

Clinicopathological Conference

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Case Introduction

54 year old male

15 pack year history smoking

Shortness of breath

Hashimoto's Thyroiditis, on levothyroxine
COPD, asthma

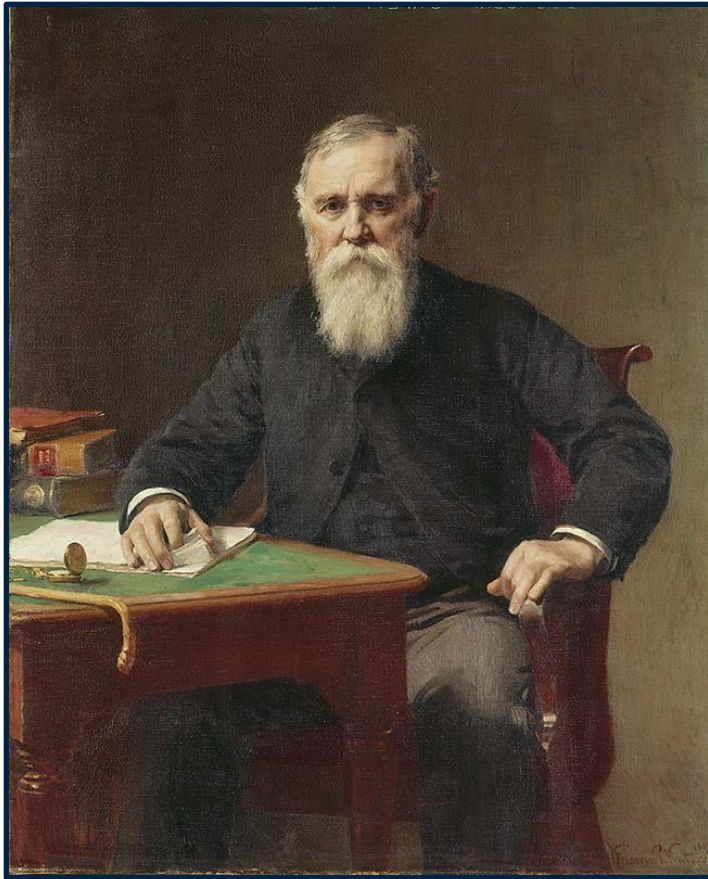
Na 114, hypertonic saline

Left upper lung mass

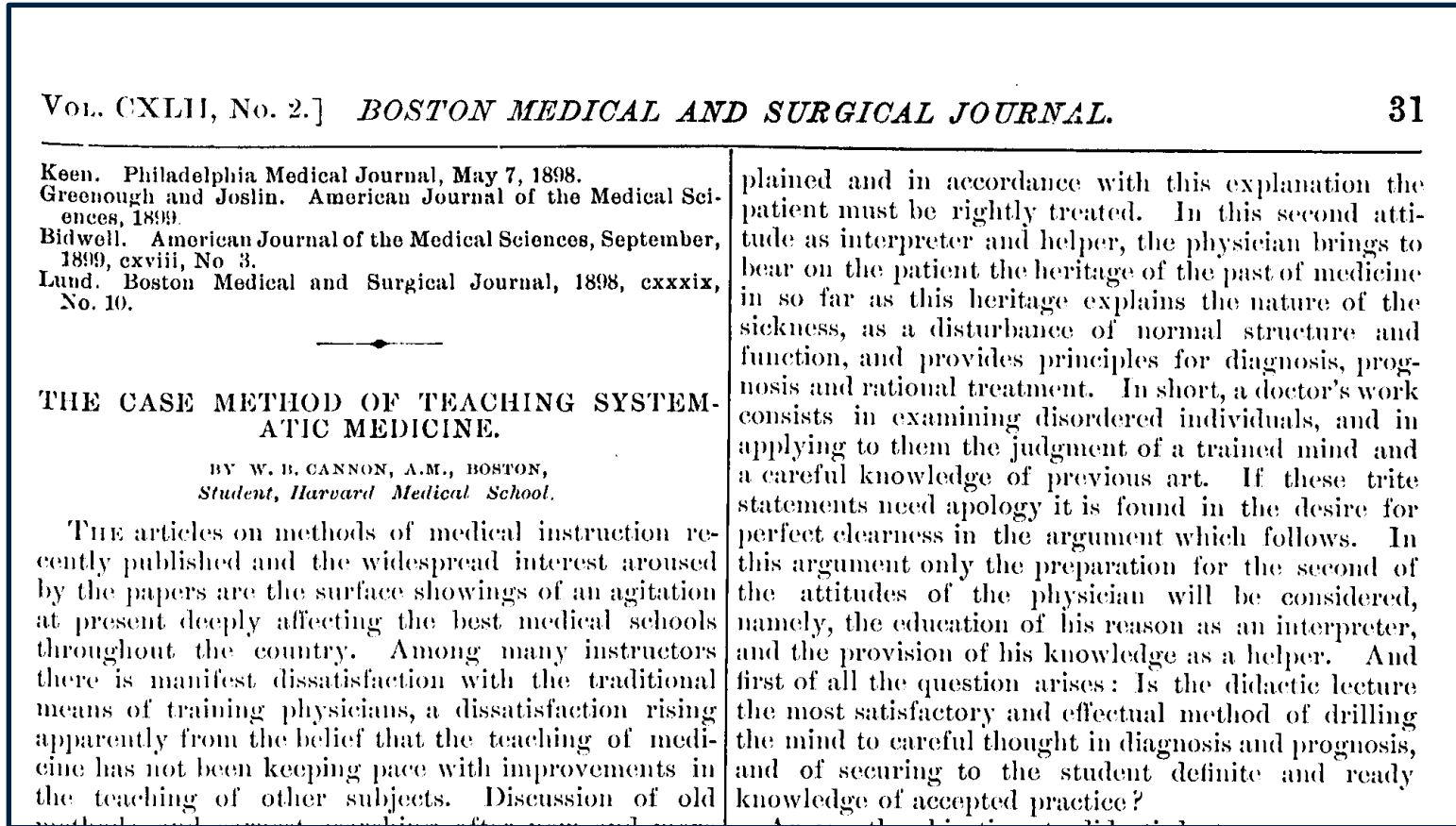
PET/CT w/ osseous dz

Bronchoscopy w/ biopsy

CPC History

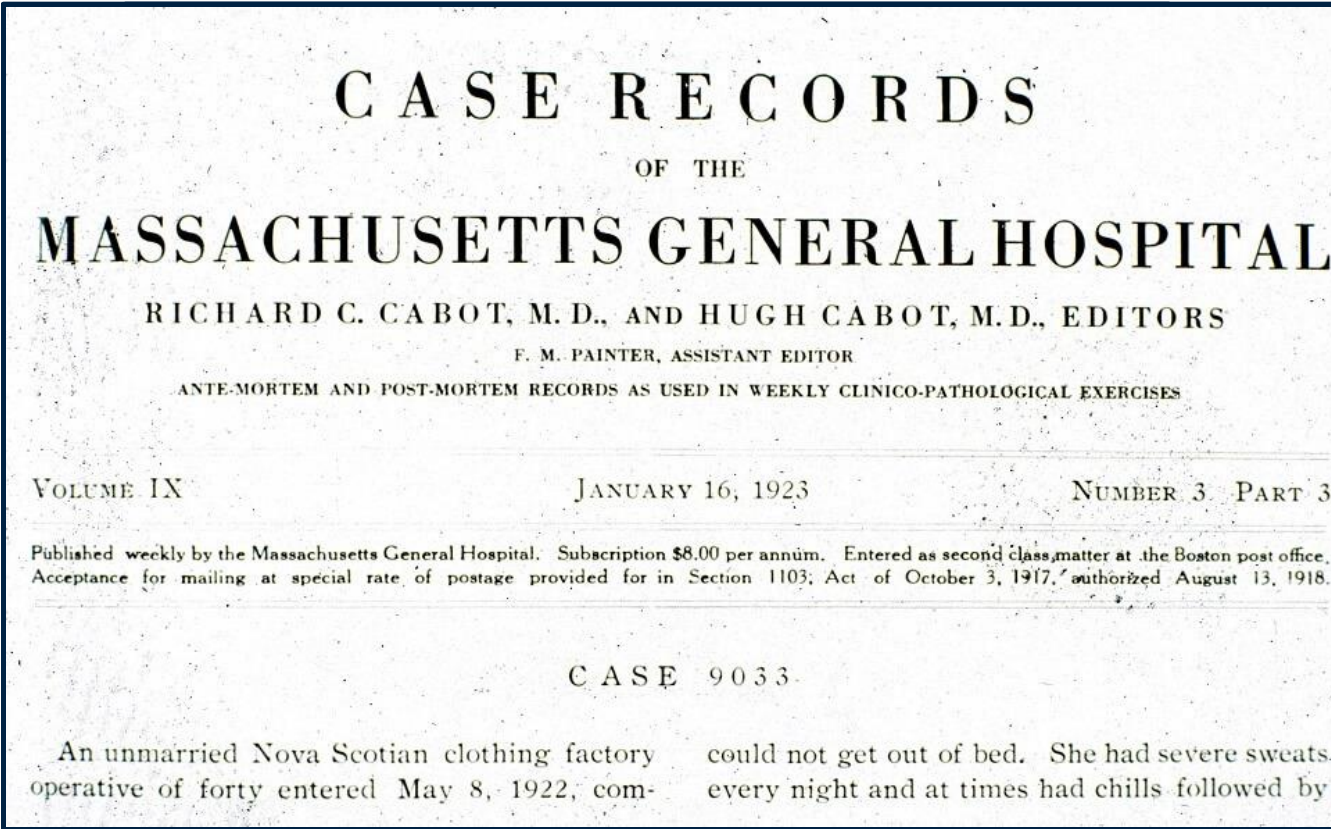


1870 – Case Method in Law
Christopher Columbus Langdell



1900 – Case Method in Medicine
Walter Bradford Cannon

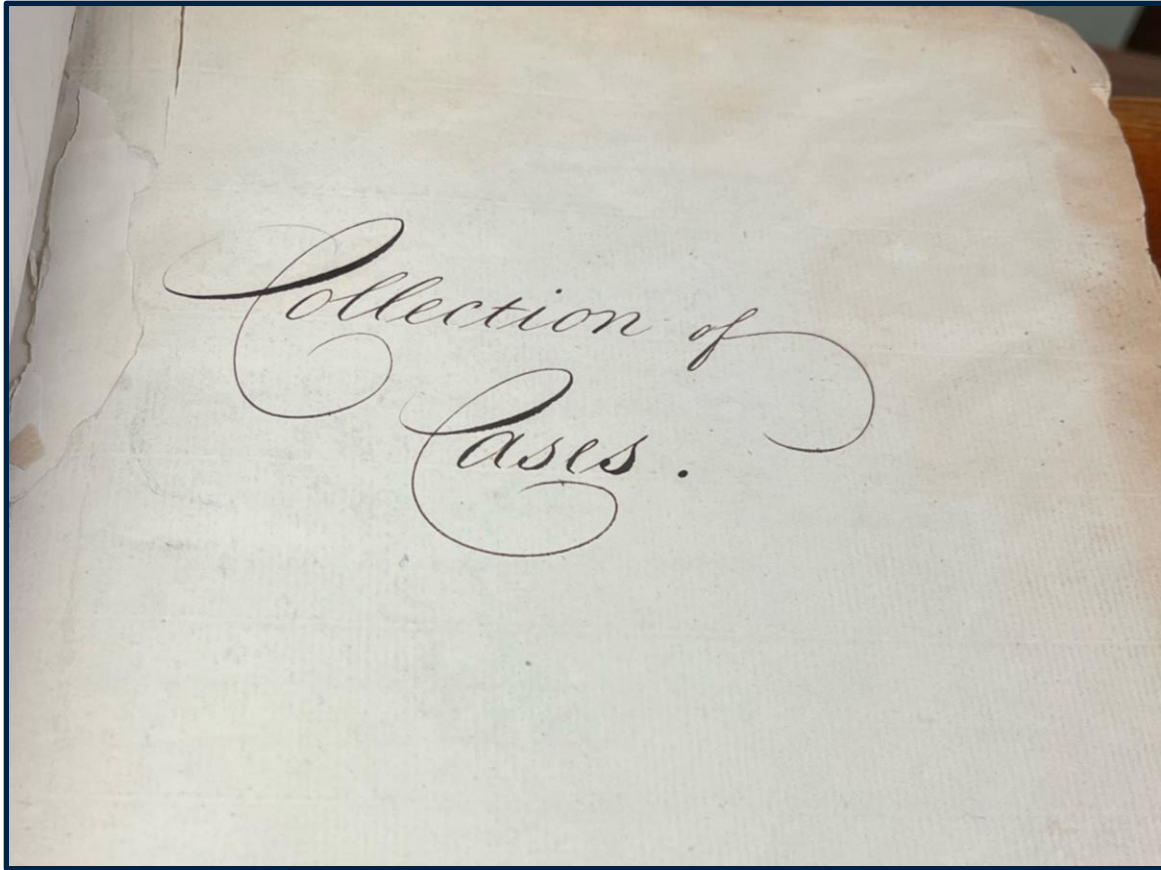
CPC History



1900-1923 – Case Teaching in Medicine Richard C. Cabot

Early CPCs

CPC History

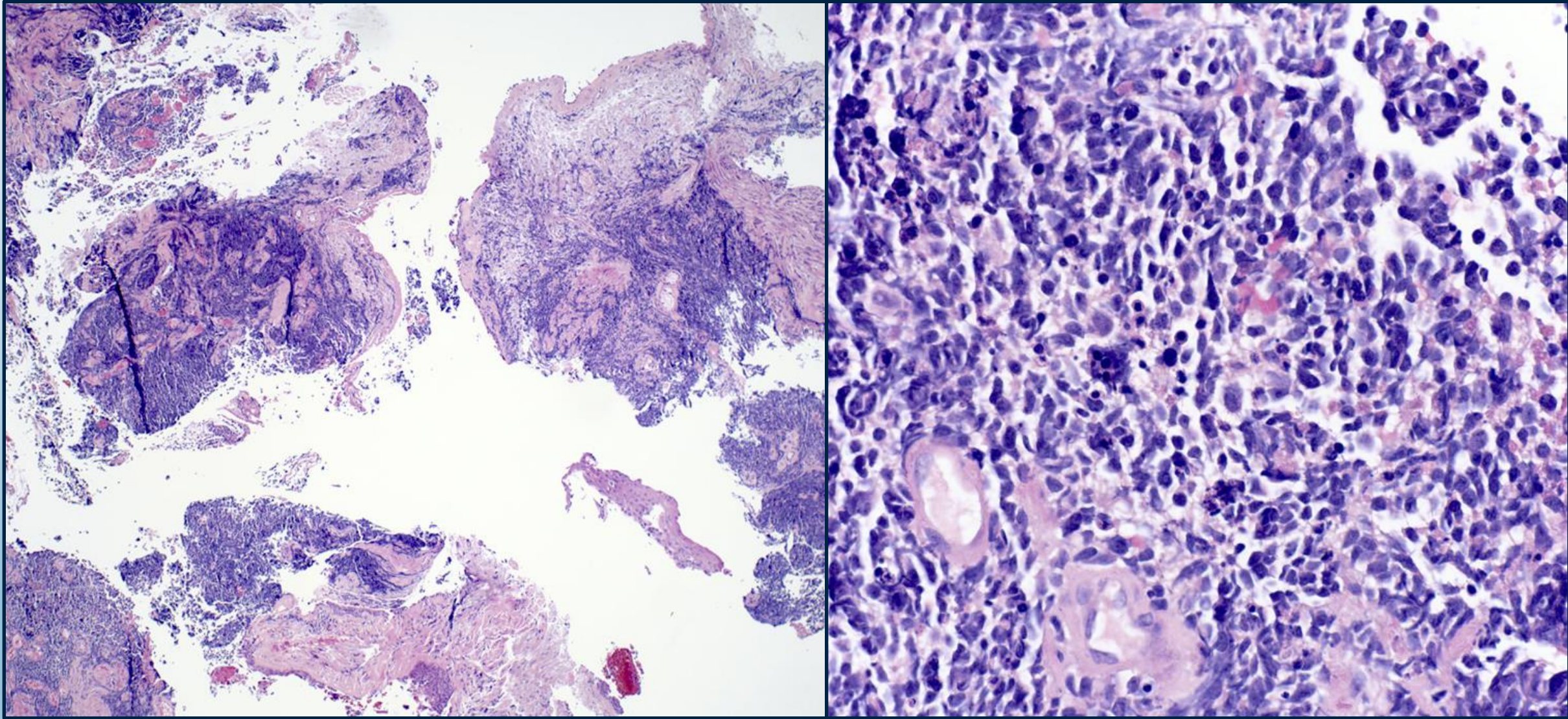


Collection of Cases at PAH, 1803



Residents at Pennsylvania Hospital, 1924

Pathology



Evaluation of patient's SCLC

Left upper lobe mass

PET/CT extensive osseous metastatic disease

MRI brain negative

No symptomatic sites of disease



Case summary to this point

This is a 54-year-old male with past medical history of **Hashimoto's thyroiditis** and **tobacco use disorder**, found to have extensive stage **small cell lung cancer** with osseous metastasis, complicated by **SIADH** on urea, initiating cancer treatment.

Small cell lung cancer classification

Bronchogenic Carcinoma

Treatment of extensive-stage SCLC with good PS

Carboplatin or Cisplatin

&

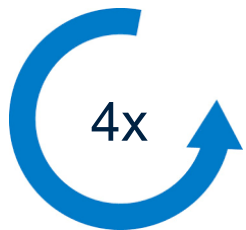
Etoposide

&

Atezolizumab or durvalumab



Maintenance atezolizumab
or durvalumab



Case update

PET/CT complete anatomic
and metabolic response

Na normal on urea

Shortness of breath and cough
improved

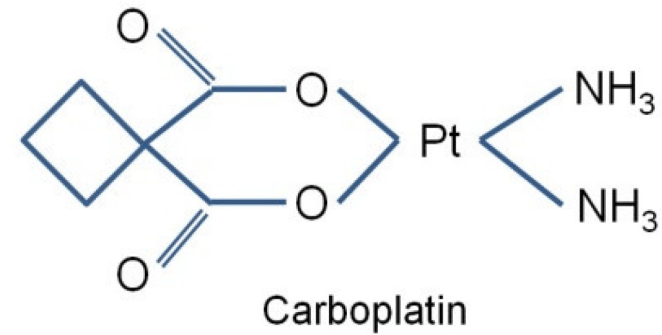
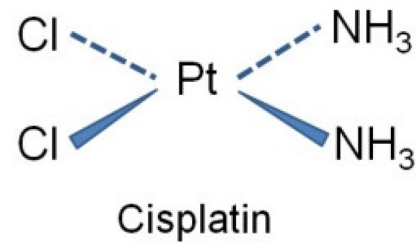
Tolerated chemoimmunotherapy well

Case summary to this point

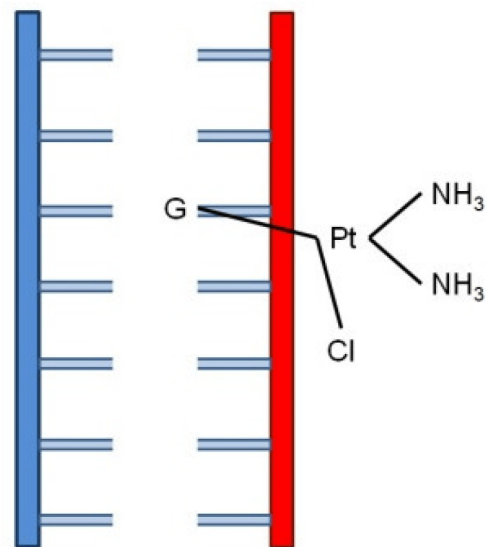
This is a 54-year-old male with past medical history of Hashimoto's thyroiditis and tobacco use disorder, found to have extensive stage small cell lung cancer with osseous metastasis, complicated by SIADH on urea, **s/p chemoimmunotherapy with complete response, now on maintenance atezolizumab.**

Carboplatin and cisplatin

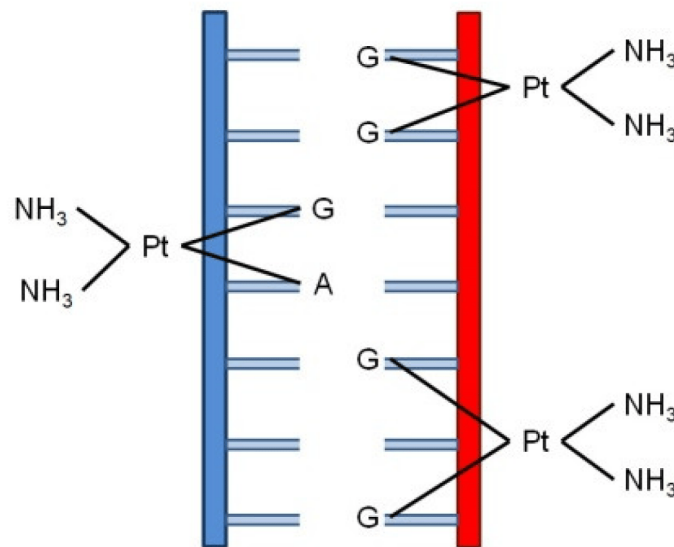
A



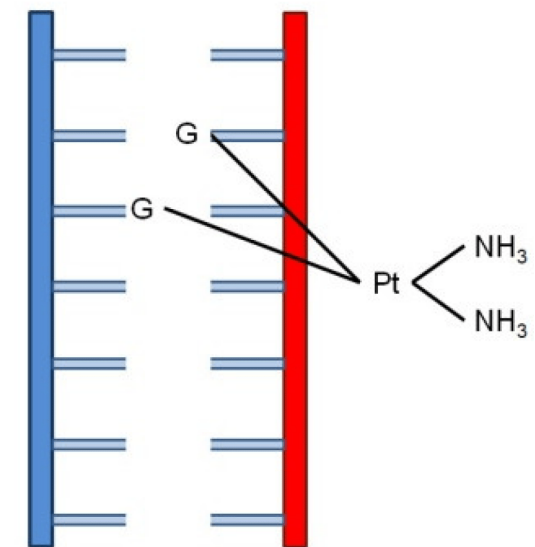
B



Monoadducts

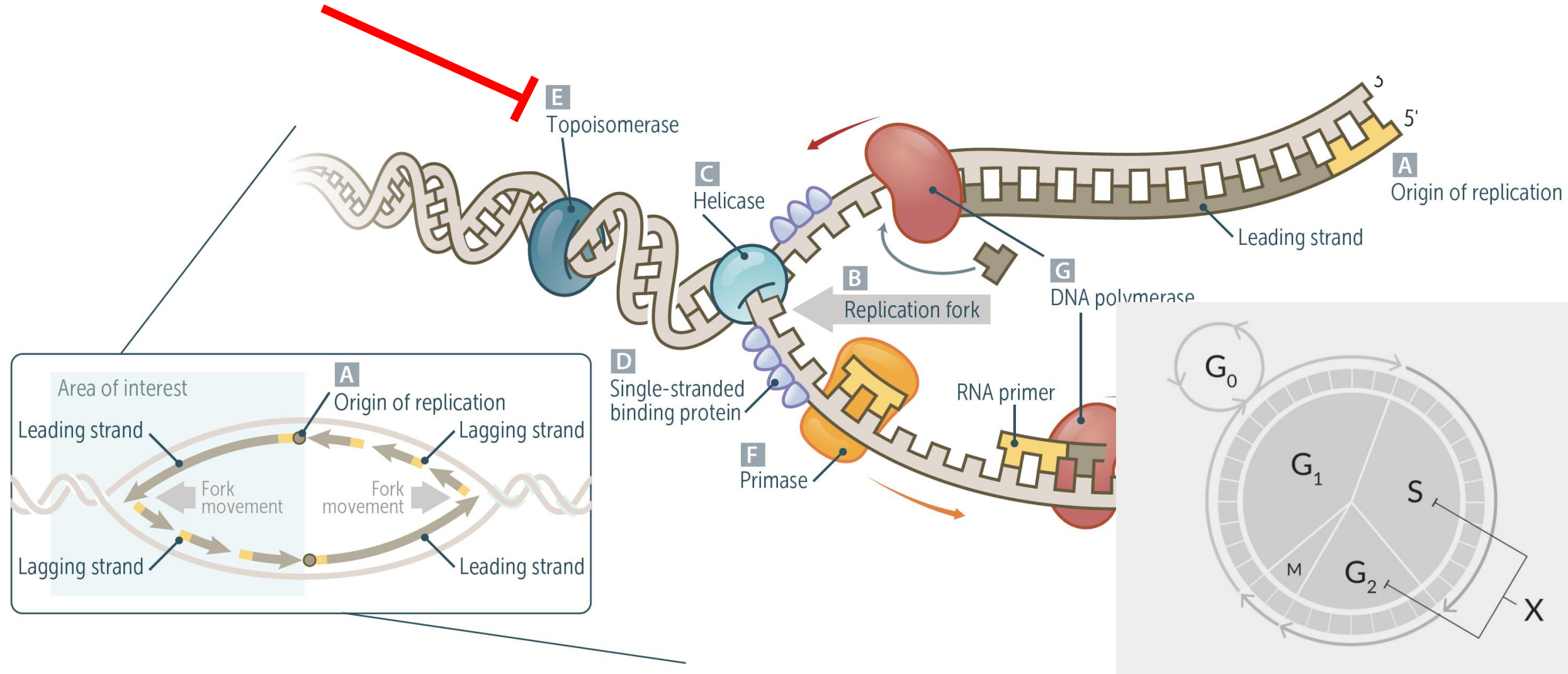


Intrastrand cross-links

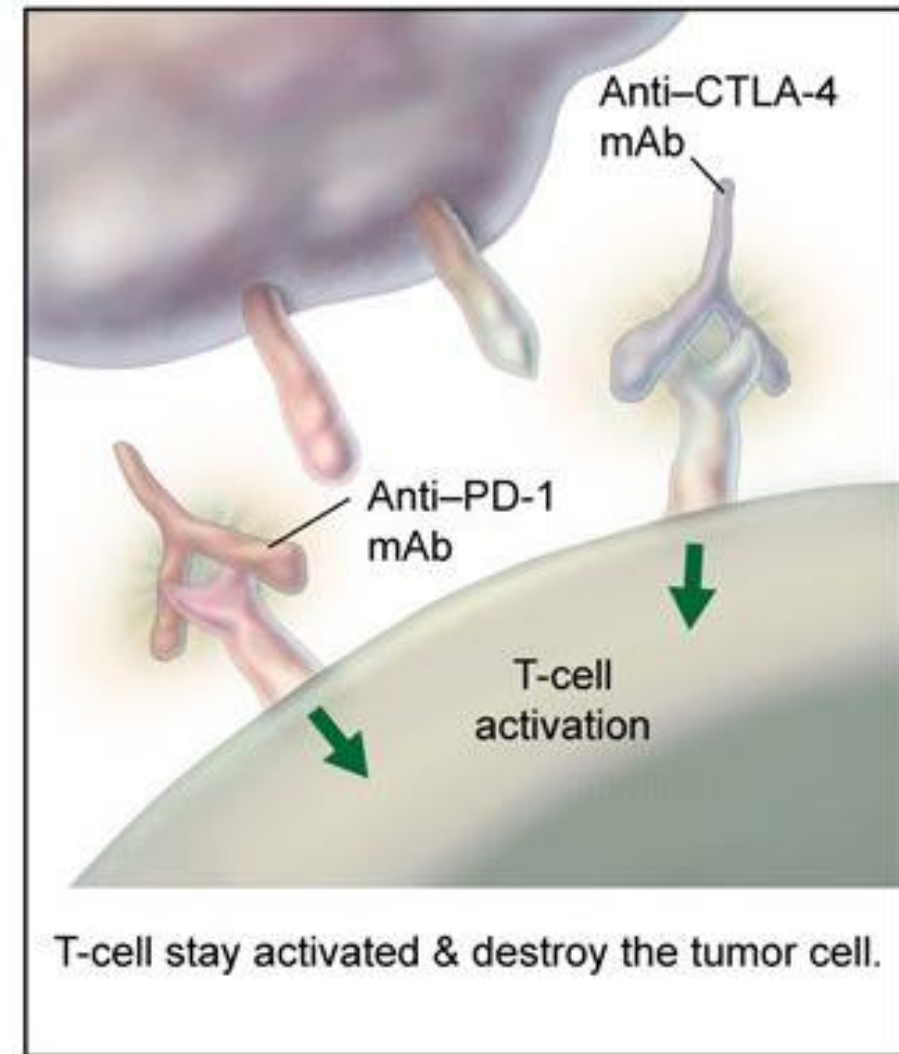
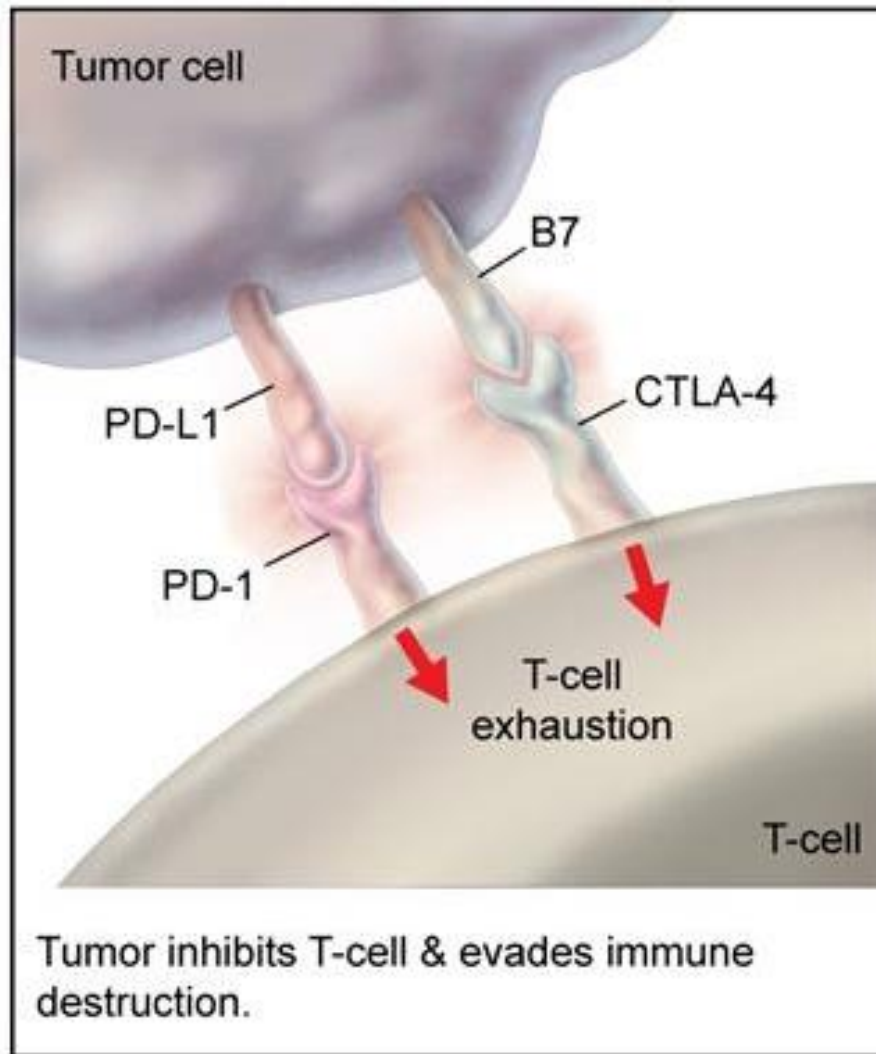


Interstrand cross-links

Etoposide



Atezolizumab and durvalumab



Final Aliquot

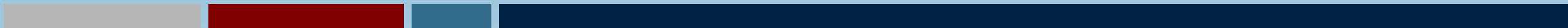
TSH high,
increased levothyroxine

“Felt terrible” 2 weeks
Nausea, lightheadedness

BP 105/70
HR 98

K 5.2

Na 128



Case summary to this point

This is a 54-year-old male with past medical history of Hashimoto's thyroiditis and tobacco use disorder, found to have extensive stage small cell lung cancer with osseous metastasis, complicated by SIADH on urea, s/p chemoimmunotherapy with complete response, on maintenance atezolizumab, **complicated by worsening hypothyroidism, malaise, hypotension, mild hyperkalemia, and moderate hyponatremia.**

Differential diagnosis

Cancer:

- Recurrent disease
- New primary cancer
- Paraneoplastic syndrome (e.g. SIADH)

Treatment-related:

- Carboplatin
- Etoposide
- Atezolizumab

Other

- Sepsis, opportunistic infection

Differential diagnosis

Cancer:

- Recurrent disease
- ~~New primary cancer~~
- Paraneoplastic syndrome (e.g. SIADH)

Treatment-related:

- ~~Carboplatin~~
- ~~Etoposide~~
- Atezolizumab

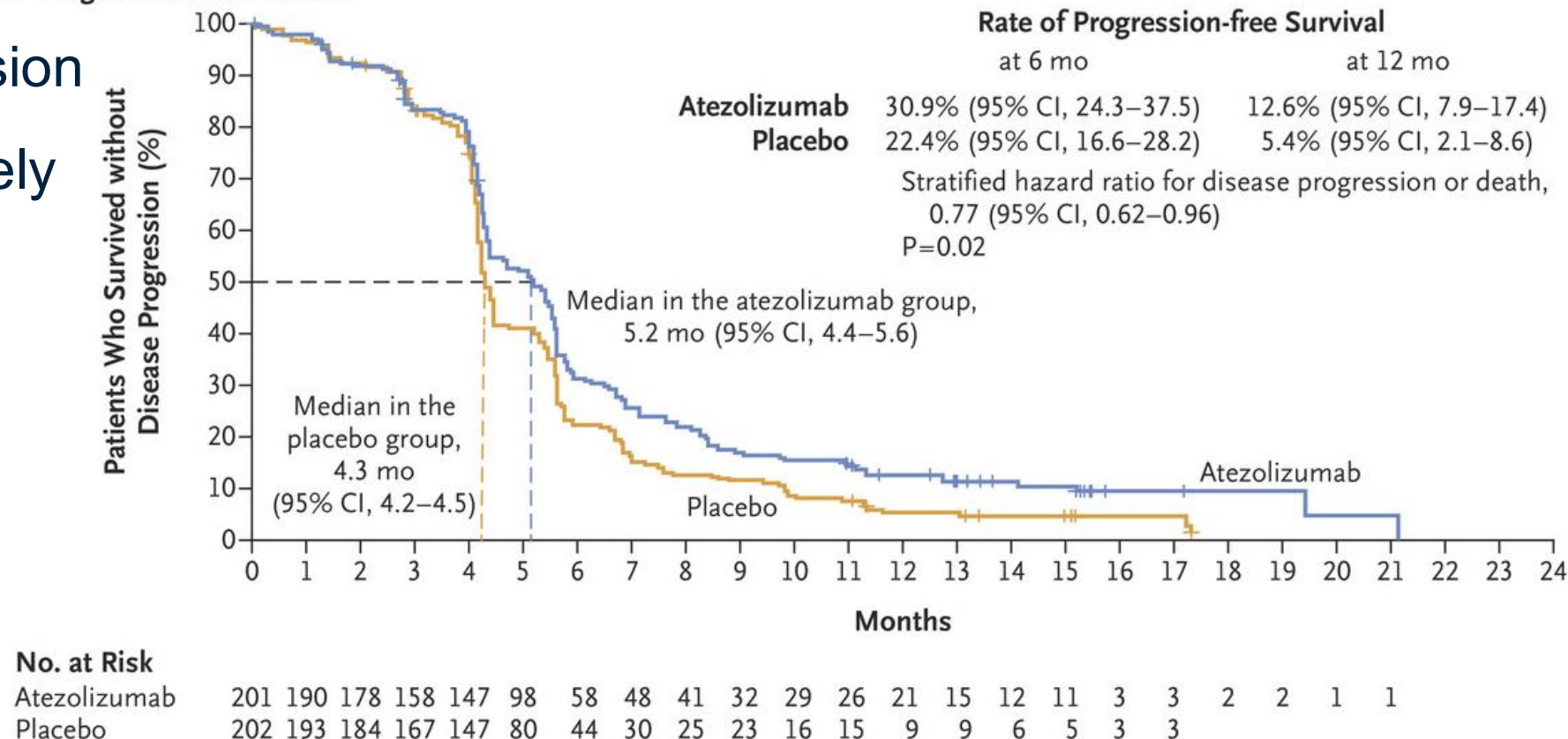
Other

- ~~Sepsis, opportunistic infection~~

Recurrence of SLCL

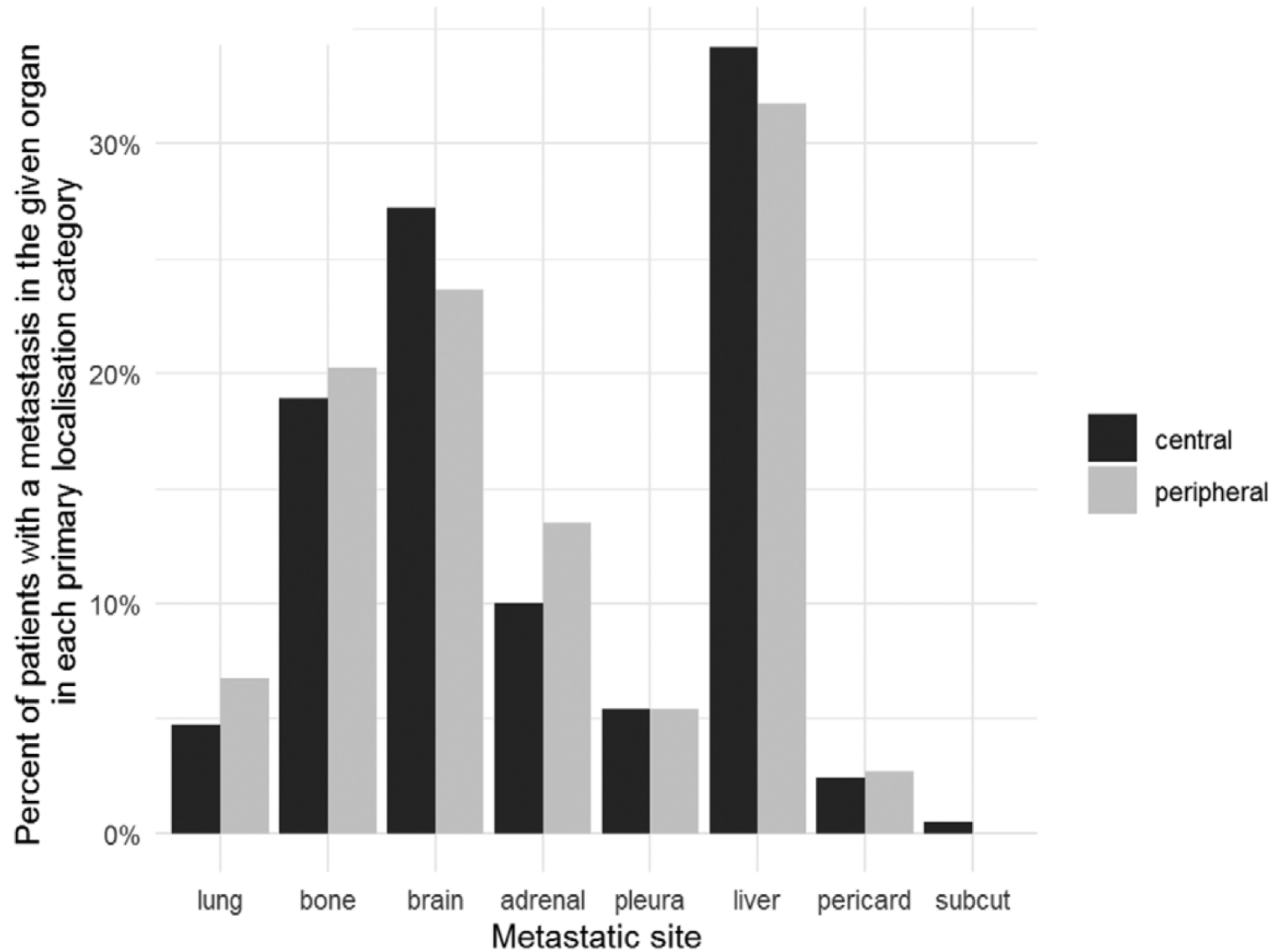
- High rate of progression
- Metastasis highly likely
- Unlikely related to overall symptoms

B Progression-free Survival



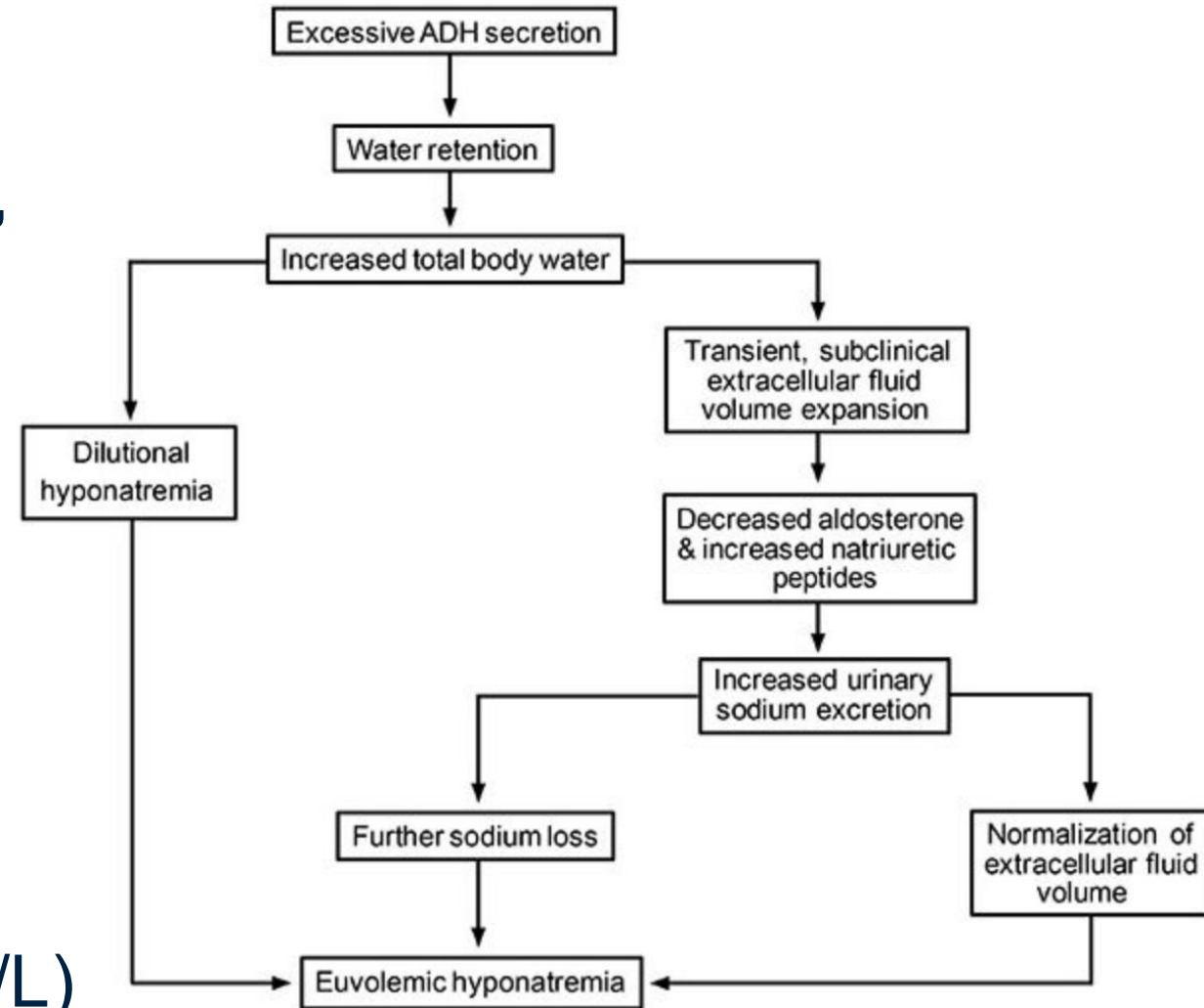
Recurrence of SLCL ^C

- High rate of progression
- Metastasis highly likely
- Unlikely related to overall symptoms
- Warrants interval scan



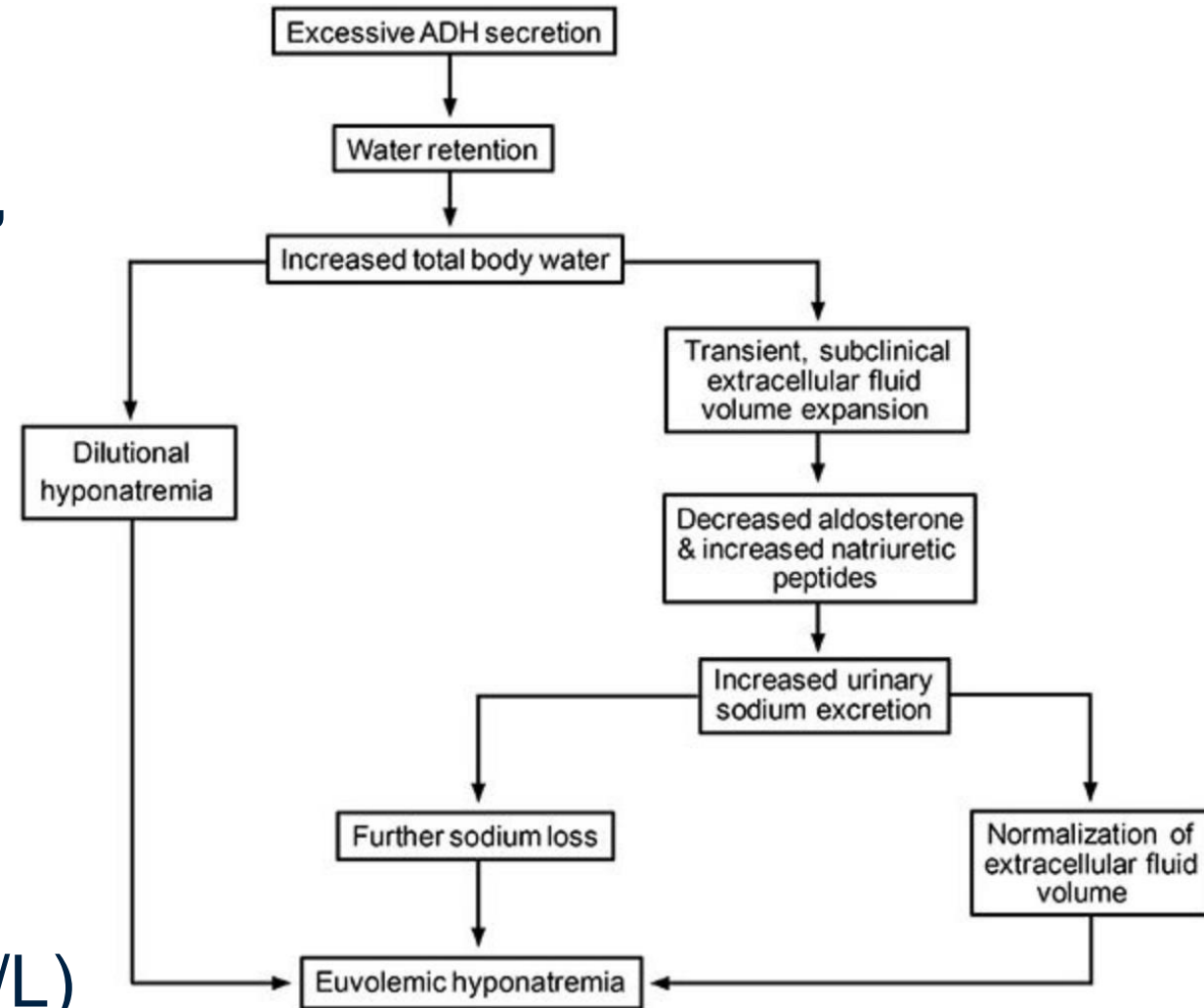
SIADH

- Clinical presentation
 - Gait disturbances, falls, headache, nausea, fatigue, muscle cramps, anorexia, confusion, lethargy, seizures, respiratory depression
- Lab findings
 - Hyponatremia
 - Hypoosmolality ($<275\text{mOsm/kg}$)
 - Increased urine osmolality ($>100\text{mOsm/kg}$)
 - Increased urine sodium ($>40\text{ mEq/L}$)



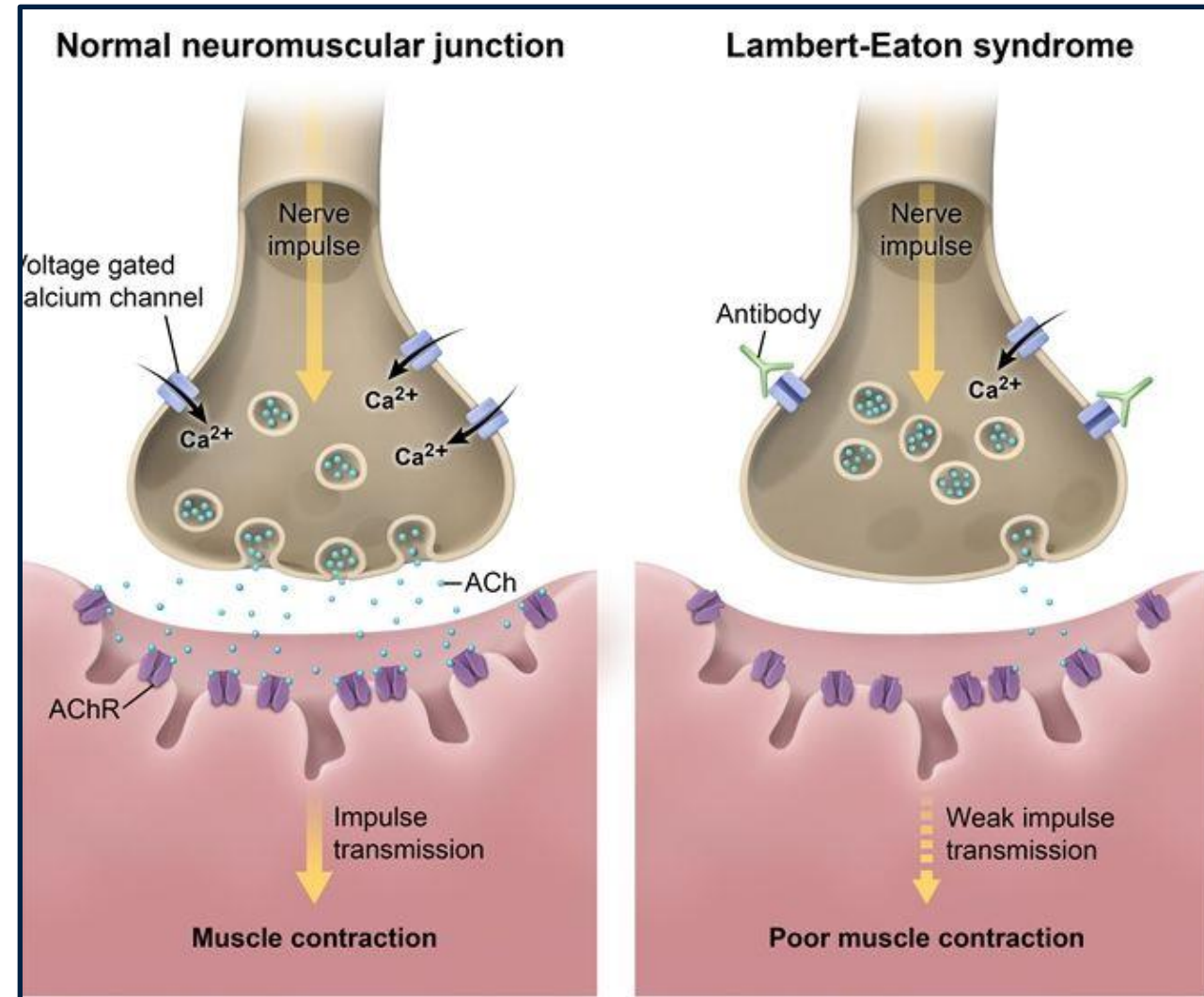
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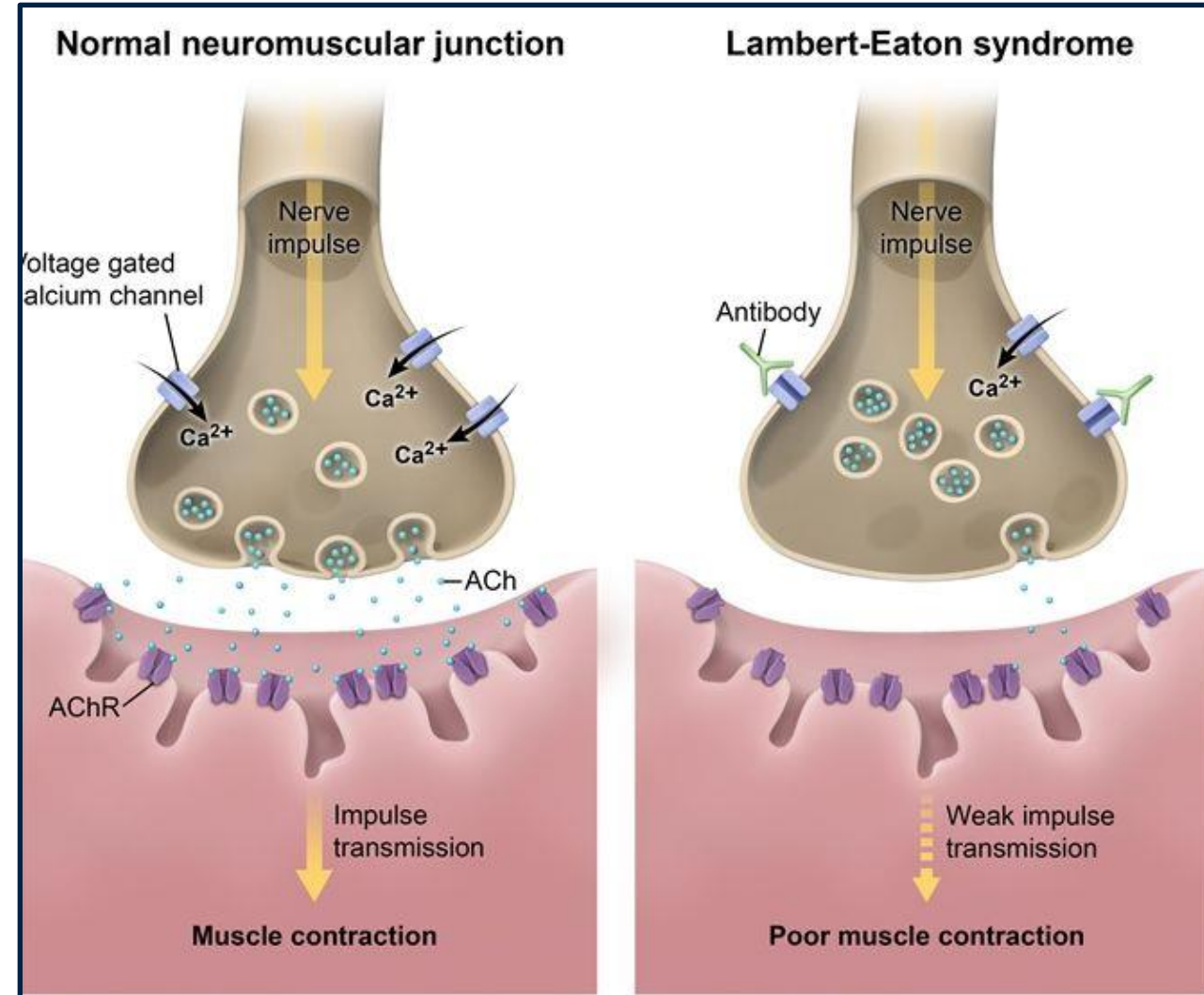
Lambert-Eaton Myasthenia Syndrome

- Clinical presentation
 - BLE proximal muscle weakness, fatigue, diaphragm weakness, bulbar symptoms
- Notable workup
 - Anti-VGCC (P/Q) type Abs
 - EMG: low compound amplitude



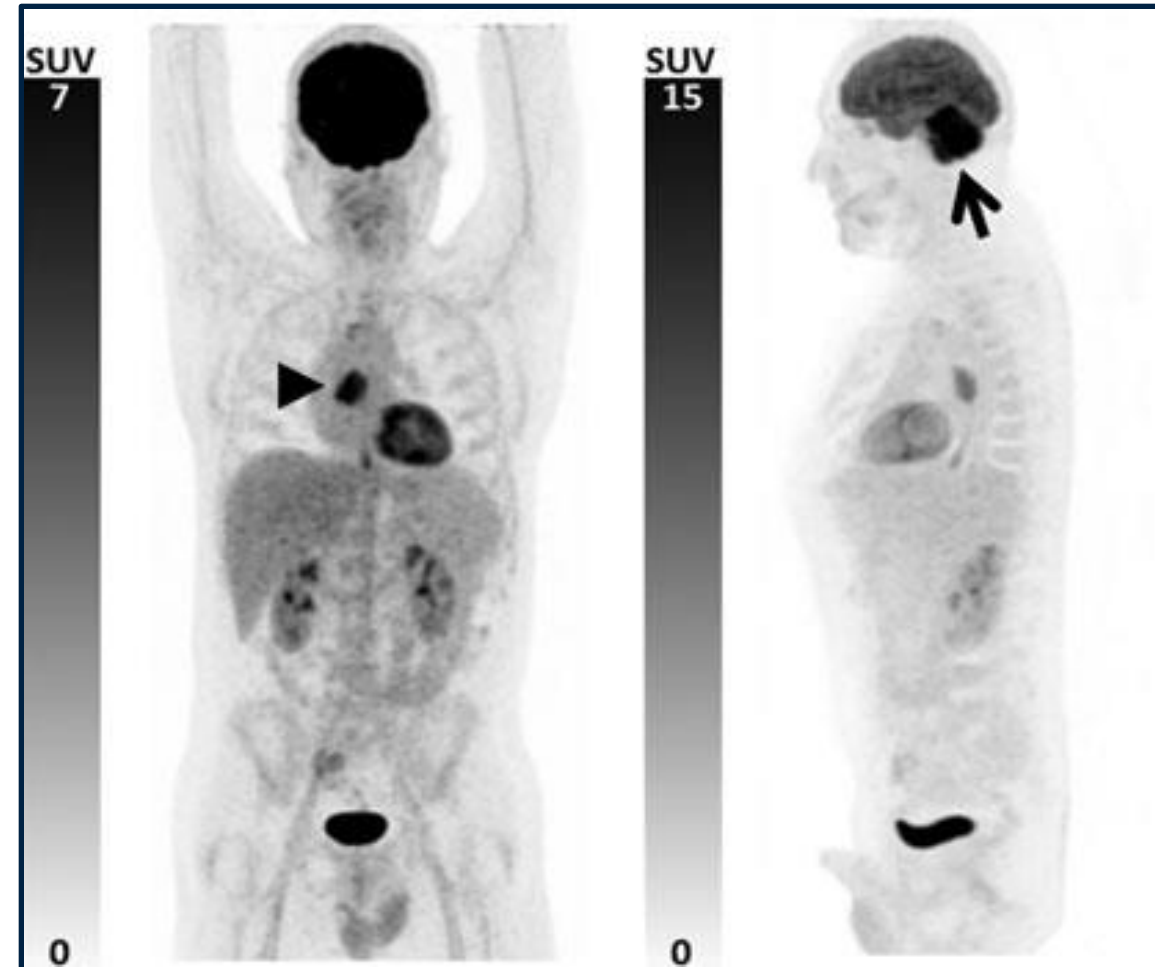
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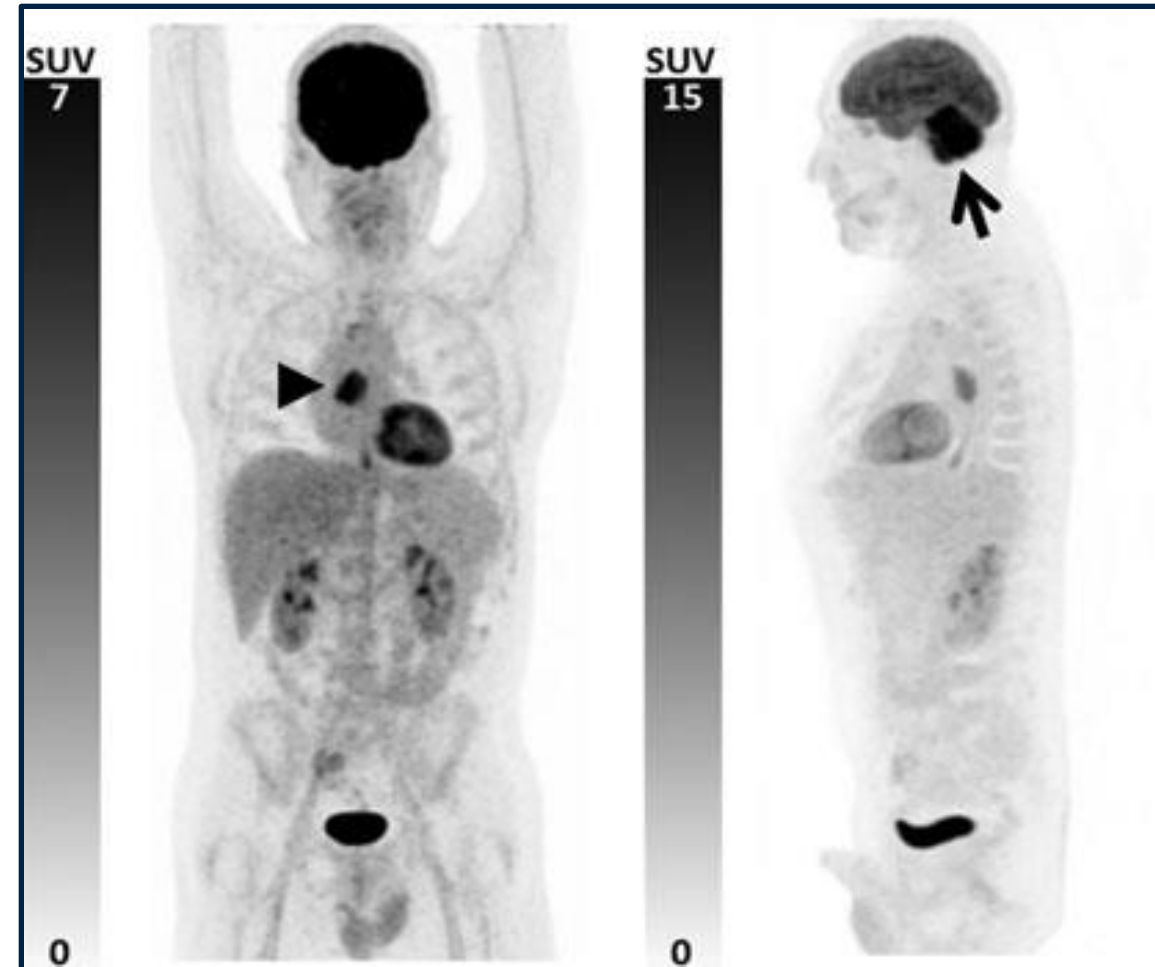
Paraneoplastic Cerebellar Degeneration

- Clinical presentation
 - Ataxia, diplopia, dysphagia, dysarthria, prodrome of dizziness, nausea, vomiting
- Notable workup
 - Antibodies to Yo, Hu, CRMP5, Ma, Tr, Ri, VGCC, mGluR1
 - FDG-PET: increased cerebellar avidity, then decreased



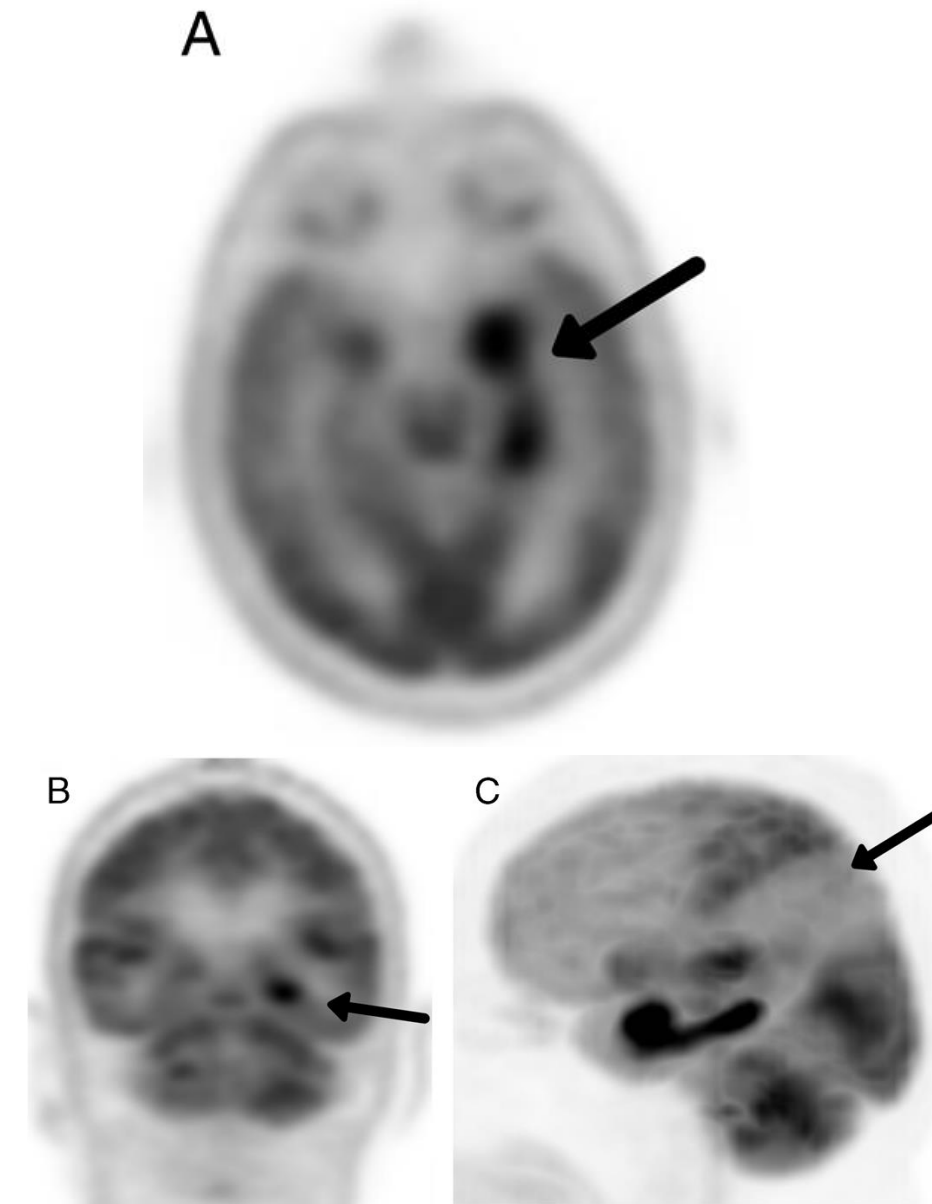
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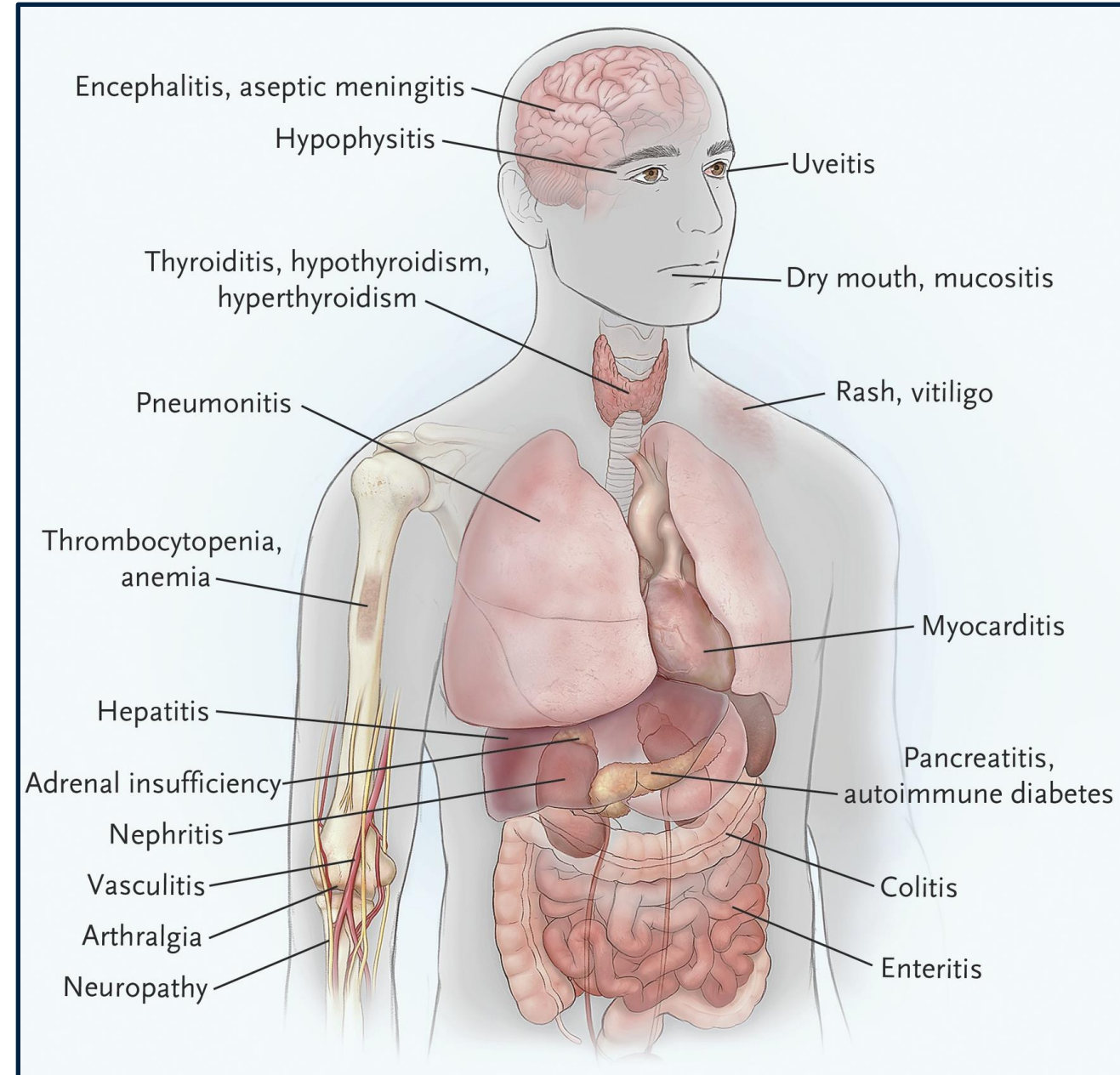
Paraneoplastic Limbic Encephalitis

- Clinical presentation
 - Mood changes, hallucinations, memory loss, seizures
- Notable workup
 - Antibodies to Hu, Ma2, CRMP5, amphiphysin
 - EEG: Epileptic foci in temporal lobes
 - PET/CT: Increased metabolism in medial temporal lobe



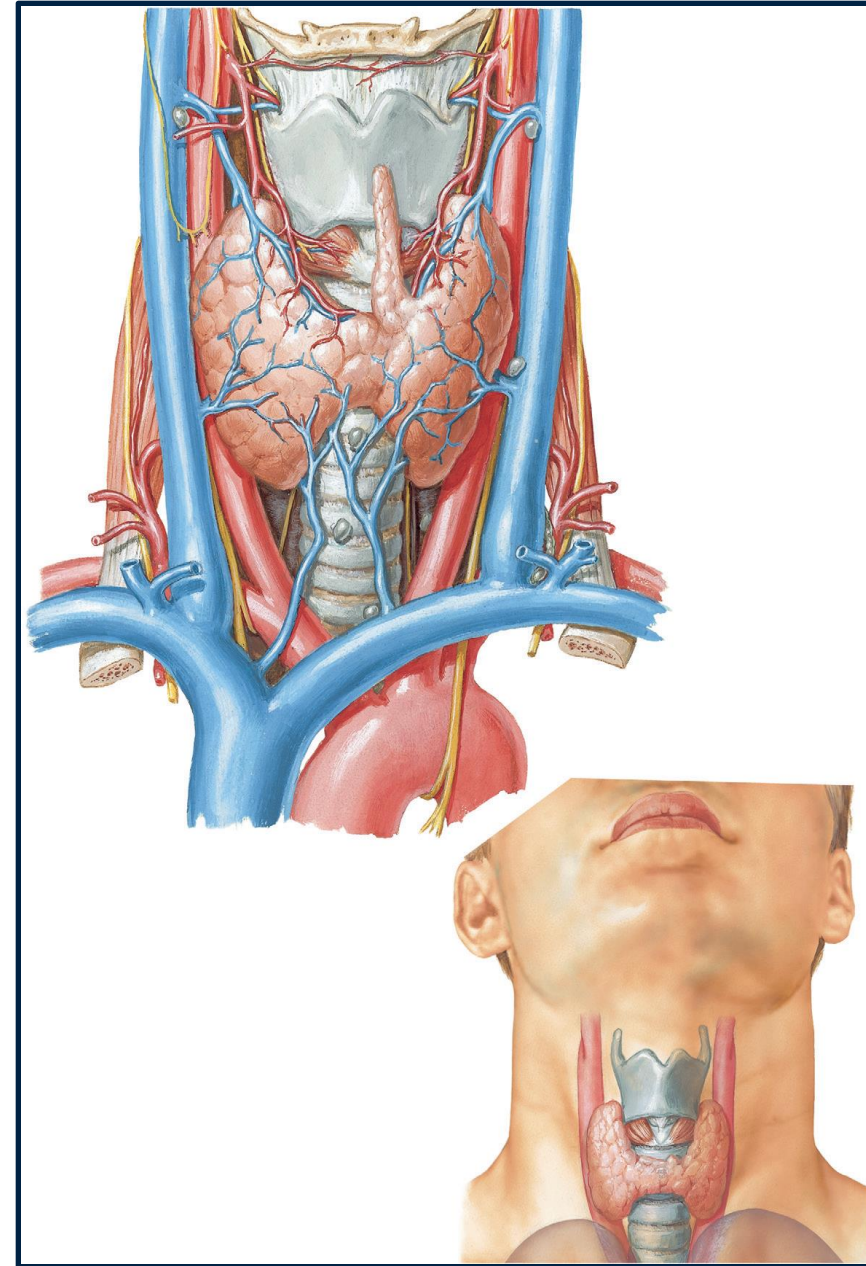
Immune-related adverse events

- Onset: wks to months after tx
- Cause: T-cells, Abs, cytokines
- Risk: Prior autoimmune dz
- Tx: Immunosuppression
- Not always associated with prognosis



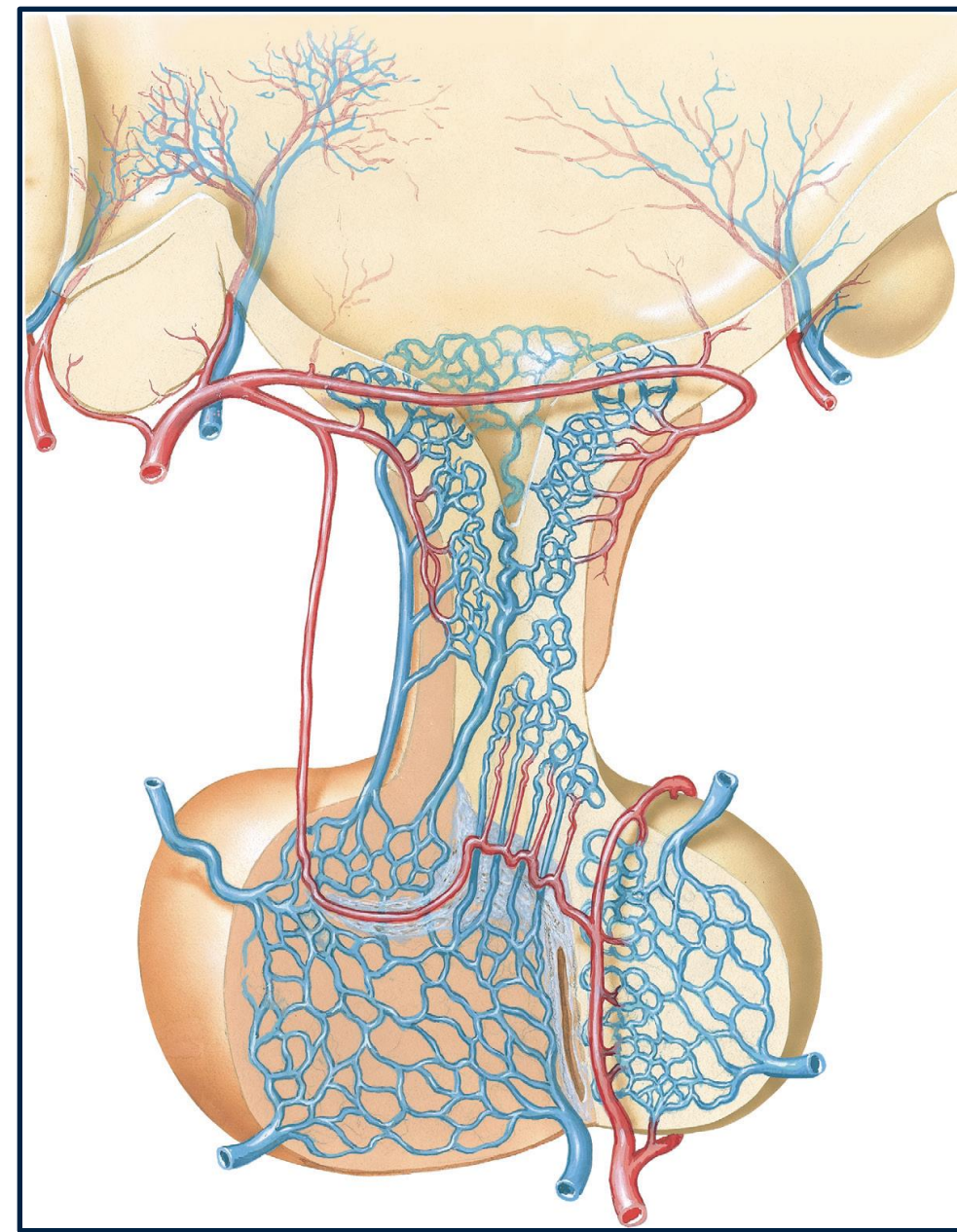
Immune-related thyroid disease

- Symptoms
 - Typical hypothyroid sx
- Notable labs
 - High TSH
 - Low T4
- More likely given history of Hashimoto



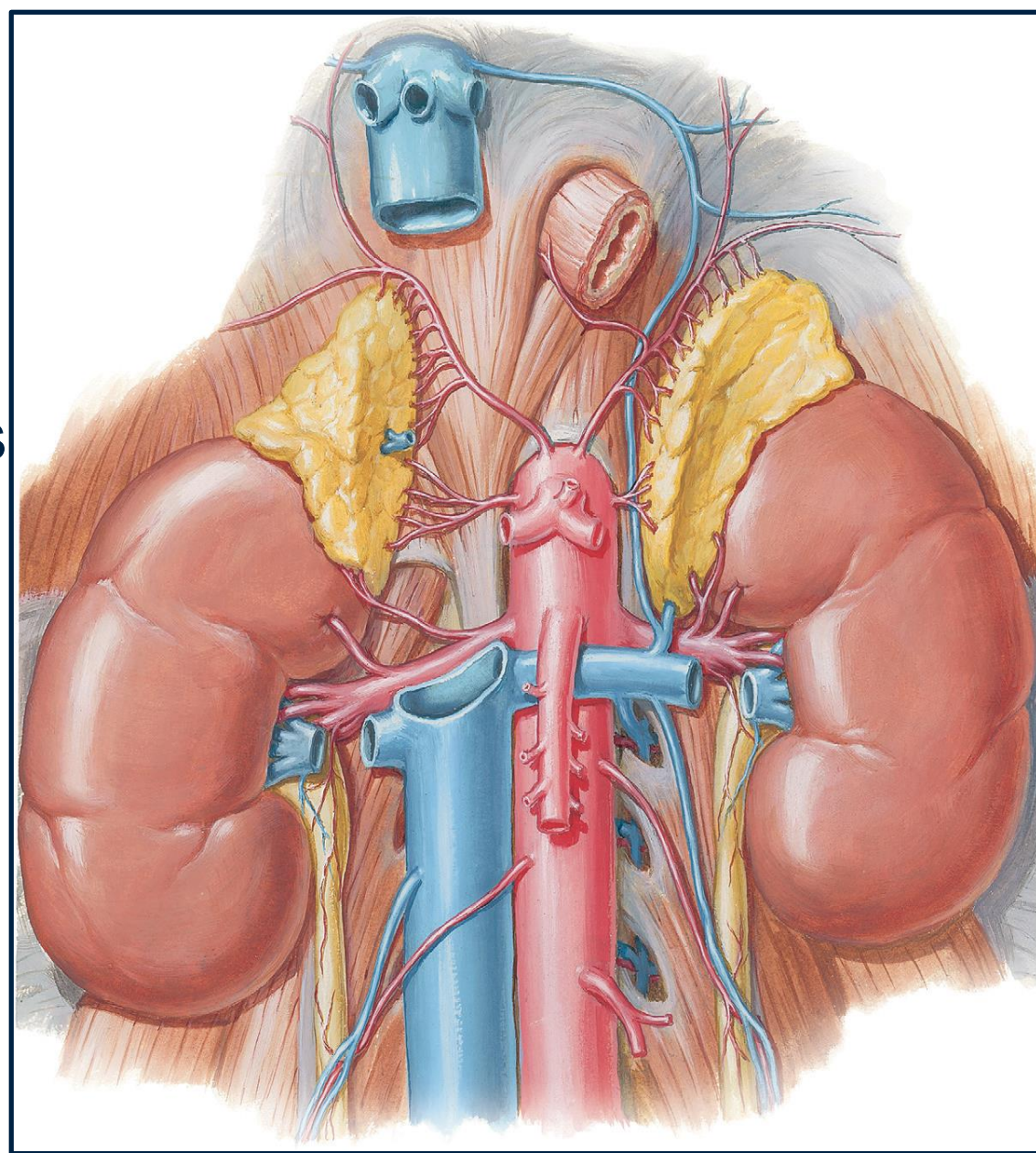
Immune-related hypophysitis

- Symptoms
 - Fatigue, headache
- Exam
 - Unremarkable
- Vital signs
 - Hypotension uncommon



Immune-related adrenal insufficiency

- Symptoms
 - Anorexia, n/v, abd pain, weakness
- Exam
 - Abd tender, fever sometimes
- Vital signs
 - Hypotension, tachycardia



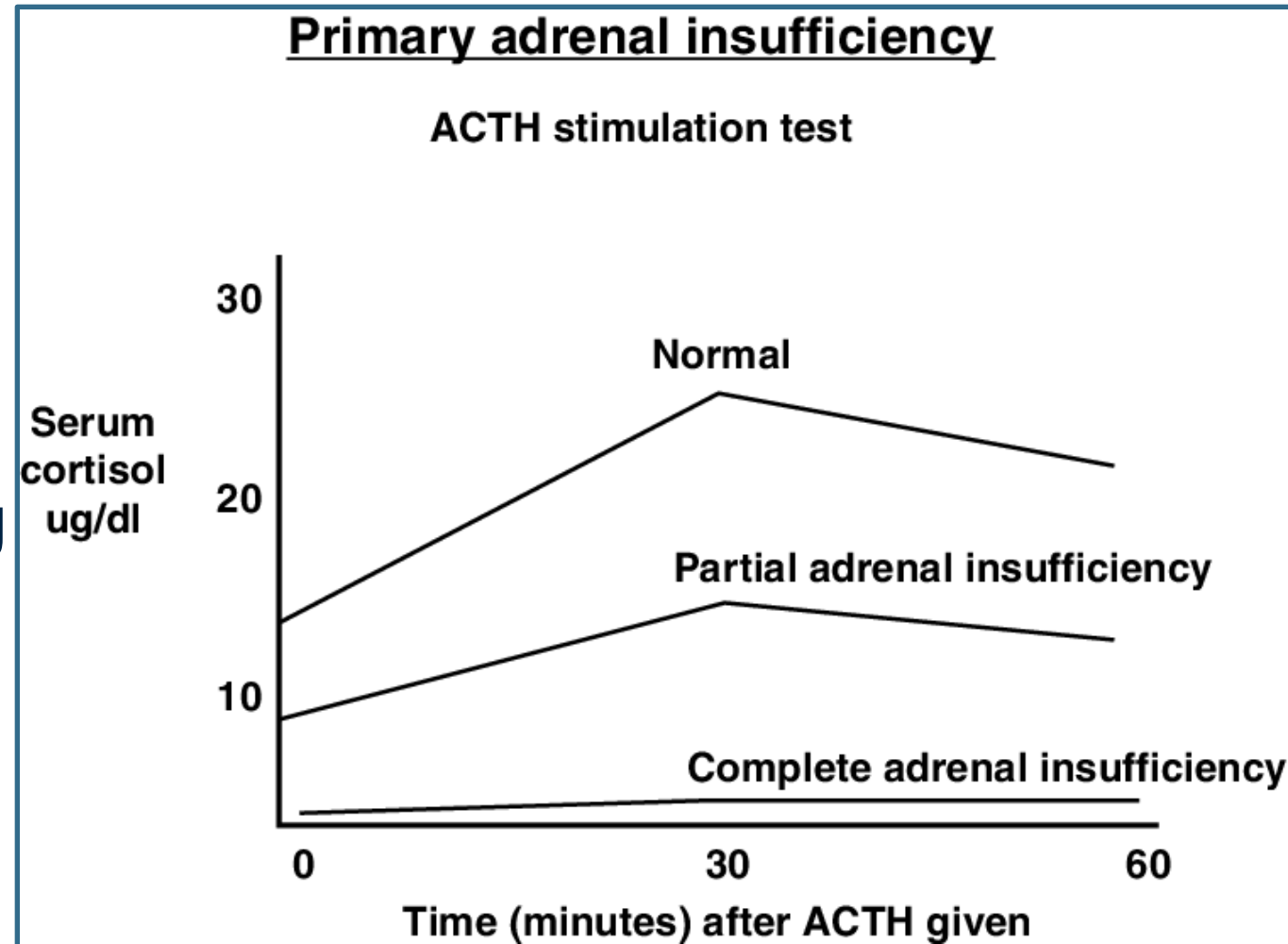
Adrenal insufficiency (AI) identification

	Primary AI	Secondary AI
Defect	Adrenal gland	Pituitary gland
CRH		
ACTH		
Cortisol		
Aldosterone		
Renin		
Potassium		
Sodium		
Overall severity		



Adrenal insufficiency diagnosis

- Warrants inpatient admission
- AM cortisol level
- ACTH stimulation test
- Aldosterone, renin
- Unclear role for antibody testing



Adrenal insufficiency management

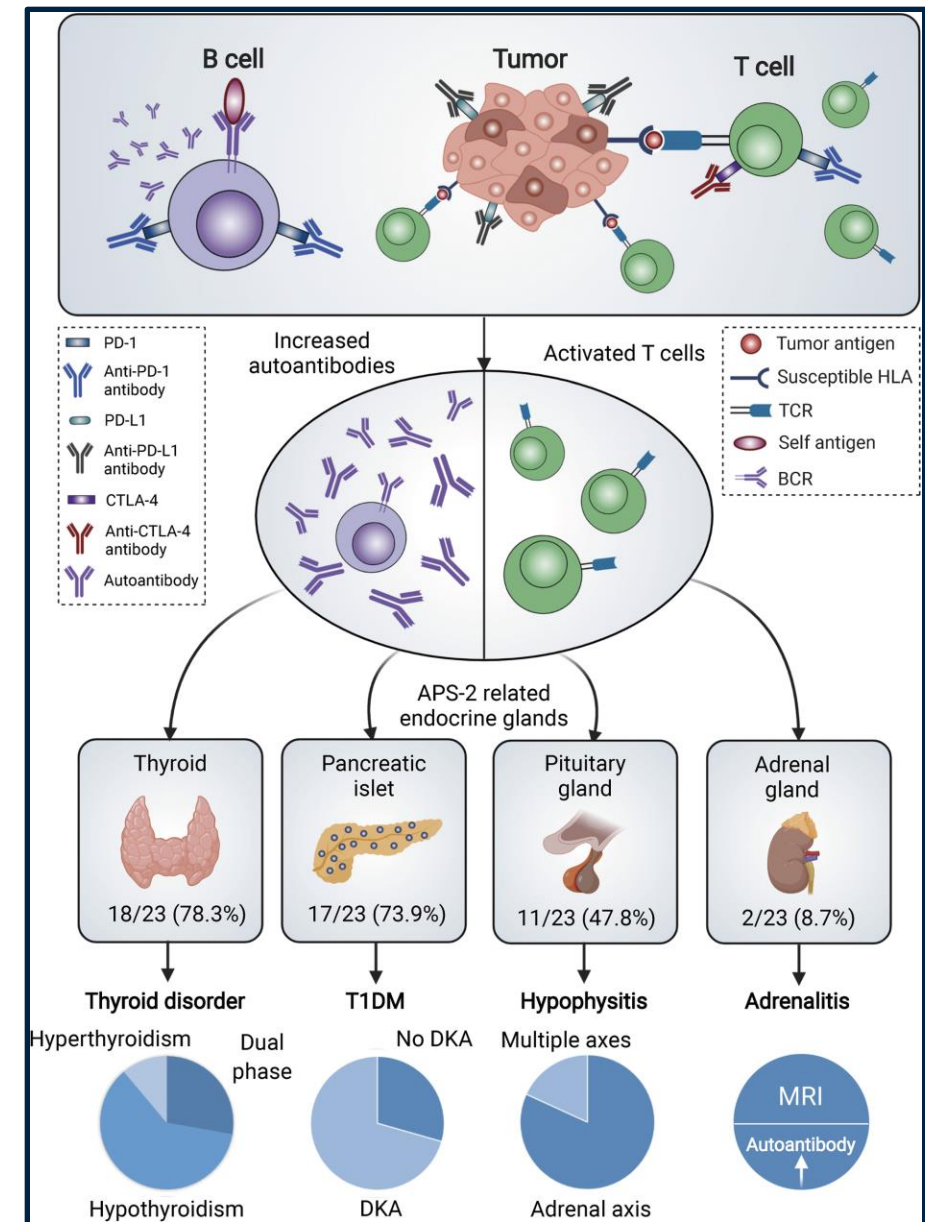
- IV hydrocortisone
 - Transition to PO hydrocortisone or prednisolone, and fludrocortisone
- IV isotonic crystalloid fluids
- Endocrinology consultation
- Serial basic metabolic profile, glucose level
- Likely continuation of immunotherapy

Case conclusion

This is a 54-year-old male with past medical history of Hashimoto's thyroiditis and tobacco use disorder, found to have extensive stage small cell lung cancer with osseous metastasis, complicated by SIADH on urea, s/p chemoimmunotherapy with complete response, on maintenance atezolizumab, **complicated by likely immune-related primary adrenal insufficiency and hypothyroidism**

Iatrogenic Polyendocrinopathy

- E.g. polyglandular autoimmune syndrome type 2 (PAS-2)
- Defined as 2 of the following 3
 - **Autoimmune thyroid disease**
 - Type 1 diabetes
 - **Autoimmune adrenal insufficiency**
- Warrants antibody testing



Learning points:

- A sprinkle of CPC history
- Pathology of SCLC
- Chemoimmunotherapy for SCLC
- Progression and metastasis of SCLC
- Paraneoplastic syndromes of SCLC
- Immune-related adverse events
- Diagnosis of 1° vs 2° adrenal insufficiency



References

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Thank You!

