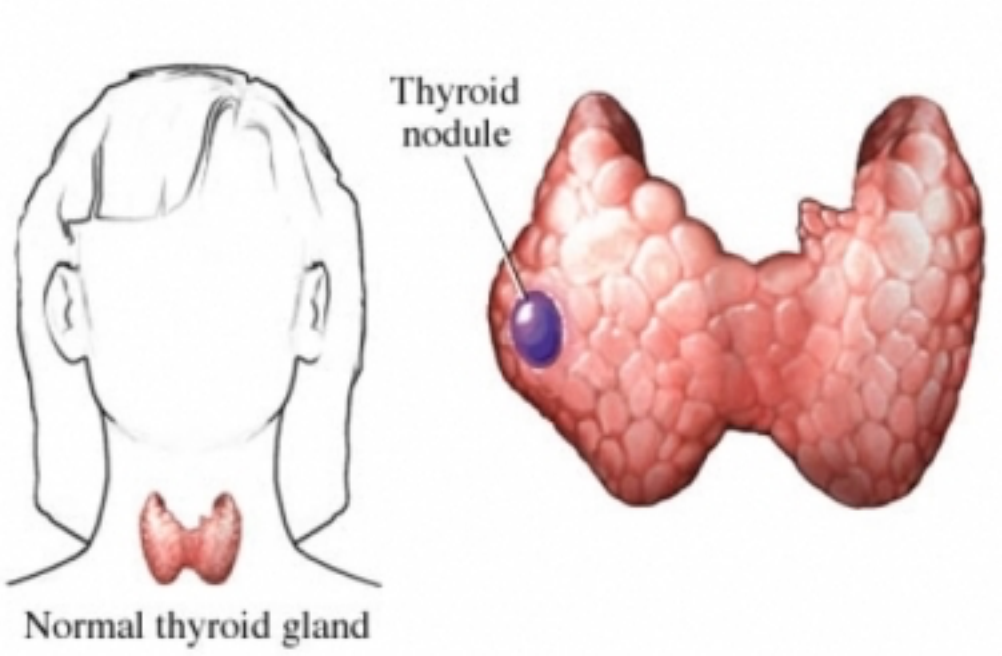


Fine-needle aspiration biopsy

- For solid neck masses suspected of being malignant
- Outpatient procedure performed under local anesthetic
- Often facilitated by utilizing ultrasound for guidance

Thyroid nodules

- Extremely common:
  - Palpable in 5% of women and 1% of men in the US
  - 19-**68**% of the population in ultrasound examination or autopsy studies
  - Higher incidence in older patients



B. Haugen, Thyroid, 2015

Thyroid nodules – risk of cancer

- Depends on multiple factors: age, gender, family history, radiation exposure
- 7-15% of thyroid nodules will be malignant

Thyroid nodules - evaluation

- Complete history of physical examination
- Thyroid function test (TSH usually sufficient)
- Ultrasound
- FNA when appropriate

Thyroid FNA – not so simple anymore

Diagnostic category	Risk of malignancy (%)	Usual management
I. Nondiagnostic or unsatisfactory		Repeat FNA with ultrasound guidance
II. Benign	0–3	Clinical follow-up
III. Atypia of undetermined significance or follicular lesion of undetermined significance	5–15	Repeat FNA
IV. Follicular neoplasms or suspicious for a follicular neoplasm	15–30	Surgical lobectomy
V. Suspicious for malignancy	60–75	Near-total thyroidectomy or surgical lobectomy
VI. Malignant	97–99	Near-total thyroidectomy

2009 “Bethesda” criteria for thyroid FNA interpretation

Thyroid FNA – not so simple anymore

Table 1. Likelihood of Malignancy Based on Ancillary Molecular Profiling Results and Recommended Management

Bethesda Cytology Category	Ancillary Testing		PPV	NPV	Recommendation
III (AUS/FLUS)	GEC	suspicious	38%		Diagnostic lobectomy
		benign	5%		Active surveillance
	7-gene MT	positive	88%		Oncologic thyroidectomy
		negative	6%		Active surveillance or diagnostic lobectomy
IV (FN/FL)	GEC	suspicious	37%		Diagnostic lobectomy
		benign	6%		Active surveillance
	7-gene MT	positive	87%		Oncologic thyroidectomy
		negative	14%		Diagnostic lobectomy
	ThyroSeq 2.0 panel	positive	87%		Oncologic thyroidectomy
		negative	5%		Observation
V (SMC)	GEC	suspicious	76%		Oncologic thyroidectomy
		benign	15%		Diagnostic lobectomy
	7-Gene MT	positive	95%		Oncologic thyroidectomy
		negative	28%		Diagnostic lobectomy

AUS, atypia of uncertain significance; FLUS, follicular lesion of undetermined significance; FN, follicular neoplasm/suspicious for follicular neoplasm; GEC, gene expression classifier; 7-gene MT, 7-gene molecular panel; NPV, negative predictive value; PPV, positive predictive value; SMC, suspicious for malignant cells. Data extracted from Ferris RL, et al. *Thyroid*. 2015 May 18. [Epub ahead of print]

Thyroid FNA – not so simple anymore

Table 3. Interpretation of Commercially Available Molecular Tests in Cytologically Indeterminate Nodules and Proposed Clinical Use

Test	Result	Cancer Risk	Clinical Utility[a]
Veracyte GEC	Suspicious	16%-57%, dependent on cancer prevalence	Surgery
	Benign	2%-25%, dependent on cancer prevalence	If cancer risk <5%, surveillance
Asuragen MiRInform (ie, 7GP)	Positive for *BRAF* V600E or *RET/PTC* rearrangement	>99% and likely to be conventional PTC	Surgery
	Positive for *RAS*, *BRAF* K601E, or *PAX8/PPARG* rearrangement	75%-90% and most likely to be follicular-variant PTC	Surgery
	Negative	6%-56%, dependent on cytology category	Surgery vs surveillance
CBLPath ThyroSeq version 2.1	Positive for *BRAF* V600E or *RET/PTC* rearrangement	>99% and likely to be conventional PTC	Surgery
	Positive for *RAS*, *BRAF* K601E, or *PAX8/PPARG* rearrangement	33%-90% and most likely to be follicular-variant PTC	Surgery
	Positive for *PTEN*, *TSHR*, *AKT1*, *CTNNB1*, *EIF1AX*, *GNAS*, *PTEN*, *NTRK1/3*, *ALK*, or *IGF2BP3* rearrangement	Studies are ongoing but all have been identified in thyroid cancers	Surgery
	Positive for *TERT*, *p53*, or *PIK3CA* mutation	>99% and likely to be aggressive cancer	Surgery
	Negative	3%-4% if cytologic results show FN or AUS/FLUS	Surveillance

Abbreviations: AUS/FLUS, atypia or follicular lesion of undetermined significance; FN, follicular neoplasm; GEC, gene expression classifier; PTC, papillary thyroid cancer; 7GP, 7-gene panel.

[a] When surgery is indicated, decision for total thyroidectomy vs lobectomy should depend on clinical variables and ultrasonographic features.

L. Yip, JAMA Surgery, 2016

Overdiagnosis/Overtreatment: a major US health problem

- An estimated >$200 billion dollars is spent in the US each year on unnecessary testing/treatment

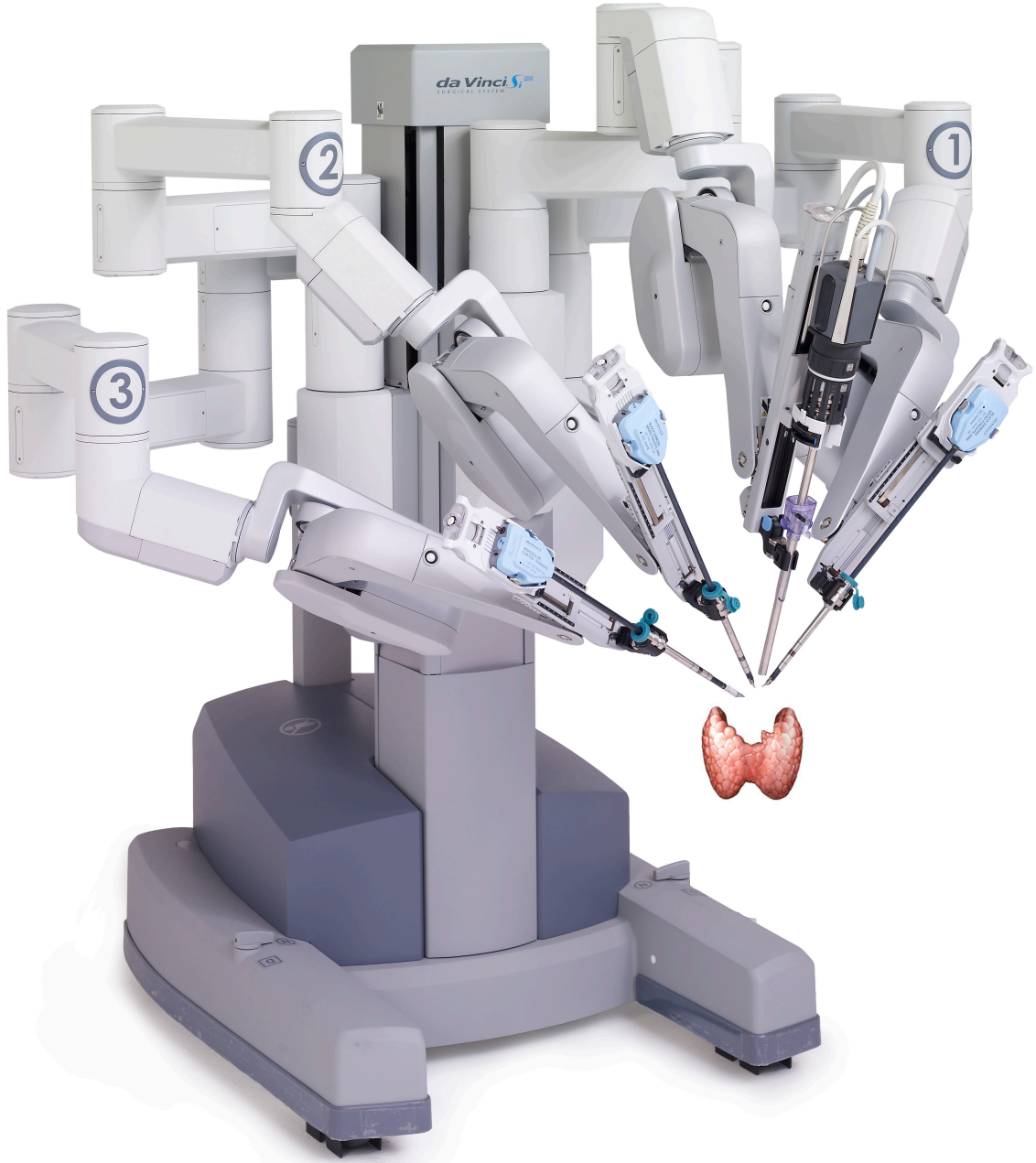
1st International Conference on Overdiagnosis, September 2013

Overdiagnosis/Overtreatment: South Korea and thyroid cancer

- 1999: National screening program for various cancers instituted
- Routine cervical ultrasound, even for younger patients
- Explosion in diagnoses and operations for thyroid cancer

South Korea's thyroid cancer "epidemic"

- 15-fold increase in diagnoses in 2000s
- Most were micro cancers (<1cm)
  - 1995: 15% of all operations were for microcancers
  - 2005: **56%** of all operations for microcancers
- Treatment comes at a cost, both in terms of financial expenditures and in morbidity
  - 11% permanent hypoparathyroidism
  - 2% permanent vocal cord paralysis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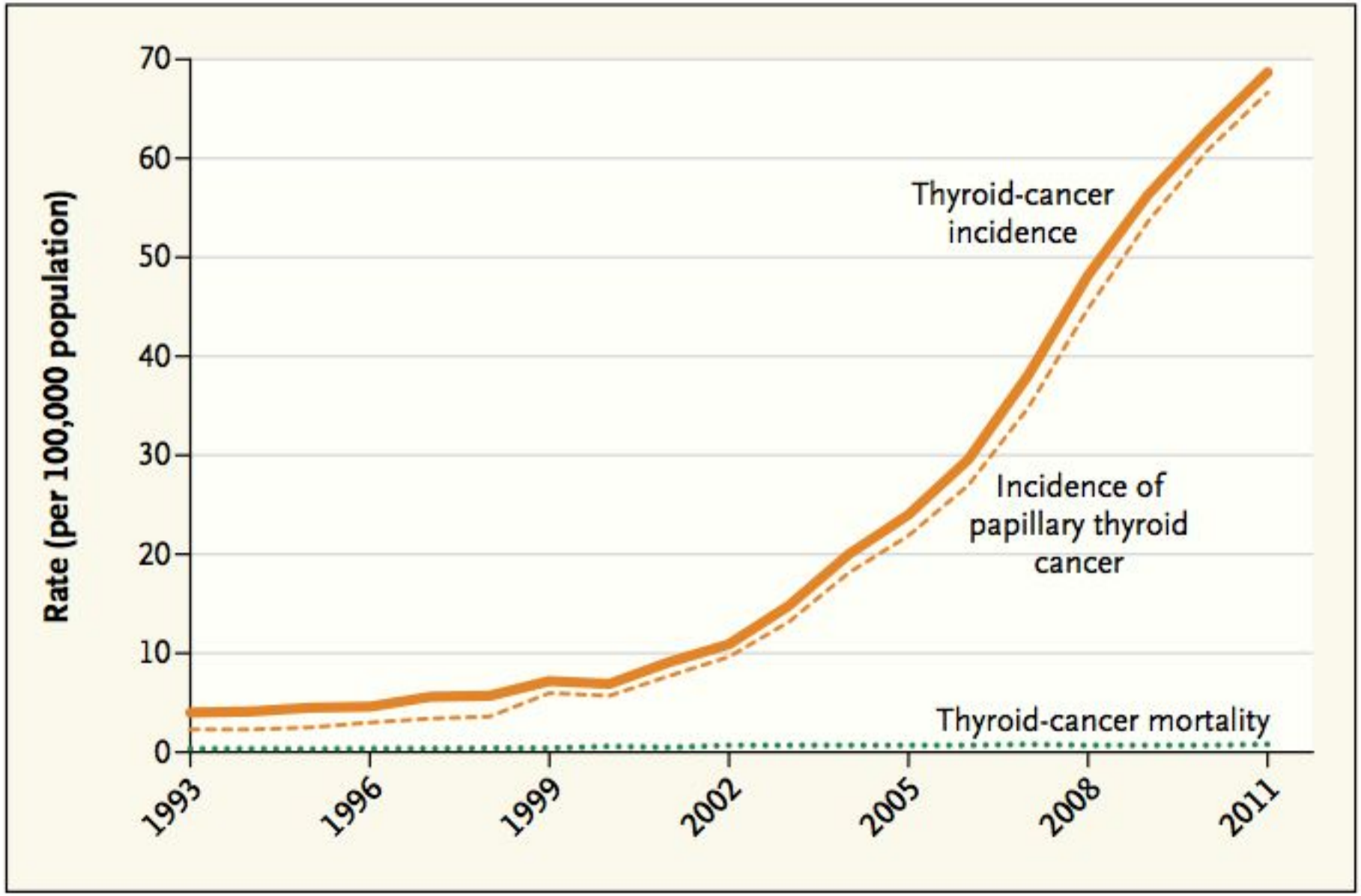


G. Welch, et al., NEJM, 2014

Benefits of early diagnosis?

- NO change in overall death rates
- Huge increase in costs, operations, morbidity, etc.
- Recent call for scaling back of screening but difficult to change entrenched practices…

HEALTH

Study Points to Overdiagnosis of Thyroid Cancer

By GINA KOLATA NOV. 5, 2014

To the shock of many cancer experts, the most common cancer in South Korea is not lung or breast or colon or prostate. It is now thyroid cancer, whose incidence has increased fifteenfold in the past two decades. "A tsunami of thyroid cancer," as one researcher puts it.

Similar upward trends for thyroid cancer are found in the United States and Europe, although not to the same degree. The thyroid cancer rate in the United States has more than doubled since 1994.

Cancer experts agree that the reason for the situation in South Korea and elsewhere is not a real increase in the disease. Instead, it is down to screening, which is finding tiny and harmless tumors that are better left undisturbed, but that are being treated aggressively.

New York Times, Nov. 5, 2014

An Epidemic of Thyroid Cancer?

By H. GILBERT WELCH NOV. 5, 2014

HISTORICALLY, the science of epidemiology was directed toward identifying and controlling epidemics of infectious disease. In a study just published in the New England Journal of Medicine, my colleagues and I highlight another important job for epidemiologists: identifying and controlling epidemics of medical care.

The setting is South Korea, where, over the last two decades, the incidence of thyroid cancer has increased fifteenfold. Nowhere in the world is the rate of any cancer growing faster.

We've all been taught to seek biological explanations for a significant rise in disease — perhaps a new infectious agent or environmental exposure. But in South Korea, we are seeing something different: an epidemic of diagnosis.

New York Times, Nov. 5, 2014

HEALTH & BEHAVIOR

Sometimes You Should Just Say No to Surgery

The introduction of national thyroid cancer screening in South Korea led to a 15-fold increase in diagnoses and a corresponding explosion of operations—but no difference in mortality rates. This is a prime example of over-diagnosis that's contributing to bloated health care costs.

WEN SHEN · NOV 25, 2014

"When in doubt, cut it out." This is a favorite mantra of surgeons, codified over centuries of treating the vast spectrum of diseases that can be ameliorated and cured with the knife. Surgeons love to operate; very little can match the highs of performing a successful operation that definitively takes care of a problem and helps a suffering patient. One of the keys, however, is making sure that there is actually a problem to take care of.

Pacific Standard, Nov 25, 2014

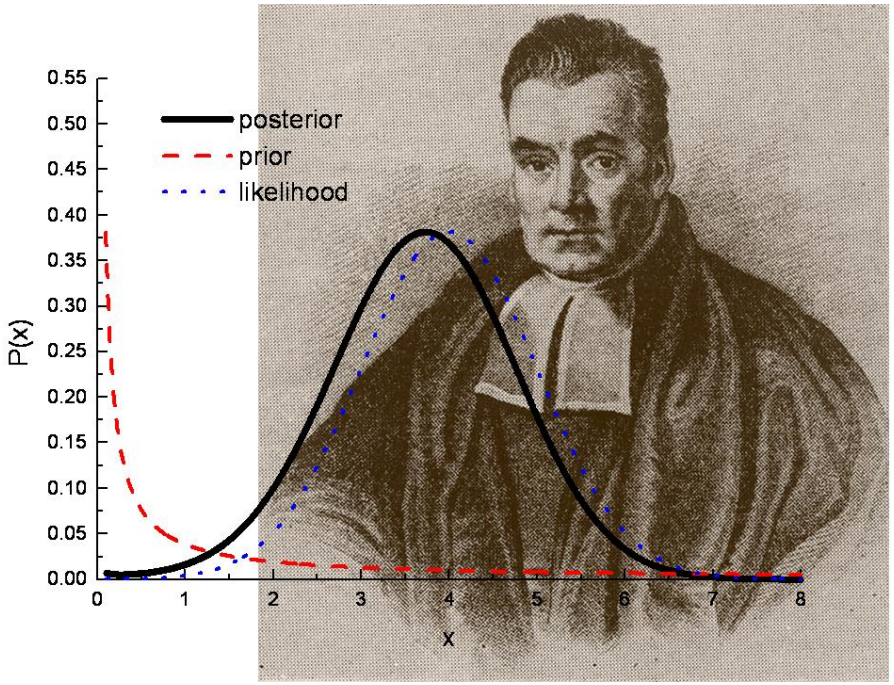
Here in the US?

- Even without a national screening program, overdiagnosis and overtreatment of thyroid cancer is an increasing problem in the US
- NCI estimates >60,000 new cases in US in 2015 (<2000 deaths)
- MSKCC published trial of observation vs. operation for microcancers demonstrating excellent outcomes (corroborating prior Japanese data)

M. Tuttle, JAMA OHNS, 2017

What should clinicians do?

- Think before ordering a test!
- Discuss with the patient the indications for the test, the possible outcomes (in context of pretest probabilities), and alternatives to testing



Thomas Bayes, 1702-1761