61 yo M w/heart disease presenting in decompensated HF

1/24/13

Jess Hwang

HPI

- 3 weeks worsening orthopnea, PND, DOE
- Referred to UCMC for transplant evaluation
- Found to have 100% afib burden 1 month prior to admission
- 3 weeks ago complained to tremors to his cardiologist, amiodarone was stopped
- Does not recall having thyroid function tested in the past

HPI cont.

- URI symptoms 2 weeks ago
- No chest pain, no palpitations
- Mild diarrhea
- No weight loss
- No visual complaints
- No family history of thyroid disease

Heart failure history

- Diagnosed in 2008 after massive MI
- Was medically managed for 4 years
- 3-4 weeks ago noticed decreased exercise tolerance, DOE, PND
- Had been on amiodarone since 2008

PMH

- HTN
- CAD (s/p MI in 2008 and 5V CABG)
- CHF (class IV)
- Afib
- Dyslipidemia

SHx

- Quit tobacco in 1999 (50 pack year history)
- No EtOH or illicits

Fam Hx

- Mother: DM2, CHF, breast cancer
- PGF: lung cancer

Meds

- ASA
- Lipitor
- Coreg
- Digoxin
- Cymbalta
- Lasix
- Aldactone
- Valsartan
- Coumadin

Physical exam

Vitals 36.5, 97, 73/43, 97% RA, BMI 24
Gen: no apparent distress. Thin.
HEENT: no scleral icterus, no proptosis.
Neck: no thyromegaly/nodules/thyroid pain.
CV: irregularly irregular, tachy.
Pulm: basilar crackles
GI: soft, nontender, normal bowel sounds
Ext: mild tremor, normal reflexes
Neuro: alert and oriented

Labs

134	97	28
4.1	25	1.0

130

8.8

2.4

3.9

13.7

10.2 418

41

6.4	2.8
2.8	0.6/2.2
67	78

194

BNP 4774 (RR < 125)

EKG: afib w/RVR (HR 110)

Labs cont.

- TSH 0.01 (RR 0.3-4.0)
- FT4 3.07 (RR 0.9-1.7), TT4 10.8 (RR 5-11.6)
- TT3 121 (RR 80-195)
- rT3 1188 (RR 160-353)
- AntiTPO/Tg/TSI Ab neg
- Urine iodine: 388,874 (RR 26-705)
- IL-6 < 6.2 (RR <17.4)

	10/19	10/22	11/1
TSH (0.3-4.0)	0.01	0.01	0.01
FT4 (0.9-1.7)	3.07	3.17	2.44
TT3 (80-195)	121	92	113
FT3 (230-420)	320	257	
rT3 (160-353)	1188		1251

Thyrotoxicosis differential

- Thyroiditis
  - Medications
  - Viral
- Autoimmune- Graves
- Multinodular goiter
- Autonomous hyperfunctioning nodule

Thyroid US

R lobe: 5.7 x 2.2 x 2 cm

- mildly heterogeneous echotexture

L lobe: 4.6 x 1.6 x 2 cm

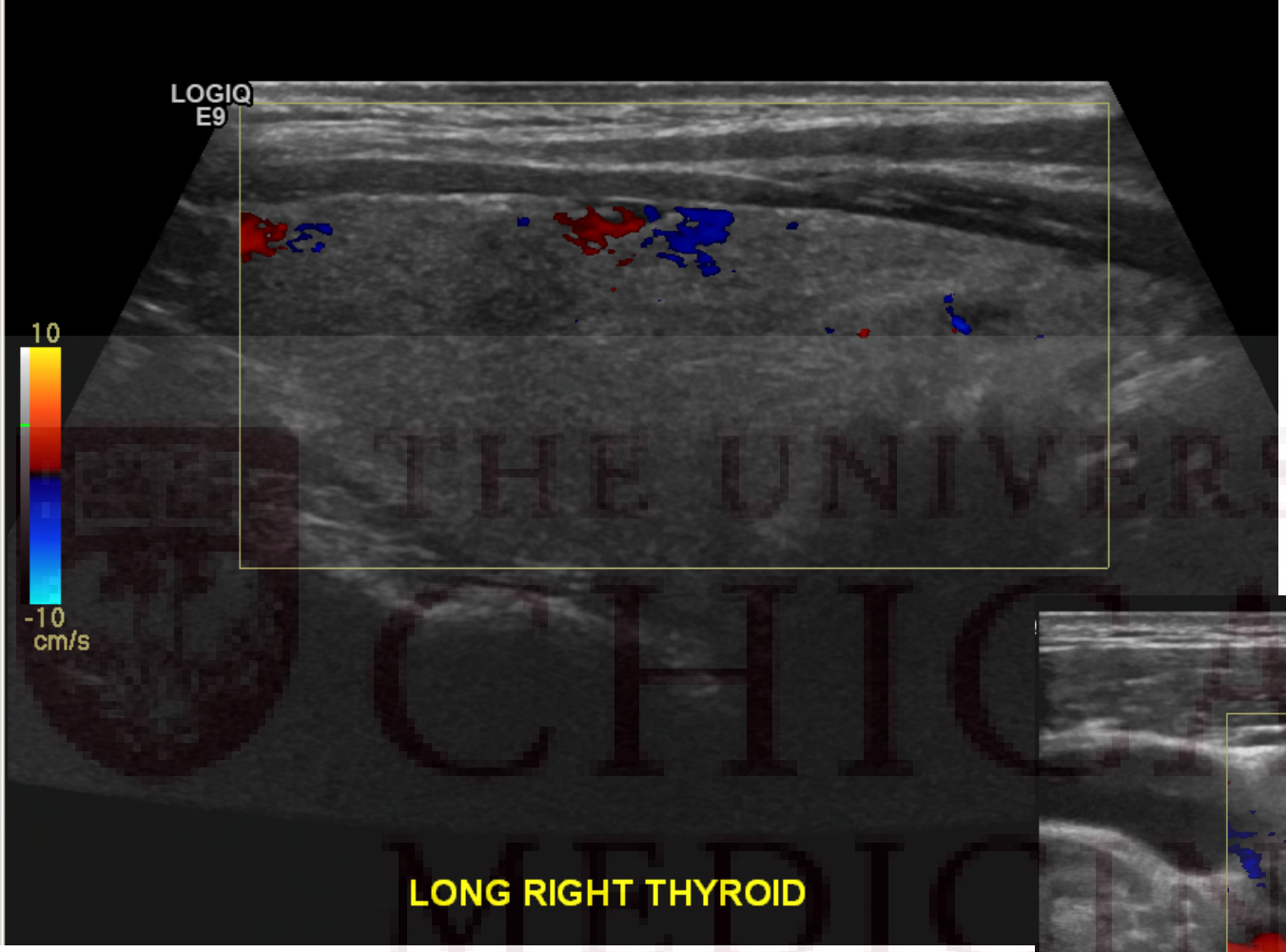
- mildly heterogeneous echotexture

Isthmus: 0.4 cm

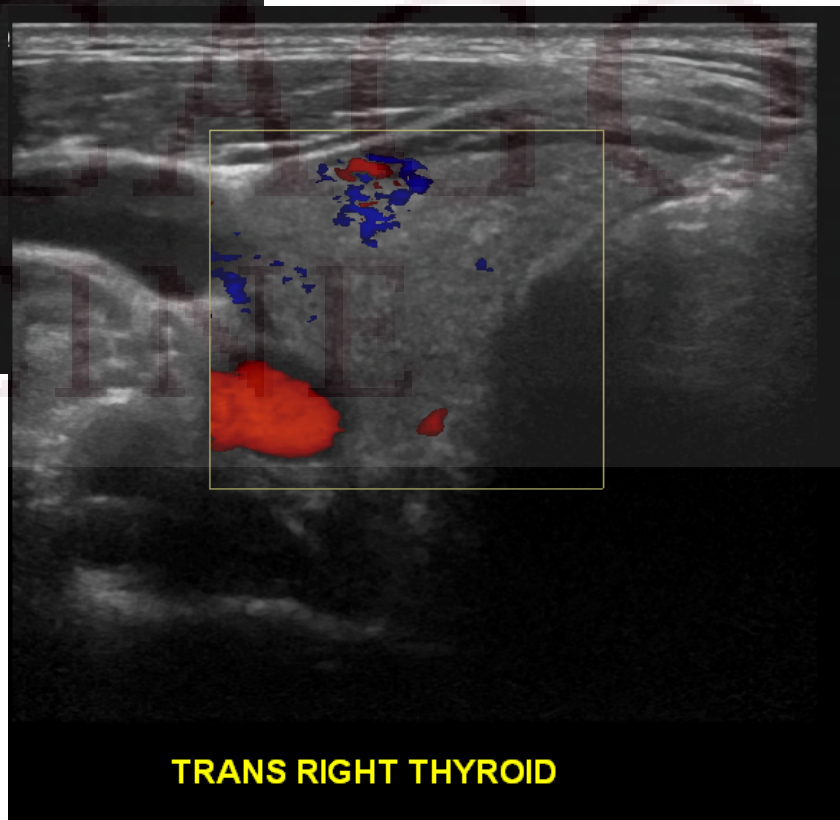
Subcentimeter hypoechoic nodules measuring 0.3 and 0.4 gm in R/L lobes

No lymphadenopathy

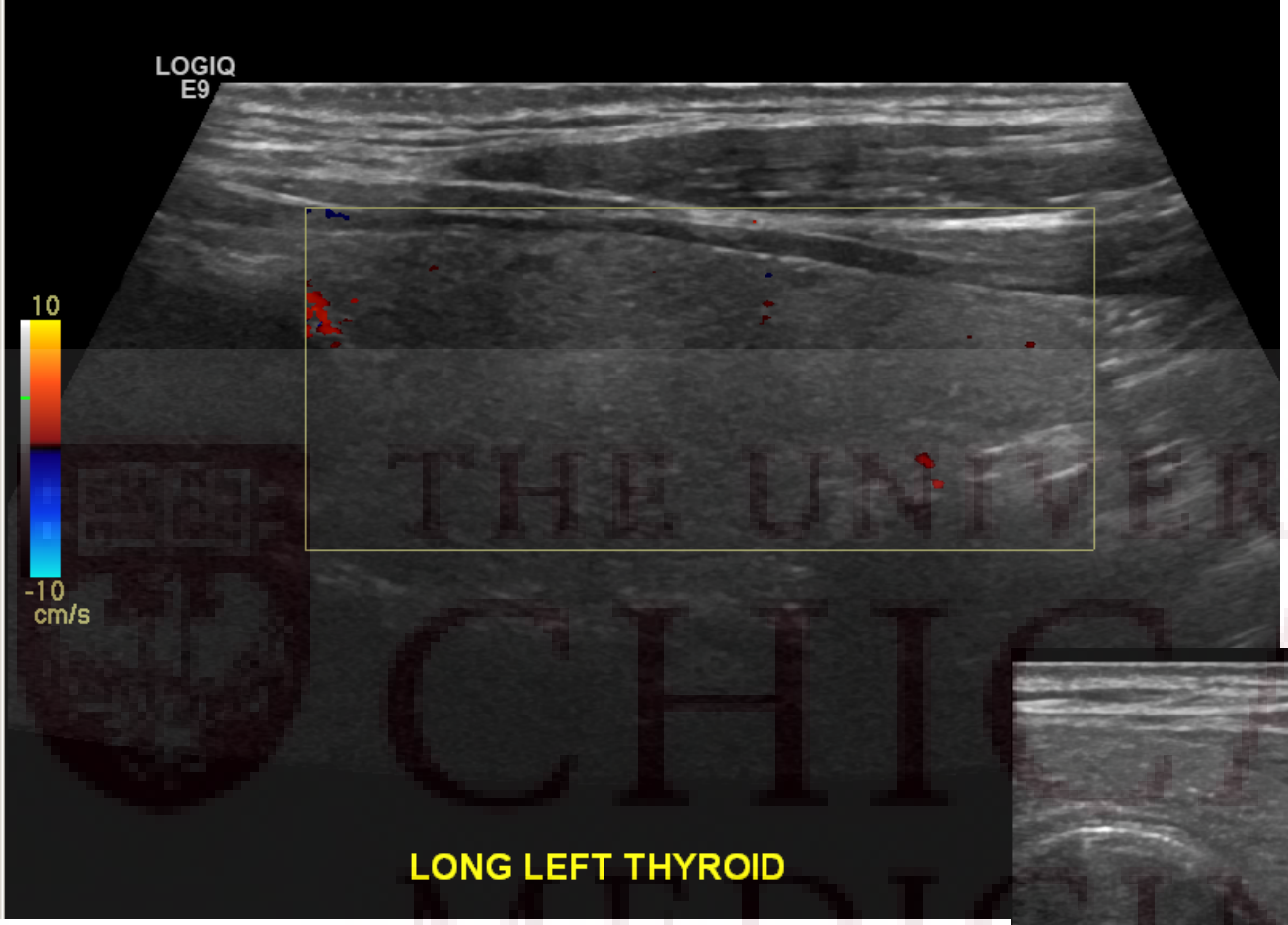
IMPRESSION: mildly heterogeneous echotexture consistent with thyroiditis



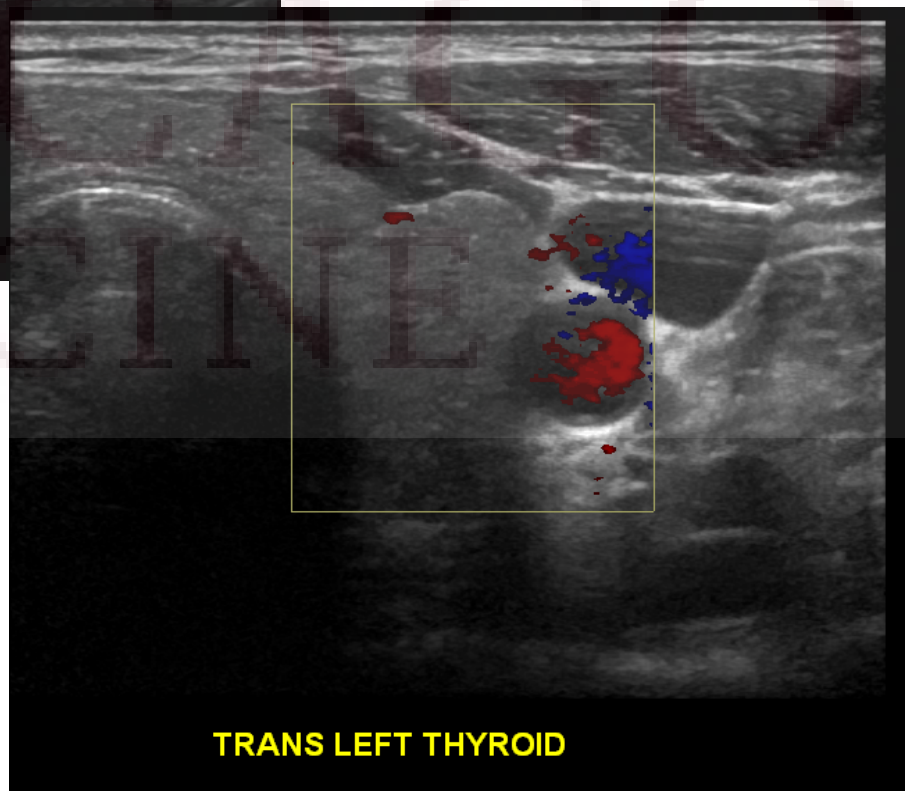
LONG RIGHT THYROID



TRANS RIGHT THYROID



LONG LEFT THYROID



TRANS LEFT THYROID

Hospital course

- Started on PTU 200 mg TID
- Started Prednisone 40 mg daily which he was on for a week with plan for taper
- Continued on Coreg BID

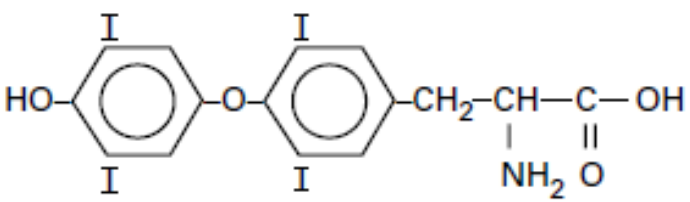
- Underwent CV and remained in NSR
- HF team said he does not require a heart transplant or LVAD at this time

Post-discharge course

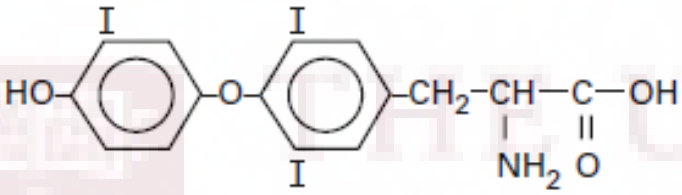
- Followed in endocrinology clinic 1 week post-discharge and at that time (likely AIT type II vs mixed)
  - Switched to MMI 20 mg daily
  - Re-started Prednisone 20 mg daily
- Was to repeat TFTs in 2 weeks but is now following up closer to home

Clinical objectives/questions

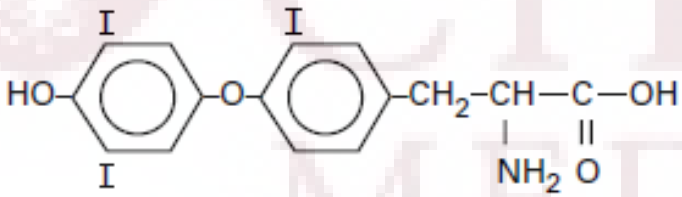
- Review properties/effects of amiodarone
- Review features/treatment strategies of the AIT I vs II vs mixed
- Is IL-6 useful in differentiating between types



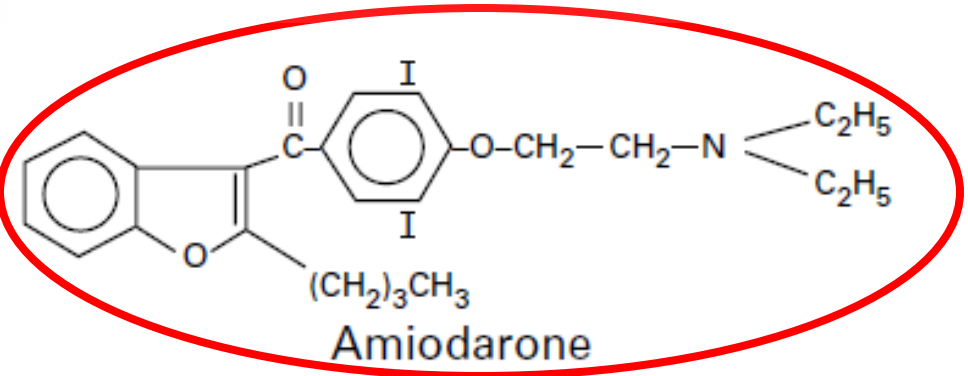
Thyroxine (T_4)



3, 5, 3′-Triiodothyronine (T_3)



3, 3′, 5′-Triiodothyronine (reverse T_3, rT_3)



Amiodarone

Amiodarone Properties

- Similar in structure to T4
- Benzofuran ring
- 37% iodine by weight
- Elimination half-life ~50d
- 2-24% thyroid dysfunction

Mechanisms of interaction

- Inhibits type I 5’-deiodinase activity
  - Decreased peripheral conversion of T4→T3
  - Decreased conversion of rT3→T2
- Inhibit type II 5’-deiodinase activity
  - Decreased conversion of T4→T3 in pituitary
- Inhibits thyroid hormone entry into peripheral tissue

Effect of Amiodarone on TFTs

Table 1 Effects of amiodarone on thyroid hormone profile in euthyroid subjects

Parameters (serum)	*Duration of treatment*	
	<3 months	*>3 months*
T4 or free T4	↑	↑ (up to 40% > baseline)
T3 or free T3	↓	↓ or low-normal
Reverse T3	↑	↑
TSH	↑ (up to 20 mU/l)	normal

Loh KC. Postgrad Med J 2000;76:133-140.

Pathogenesis AIT Type I vs II

	Type I AIT	Type II AIT
Underlying thyroid abnormality	Yes	No
Pathogenetic mechanism	Excessive hormone synthesis due to iodine excess	Excessive release of preformed hormones due to thyroid destruction
Goitre	Multinodular or diffuse goitre normally present	Occasionally small, diffuse, firm, sometimes tender
Thyroidal radioiodine uptake	Normal/raised (can also be low due to diluting effects of excess iodine)	Low/absent
Serum interluekin-6	Normal/slightly raised	Profoundly raised
Thyroid ultrasound	Nodular, hypoechoic, increased volume	Normal
Colour flow Doppler sonography	High vascularity	Absent vascularity

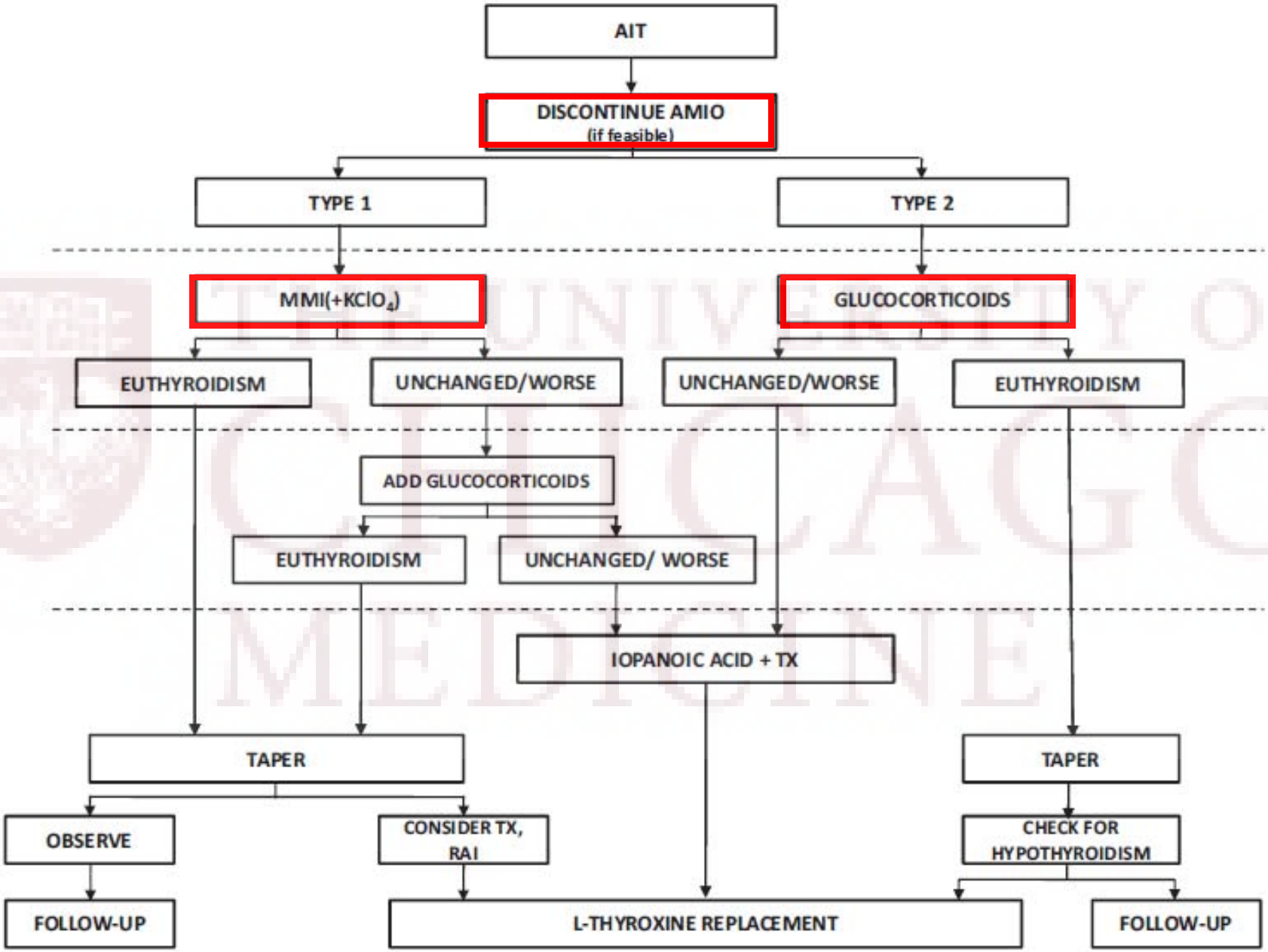
AIT, amiodarone-induced thyrotoxicosis.

Narayana S. Thera Adv in Endo and Metab 2011.2:115-126.

Amiodarone-induced thyrotoxicosis: Type 1 or type 2?

FINDING	RELATIVE WEIGHT OF FINDING*	
	TYPE 1 (OVERACTIVITY)	TYPE 2 (INFLAMMATION)
Goiter		
Clearly present (diffuse or nodular)	+2	−1
No or minimal goiter	0	+2
Thyroid autoantibodies > twofold of upper normal		
Antimicrosomal (anti-thyroid peroxidase)	+1	0
Antithyroglobulin	+1	0
Anti-receptor antibodies	+1	0
Radioactive iodine thyroid uptake (24-hour values)		
< 1%	−1	+1
1%–3%	+1	−1
> 3%	+2	−2
Interleukin 6 (IL-6) levels		
> twofold of upper normal	−2	+2
Normal (or minimal elevation)	0	0
Color flow Doppler sonography		
Decreased blood flow (pattern 0)	−2	+2
Normal to increased flow (patterns 1–4)	+2	−2
Satisfactory response to a specific therapeutic trial		
Prednisone 30–40 mg/day alone (within 4 weeks)	−2	+2
Thionamide with or without perchlorate (within 8 weeks)	+2	0
Combination of both modalities of treatment	0	0
TOTAL	**+2**	**0**

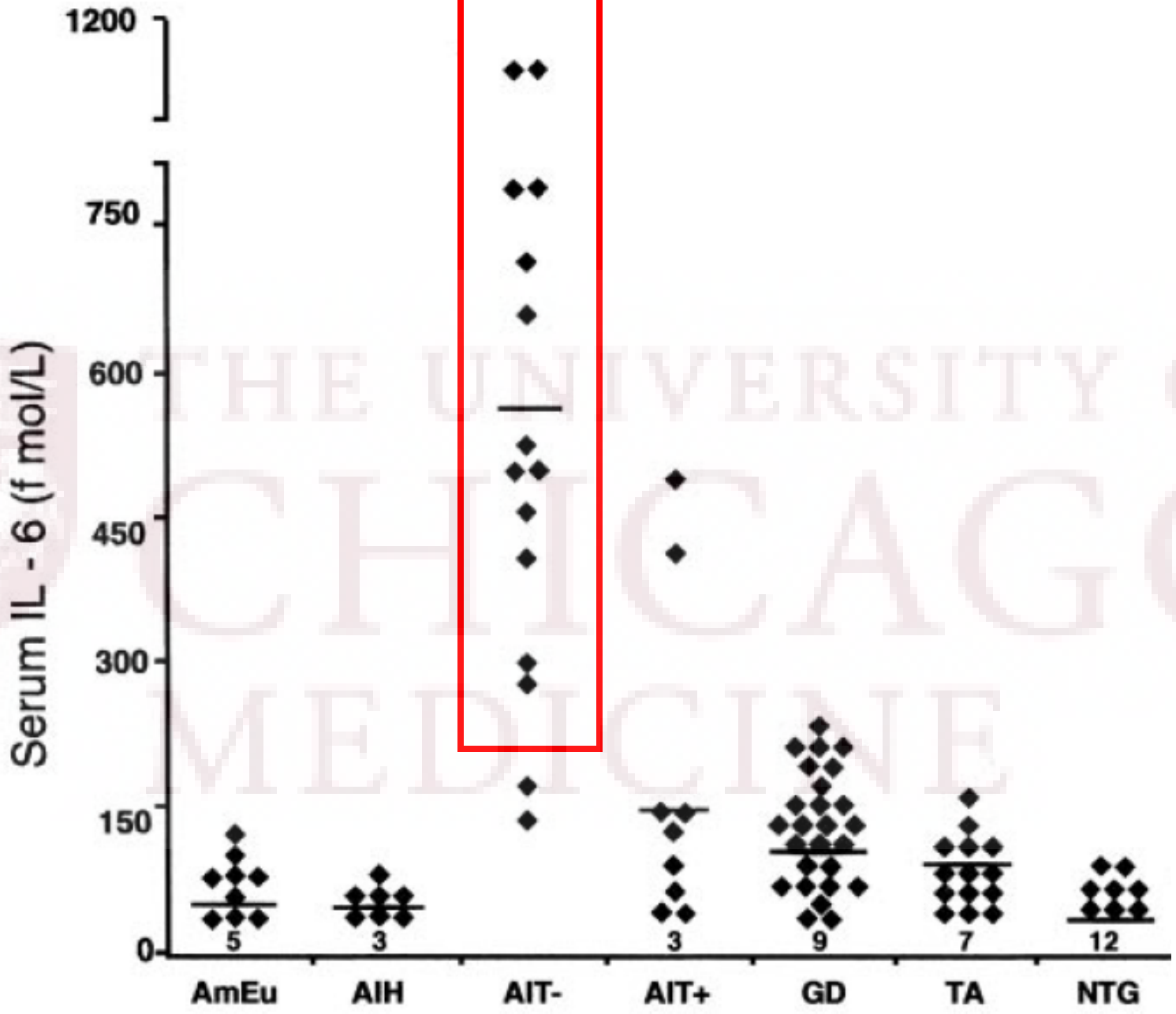
Cardenas GA et al. CCJM 2003;70(7):624-631.



JCEM 2010. Approach to AIT.

Significance of IL-6 levels?

- JCEM 1994
- Cross-sectional study:
  - 27 AIT (15 AIT+/12 AIT-)
  - 14 euthyroid on amiodarone
  - 10 AIH
  - 56 with hyperthyroidism (Graves/adenoma)
  - 50 controls
- Implications for treatment


Serum IL - 6 (f mol/L)
1200
750
600
450
300
150
0
5
3
3
9
7
12
AmEu
AIH
AIT-
AIT+
GD
TA
NTG

Take home points

- Type I AIT- iodine-induced excessive thyroid hormone synthesis, underlying abnormal thyroid.
  - Treatment: thionamides
- Type II AIT- destructive thyroiditis, normal thyroid.
  - Treatment: glucocorticoids
- IL-6 can be a useful marker

References

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