



WHEN IS LVH NOT JUST LVH?

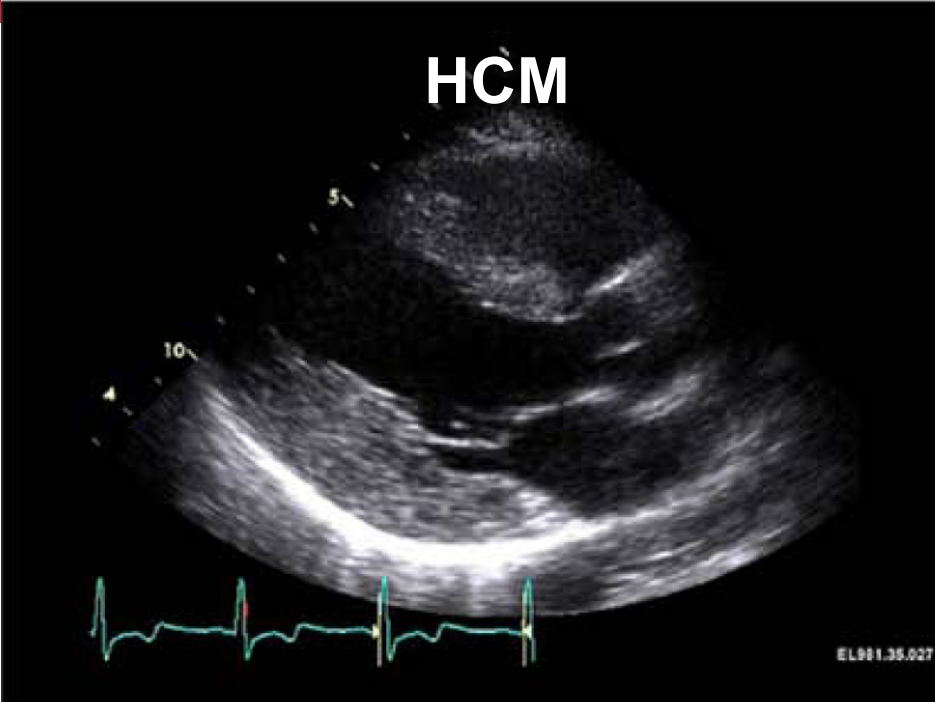
PRACTICAL CLINICAL ALGORITHMS WHEN YOU SUSPECT CARDIAC AMYLOID

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Section of Heart Failure and Cardiac Transplant
Cleveland Clinic

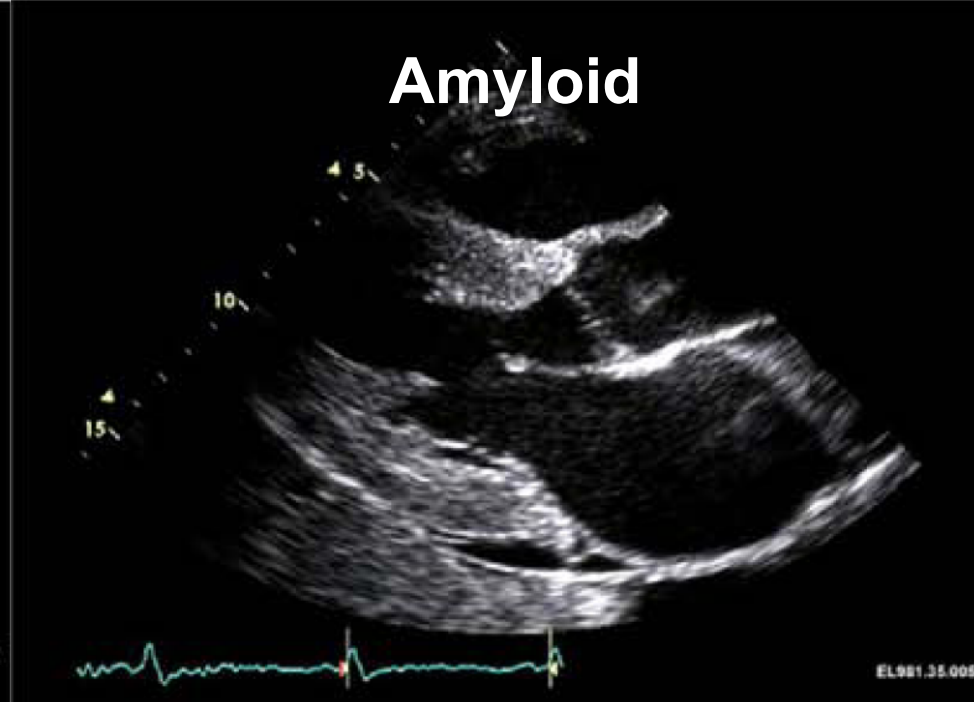
Disclosures

- **Grants/research support:** Term chair for Amyloid Heart Disease, Philanthropic donation
 - **Consulting fees:** Pfizer, Alnylam, Akcea, Eidos (served on an advisory board)
 - **Speaker fees:** Alnylam, Akcea
 - **Other:**
-
- I will not be discussing names of medications for treatment during this lecture. _____

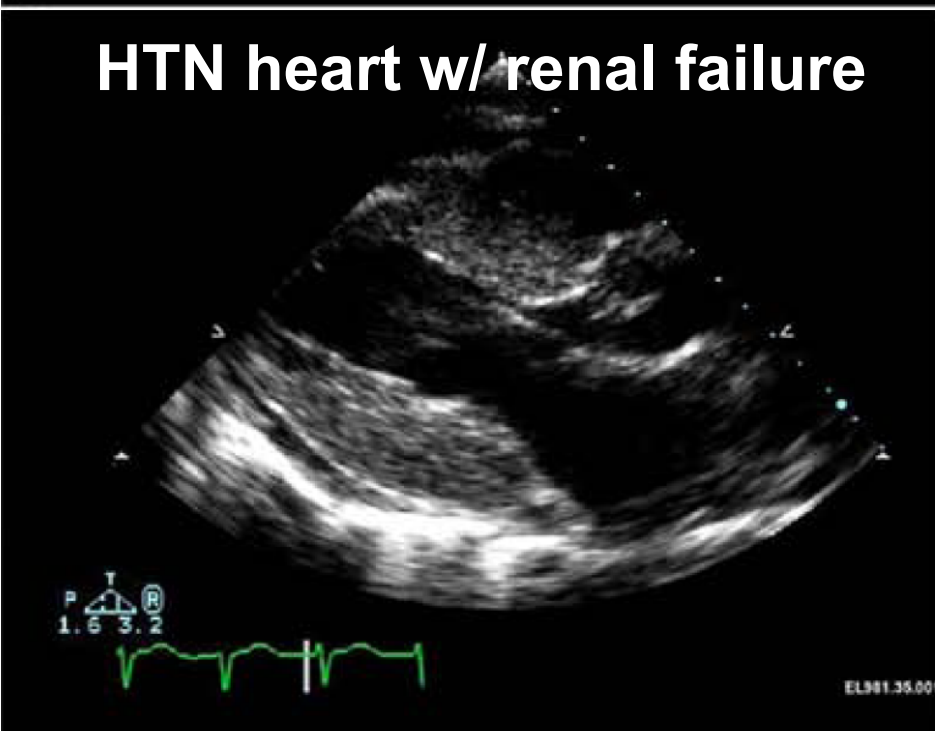
HCM



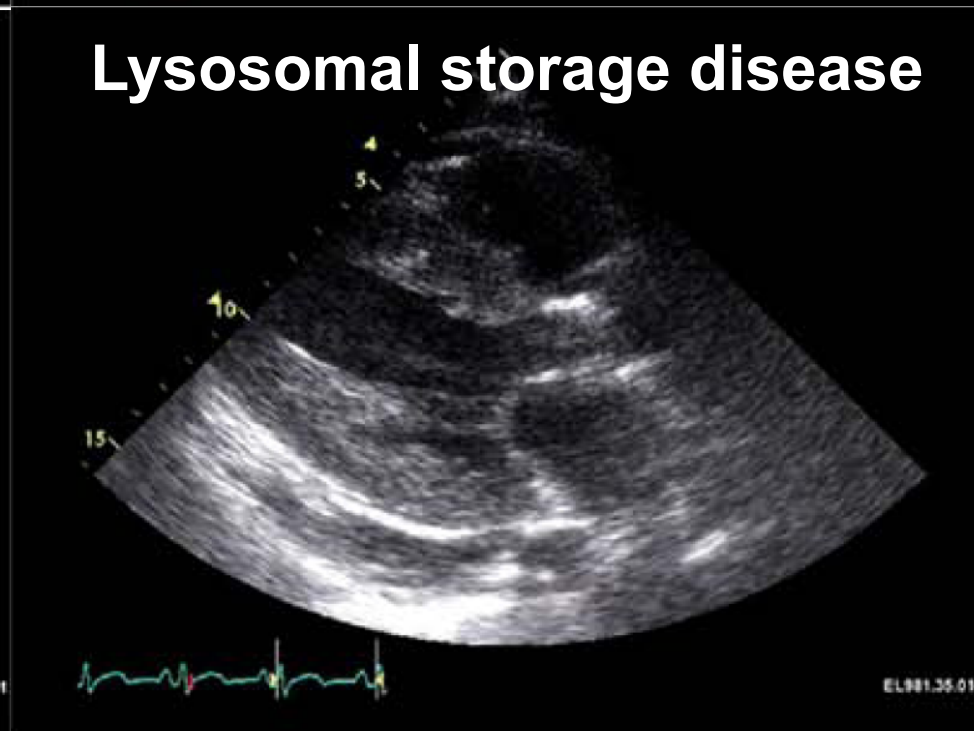
Amyloid



HTN heart w/ renal failure



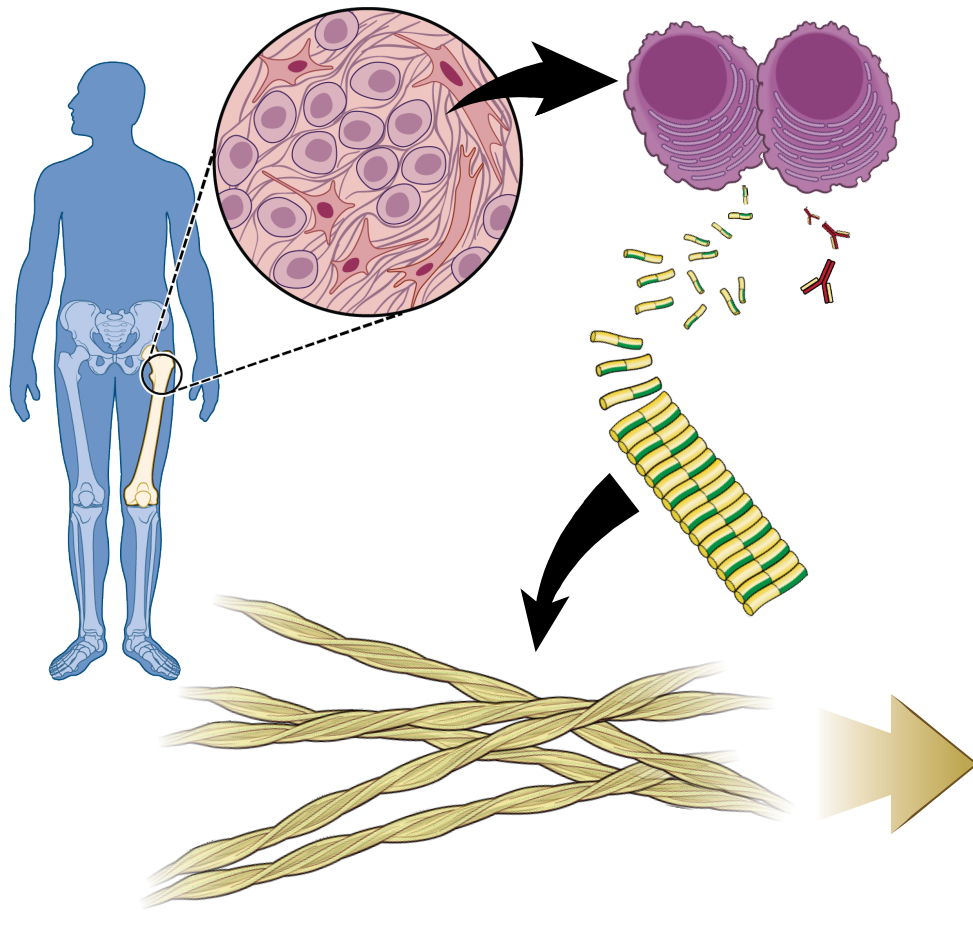
Lysosomal storage disease



Two Main Types of Amyloid That Affect the Heart

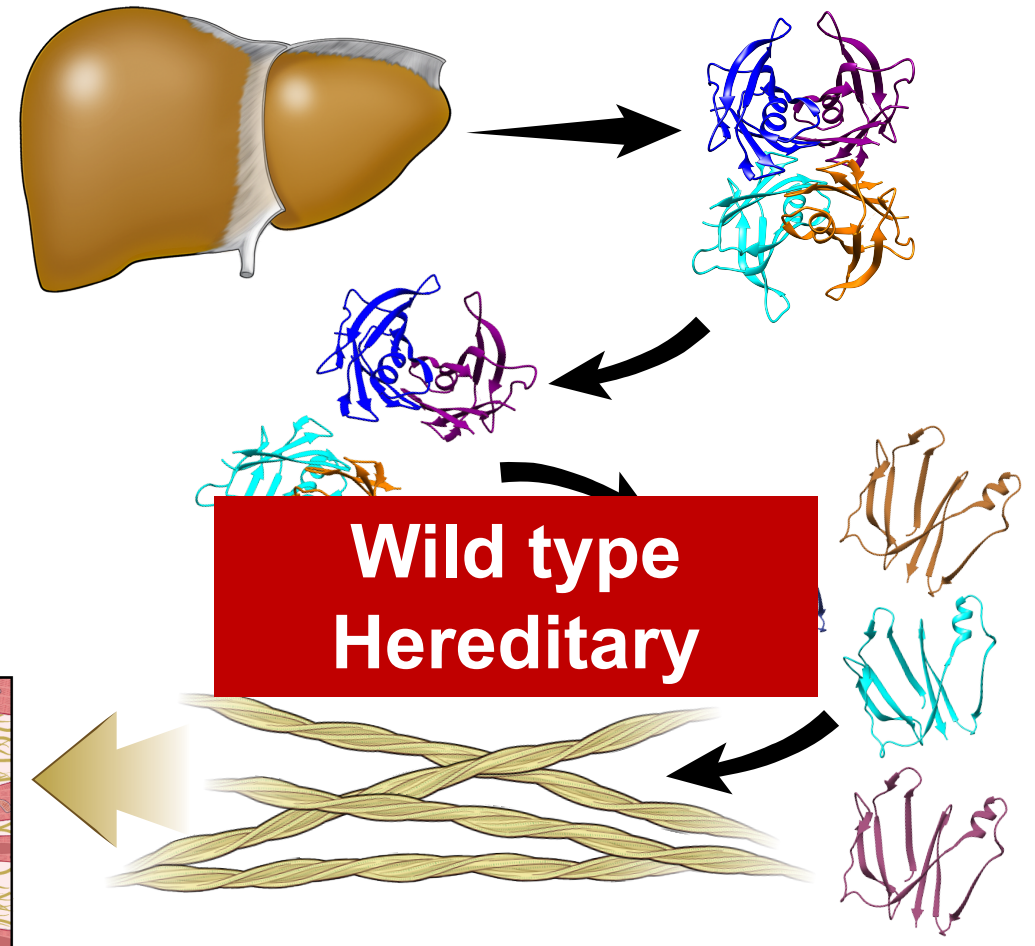
AL

Light chain amyloidosis



ATTR

Transthyretin amyloidosis

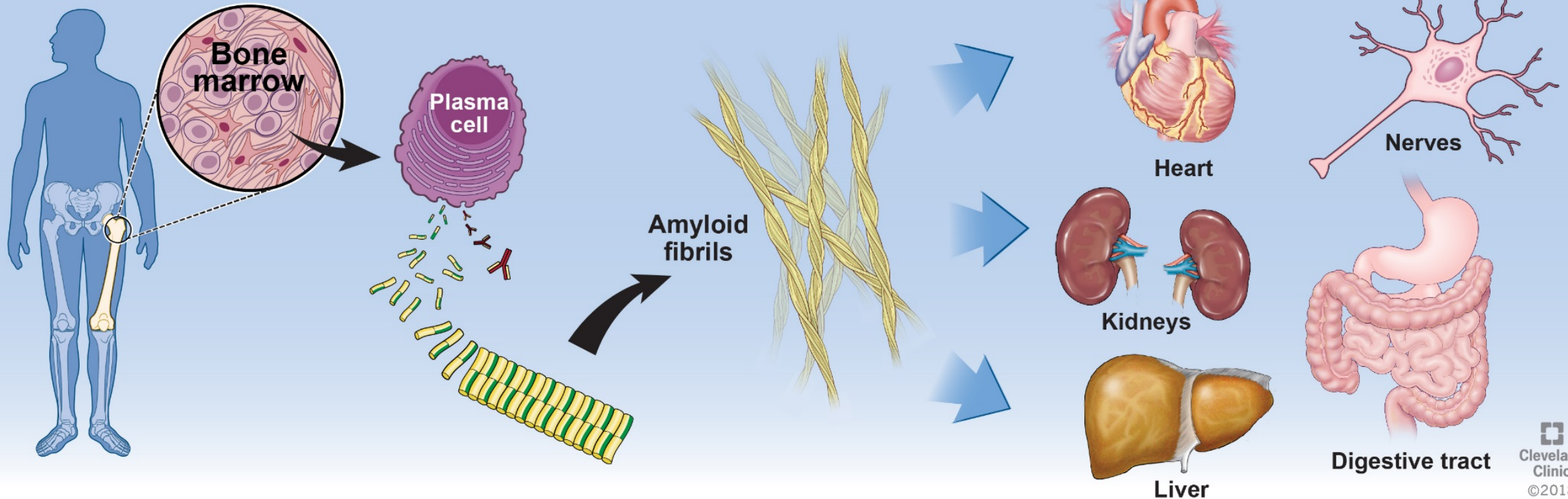


AL Amyloidosis (Light Chain amyloidosis)

Light Chains are Produced by Plasma Cells in the Bone Marrow

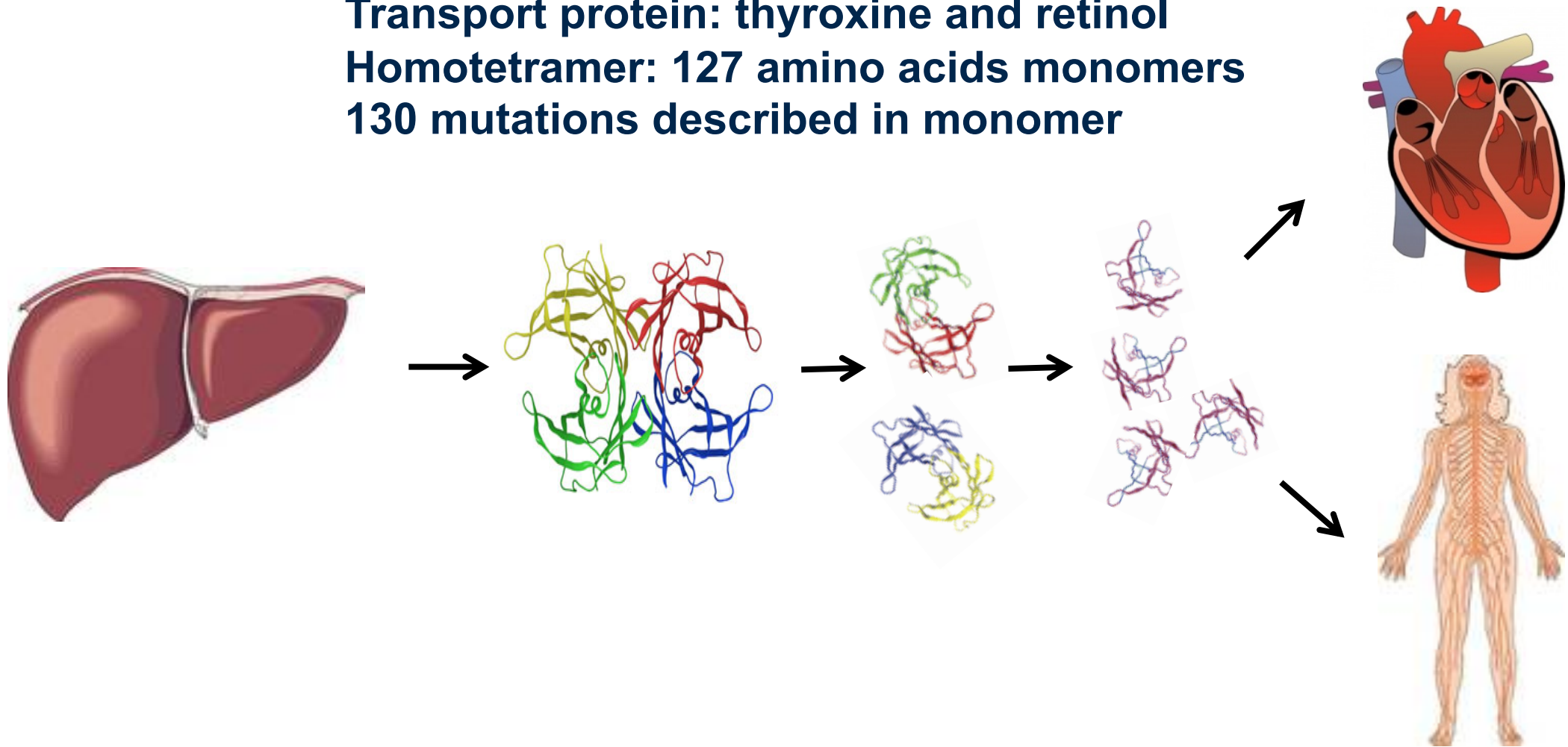
Light Chains Clump & Form Amyloid Fibrils

Amyloid Fibrils Deposit in Organs



Transthyretin (TTR) “Prealbumin”

Transport protein: thyroxine and retinol
Homotetramer: 127 amino acids monomers
130 mutations described in monomer



Wild Type Transthyretin Amyloidosis (wtATTR)

“Senile systemic amyloidosis” (SSA)

Median age at dx 74 years

Cardiomyopathy/ Atrial fibrillation/ Conduction disease

Bilateral carpal tunnel syndrome/ Spinal Stenosis *

The most common type of amyloidosis!!

Median survival 3-4 years

Hereditary TTR amyloidosis (hATTR)

> 130 point mutations

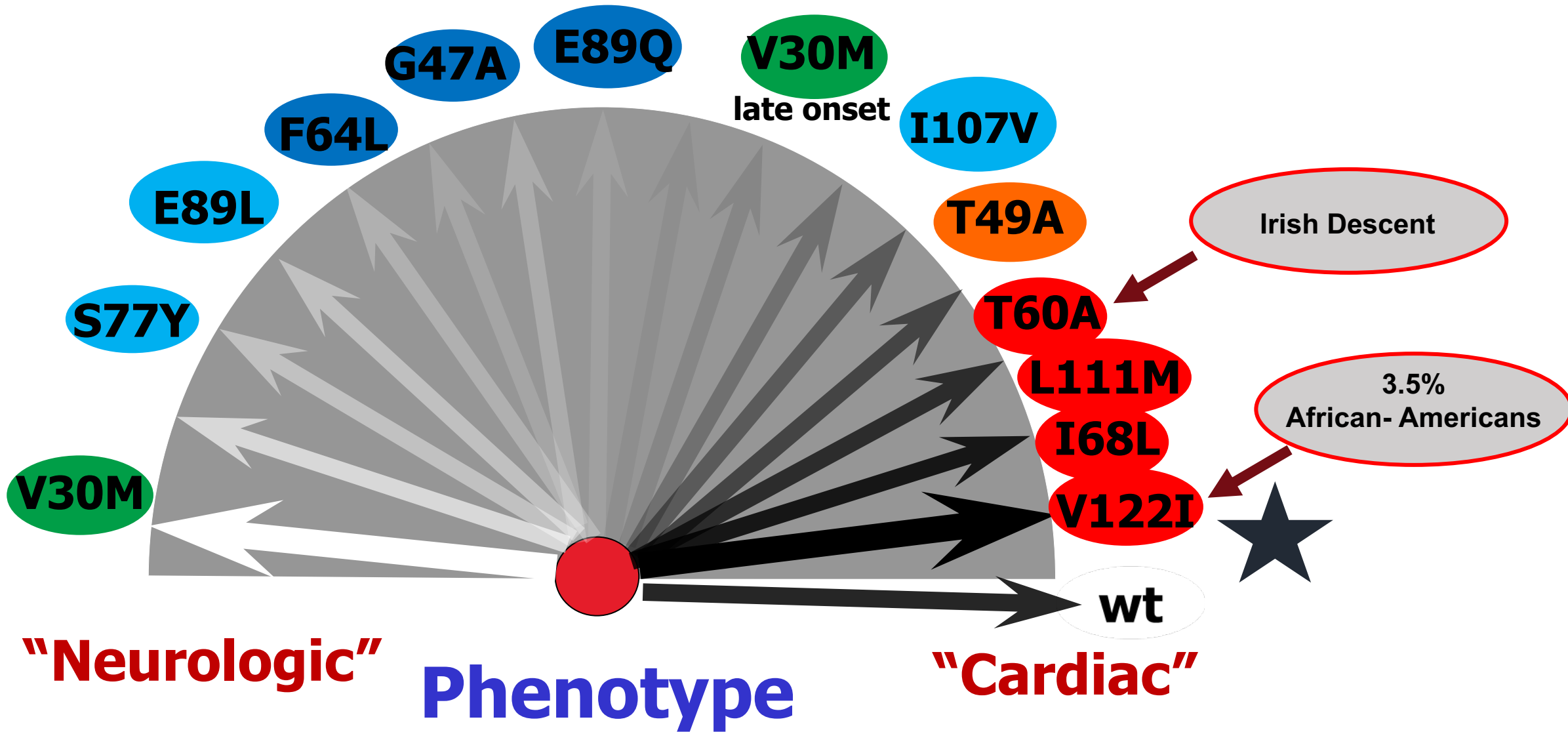
Autosomal dominant inheritance



**Familial amyloid polyneuropathy
(FAP)**

**Familial amyloid cardiomyopathy
(FAC)**

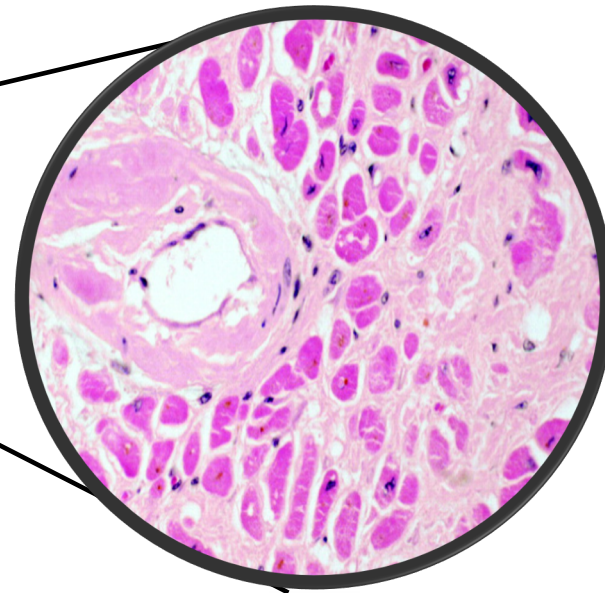
Mixed Phenotype Common



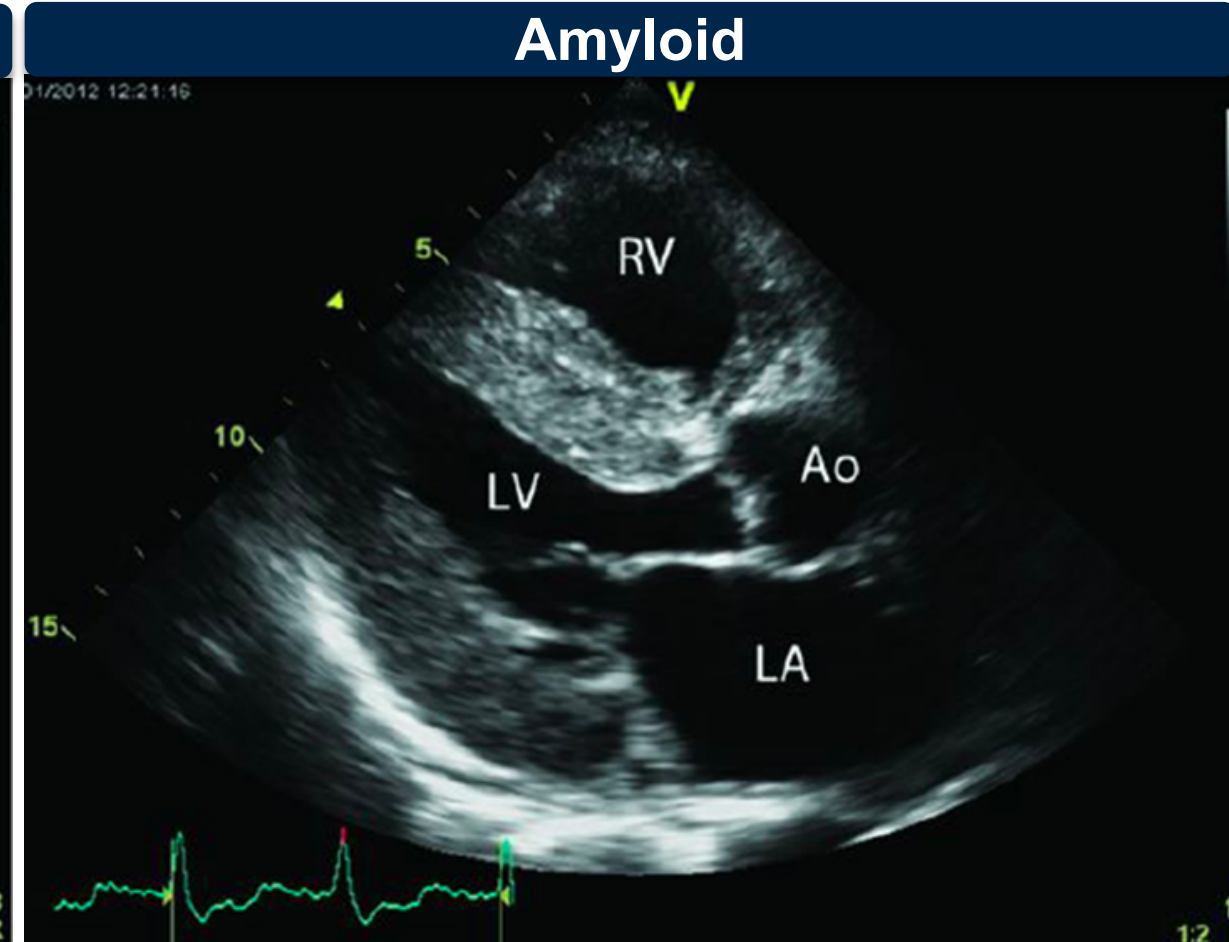
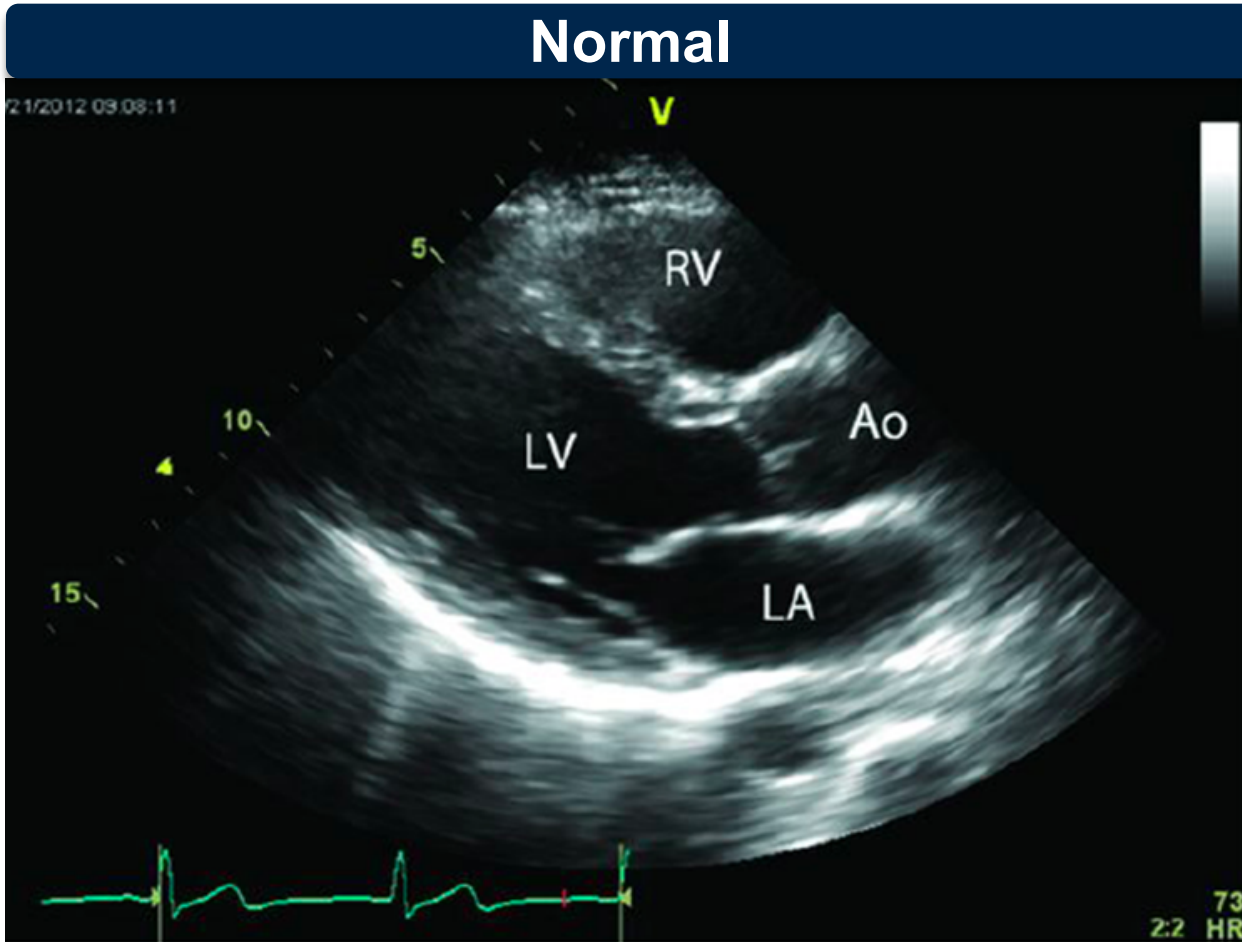


Pathology: Diffuse involvement

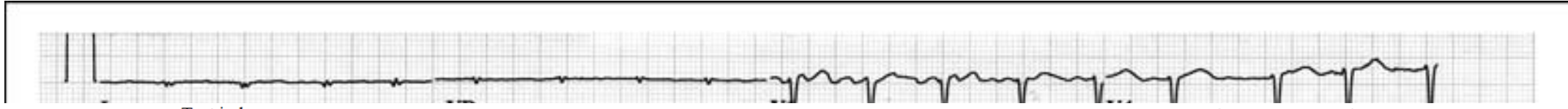
- Increase in LV mass w/out dilatation
- Atrial infiltration impairing atrial contraction
- Conduction system / valves
- Microvascular ischemia



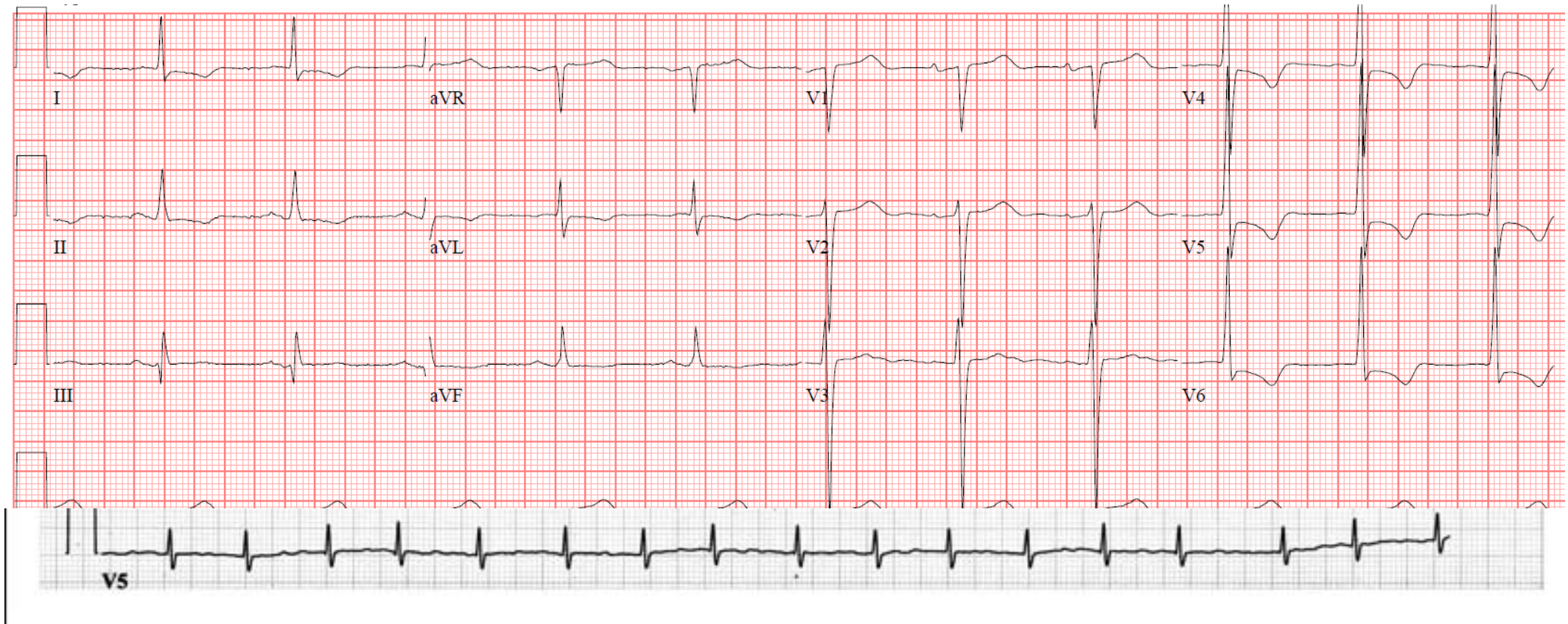
Echocardiogram: Prompts Suspicion



- **Classic Low-Voltage Electrocardiogram in Cardiac Amyloidosis^{1,2}**



81 year old white male with biopsy proven ATTR cardiac amyloidosis



55 year old male with nephrotic syndrome and HF

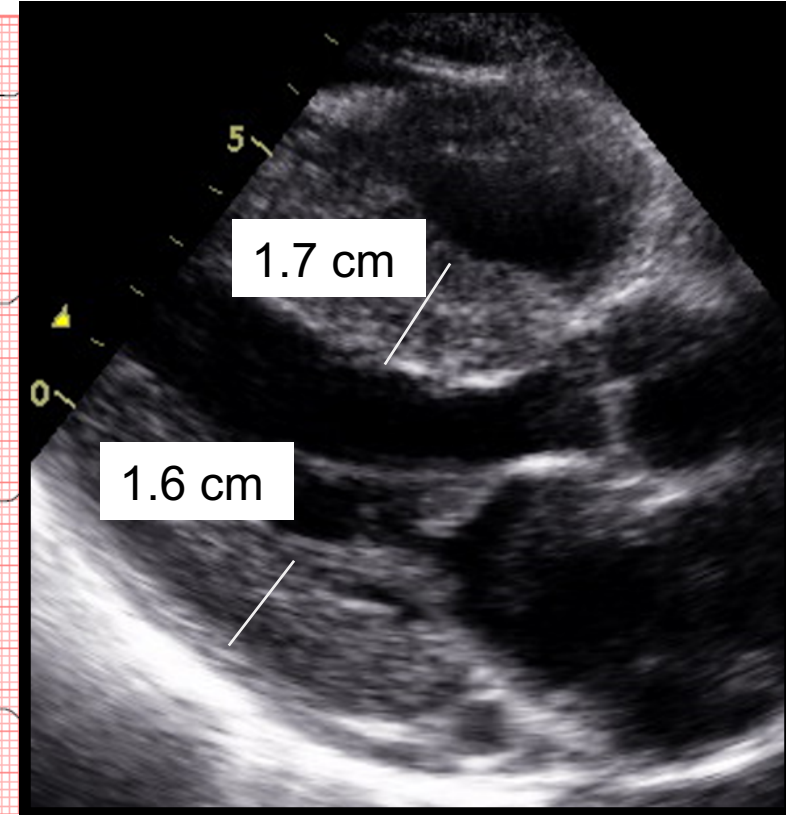
LV & RV Thickening, Atrial Dilation, Thickened Valves, Pericardial Effusion



55 year old male

Nephrotic syndrome and heart failure

AL Amyloid



Clinical Presentation

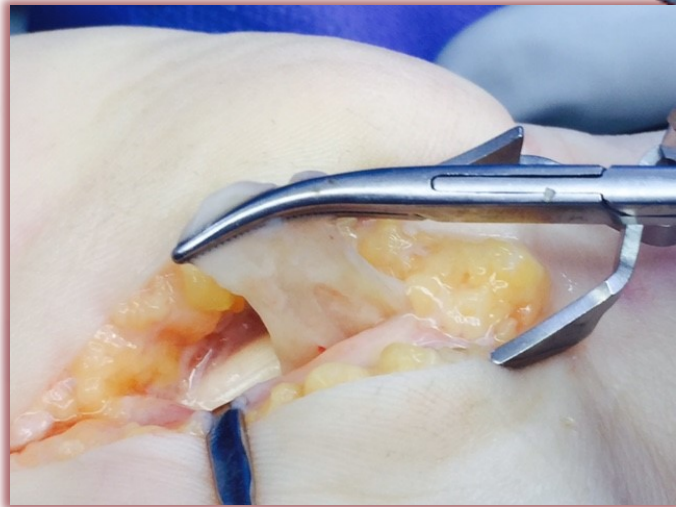
Cardiac¹⁻⁵

- HFpEF (“right sided”)
- “Hypertrophic cardiomyopathy”
- Low-flow low-gradient AS
- Afib/cardioembolic stroke
- Pacemaker/Heart Block
- Angina with normal course

Non-Cardiac^{6,7}

- Orthostasis
- Neuropathy
- Peripheral
- Autonomic
- Bilateral CTS (TTR > AL)
- Spinal stenosis (TTR)

Amyloid Fibril



Carpal tunnel syndrome



Cardiac symptoms



Time

Physical Exam Findings Specific to AL Amyloidosis

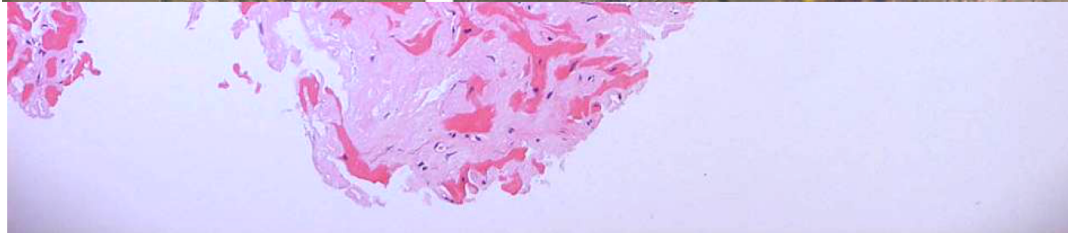
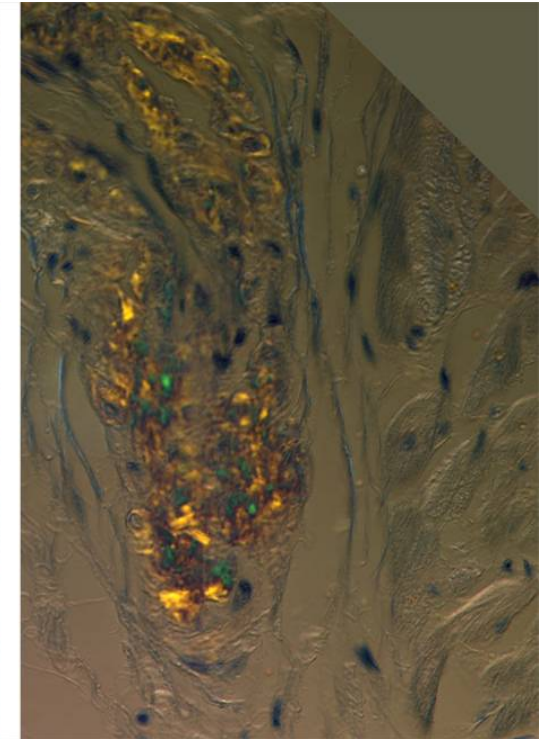
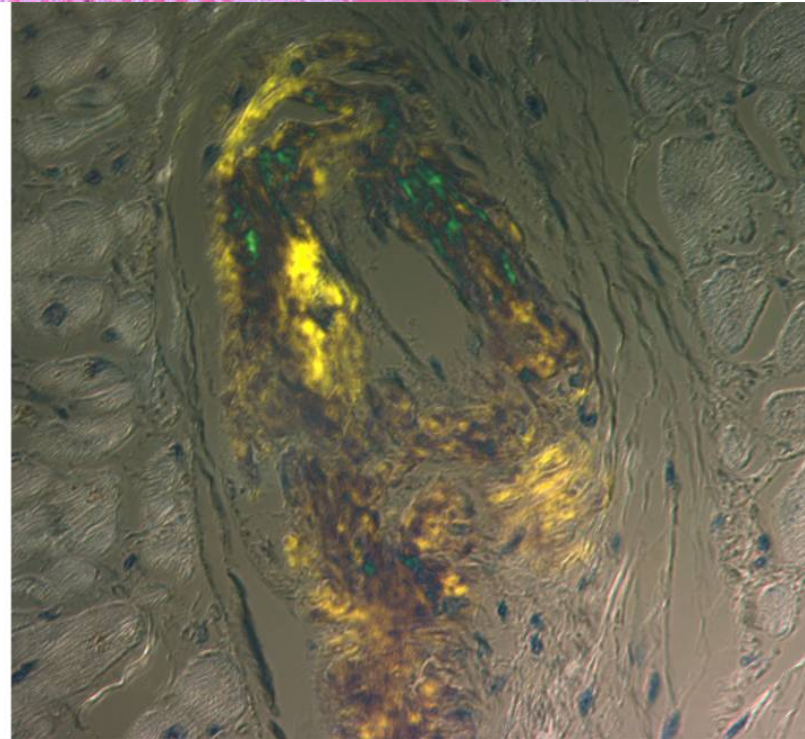
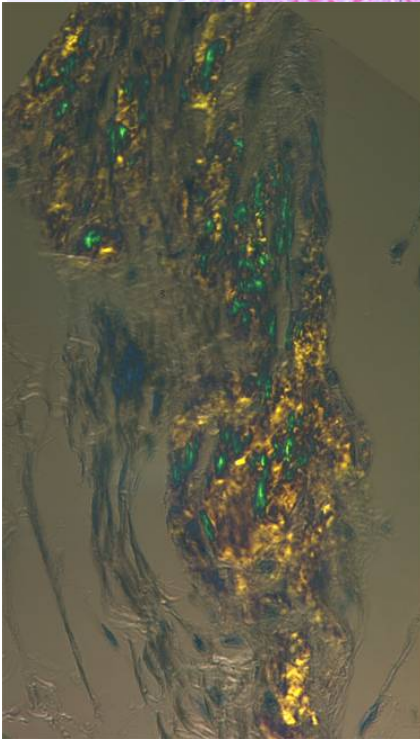
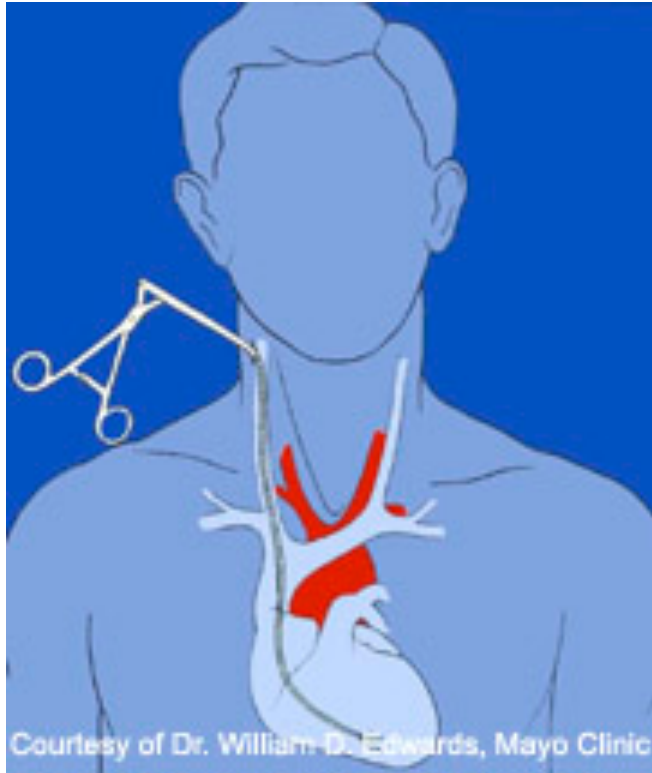
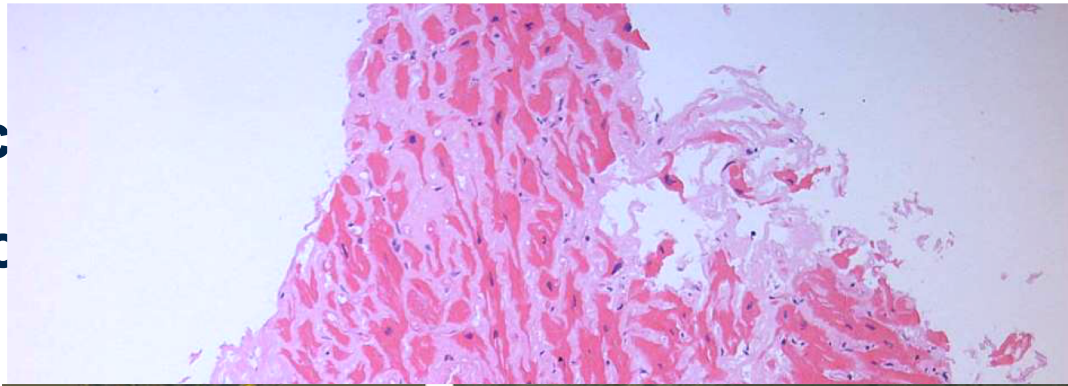
Macroglossia



Periorbital Purpura



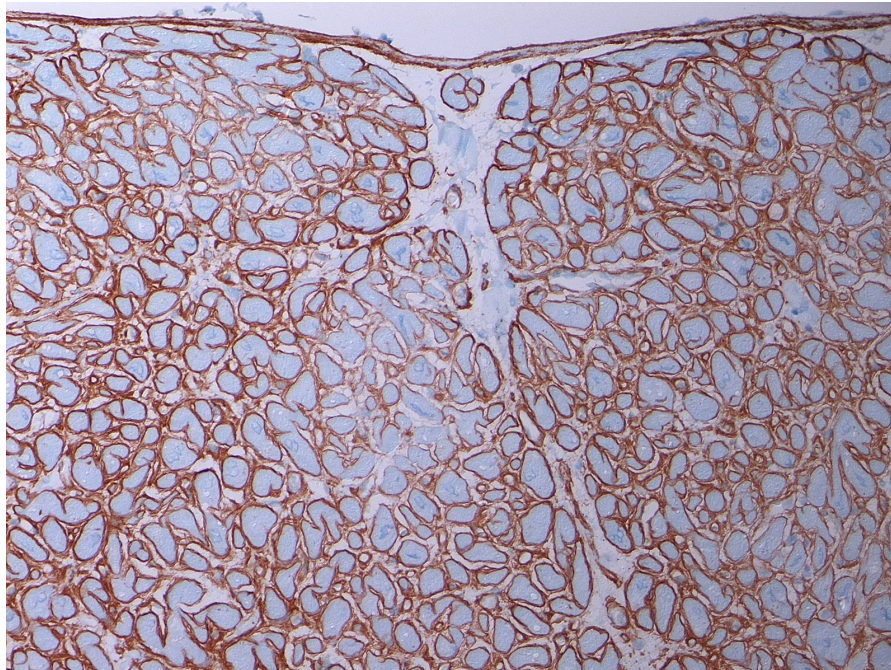
- Diagnosing Cardiac
- Endomyocardial biopsy



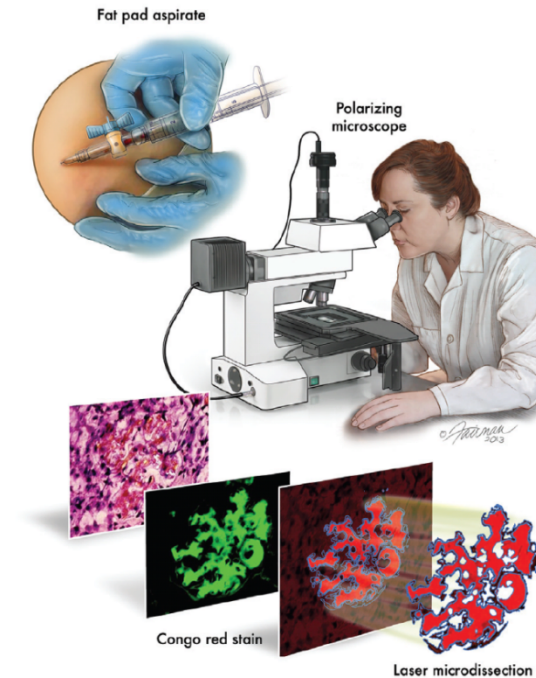
MUST SUBTYPE THE AMYLOID

Determines further testing
Prognosis
Treatment

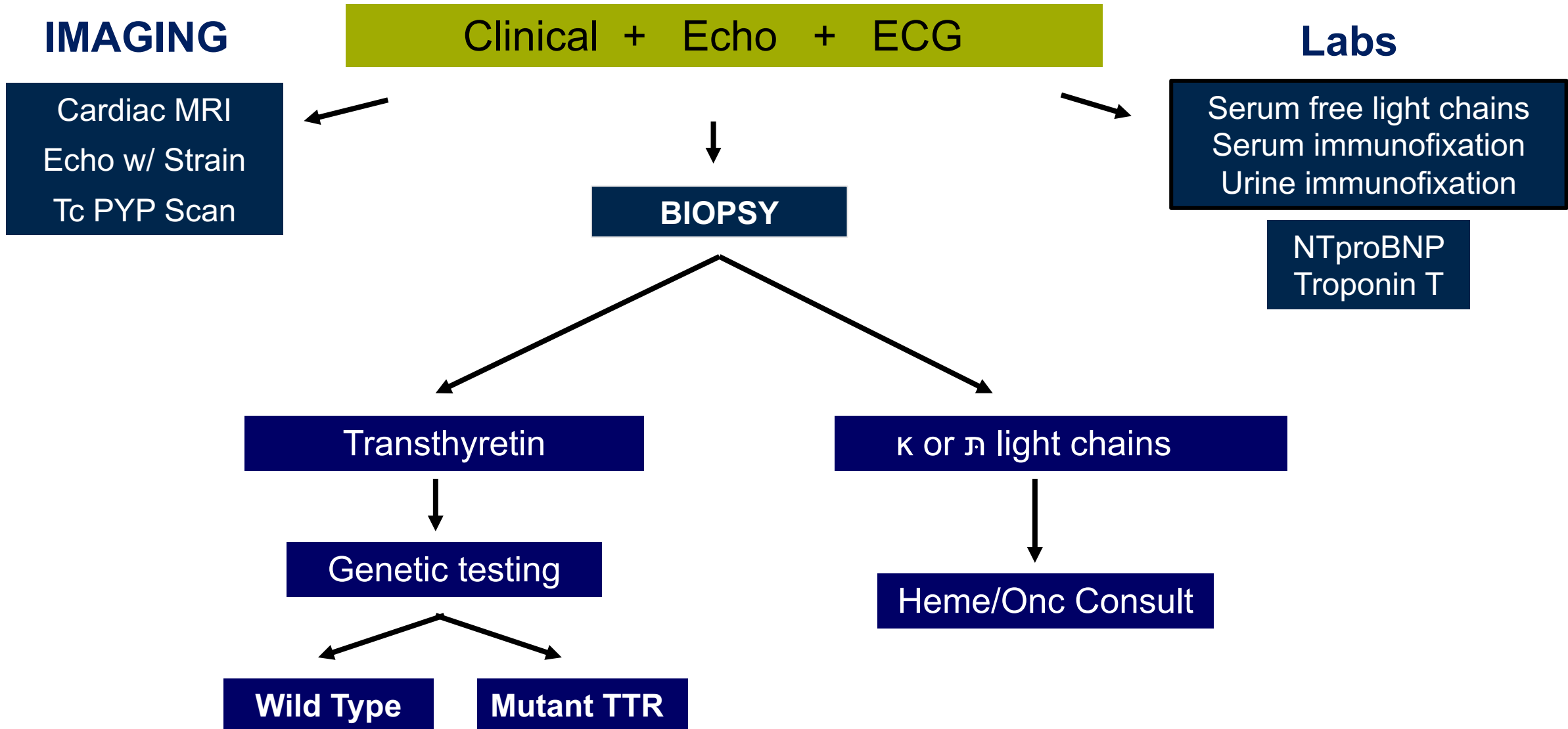
Immunohistochemistry



Mass Spectrometry



Diagnostic Approach



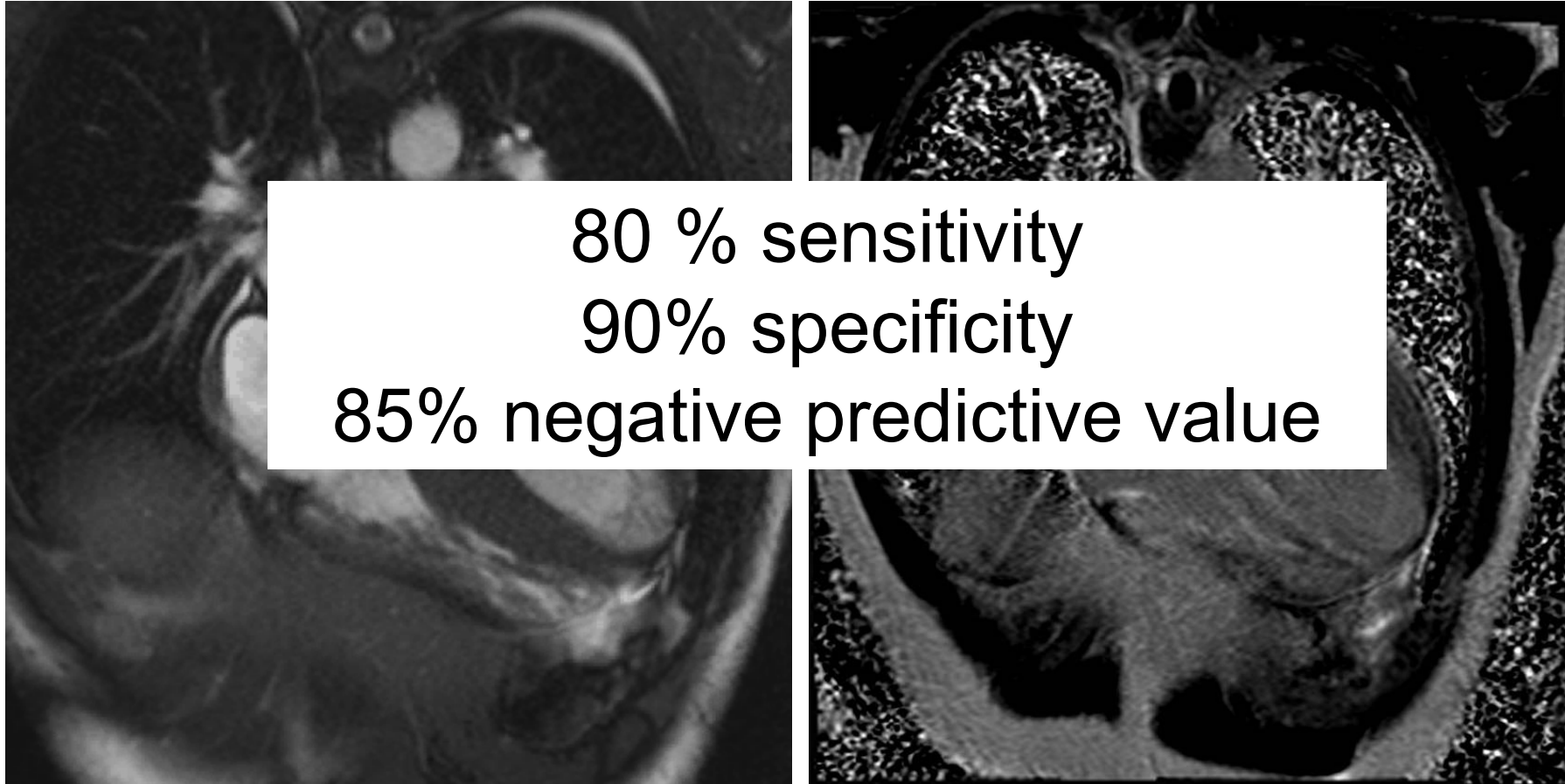
Laboratory Testing for work up of AL

~~SPEP and UPEP~~

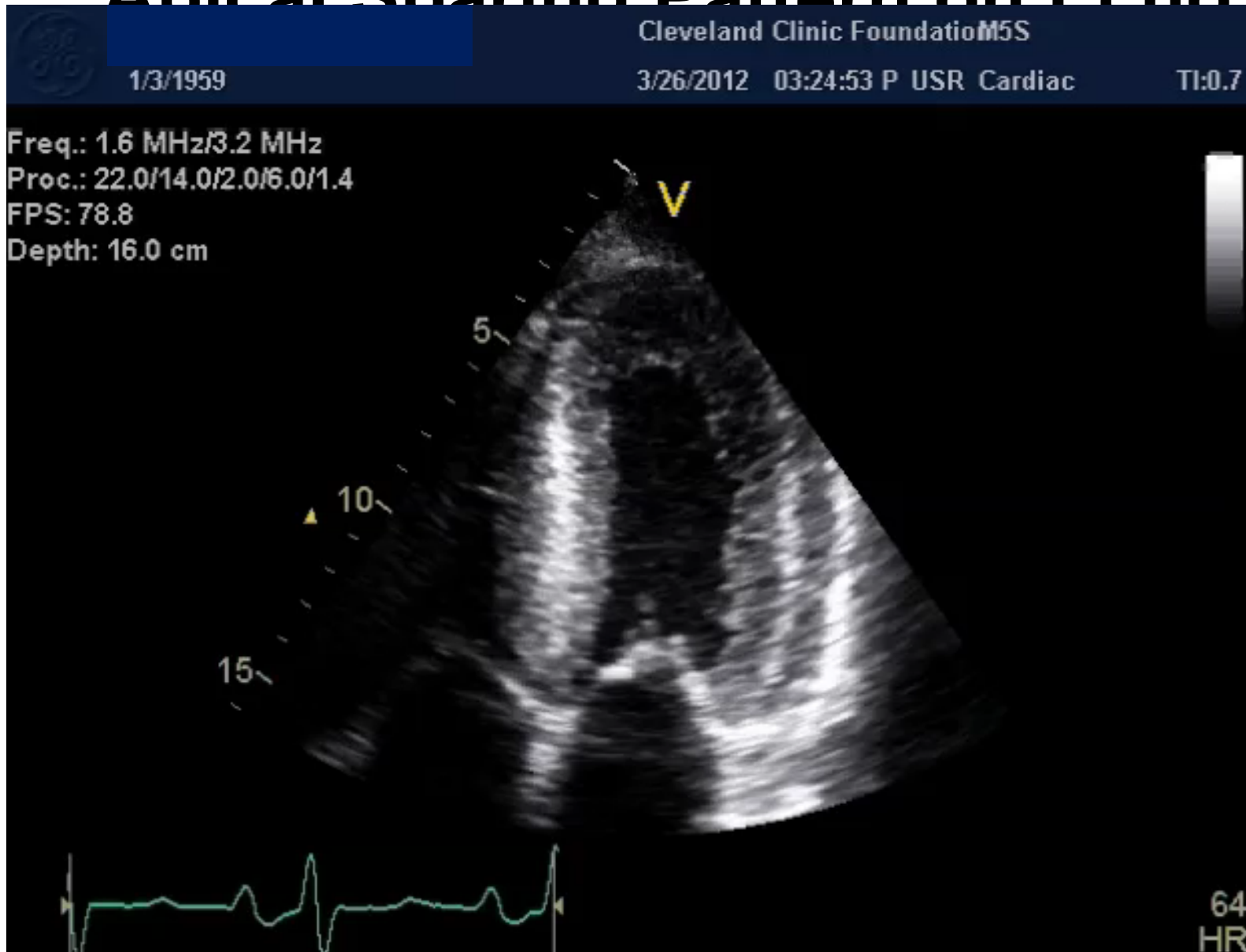
Kappa Free, Serum	3.30 - 19.40 mg/L	34.3 (H)
Lambda Free, Serum	5.7 - 26.3 mg/L	475.0 (H)
K/L Ratio, Serum	0.26 - 1.65	0.07 (L)

- Urine Immunofixation

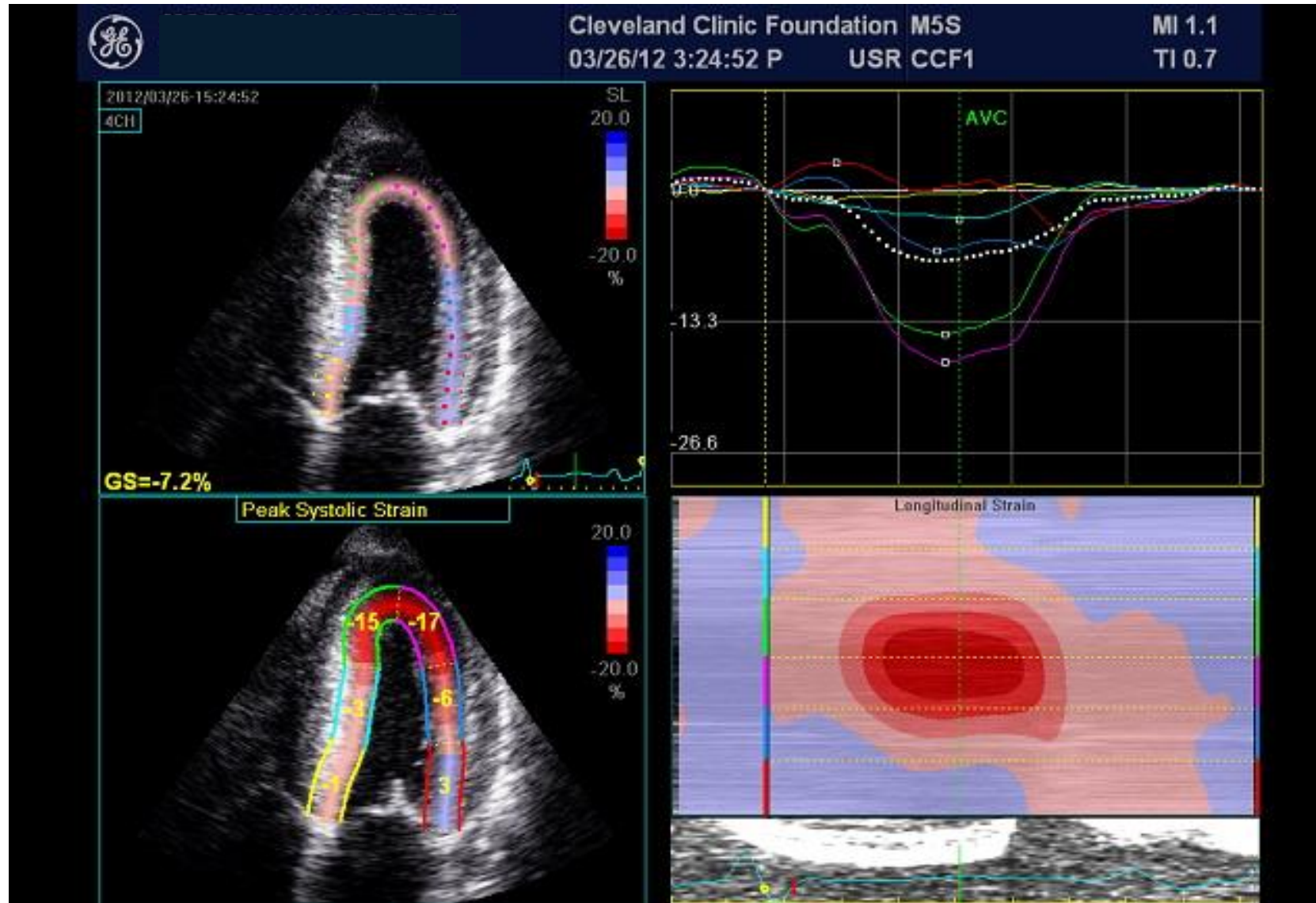
Diagnosis Cardiac Amyloid by MRI



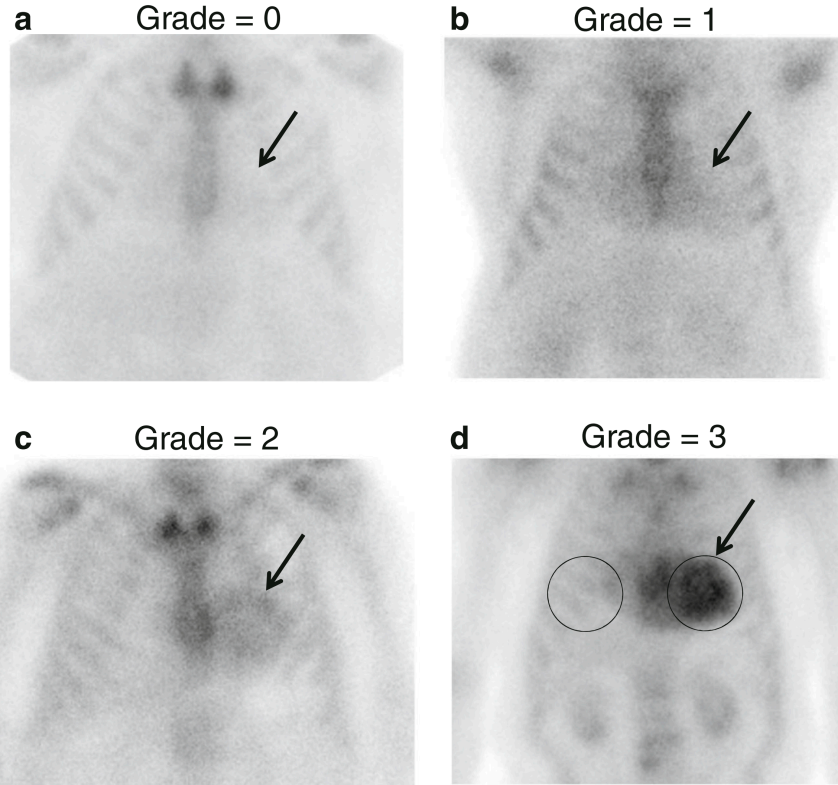
Apical Sparing Pattern on Echo



Apical Sparing Pattern: Longitudinal Strain



99mTechnetium pyrophosphate (PYP)



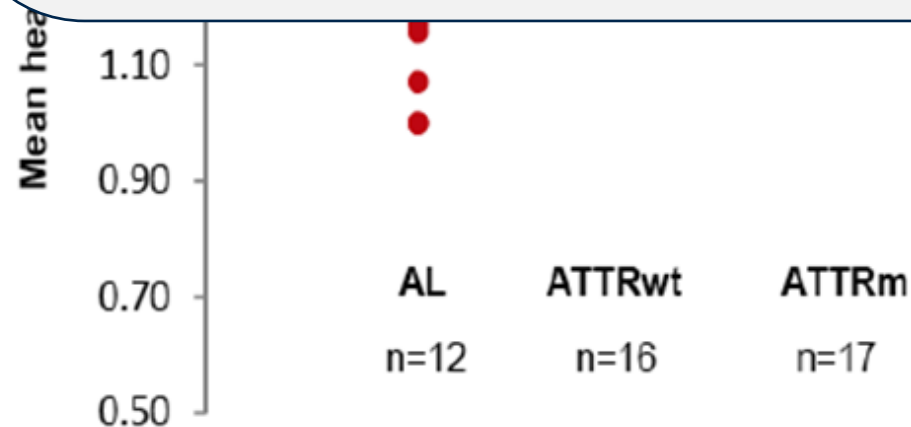
Perugini score

- 0 – absent uptake - NEGATIVE
- 1 – less than rib – INDETERMINATE
- 2 – equal to rib – LIKELY POSITIVE**
- 3 – greater than rib – POSITIVE**

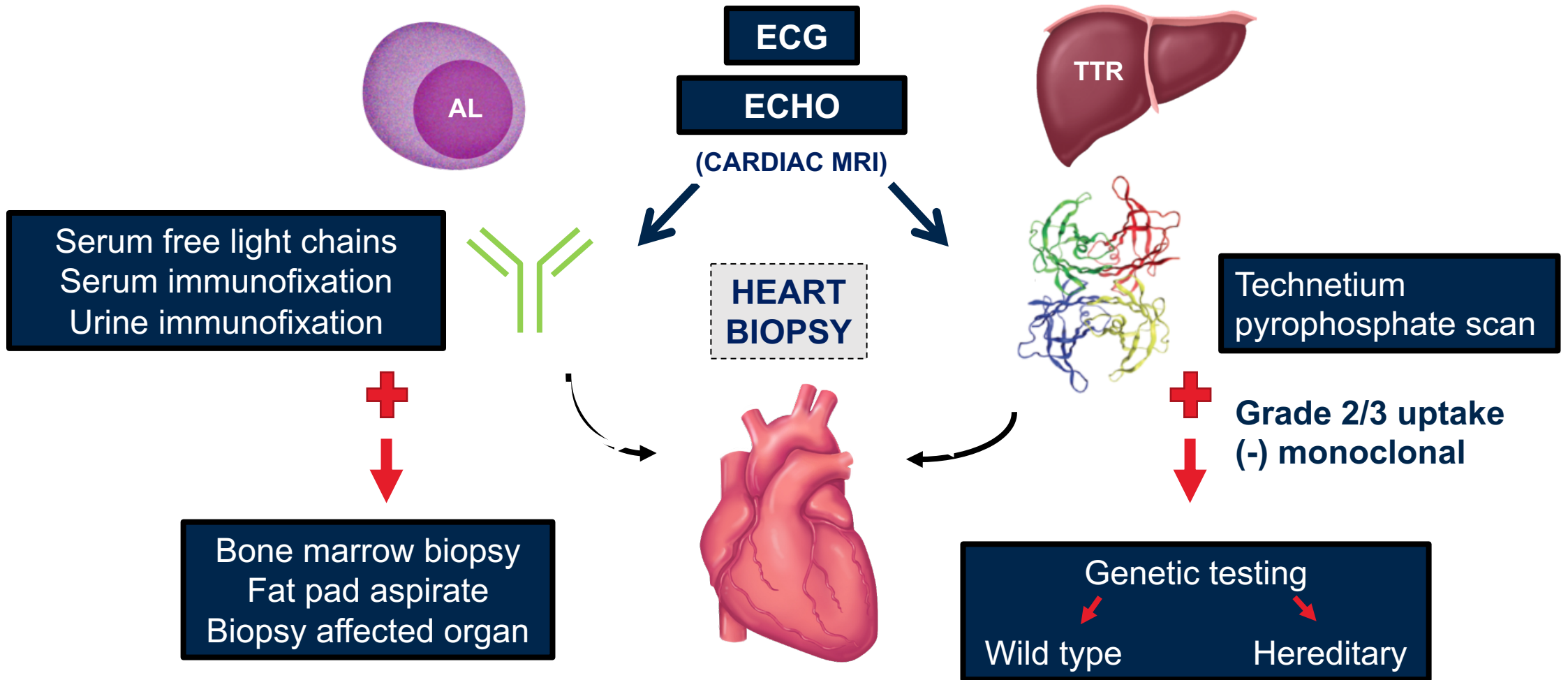
Rapezzi *Eur J Nuc*
Banyersad, *JAHA*

Diagnostic of ATTR Cardiac Amyloidosis

- 1) Grade 2 or 3 scan
- 2) Negative monoclonal lab testing
- 3) 91% sensitivity and 100% specificity for ATTR amyloidosis

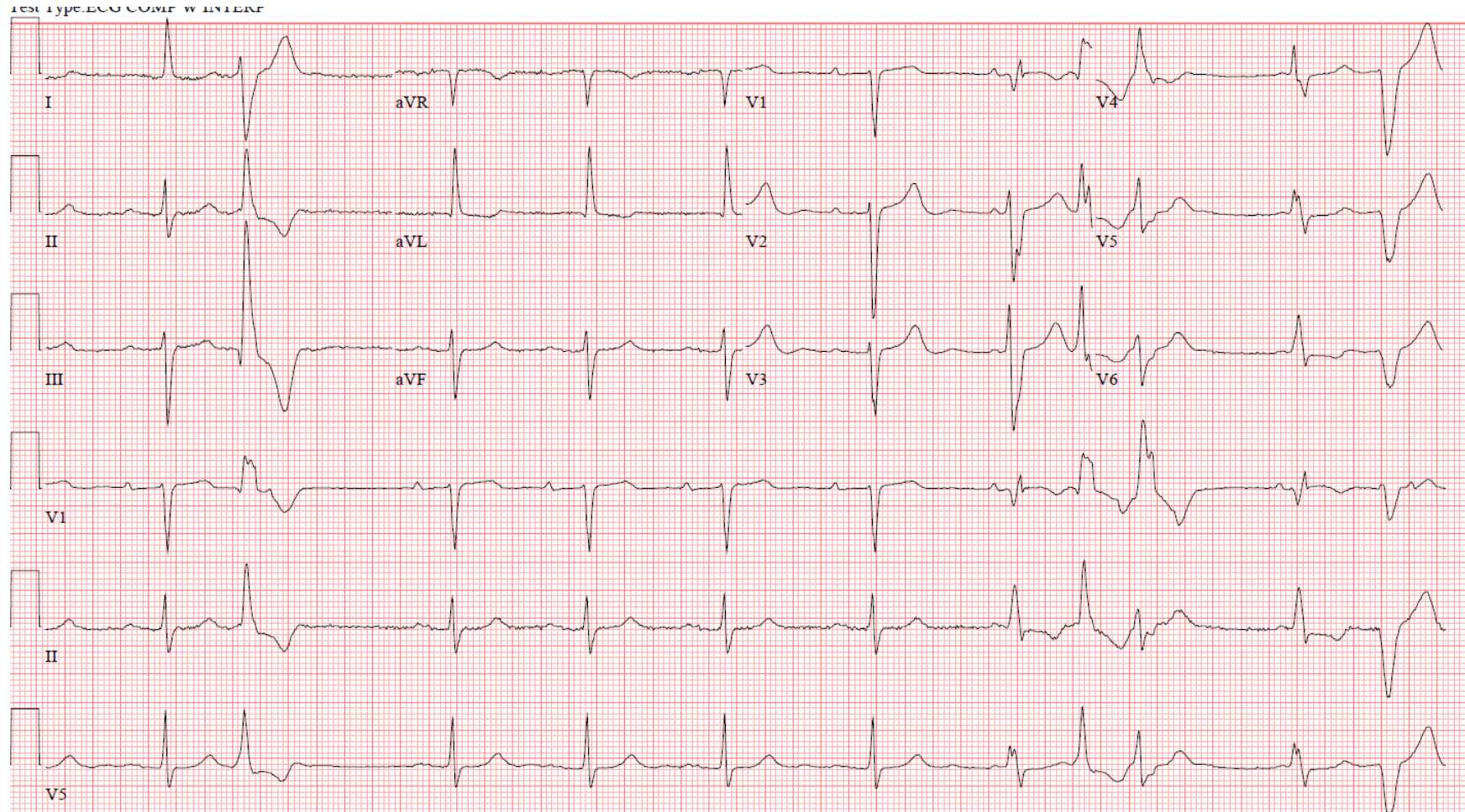


Starts With Clinical Suspicion

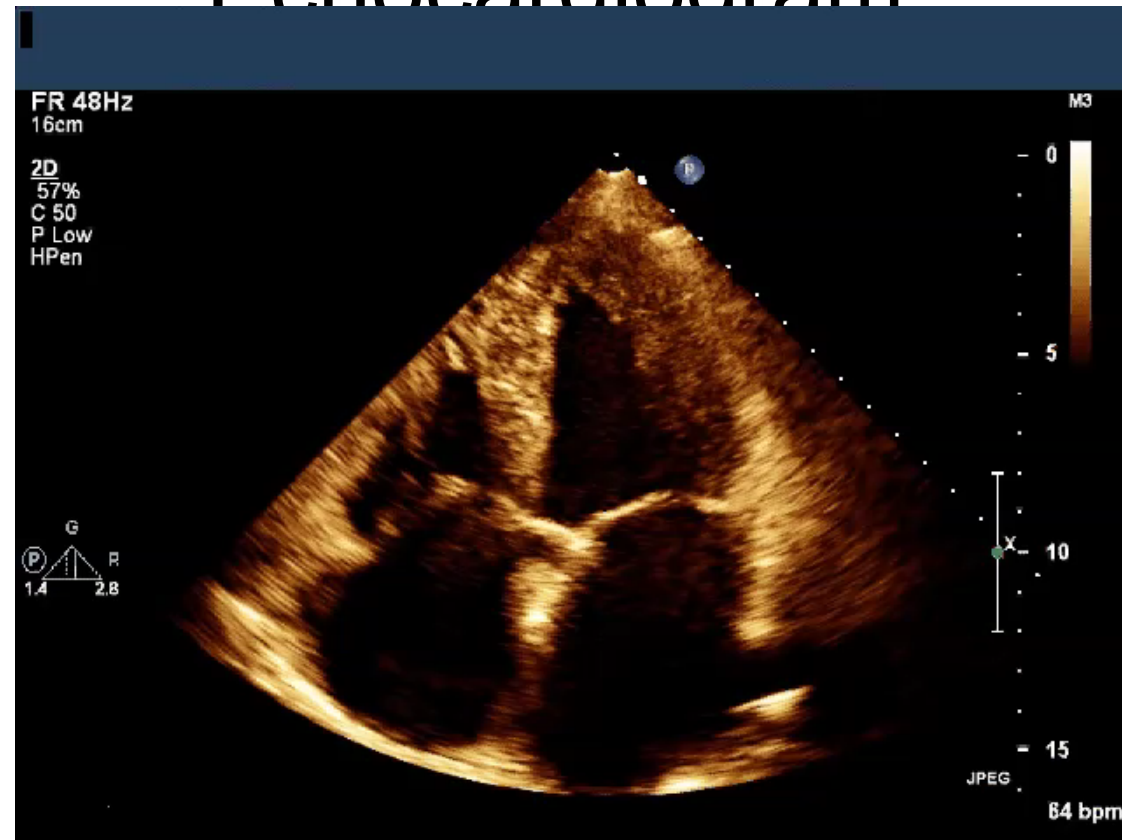


78 yo AA female h/o HTN & EF 45%

Referred for shortness of breath



Echocardiogram

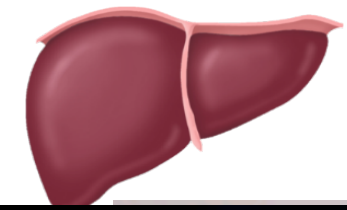




AL

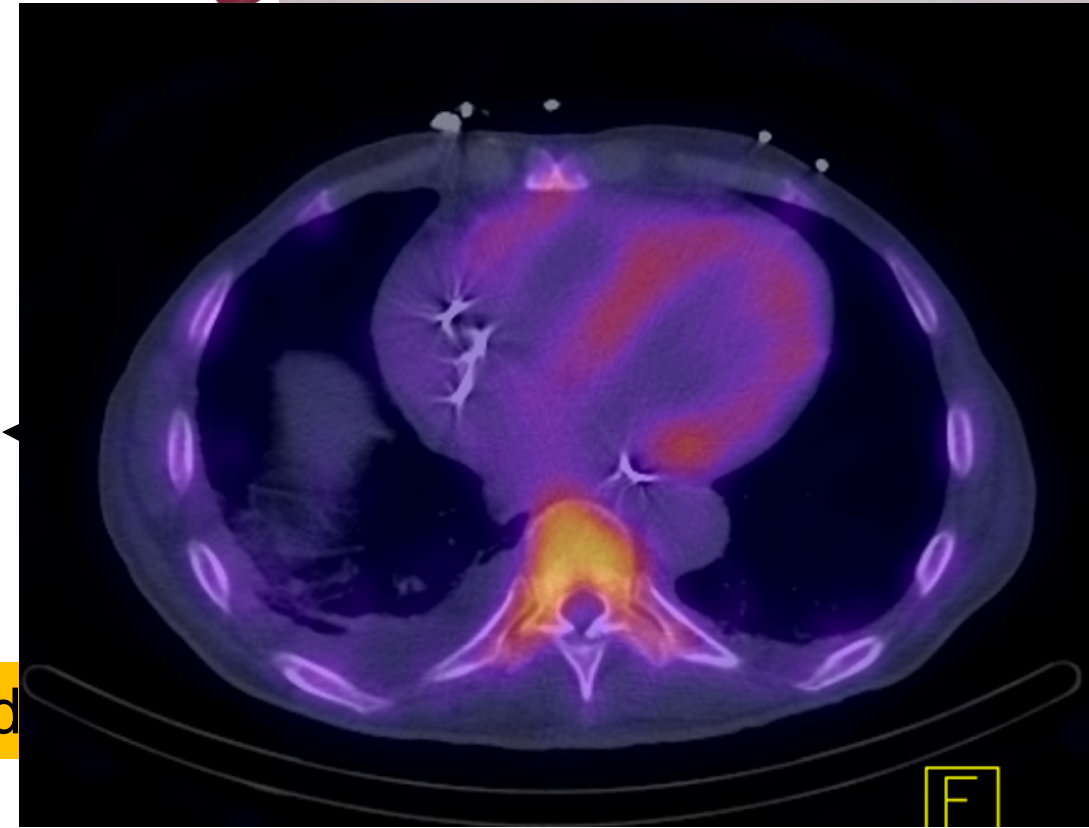
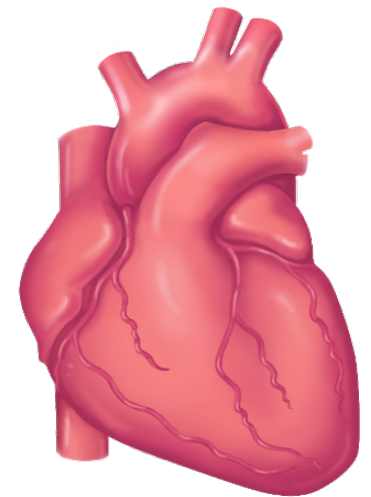
ECG

ECHO
(with strain)



TTR

NORMAL fLC
No M protein



Hereditary transthyretin cardiac amyloid

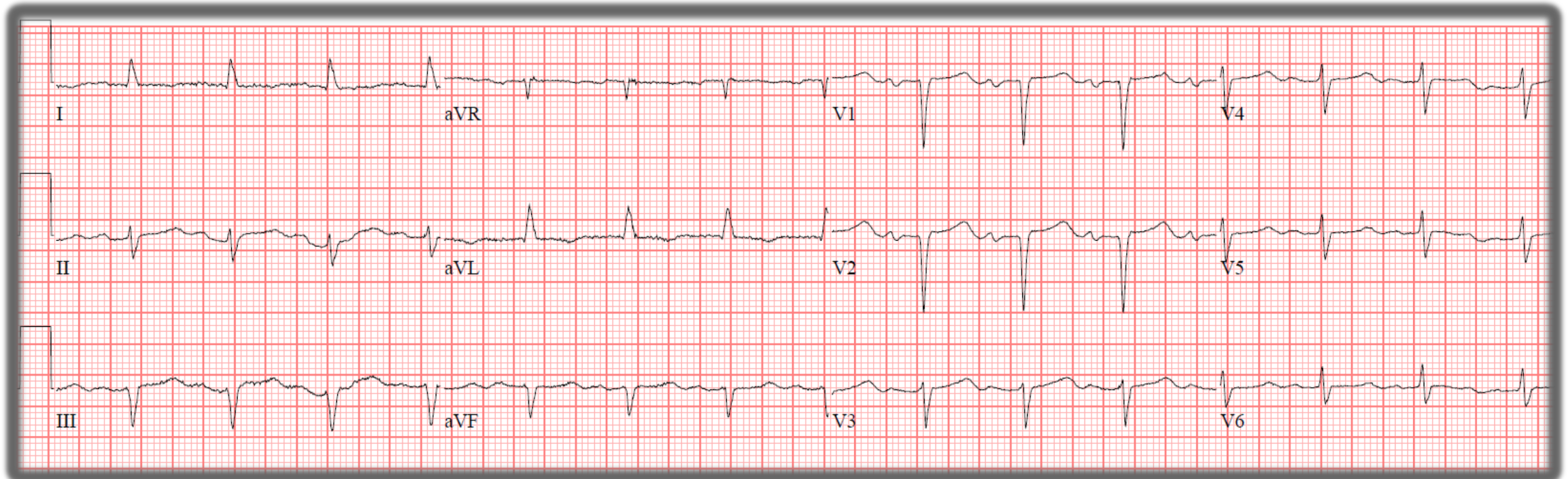
F

61 yo white female

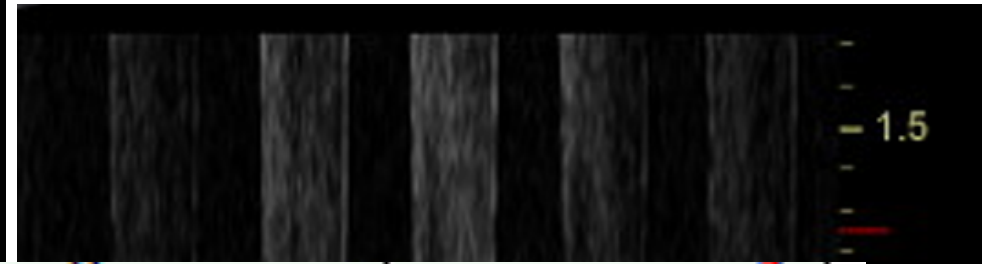
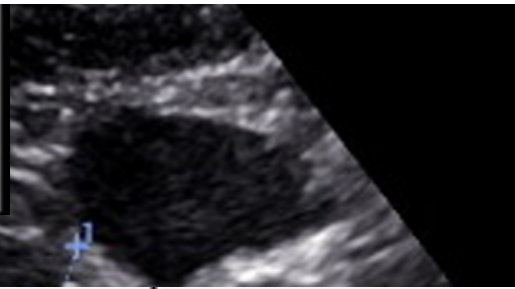
- SOB and edema X 1 year
- Urine with 9 grams proteinuria

ECG: 1st degree AV block, LAFB

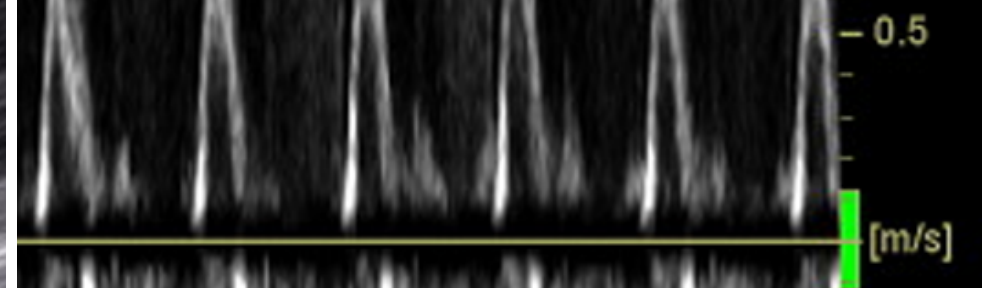
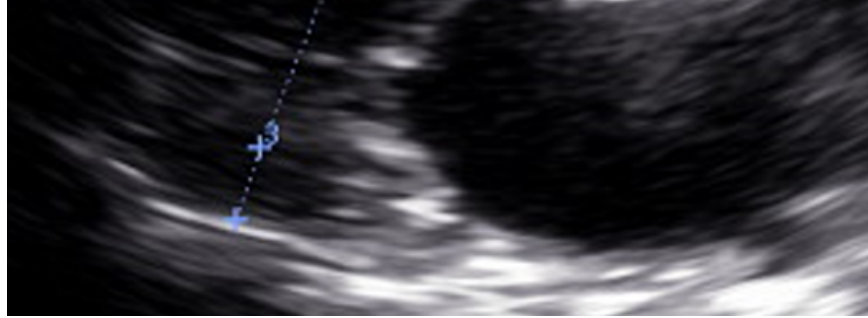
[@maz_hanna](#)



3 LVPWd 1.0 cm
2 LVIDd 4.9 cm
EDV(Teich) 110 ml
1 IVSd 1.3 cm

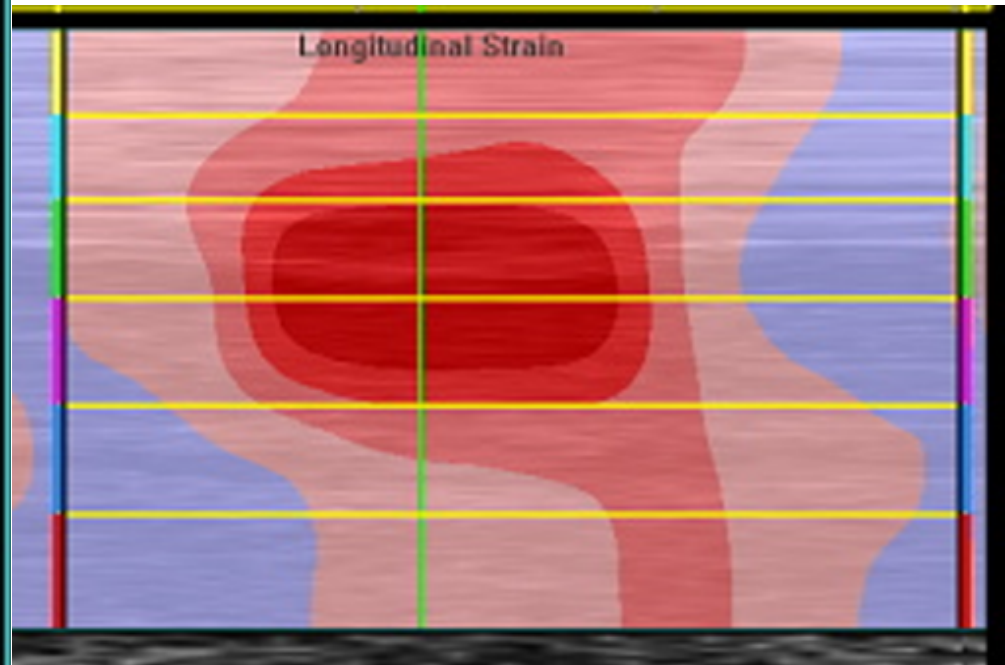
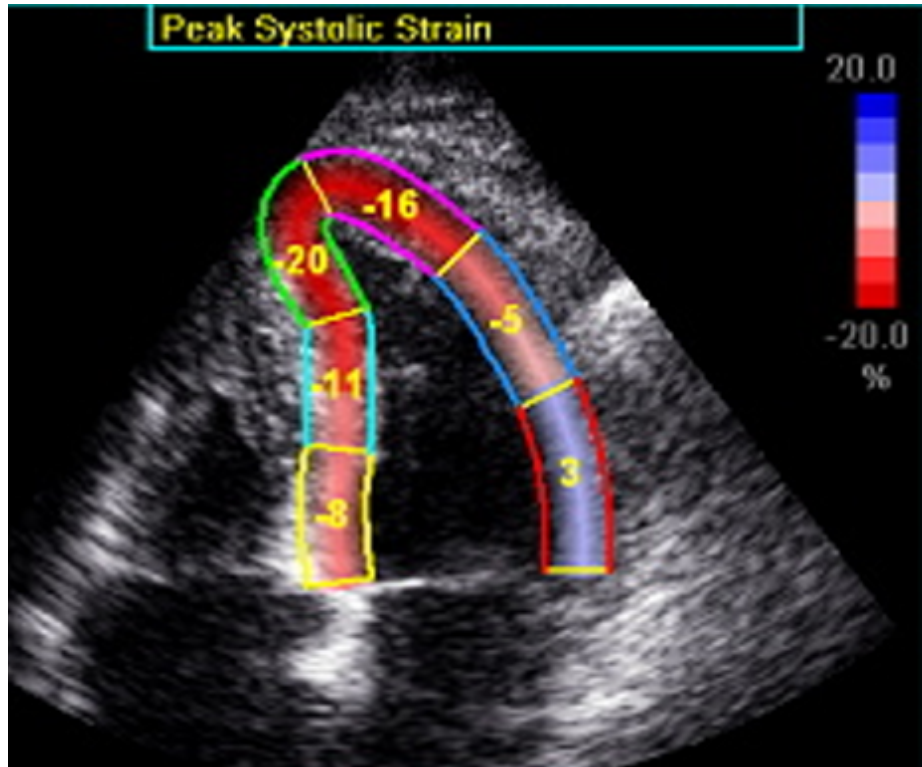


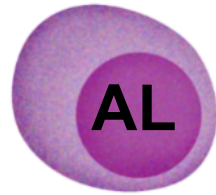
Troponin T	0.000 - 0.029 ng/mL	<0.010
NT Pro BNP	<125 pg/mL	3505 (H)



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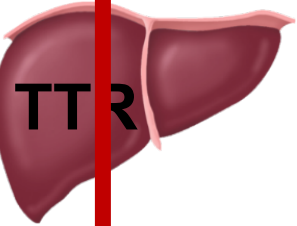
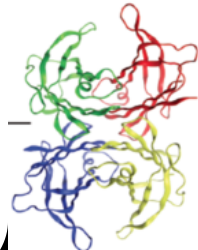
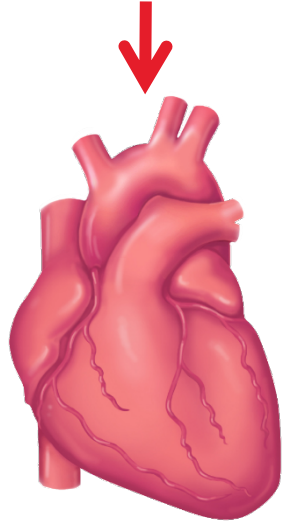




Serum free light chains
 Serum immunofixation
 Urine immunofixation



ECG
 ECHO
 (with strain)



TcPYP scan

Kappa Free, Serum	3.30 - 19.40 mg/L	311.9 (H)
Lambda Free, Serum	5.7 - 26.3 mg/L	23.5
K/L Ratio, Serum	0.26 - 1.65	13.27 (H)

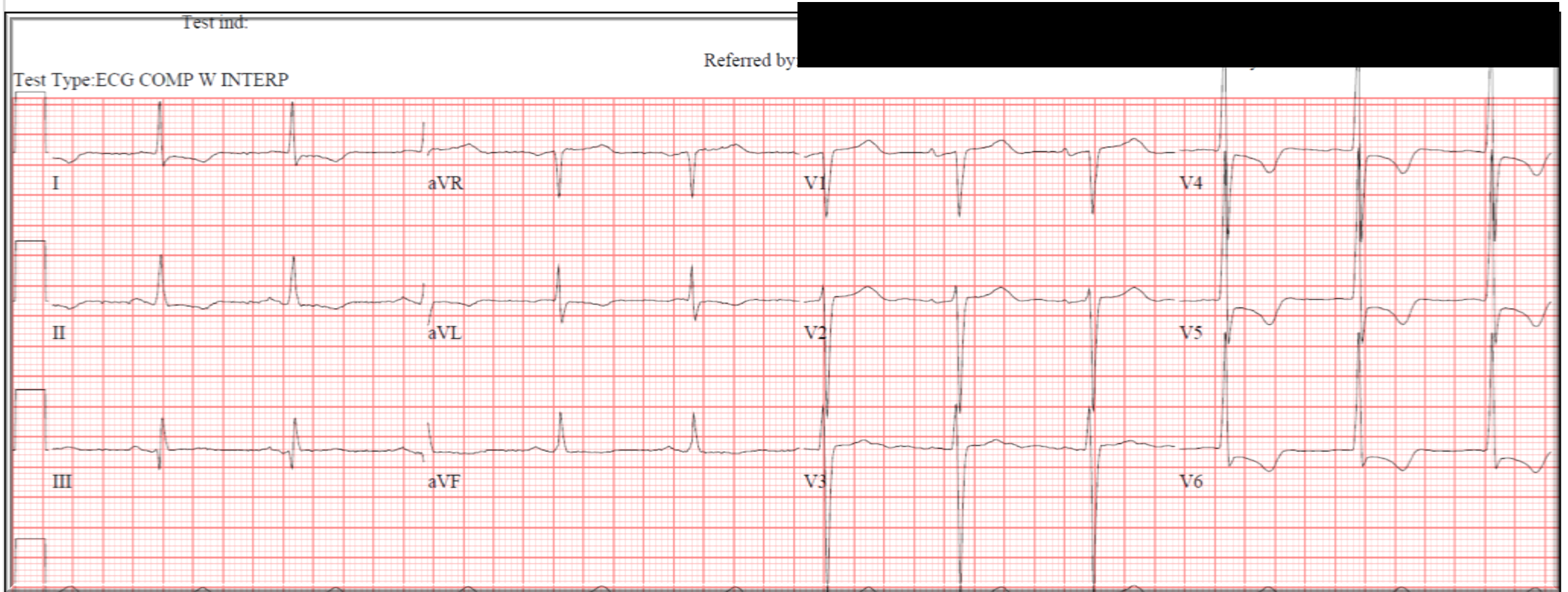
Serum and urine immunofixation: No M Protein

Kidney Biopsy
 + Kappa light chain amyloid

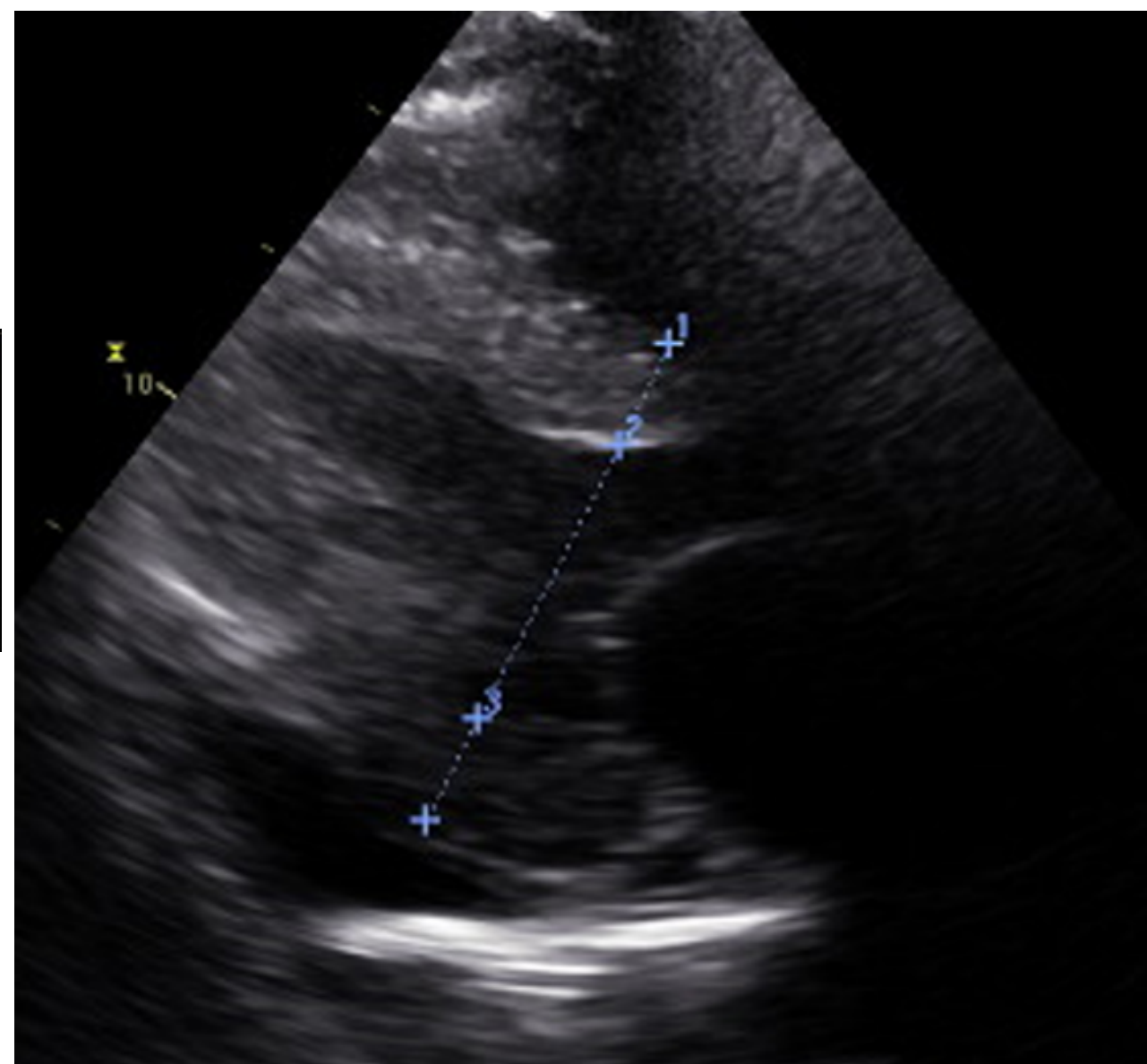
Kappa light chain AL Amyloid

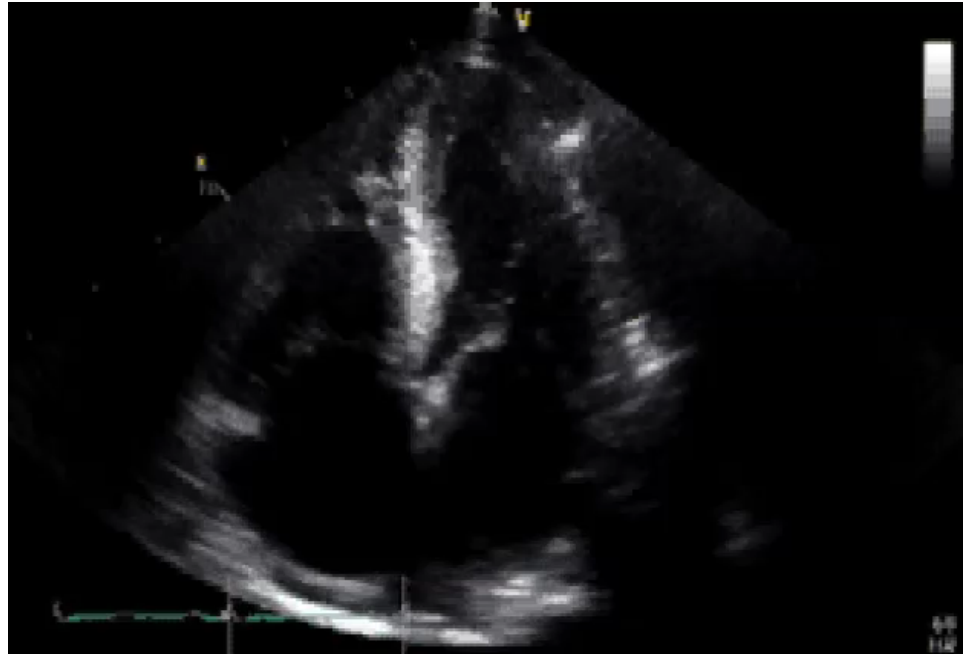
Bone Marrow biopsy
 only 1% plasma cells,
 Congo red negative

81 yr old white male

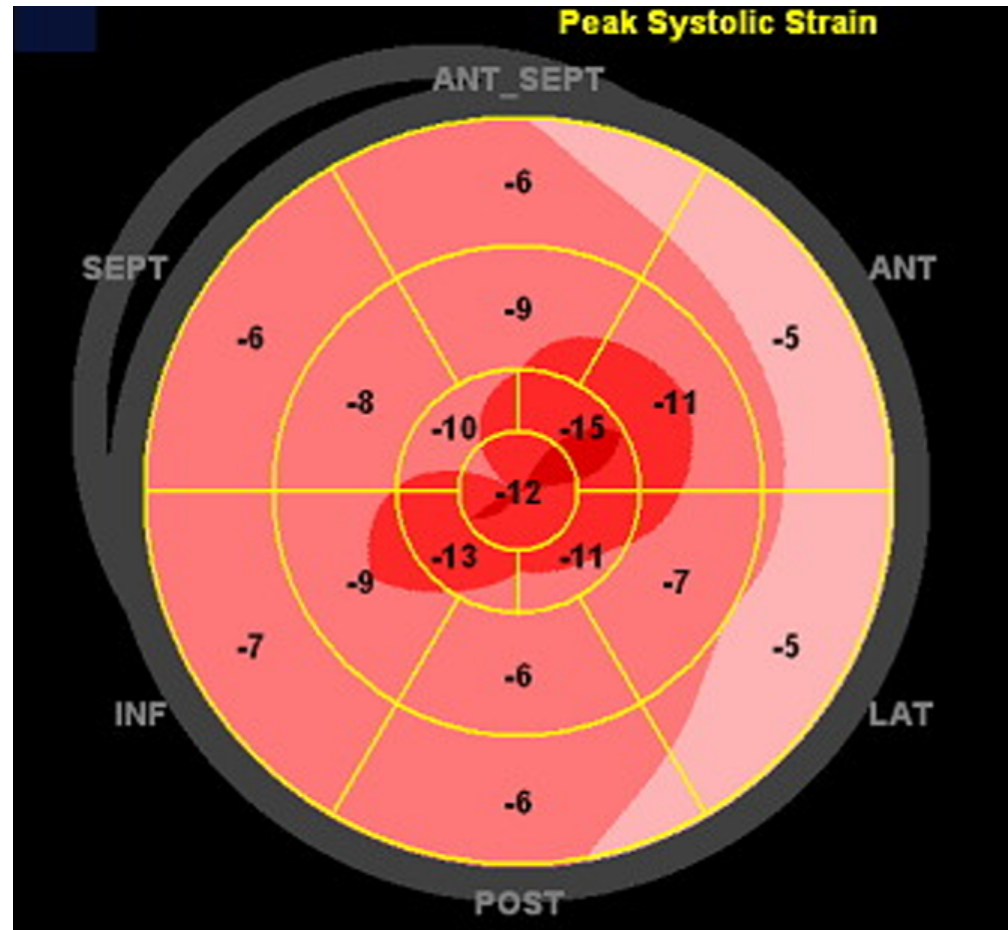


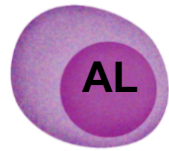
3	LVPWd	1.6 cm
2	LVIDd	4.4 cm
	EDV(Teich)	87 ml
1	IVSd	1.6 cm





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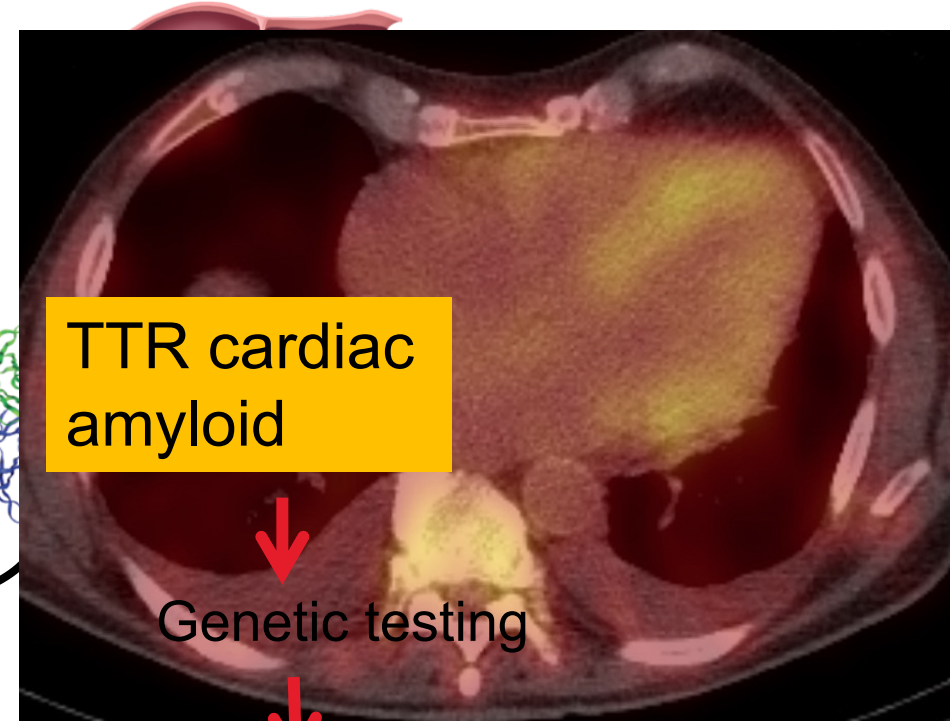
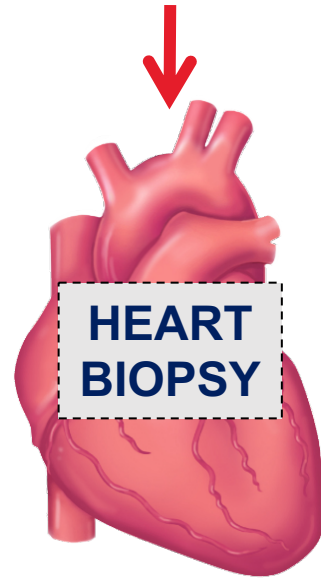


ECG

ECHO
(with strain)

Component	Latest Ref Rng & Units	5/24/2017
Kappa Free, Serum	3.30 - 19.40 mg/L	41.6 (H)
Lambda Free, Serum	5.7 - 26.3 mg/L	23.1
K/L Ratio, Serum	0.26 - 1.65	1.80 (H)

Serum immunofixation
No M protein



Genetic testing

No mutation

Wild type transthyretin cardiac amyloid

Teaching points

- Look at ECG and wall thickness on ECHO
- Diagnostic work up
 - **DO NOT ORDER SPEP AND UPEP!!!!!!!**
 - *Rather order serum free light chains & immunofixation serum +/- urine*
 - *Technetium pyrophosphate scan specific for TTR*
- Red flags
 - *Older white male w previous carpal tunnel and diastolic HF or “HOCCM”*
 - *Older African American with “diastolic heart failure”*
 - *As about both carpal tunnel and spinal stenosis in history taking*