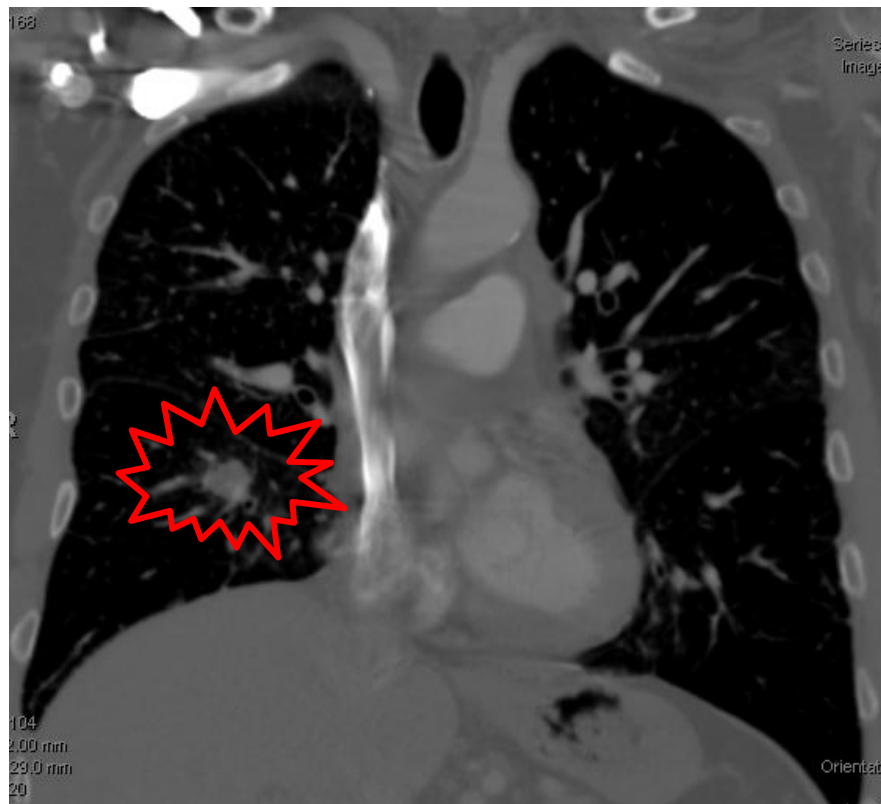
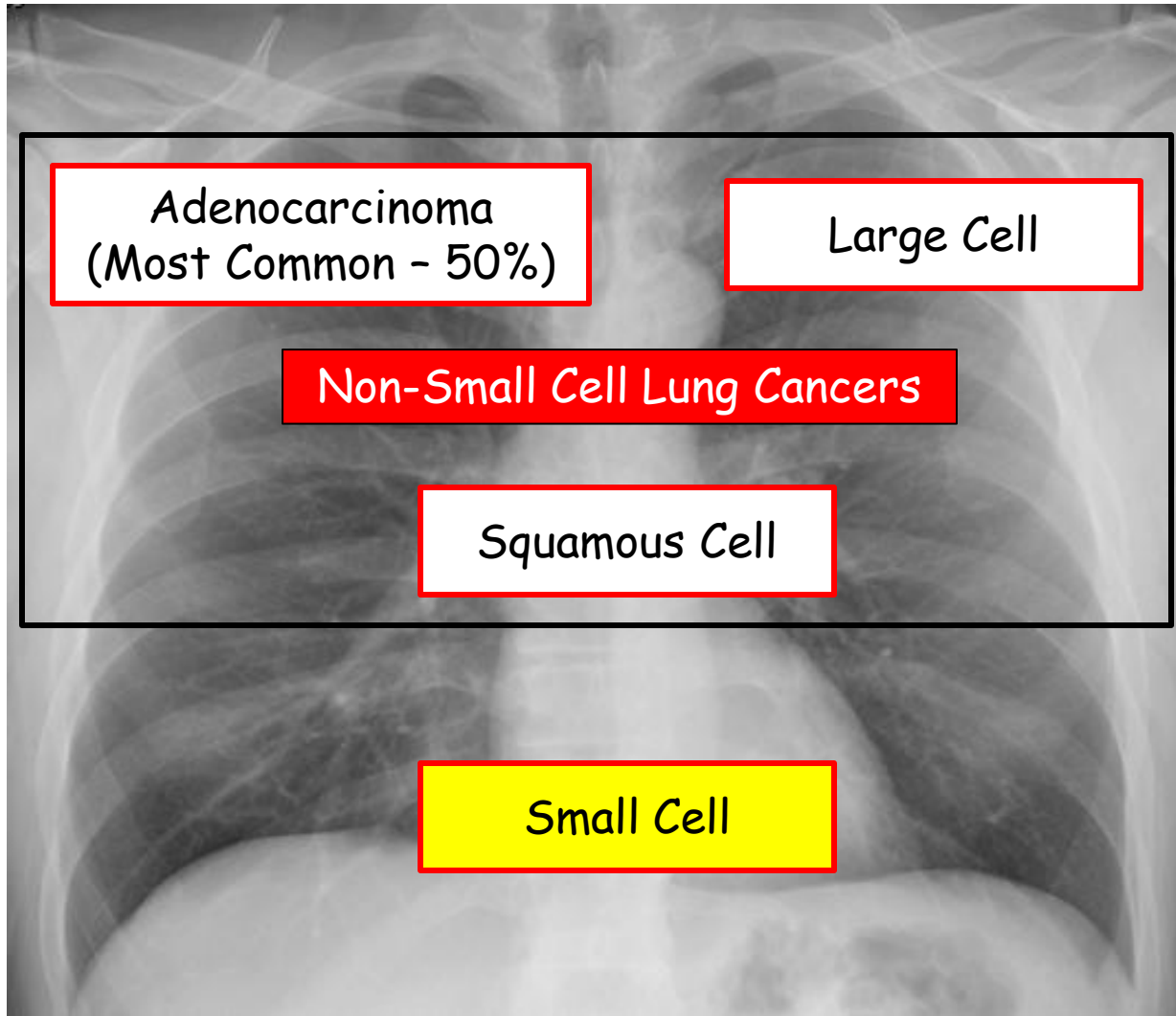


Pulmonary Neoplasm



Howard J. Sachs, MD
www.12daysinmarch.com



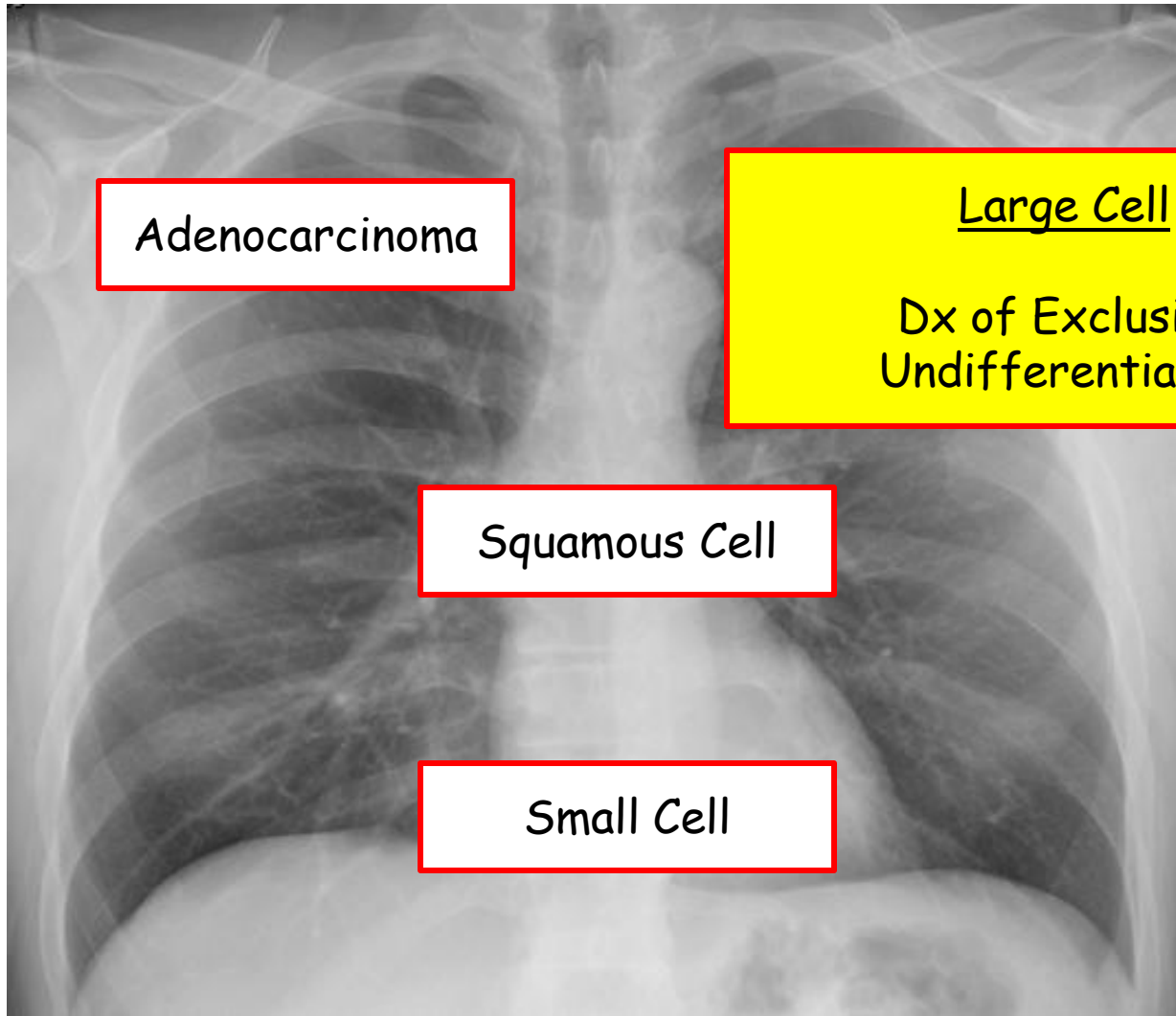
Adenocarcinoma
(Most Common - 50%)

Large Cell

Non-Small Cell Lung Cancers

Squamous Cell

Small Cell



Adenocarcinoma

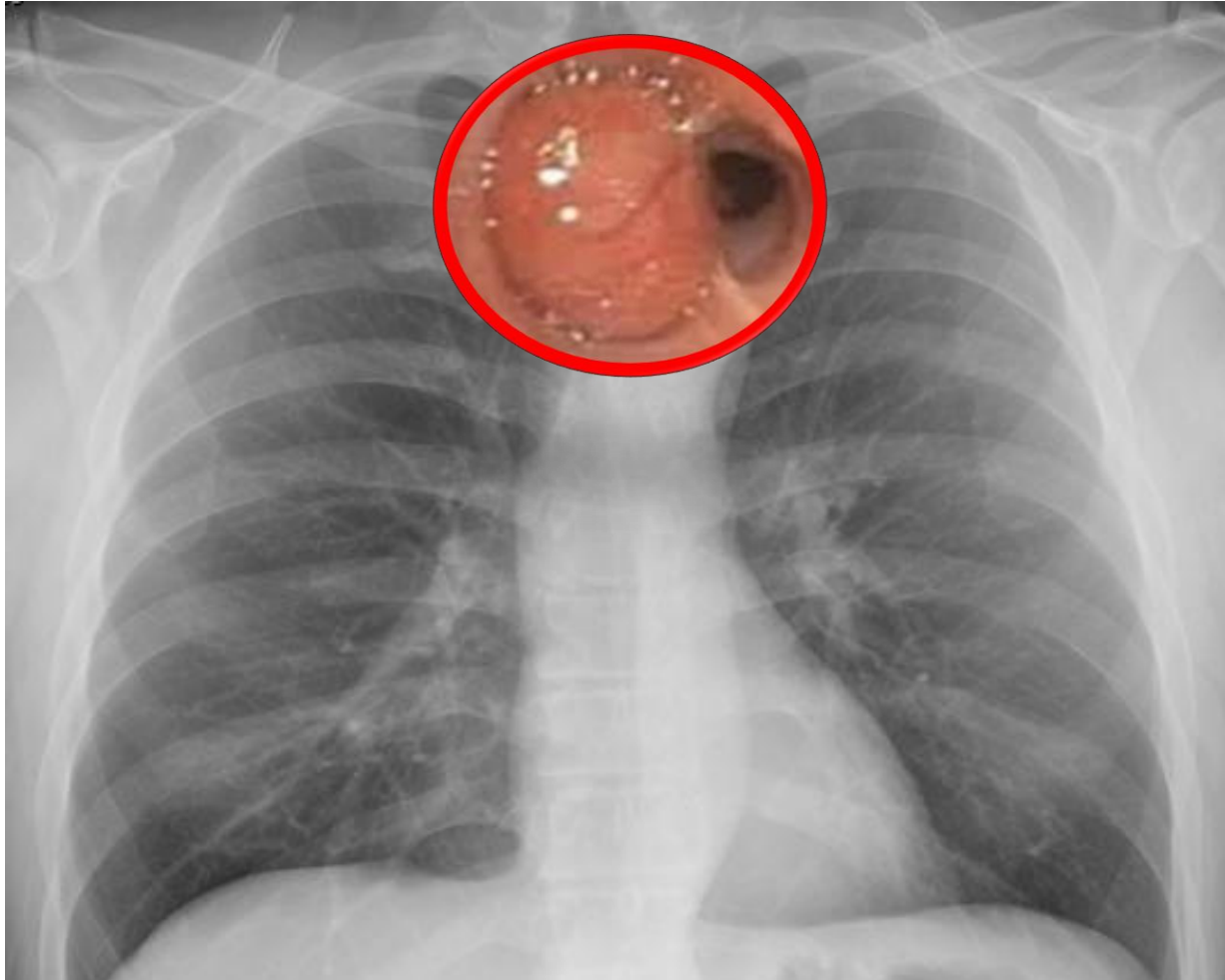
Large Cell

Dx of Exclusion
Undifferentiated

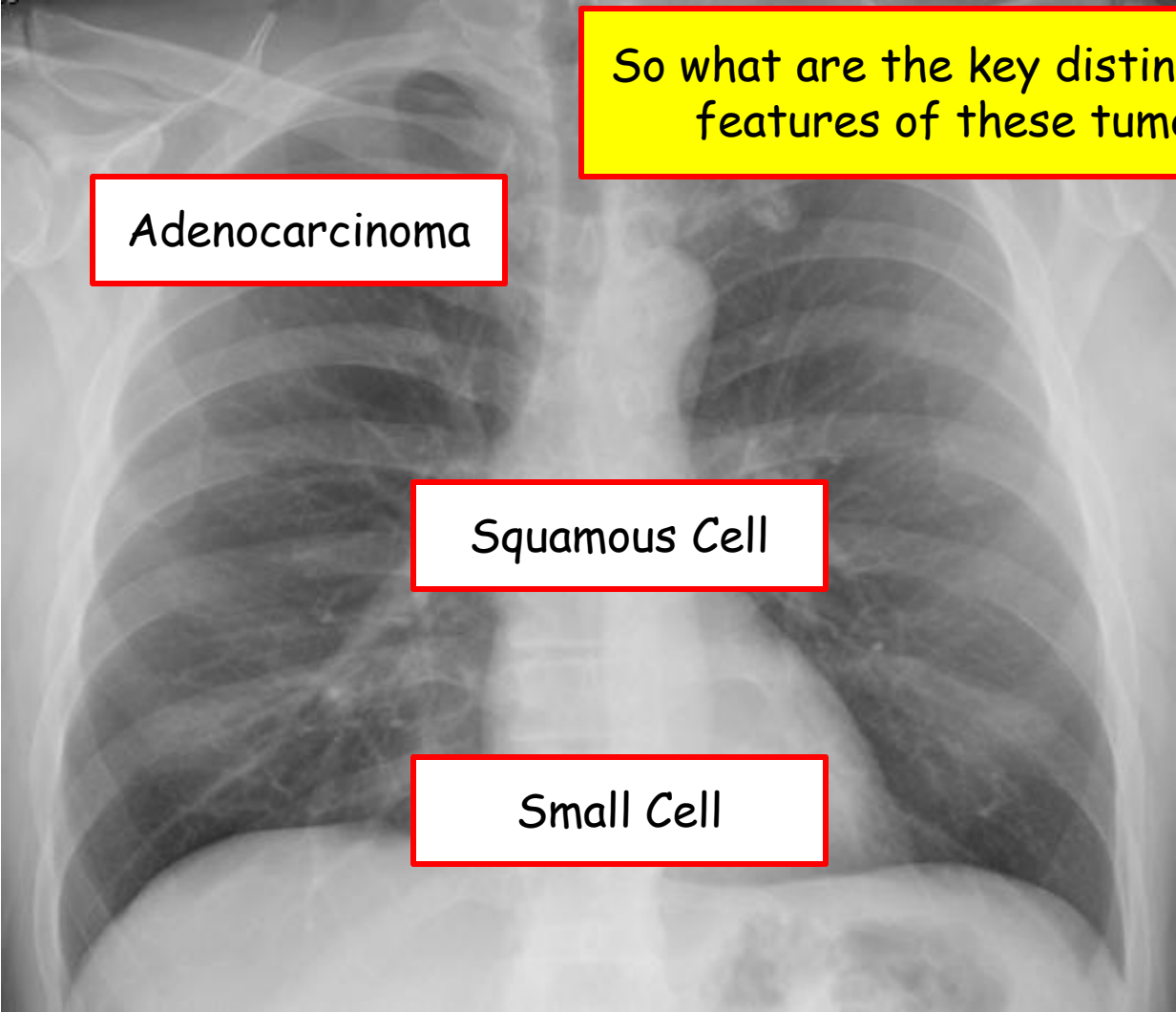
Squamous Cell

Small Cell

Carcinoid



Mesothelioma is covered in Pneumoconioses (Asbestos)

A grayscale chest X-ray showing the lungs, heart, and ribcage. Three red-bordered boxes are overlaid on the image, each containing a label for a different type of lung tumor. The labels are 'Adenocarcinoma' (top left), 'Squamous Cell' (center), and 'Small Cell' (bottom center). A yellow box with a red border is in the top right corner, containing a question.

So what are the key distinguishing features of these tumors?

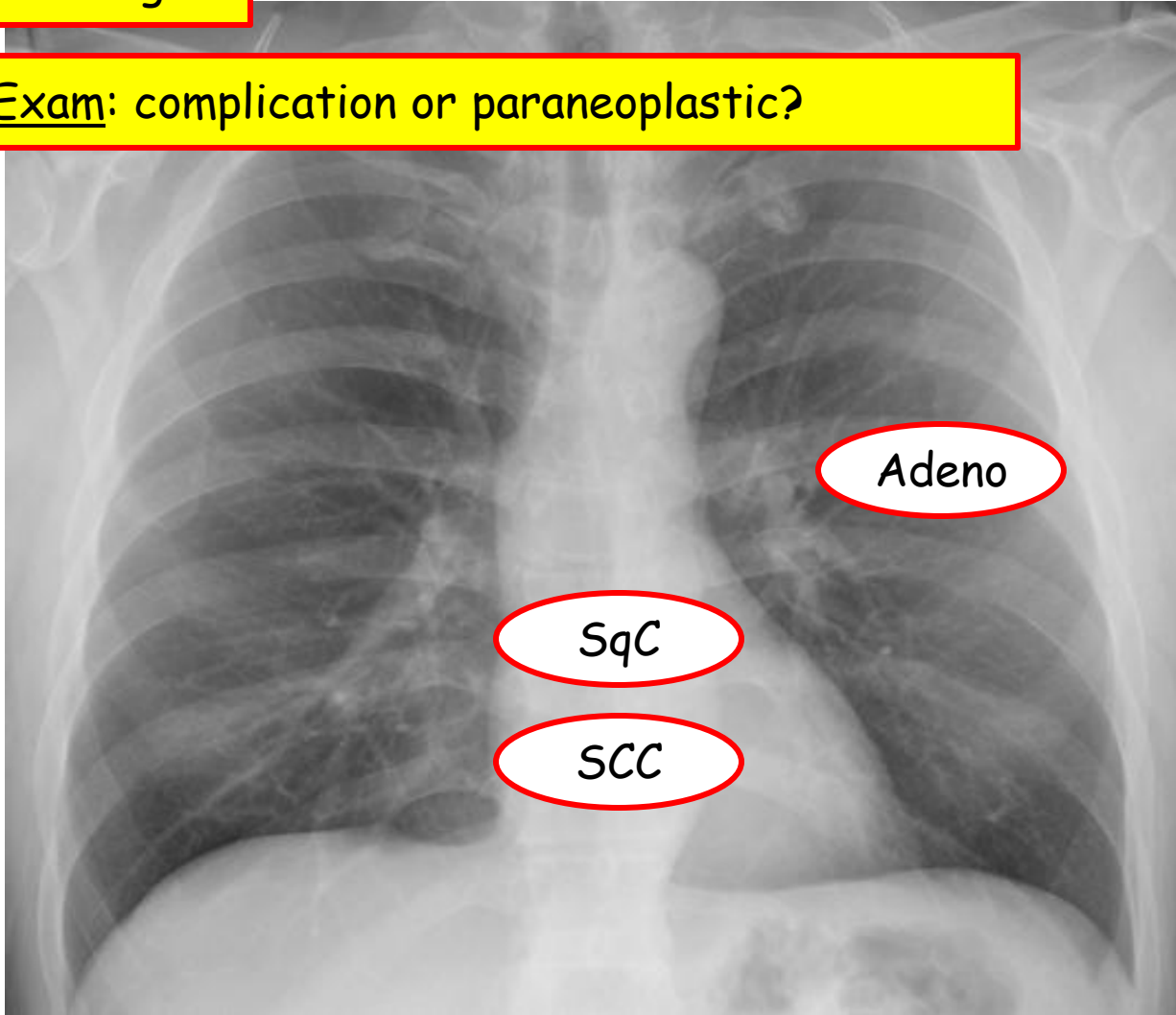
Adenocarcinoma

Squamous Cell

Small Cell

History: smoking?

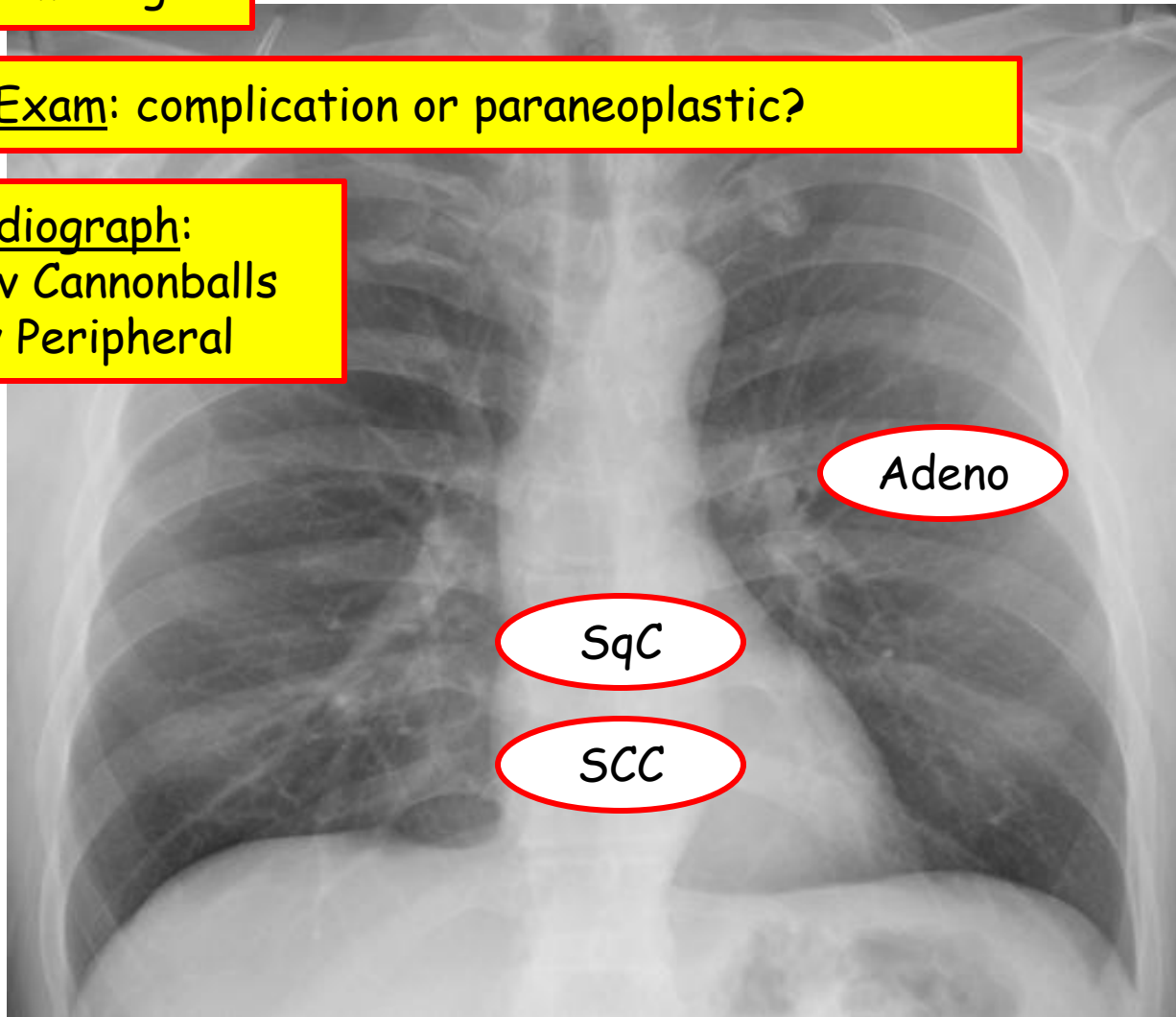
Physical Exam: complication or paraneoplastic?



History: smoking?

Physical Exam: complication or paraneoplastic?

Radiograph:
Solitary v Cannonballs
Central v Peripheral



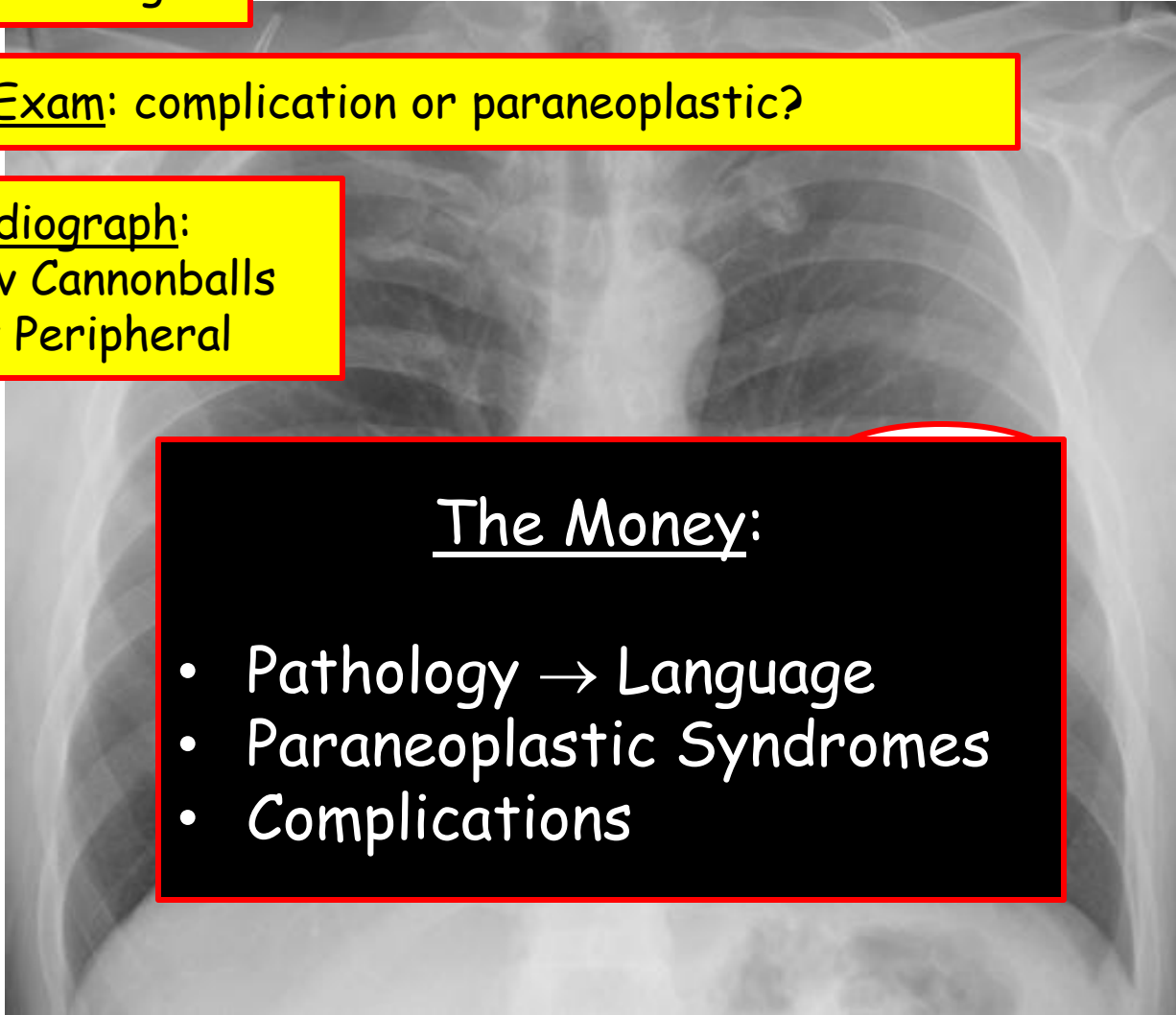
History: smoking?

Physical Exam: complication or paraneoplastic?

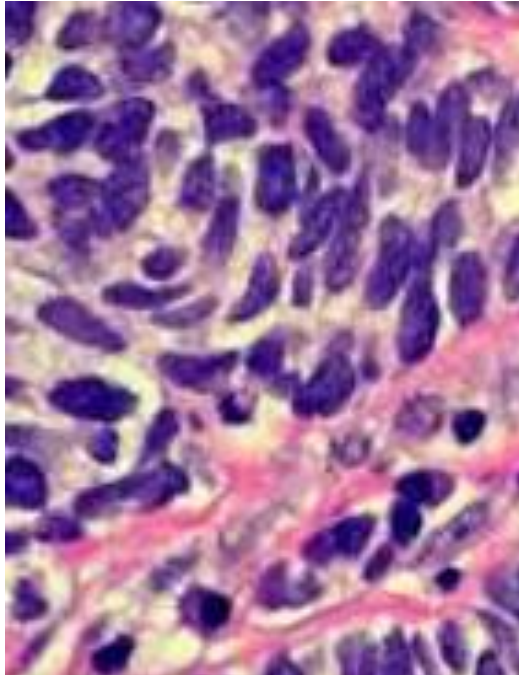
Radiograph:
Solitary v Cannonballs
Central v Peripheral

The Money:

- Pathology → Language
- Paraneoplastic Syndromes
- Complications



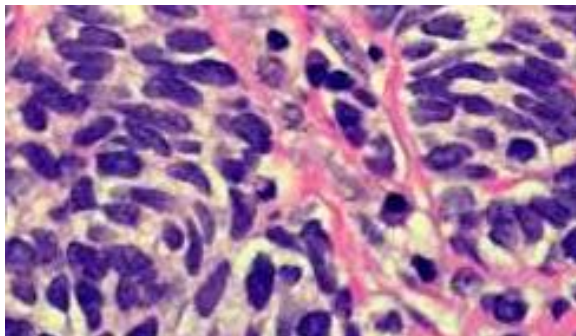
Small Cell ('oat cell'; L-MYC): Distinguishing Characteristics



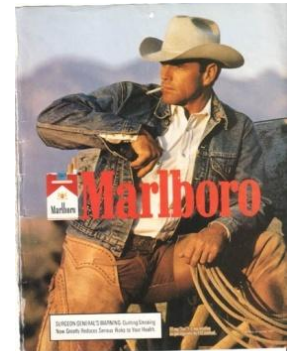
L ('Lung') - MYC
Gain of function
Transcription Factor
Promotes Cell Proliferation

Small Cell ('oat cell'; L-MYC): Distinguishing Characteristics

- Background
 - Central location; (+) Tobacco
 - Neuroendocrine origin → the paraneoplastic phenomenon
 - Neurosecretory cells, of neural crest origin include overexpression of the following markers:
 - Enolase (glycolytic enzyme)
 - Chromogranin (inhibitory peptide, precursor)
 - Synaptophysin (involved in synaptic transmission)

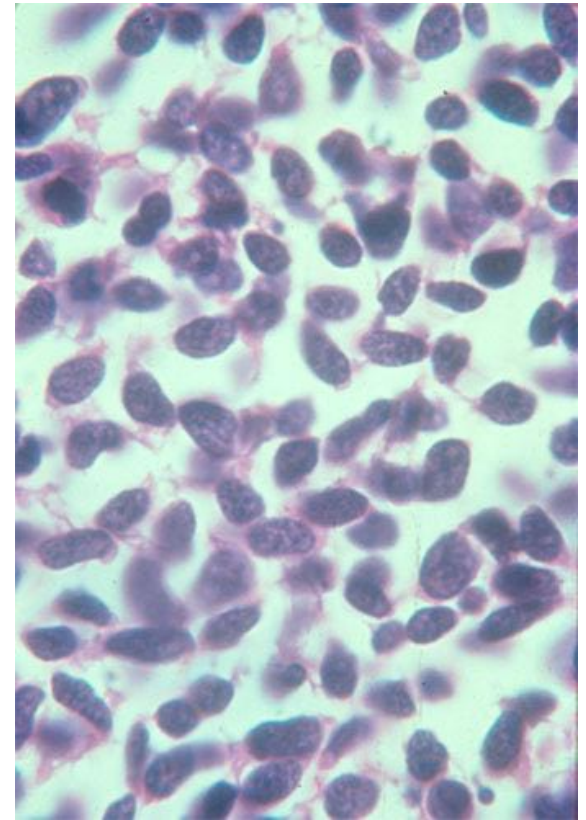


L (Lung)- MYC
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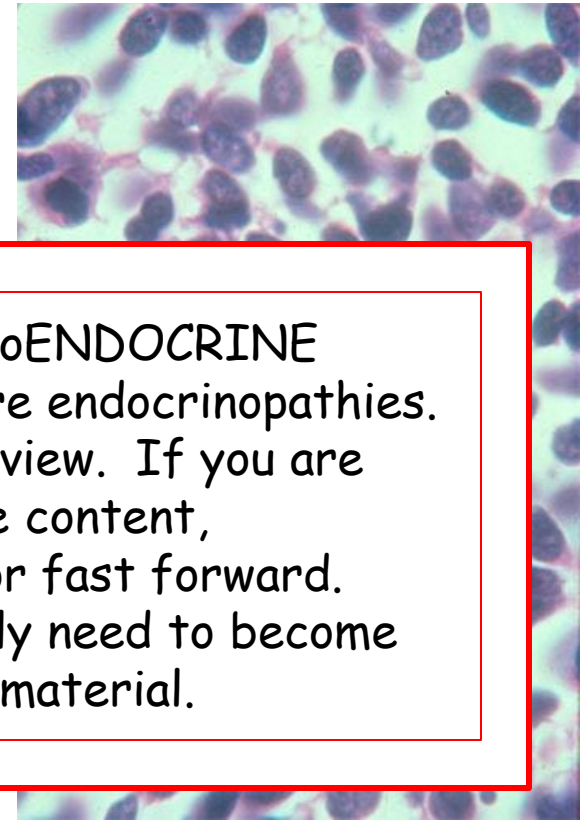


Small Cell ('oat cell'; L-MYC): Distinguishing Characteristics

- Pathology
 - Small round cells, scant cytoplasm
 - Dense, dark nuclei
 - Resemble lymphocytes, but smaller
 - EM: Neurosecretory granules
- Paraneoplastic Syndrome...\$\$\$
 - Eaton-Lambert → Presynaptic calcium channel; no response to Tensilon
 - SIADH Secretion → hyponatremia
 - Ectopic ACTH → Cushing's syndrome



Small Cell ('oat cell'; L-MYC): Distinguishing Characteristics



Warning: SCC is a NeuroENDOCRINE
SIADH and Ectopic ACTH are endocrinopathies.
Next up is a pragmatic review. If you are
unfamiliar with the content,
either grin and bear it or fast forward.
Do Note - you will eventually need to become
familiar with this material.

- Paraneoplastic Syndrome...\$\$\$
 - Eaton-Lambert → Presynaptic calcium channel; no response to Tensilon
 - SIADH Secretion → hyponatremia
 - Ectopic ACTH → Cushing's syndrome

The Syndrome of Inappropriate Anti-Diuretic Hormone Secretion (SIADH) for Small Cell Carcinoma

Hyponatremia

Euvolemia

Inappropriate
Uosm

The Syndrome of Inappropriate Anti-Diuretic Hormone Secretion (SIADH) for Small Cell Carcinoma

Hyponatremia

Euvolemia

Inappropriate
Uosm

Hyponatremia is a disease of free water excess

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Hyponatremia is a disease of free water excess

Euvolemia means there is neither need nor desire to hold onto that free water

The Syndrome of Inappropriate Anti-Diuretic Hormone Secretion (SIADH) for Small Cell Carcinoma

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Hyponatremia is a disease of free water excess

Euvolemia means there is neither need nor desire to hold onto that free water

For our body to correct hyponatremia, it should dump free water creating a maximally dilute urine.

The Syndrome of Inappropriate Anti-Diuretic Hormone Secretion (SIADH) for Small Cell Carcinoma

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For our body to correct hyponatremia, it should dump free water creating a maximally dilute urine.

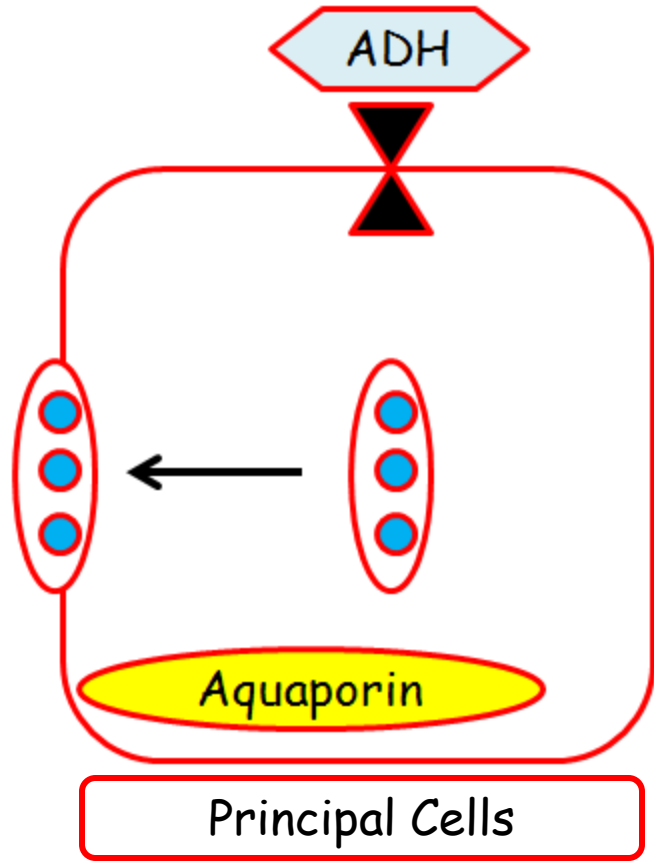
1. Hyponatremia is a disease of free water excess

What does ADH do?

Water Management



How does ADH manage water?

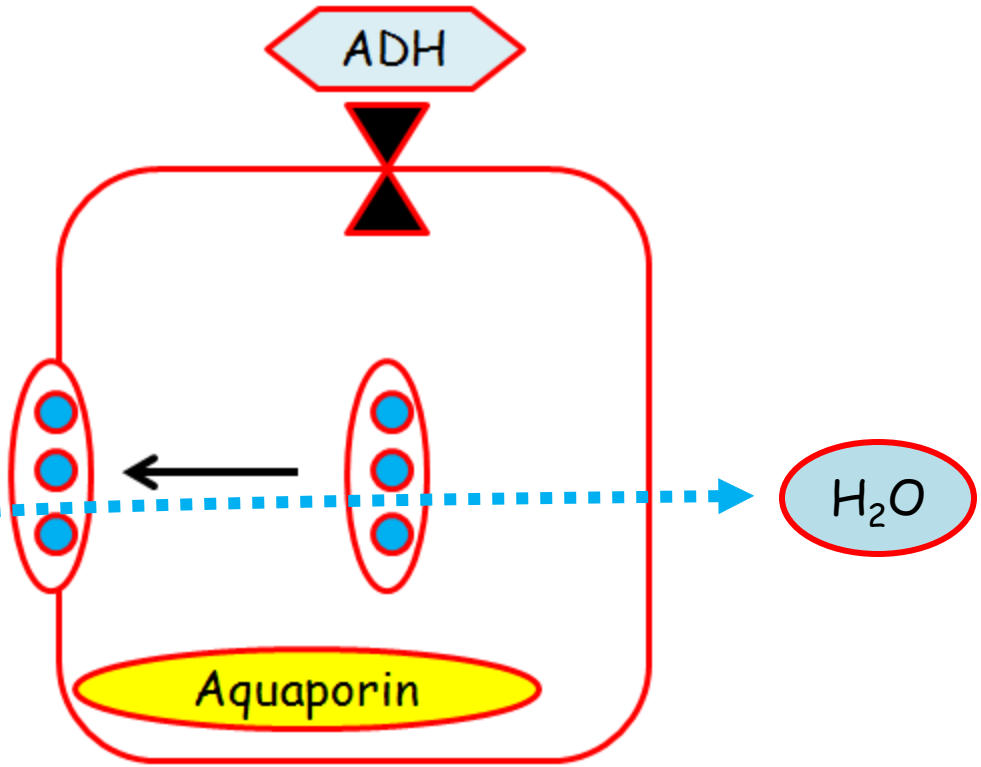


1. Hyponatremia is a disease of free water excess

What does ADH do?

How does ADH manage water?

Water Management

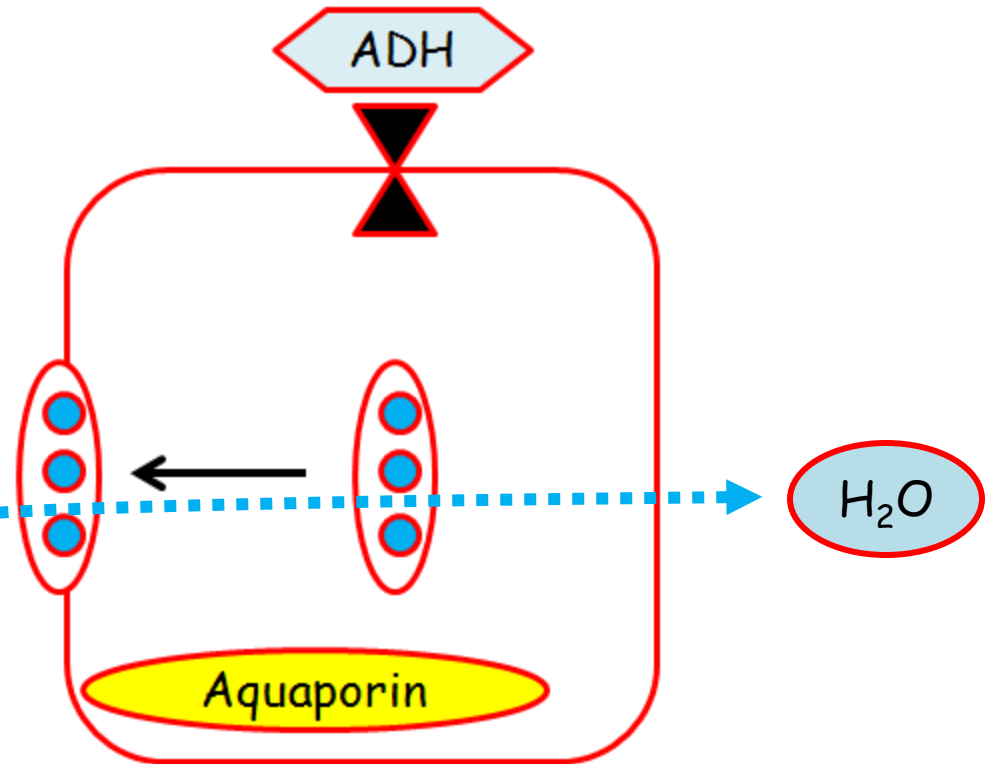


1. Hyponatremia is disease of free water excess

Through this process
ADH regulates P_{osm}



Plasma Na^+ 140 meq

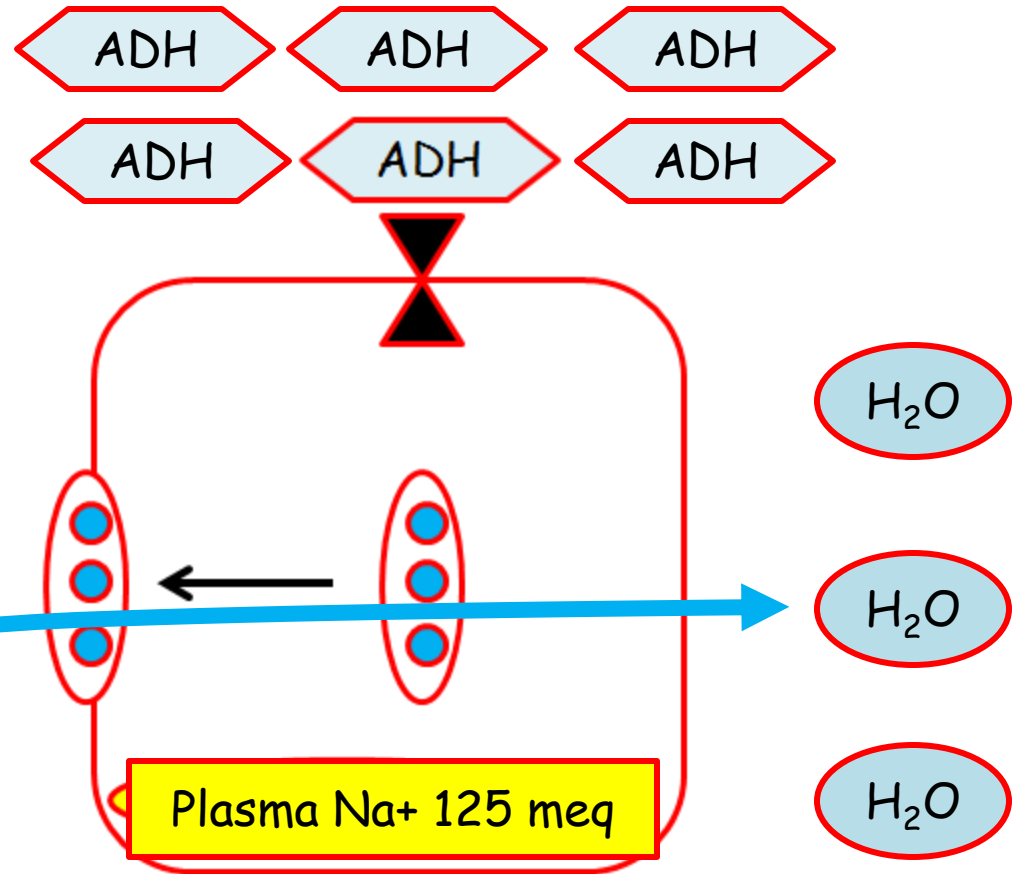


1. Hyponatremia is disease of free water excess

In SIADH, the process is dysregulated

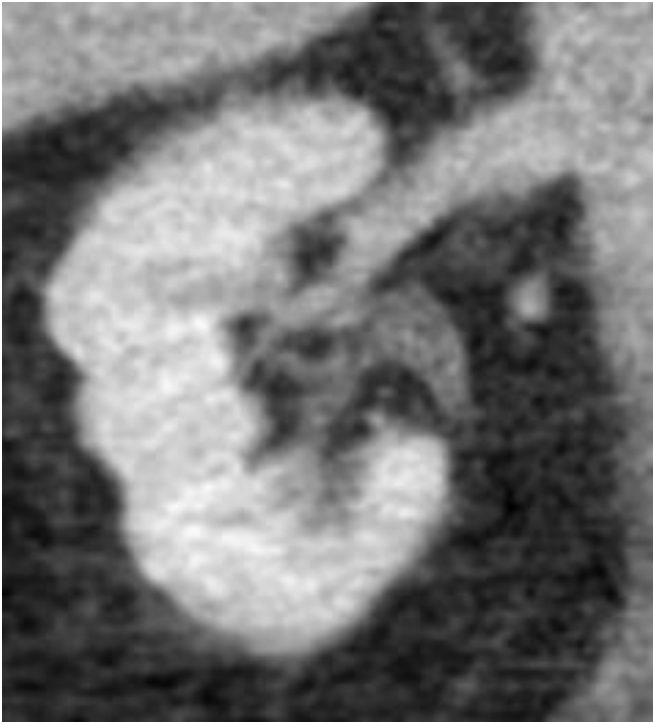


Plasma Na⁺ 140 meq



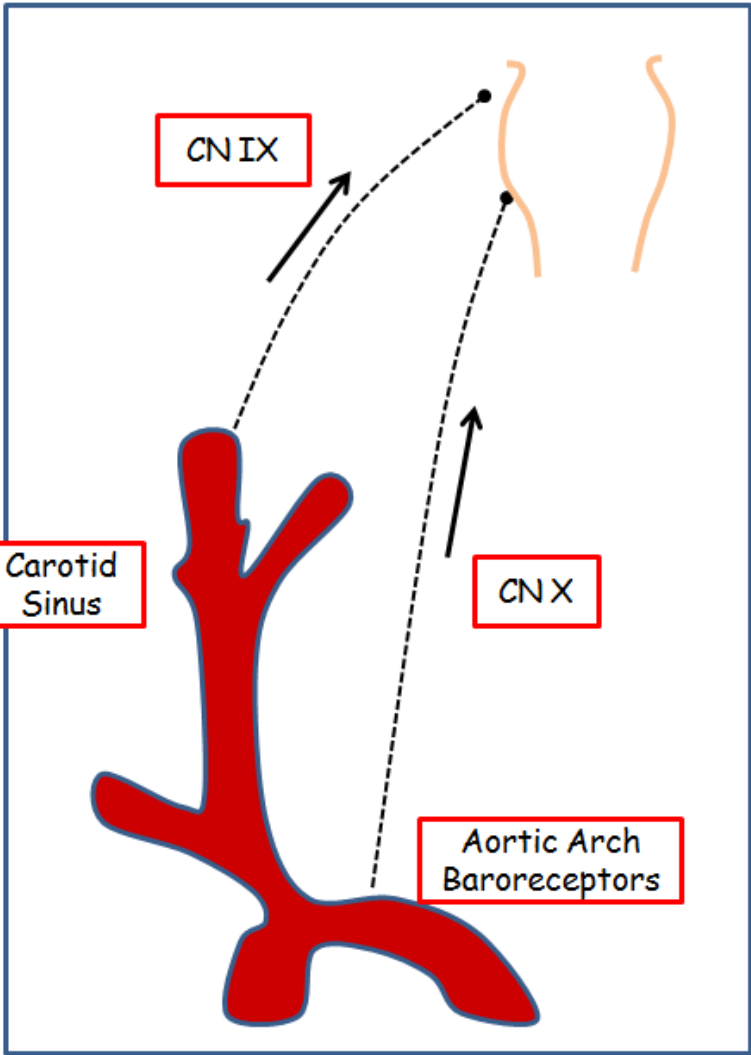
Plasma Na⁺ 125 meq

2. Euvolemia means there is neither need or desire to hold onto that free water

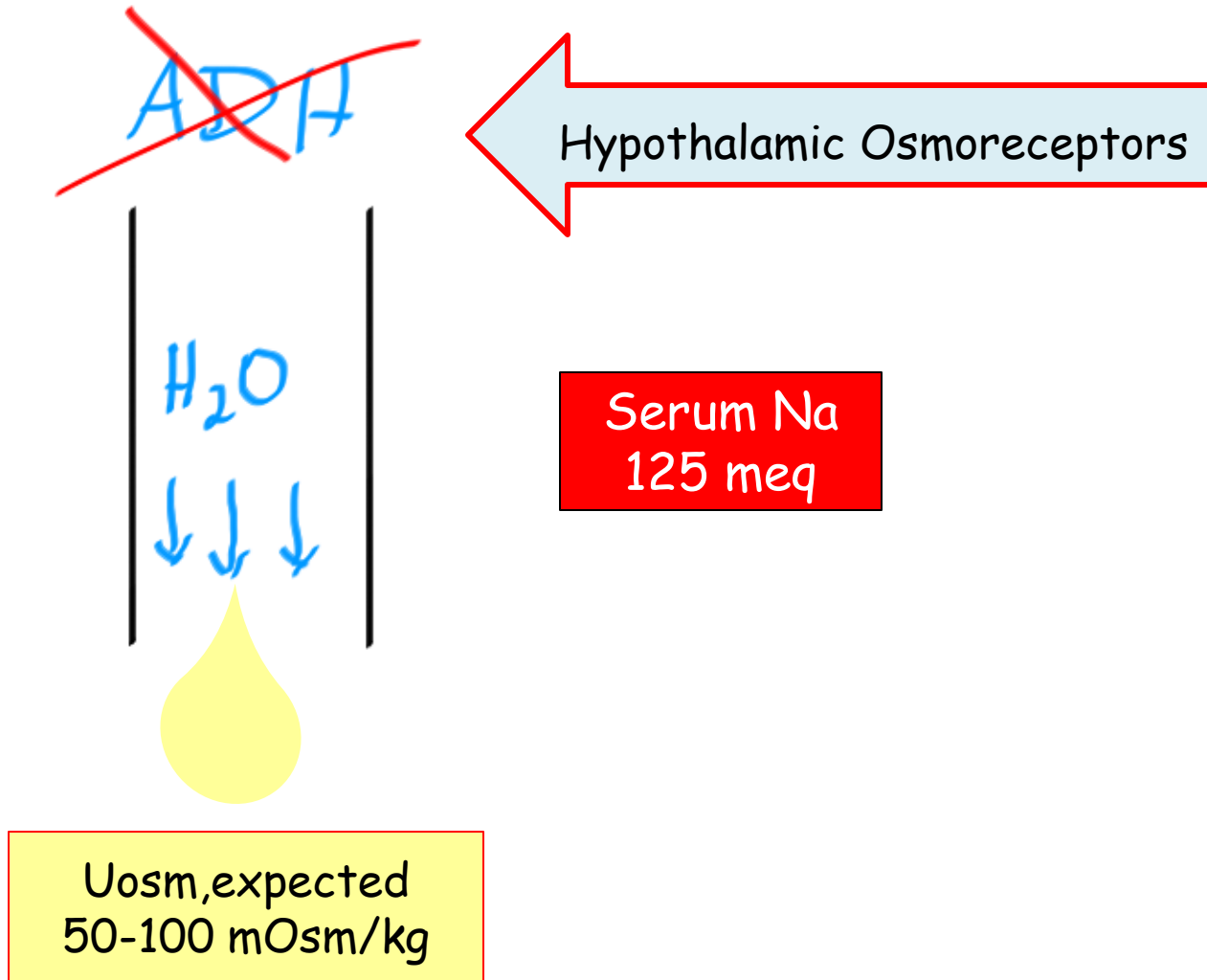


BP, pulse normal

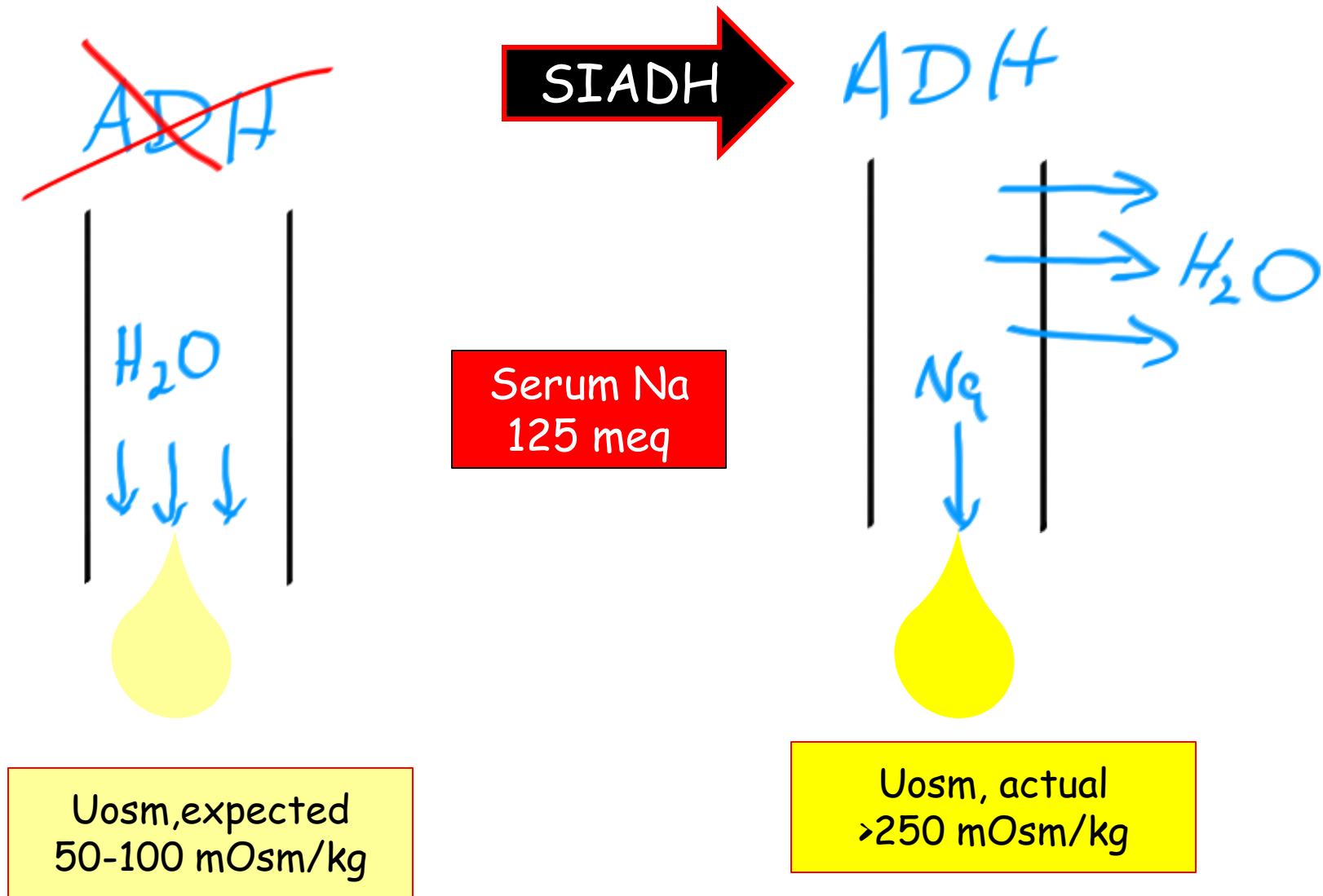
Nothing is driving release of ADH



3. For our body to correct hyponatremia, it should dump free water creating a maximally dilute urine.



3. For our body to correct hyponatremia, it should dump free water creating a maximally dilute urine.



SIADH for Small Cell Section

Hyponatremia

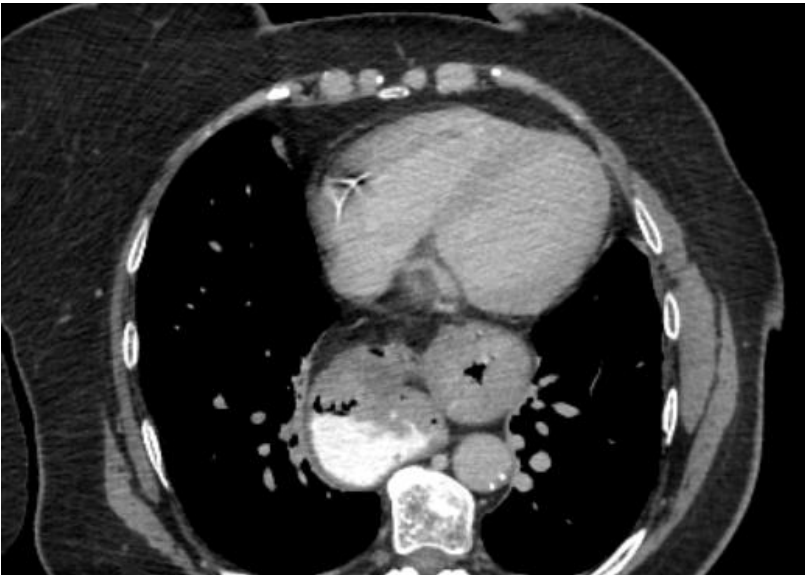
Euvolemia

Inappropriate
Uosm

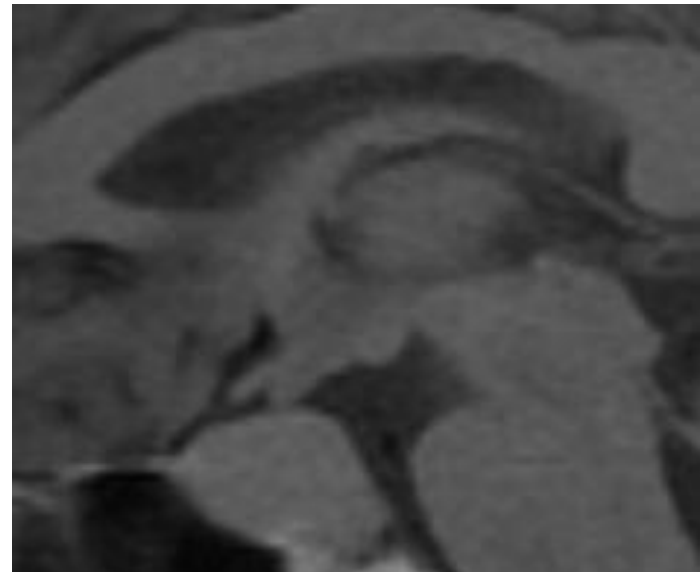
Classic Questions:

- Smoker presents with weakness and fatigue. BP normal. CXR with mass. Serum Na⁺ 120 meq/dL.
Correct diagnosis?
Choose the pathology?
Histochemical stains note the presence of which peptide?
- Smoker with Posm of 240 mOsm/kg and Uosm 280.
Choose the correct diagnosis

Small Cell Carcinoma:
Ectopic ACTH



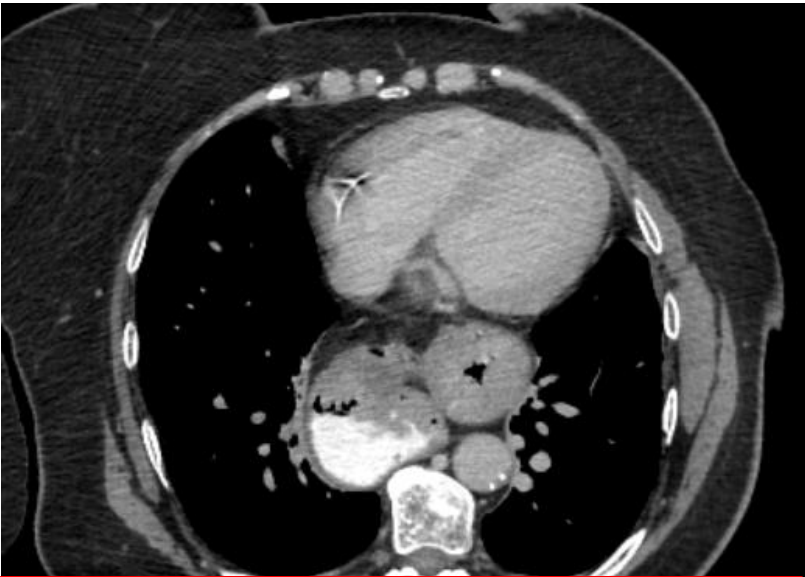
Small Cell Carcinoma



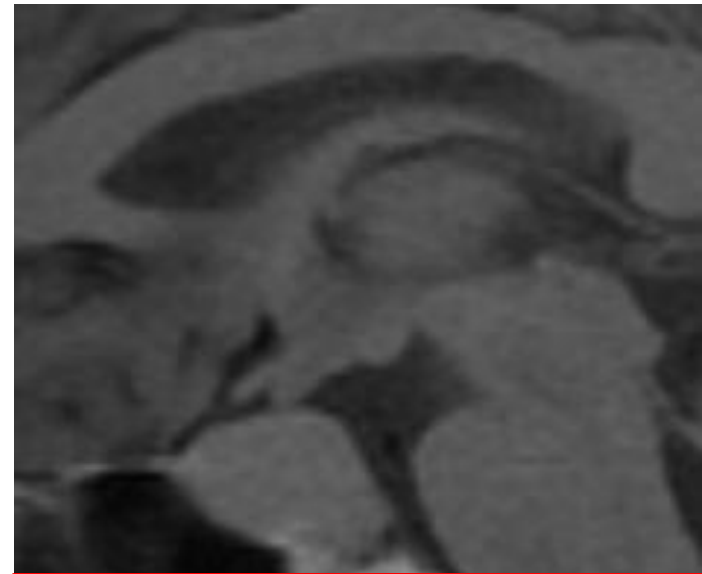
Cushing's Disease

Small Cell Carcinoma:
Ectopic ACTH

High ACTH:
Ectopic, Pituitary Adenoma



Small Cell Carcinoma



Cushing's Disease

How to distinguish the two?

High ACTH → Hypercortisolism
(Cushing's Syndrome)

Presentation:

Central Obesity

HTN

Striae

Hyperpigmentation*

Data:

Hyperglycemia/Diabetes

Low K, High HCO₃

High ACTH, Cortisol

Provocative Test

High dose DST

High ACTH → Hypercortisolism
(Cushing's Syndrome)

Presentation:
Central Obesity
HTN
Striae
Hyperpigmentation*

Data:
Hyperglycemia/Diabetes
Low K, High HCO₃
High ACTH, Cortisol

Provocative Test
High dose DST

Language of Ectopic
ACTH production

High ACTH → Hypercortisolism
(Cushing's Syndrome)

Provocative Test
High dose DST

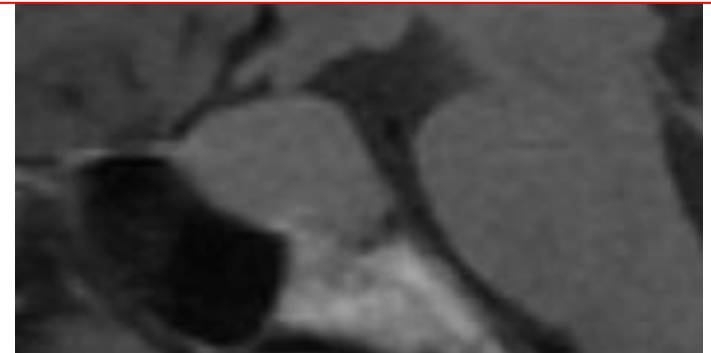
Ectopic ACTH, Small Cell:



High Dose Dexamethasone
Suppression Test: 2 mg q6h x 48h



Pituitary Adenoma (Cushing's Disease)



High ACTH → Hypercortisolism
(Cushing Syndrome)

Provocative Test
Ectopic Hormone
Does NOT Suppress

Ectopic ACTH, Small Cell:
ACTH & Cortisol remain elevated

High Dose Dexamethasone
Suppression Test: 2 mg q6h x 48h

Pituitary Adenoma (Cushing's Disease)
ACTH & Cortisol suppress

Ectopic ACTH → (↑ cortisol)

Presentation:

HTN

Striae

Hyperpigmentation*

ACTH has homology with MSH.
It can bind the MSH receptor.

Low K, High HCO₃

High ACTH

Provocative Test

No Suppression - high dose DST

Ectopic ACTH

Classic Questions:

Smoker with weakness and fatigue. PE:160/104, buccal mucosa with pigmented macules. Labs: Glucose 235, K⁺ 3.2. CXR with mass in the hilum. 24 hour urine collection reveals elevated cortisol value. ACTH level is elevated.

What is the best confirmatory test for this presentation?

- Chest CT Scan
- High Dose DST

Ectopic ACTH

Classic Question:

Smoker with weakness and fatigue. PE:160/104, buccal mucosa with pigmented macules. Labs: Glucose 235, K+ 3.2. CXR with mass in the hilum. 24 hour urine collection reveals elevated cortisol value. ACTH is elevated.

A high dose dexamethasone test is performed.

ACTH and cortisol remain elevated.

Choose the most likely diagnosis:

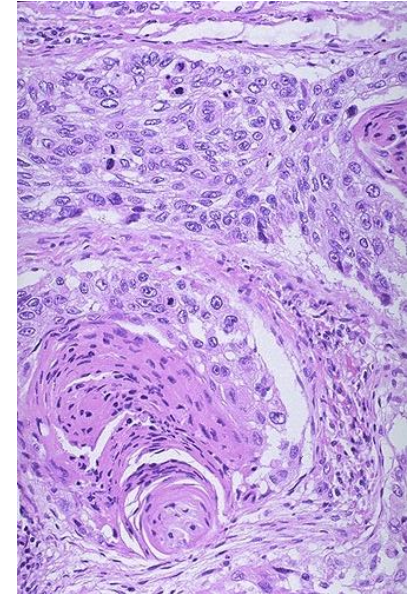
- Pituitary Adenoma
- Adrenal Adenoma
- Exogenous Glucocorticoids
- Addison's Disease
- Bronchogenic Carcinoma

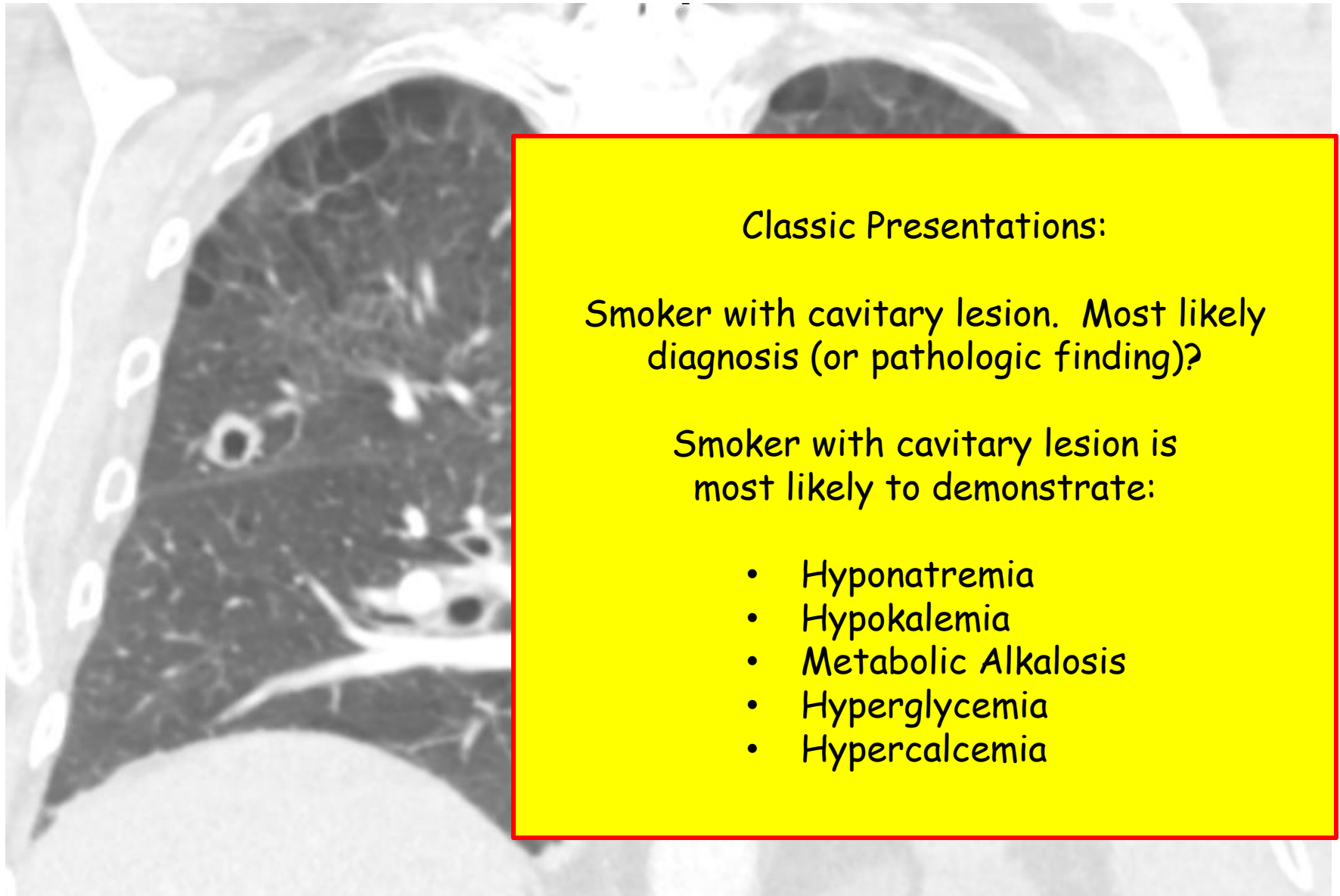
Small Cell ('oat cell'): Distinguishing Characteristics

- Background
 - Central location; (+) Tobacco
 - Neuroendocrine origin → the paraneoplastic phenomenon
 - Overexpressed markers associated with tumors of neural crest origin; Neurosecretory cells are noted with:
 - Enolase (glycolytic enzyme)
 - Chromogranin (inhibitory peptide, precursor)
 - Synaptophysin (involved in synaptic transmission)
- Pathology
 - Small round cells, scant cytoplasm
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- ParaNeoplastic Syndrome...\$\$\$
 - Eaton-Lambert → Presynaptic calcium channel; no response to Tensilon
 - SIADH Secretion → hyponatremia
 - Ectopic ACTH → Cushing's disease

Squamous Cell: Distinguishing Characteristics

- Key Background
 - Central location, Strong a/w smoking, M>F
 - Tendency to **obstruct** and **cavitate** (central necrosis)
- Pathology
 - **Keratin pearls** ('keratinization')
 - **Intercellular bridges** (desmosomes/tight junctions)
 - Polygonal cells with eosinophilic cytoplasm
- Paraneoplastic
 - **Hypercalcemia** related to **PTH-rP**



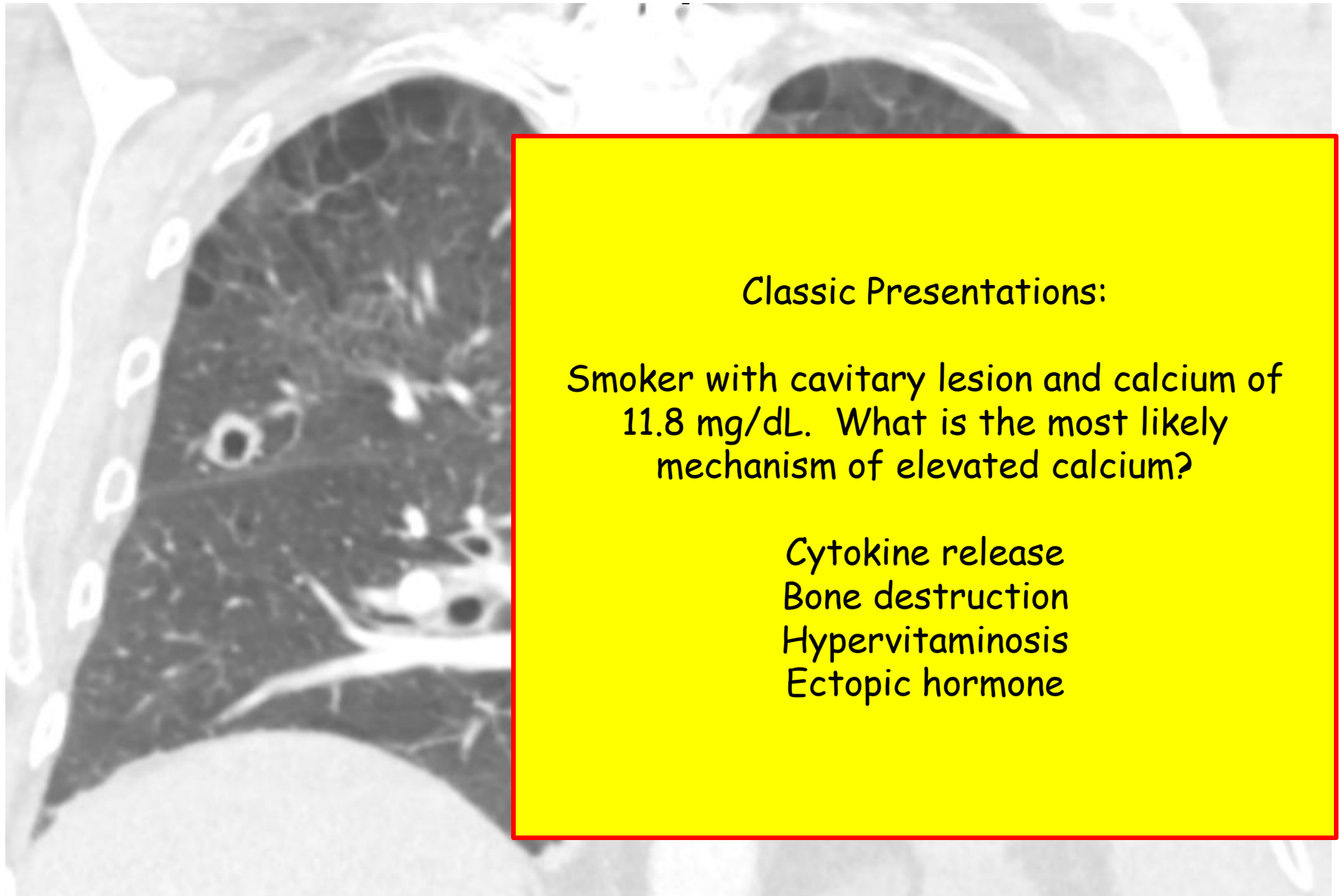


Classic Presentations:

Smoker with cavitary lesion. Most likely diagnosis (or pathologic finding)?

Smoker with cavitary lesion is most likely to demonstrate:

- Hyponatremia
- Hypokalemia
- Metabolic Alkalosis
- Hyperglycemia
- Hypercalcemia



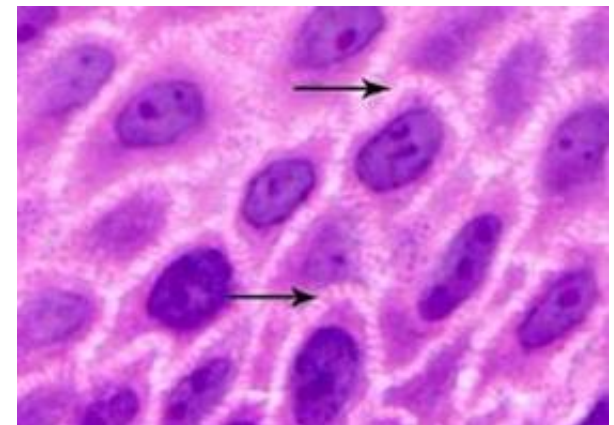
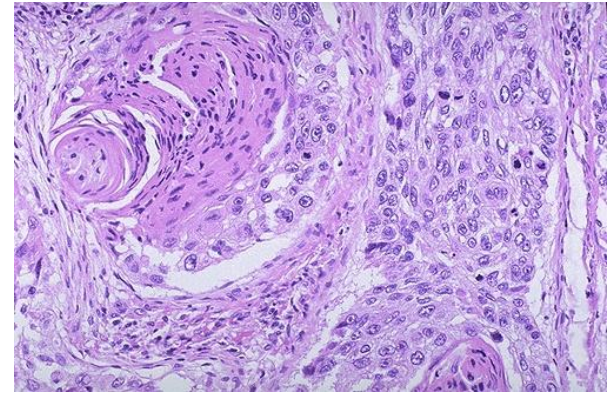
Classic Presentations:

Smoker with cavitary lesion and calcium of 11.8 mg/dL. What is the most likely mechanism of elevated calcium?

- Cytokine release
- Bone destruction
- Hypervitaminosis
- Ectopic hormone

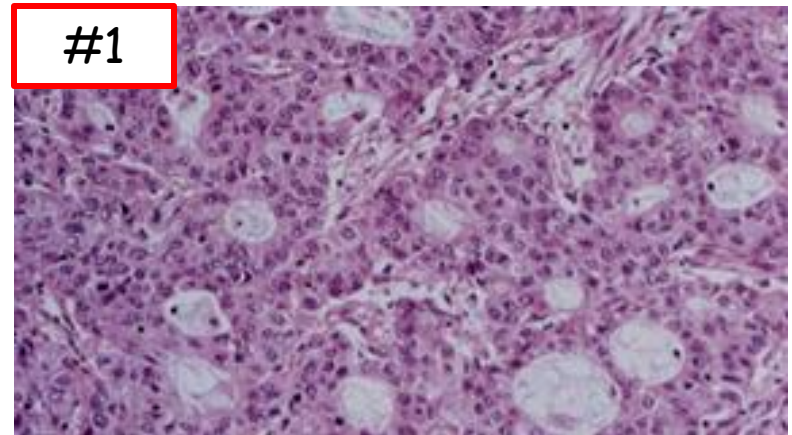
Squamous Cell: Distinguishing Characteristics

- Key Background
 - Central location, Strong a/w smoking
 - Tendency to cavitate and obstruct
 - Male predominance
- Pathology
 - Keratin pearls
 - Intercellular bridges (desmosomes/tight junctions)
 - Polygonal cells with eosinophilic cytoplasm
- Paraneoplastic
 - Hypercalcemia related to PTH-rP



Adenocarcinoma (K-RAS): Distinguishing Characteristics

- Key Background:
 - Peripheral or **scar** location
 - **Weakest smoking association**
 - Women > Men



- Pathology:
 - Form tubules, glands and papillary structures

- Paraneoplastic Syndrome:
 - **Hypertrophic osteoarthropathy**



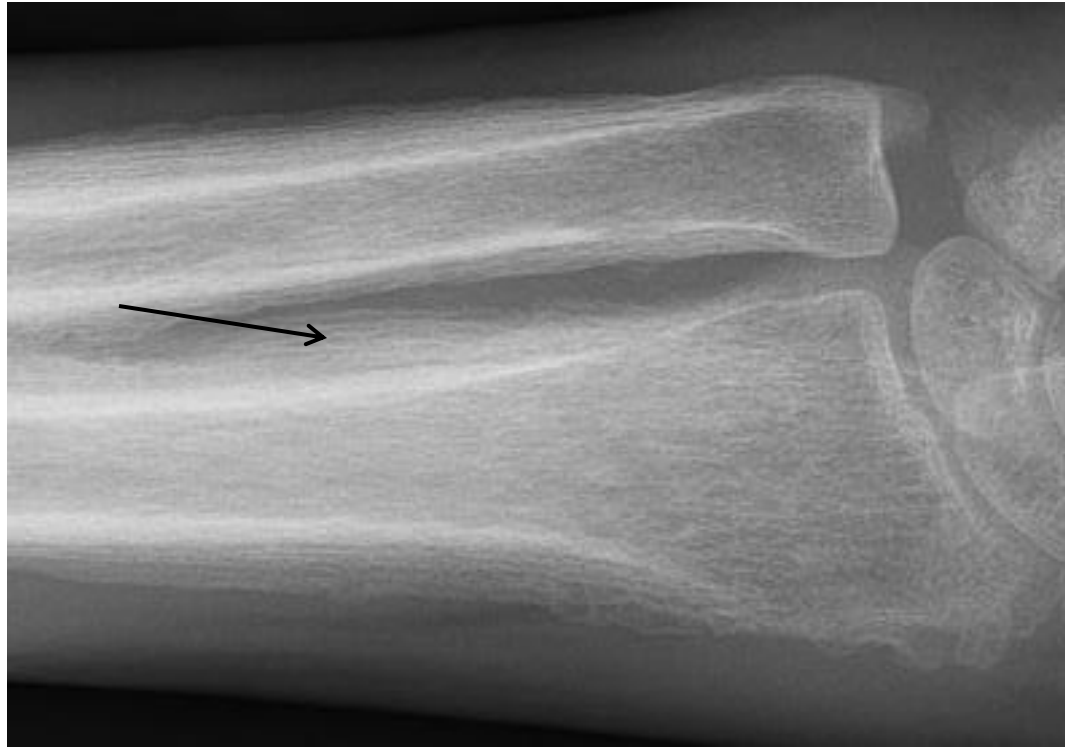
Hypertrophic Osteoarthropathy

- Advanced stage of clubbing with **painful periosteal proliferation** of long bones, especially the digits.
- The periostitis may be a/w fever, arthralgia or joint effusion.

Clubbing:

- Physical sign characterized by bulbous enlargement of the ends of one or more fingers (or toes).
- Proliferation and edema of connective tissue result in loss of normal angle between skin and nail plate and excessive sponginess of nail base.
- Pathophysiologic basis: Unknown.

Hypertrophic Osteoarthropathy



1. Characterized by periosteal reaction of long bones of distal extremities.
2. No underlying bone lesion (i.e. osteosarcoma, osteomyelitis, hyperPTH).
3. Clinical features: digital clubbing, periostosis of tubular bones and synovial effusions

Adenocarcinoma: Paraneoplastic

Long time smoker presents with dyspnea and forearm/hand pain.
A radiograph reveals marked periosteal new bone formation.

What is his likely dx?

- Paraneoplastic Syndrome:
 - Hypertrophic osteoarthropathy



Classic Question (demographics):
Woman, Nonsmoker; CXR → nodule

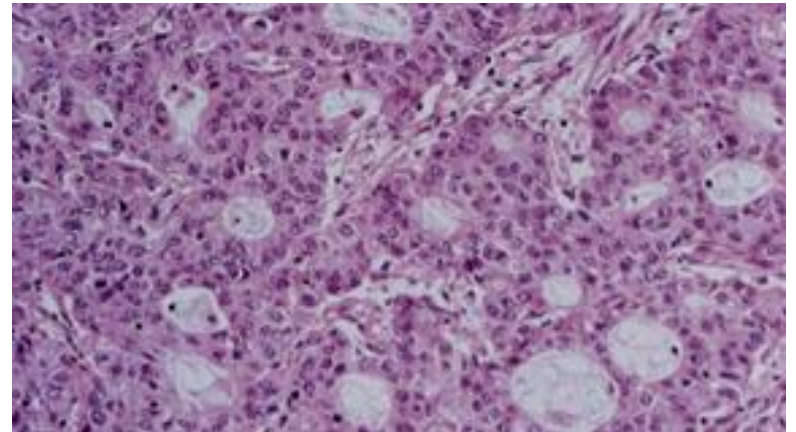
Most likely pathology?
Most likely dx?

Patient has some symptoms of a pulmonary condition (such as old TB, radiation, IPF) that caused scarring. They are now noted with nodular growth in region of prior scar tissue.
If a biopsy is performed, what pathology is noted?

Scar (Adeno)Carcinoma

Adenocarcinoma (K-RAS): Distinguishing Characteristics

- Key Background:
 - Peripheral or scar location
 - Weakest smoking association
 - Women > Men
- Pathology:
 - Form tubules, glands and papillary structures
- Paraneoplastic Syndrome:
 - Hypertrophic osteoarthropathy



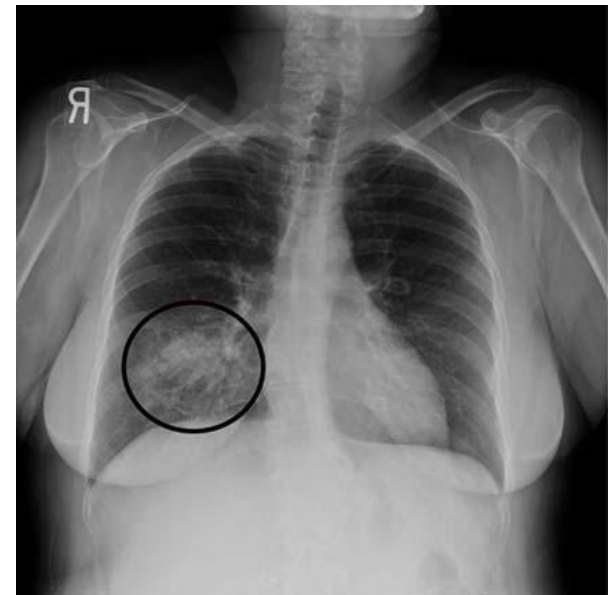
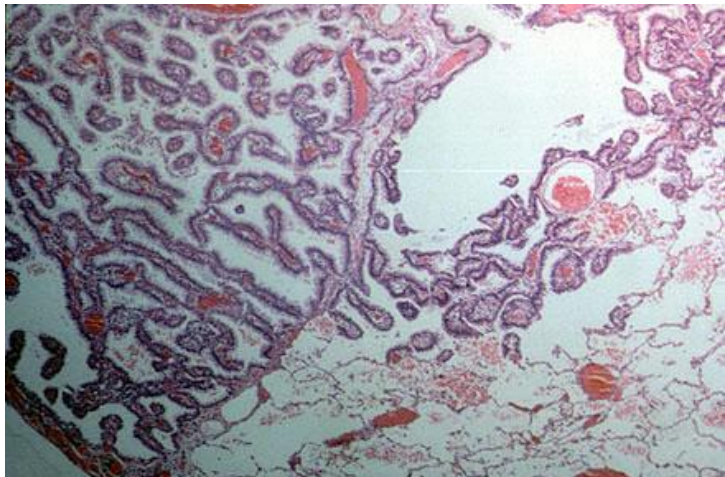
Bronchioloalveolar Carcinoma (now called adenocarcinoma-in-situ)

- Key Background

- Poor association w/ tobacco (but less common than adeno overall)
- Presents as diffuse infiltrate that may **mimic PNA**.

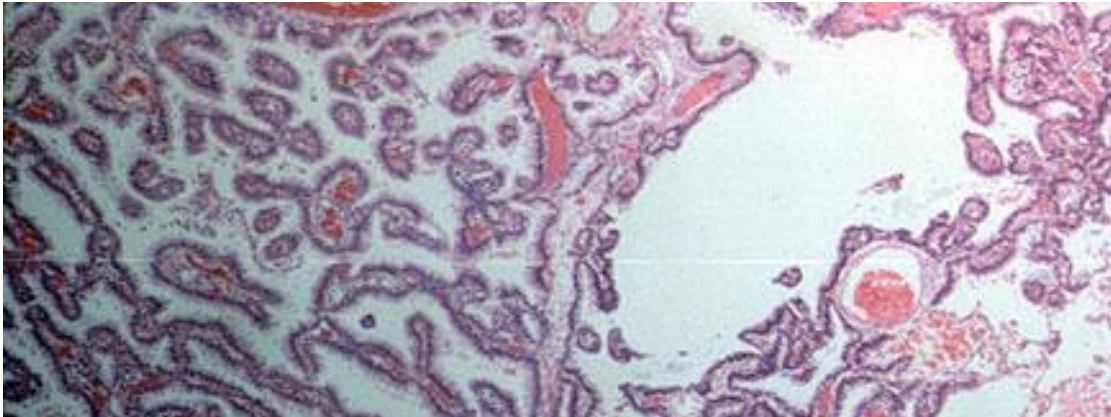
- Pathology:

- Dysplastic columnar cell growth along the alveolar septum that extends toward periphery.
- **No vascular or stromal invasion.**



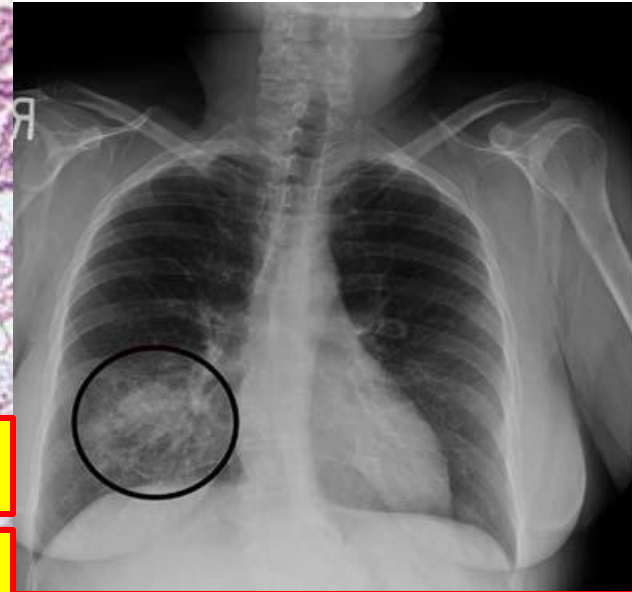
Bronchioloalveolar Carcinoma (now called adenocarcinoma-in-situ)

- Pathology:
 - Dysplastic columnar cell growth along the alveolar septum that extends toward periphery.
 - No vascular or stromal invasion.



Grows along alveolar septum → periphery

No vascular or stromal invasion



Mimics PNA

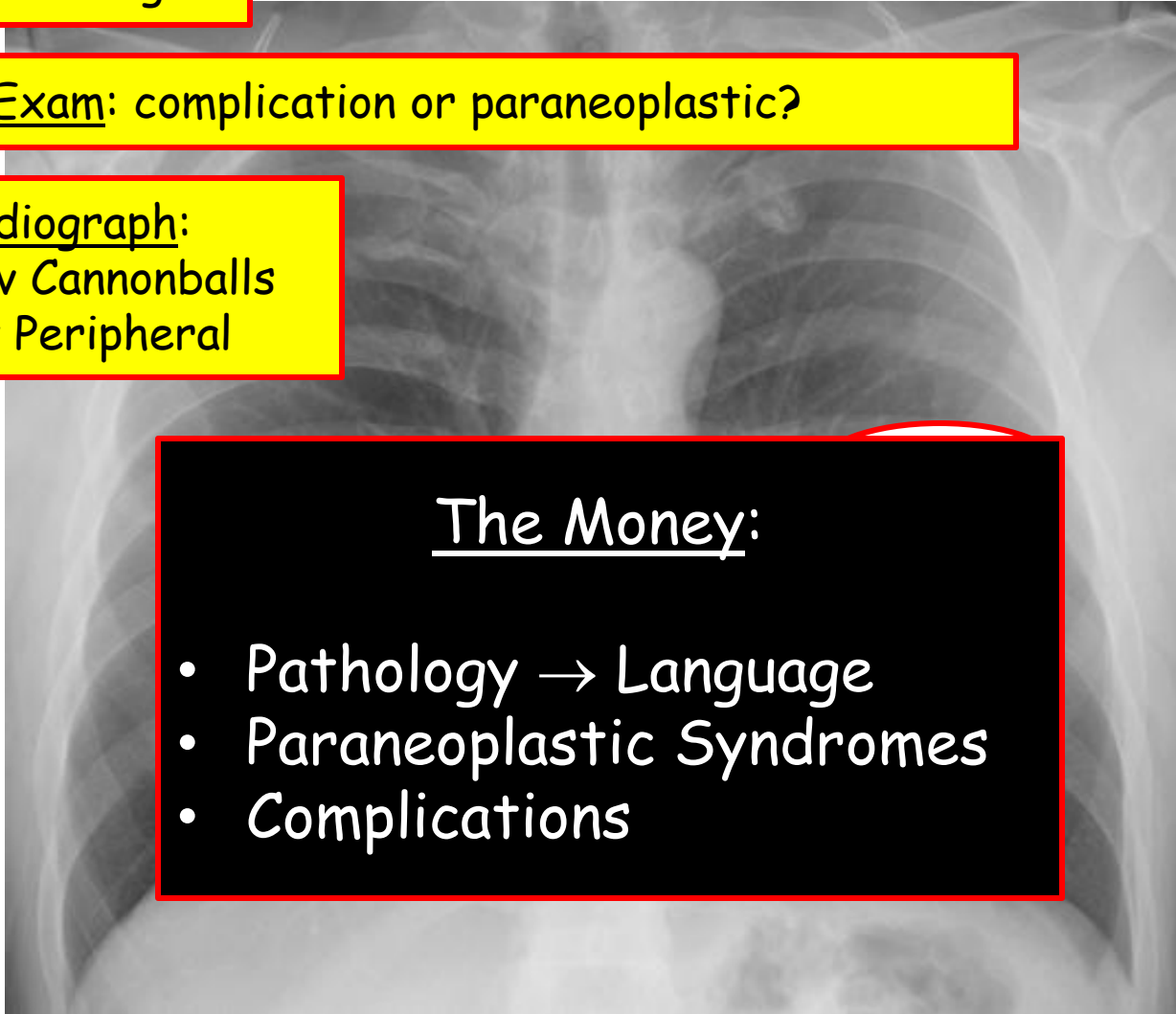
History: smoking?

Physical Exam: complication or paraneoplastic?

Radiograph:
Solitary v Cannonballs
Central v Peripheral

The Money:

- Pathology → Language
- Paraneoplastic Syndromes
- Complications



SVC Syndrome

- Bronchogenic most common cause (**lymphoma** is 2nd)
- Associated w/ mediastinal mass (i.e. **SVC compressed**)
- **Symptoms** include:
 - SOB/cough
 - Face/arm swelling
 - Headache/dizzy/visual Δ
 - Dilated collateral veins on upper torso

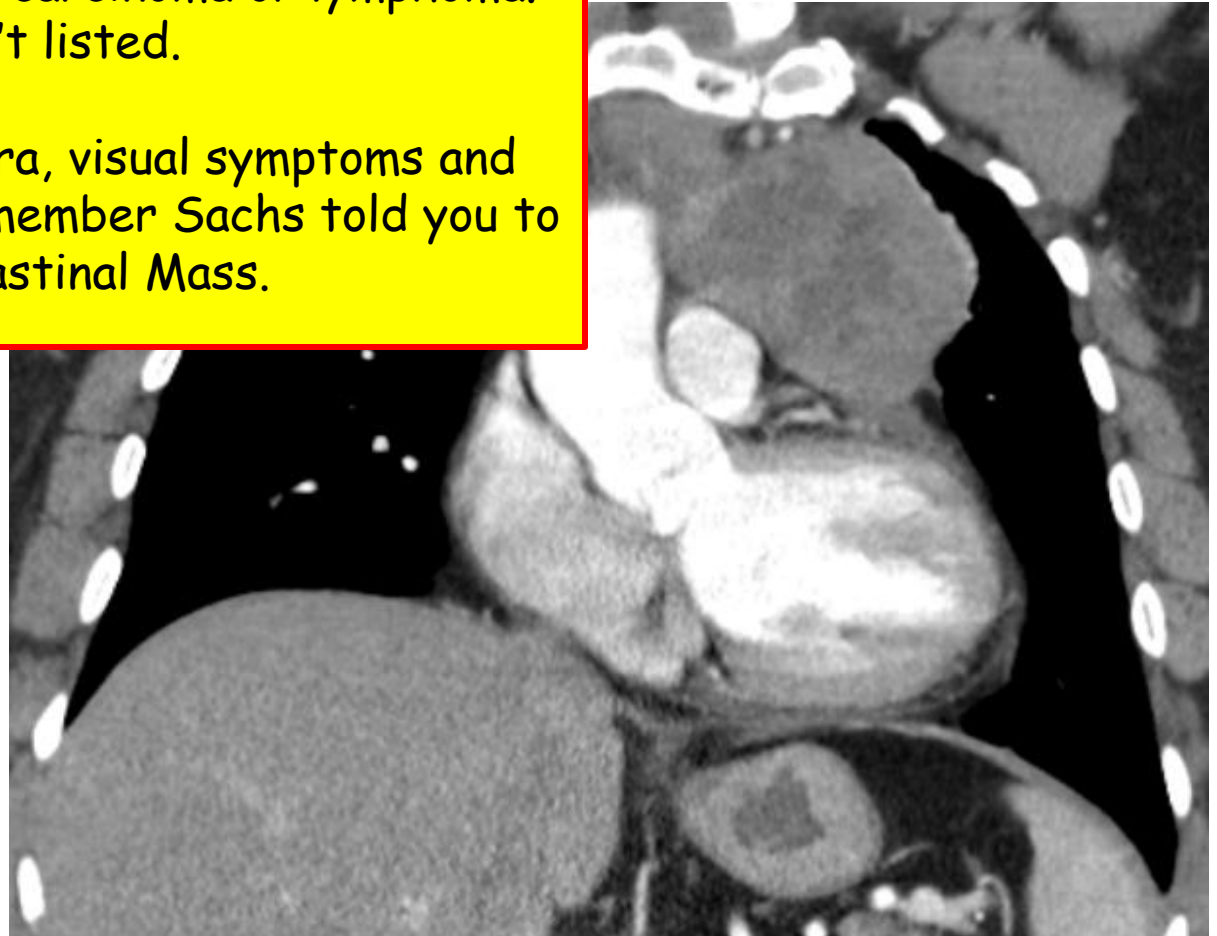


Patient presents with facial plethora, headache, dizzy, visual symptoms and dilated veins.

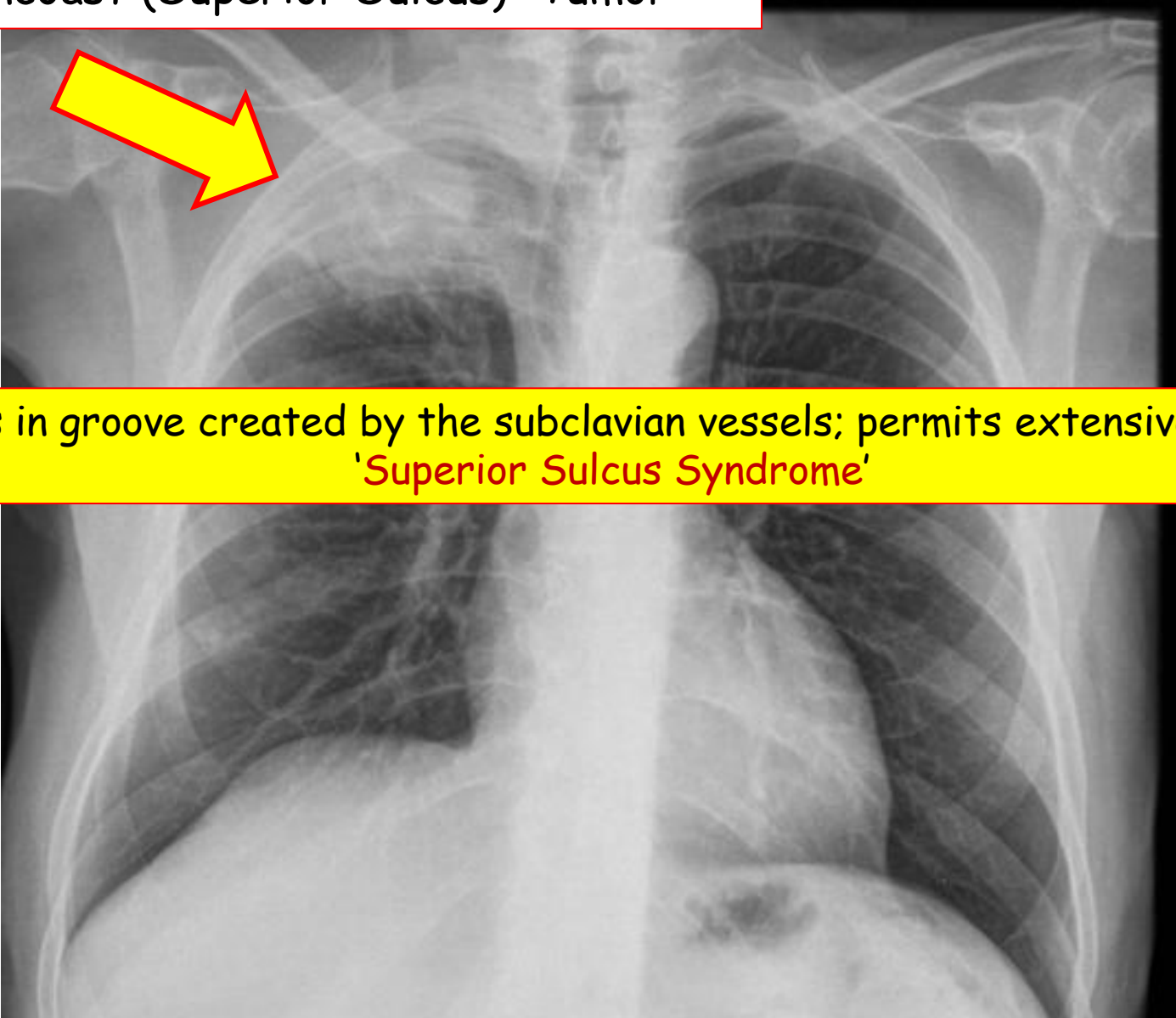
You know this is SVC syndrome.
You are proud of yourself.

You look for bronchogenic carcinoma or lymphoma.
They aren't listed.

You develop facial plethora, visual symptoms and dizziness BUT then you remember Sachs told you to look for Mediastinal Mass.



Pancoast (Superior Sulcus) Tumor



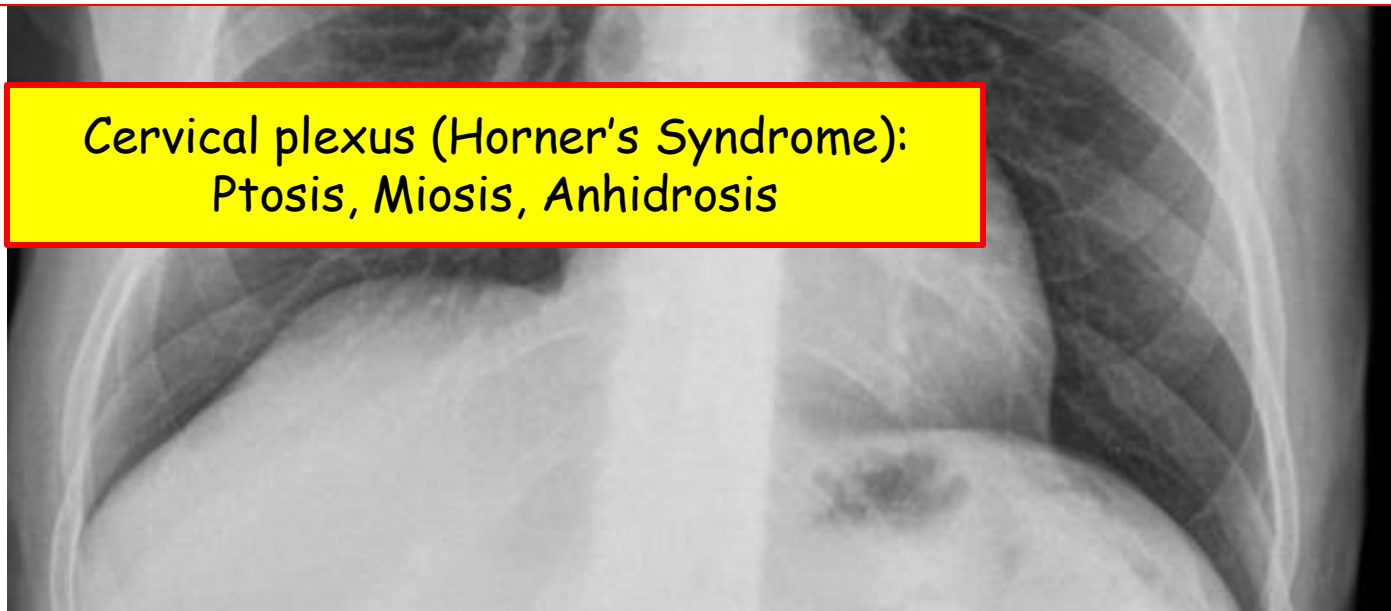
Forms in groove created by the subclavian vessels; permits extensive spread
'Superior Sulcus Syndrome'

Pancoast (Superior Sulcus) Tumor



Forms in groove created by the subclavian vessels; permits extensive spread
'Superior Sulcus Syndrome'

Cervical plexus (Horner's Syndrome):
Ptosis, Miosis, Anhidrosis



Pancoast (Superior Sulcus) Tumor



Forms in groove created by the subclavian vessels; permits extensive spread
'Superior Sulcus Syndrome'

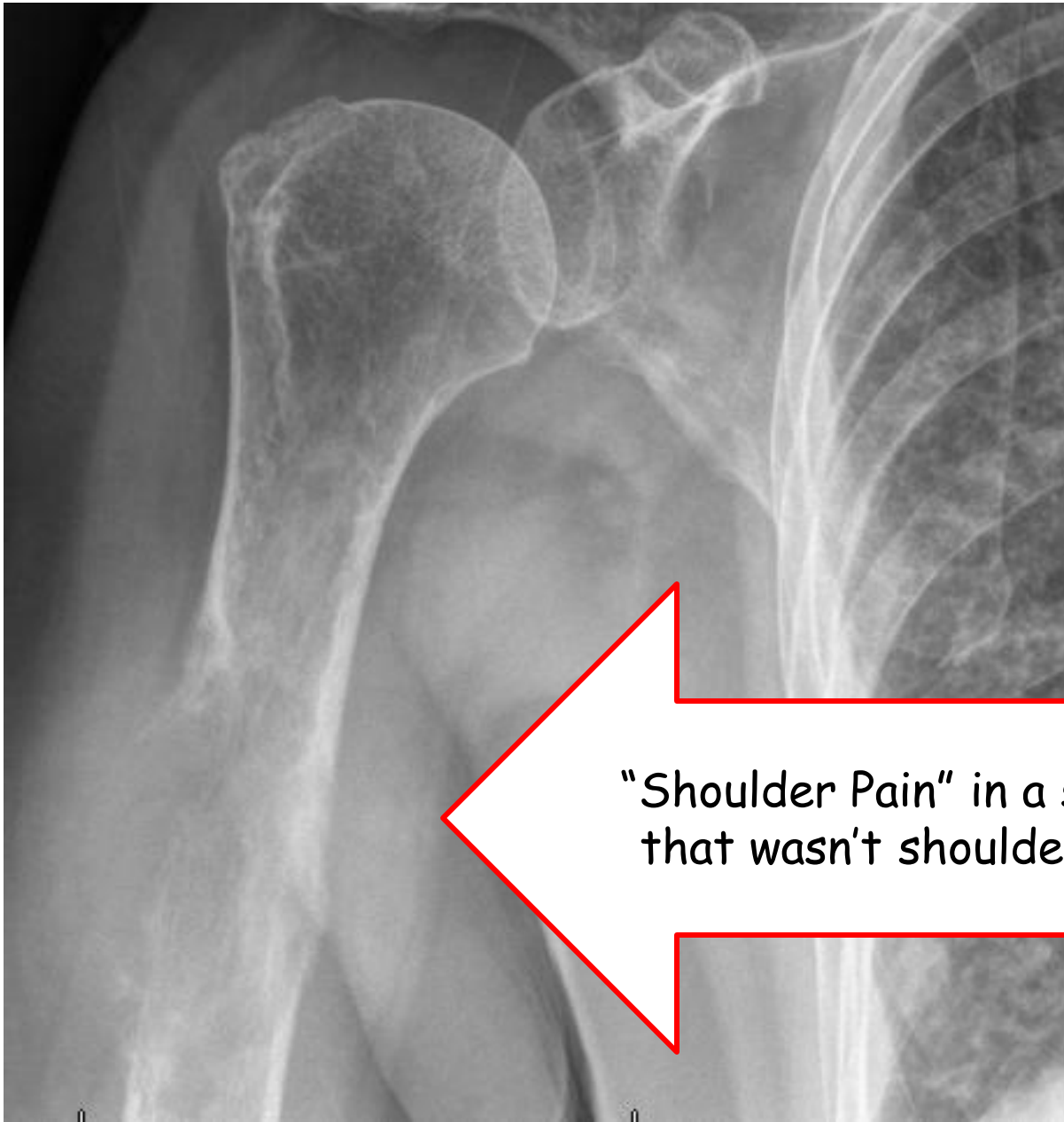
Cervical plexus (Horner's Syndrome):
Ptosis, Miosis, Anhidrosis

They assume you know
this one

So they ask this one

Brachial plexus (ulnar nv distribution):
Shoulder pain, weakness, numbness

Most common: Squamous & Adenocarcinoma



"Shoulder Pain" in a smoker
that wasn't shoulder pain.

Exudate

Pleural LDH > 200

Pleural:Serum LDH > 0.6

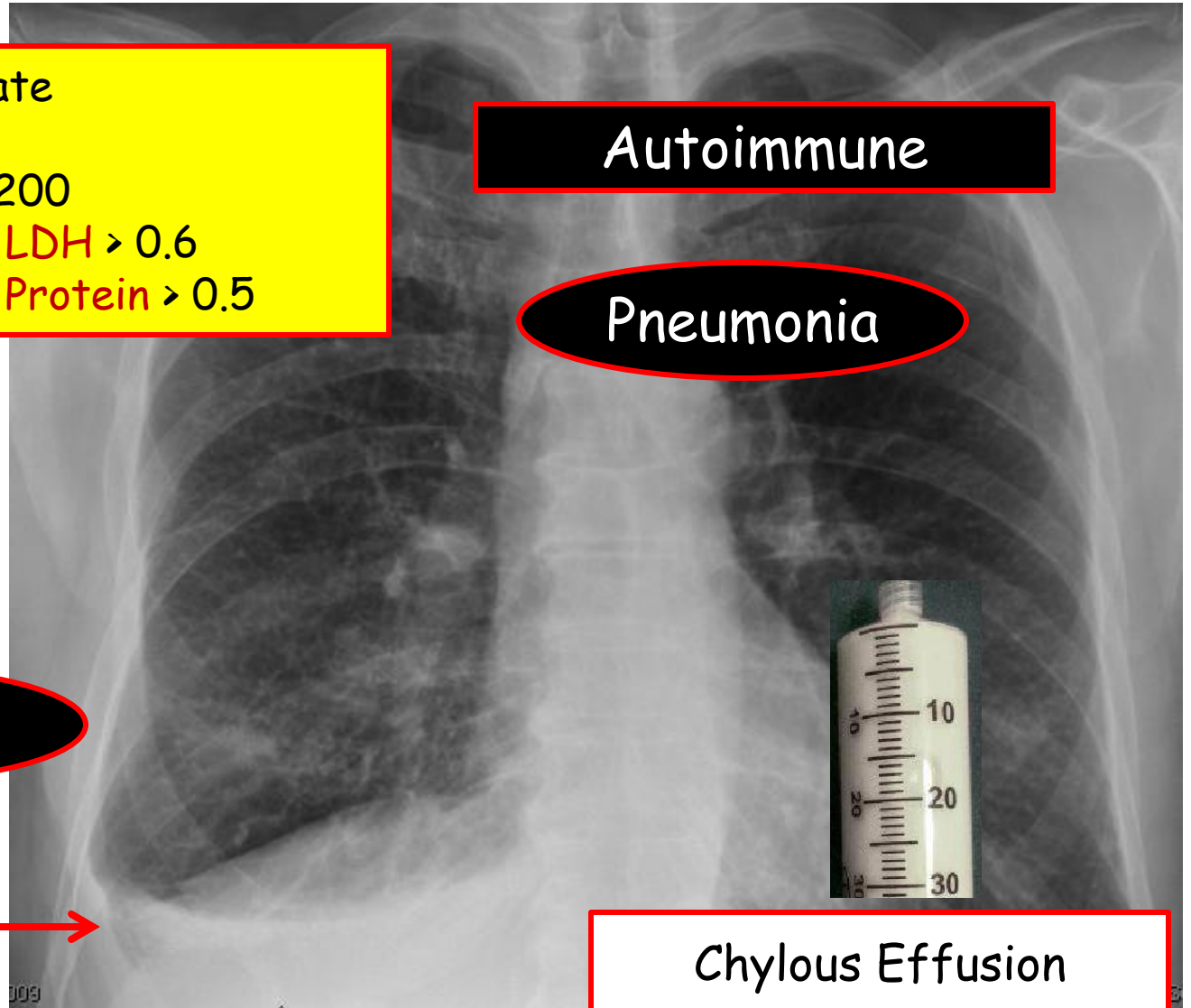
Pleural:Serum Protein > 0.5

Autoimmune

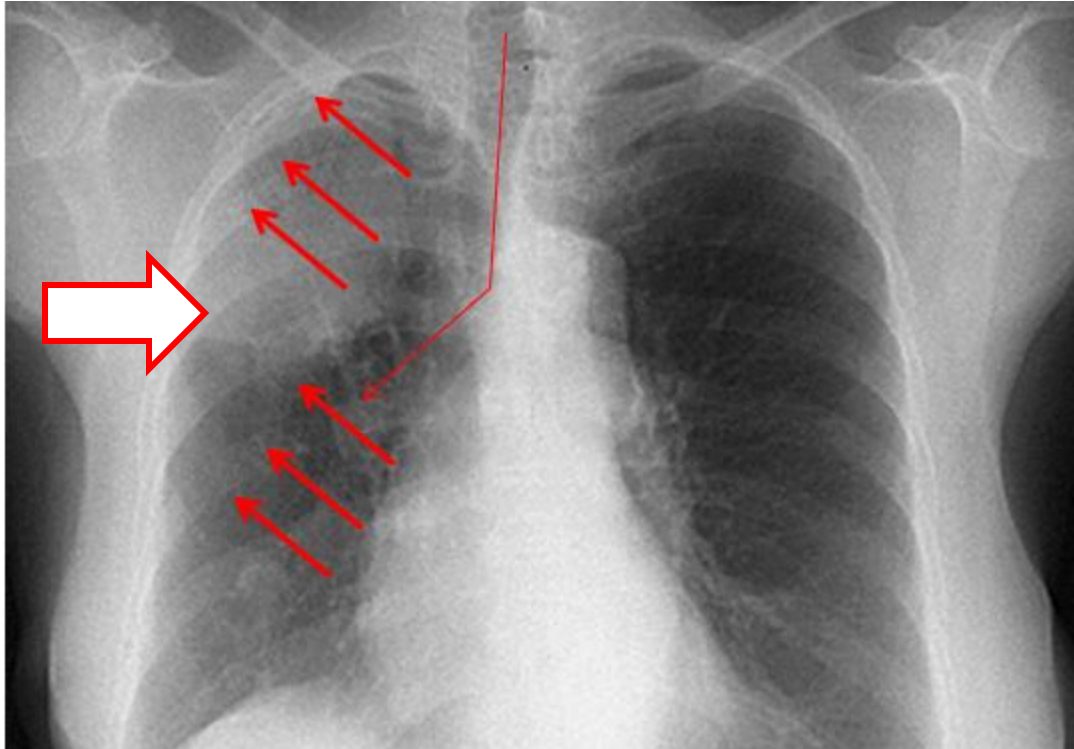
Pneumonia

Neoplasm

Chylous Effusion



Non-Pleural Physical Exam Confounders: Trachea



Opacification

Traction Atelectasis:

- **Etiology:** Mass Lesion in Bronchus
- Inspection, Trachea - Deviated (pulled) toward collapsed lung
- Auscultation - decreased breath sounds (due to lung collapse)
- Percussion - decreased (or normal); **no hyperresonance** (either side)

Pulmonary Neoplasm: Bronchial Carcinoid

GI → mets to liver
(carcinoid syndrome)

Cardiology → right
sided valvular disease

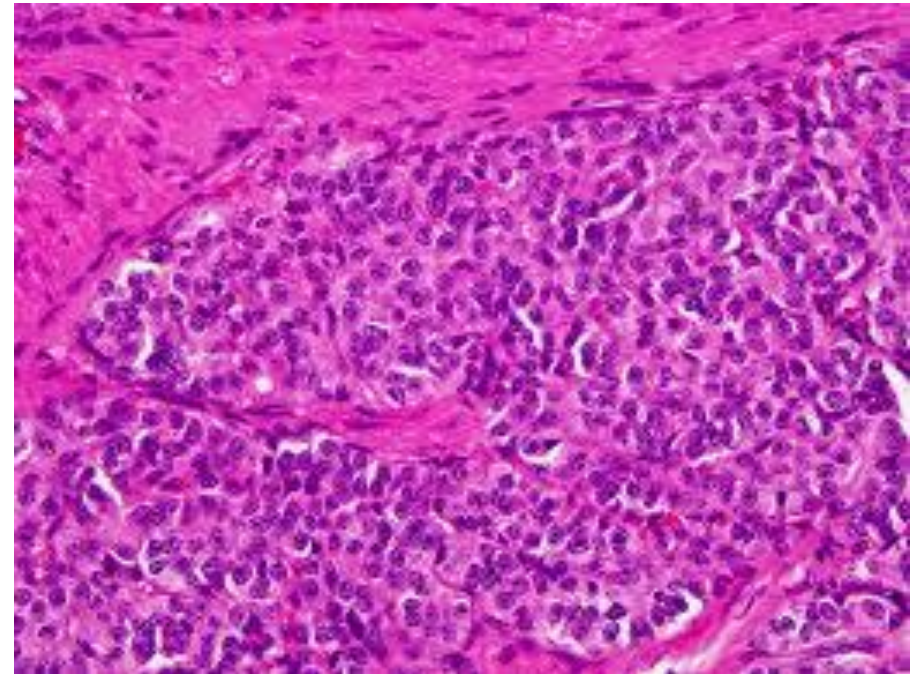
Pulmonary Neoplasm: Bronchial Carcinoid

- **Key Background:**
 - Low grade neuroendocrine tumors
- Pathology (intramural/submucosal mass)
 - Uniform bland cells arranged in packets/nests separated by delicate fibrovascular stroma (hemoptysis).
 - EM: dense-core granules
- Clinical Presentation
 - Carcinoid Syndrome → Serotonin (5-HIAA): **Flushing, wheezing, diarrhea**
- **Diagnostics: Bronchoscopy**
 - Present as **polypoid growth** within lumen of bronchus
 - Pink to red vascular mass with **intact overlying bronchial epithelium.**

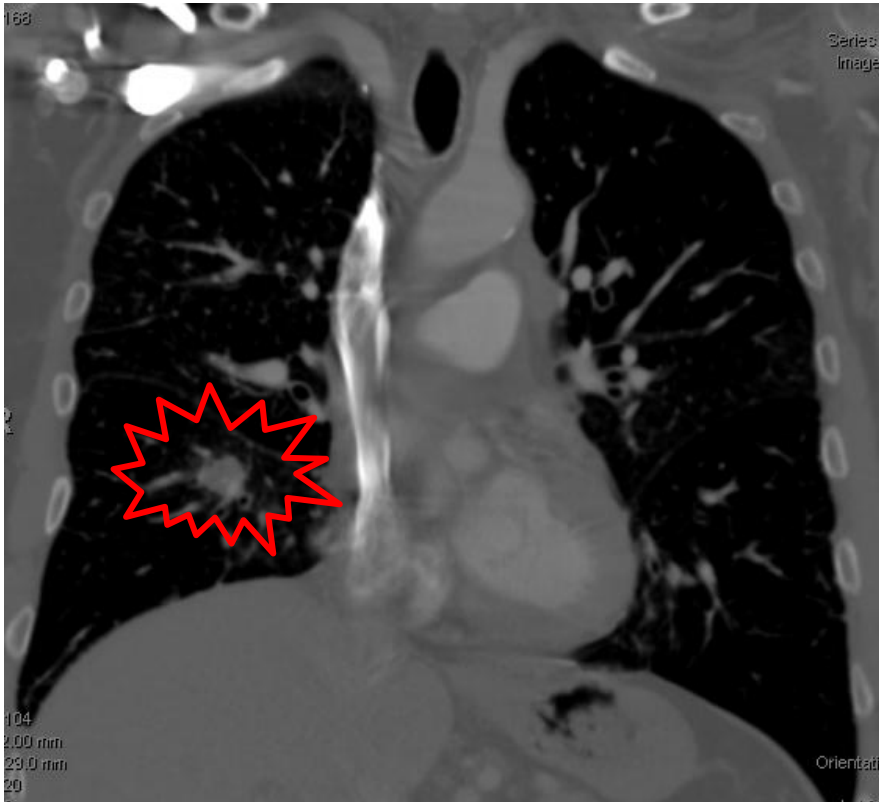


Bronchoscopic appearance
Pink to red vascular mass with **intact overlying bronchial epithelium**.
Appear as ovoid or polypoid masses

Nests or cords of uniform bland cells with central nuclei and moderate granular cytoplasm; **prominent vasculature** (hemoptysis)



Pulmonary Neoplasm



The Money:

- Pathology → Language
- Paraneoplastic Syndromes
- Complications

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