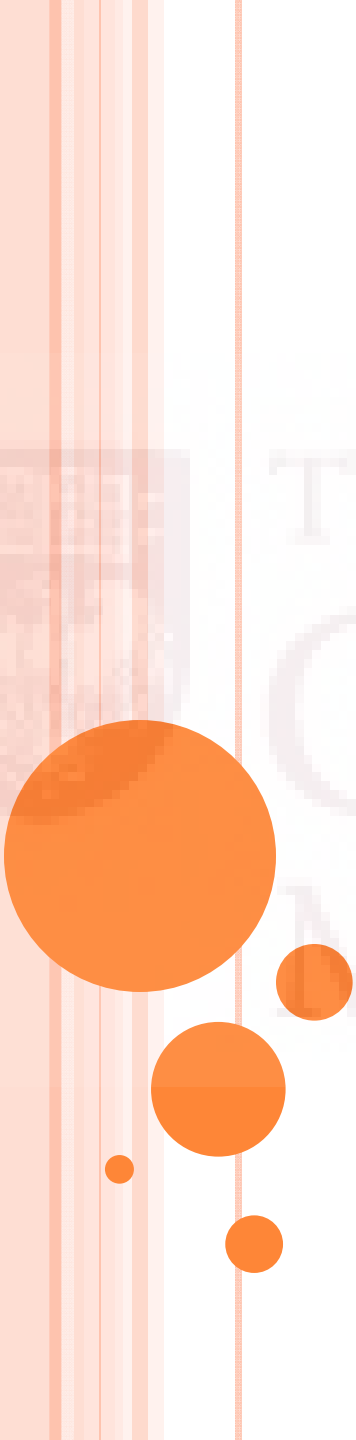




38 YO W/CROHN'S, ADRENAL INSUFFICIENCY, GRAVES' DISEASE, WITH A THYROID NODULE

Jess Hwang
Endocrinology Fellow
October 31, 2013

HISTORY OF CROHN'S/ IATROGENIC ADRENAL INSUFFICIENCY

- Diagnosed in 1990s with Crohn's
- Frequent flares → colectomy with ileostomy
- Multiple course of Prednisone (>30 mg) over years
- In 2011, he had been weaned off Prednisone 10 mg over 2-3 weeks and presented with nausea/vomiting
- In 7/2012, doing well on Hydrocortisone 10/5 mg daily. Held PM dose, had 8AM labs:
 - ACTH 26.2 (RR 7.2-63.3), Cortisol 1.6 (RR 2.3-19.4)



- PMHx

Crohn's dx 1990

Shingles 1998

Multiple abscesses-
Crohn's

2° adrenal
insufficiency

Vitamin D deficiency

Vitamin B12
deficiency

- SHx

No smoking, EtOH

Lives with girlfriend

Journalist

- FHx

No autoimmune
disease

No cancer

No thyroid disease

No diabetes

- Medications

CaCo3 1250 mg BID

Hydrocortisone 10/5

Vit B12

Vit D

Iron



MORE HISTORY

- 12/2012 admitted for parastomal hernia, conservatively managed
- Readmitted in 1/2013 with SBO requiring ex-lap, LOA, resection of distal ileum and ileostomy revision
- Discharged on Hydrocortisone 40/20 mg
- Many attempts to wean HC unsuccessful
- +hypersomnolence, fatigue, dizziness
- HR 121 in clinic



PHYSICAL EXAM

- Vitals: 107/91, 121, BMI 23
- Gen: chronically ill-appearing
- HEENT: no exophthalmos
- Neck: mildly enlarged thyroid, no palpable nodule, +bruit
- CV: tachycardic, no murmur
- Pulm: CTAB
- GI: +ostomy bag, soft, non-tender
- Ext: no edema
- Neuro: +normal reflexes
- Psych: slightly anxious



LABS

140	103	12	99	8.8	15.9	390
3.5	22	1.0				
			9.2	42		

7.7	4.2
0.7	84
31	41

Vit B12 606

25-OH Vit D37

TSH 0.01 (RR 0.3-4)

FT4 3.22 (RR 0.9-1.7)

TPO Ab 5120, Tg Ab 2560

TSIg 2.0 (RR <1.3)

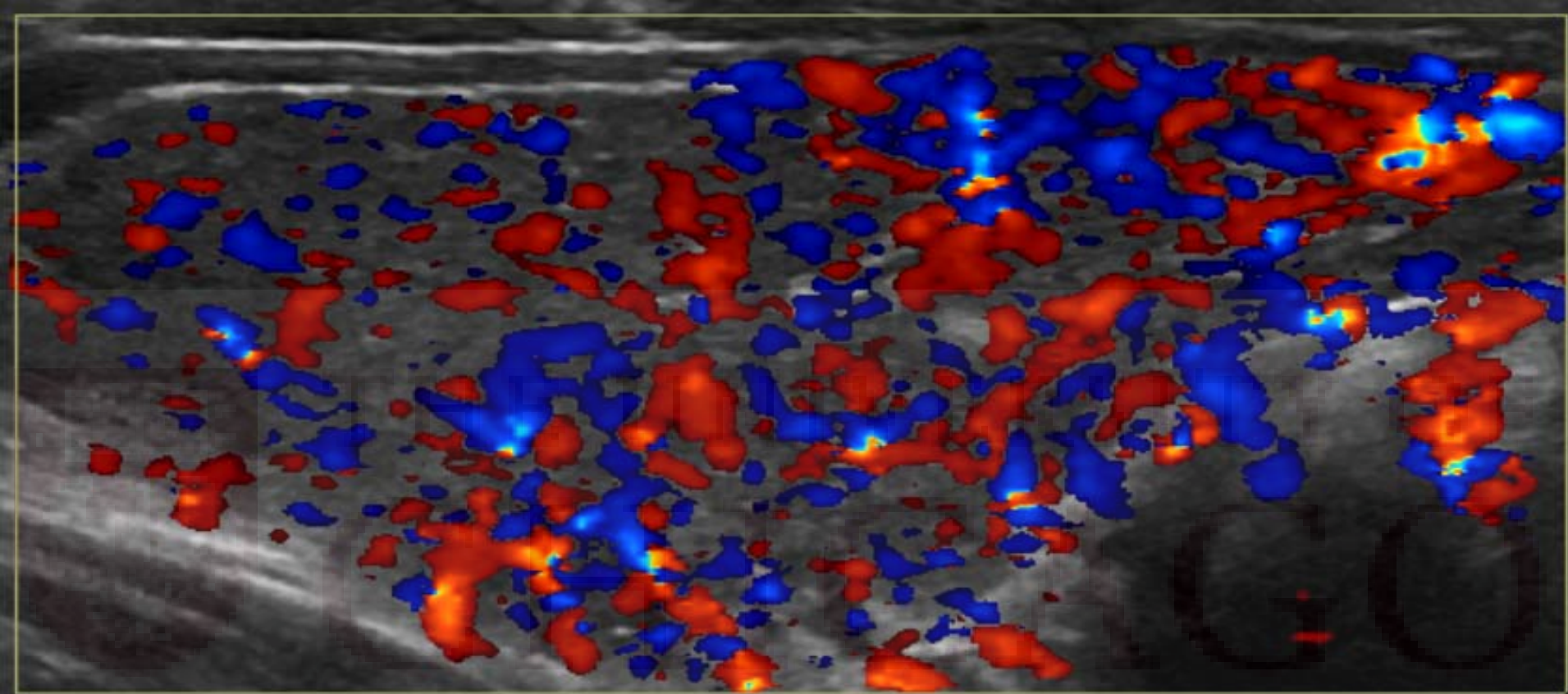


GRAVES' DISEASE TREATMENT

- Since he was so symptomatic he was started right away on Methimazole
- No RAIU and scan since he was MMI
- Thyroid US ordered

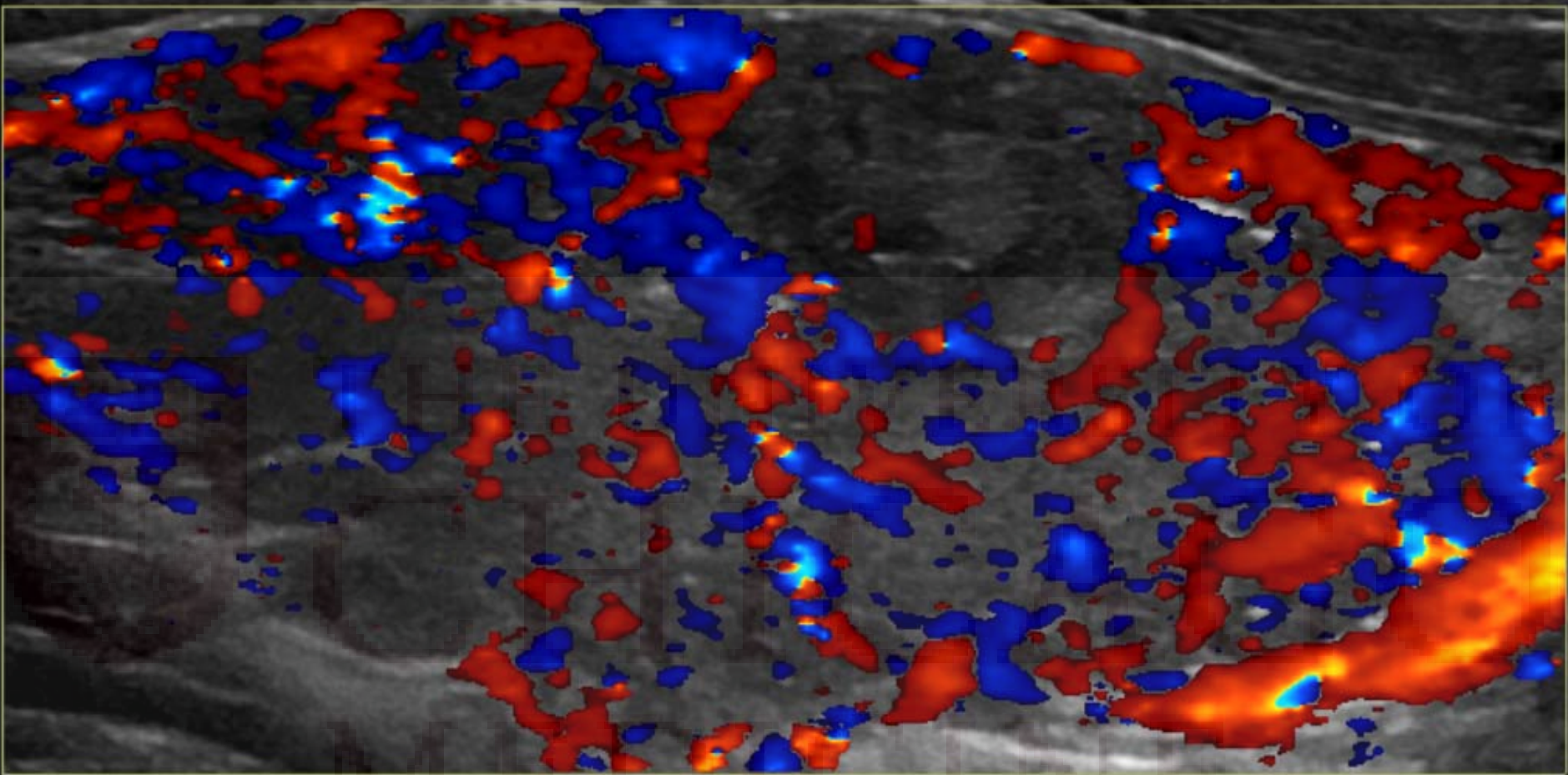
THYROID ULTRASOUND

- R LOBE: 5.6 x 1.9 x 2.4 cm.
 - L LOBE: 5 x 2 x 2.8 cm.
 - ISTHMUS: 0.5 cm.
- 



Extremely coarse texture, extreme hypervascularity.

LONG RT LOBE

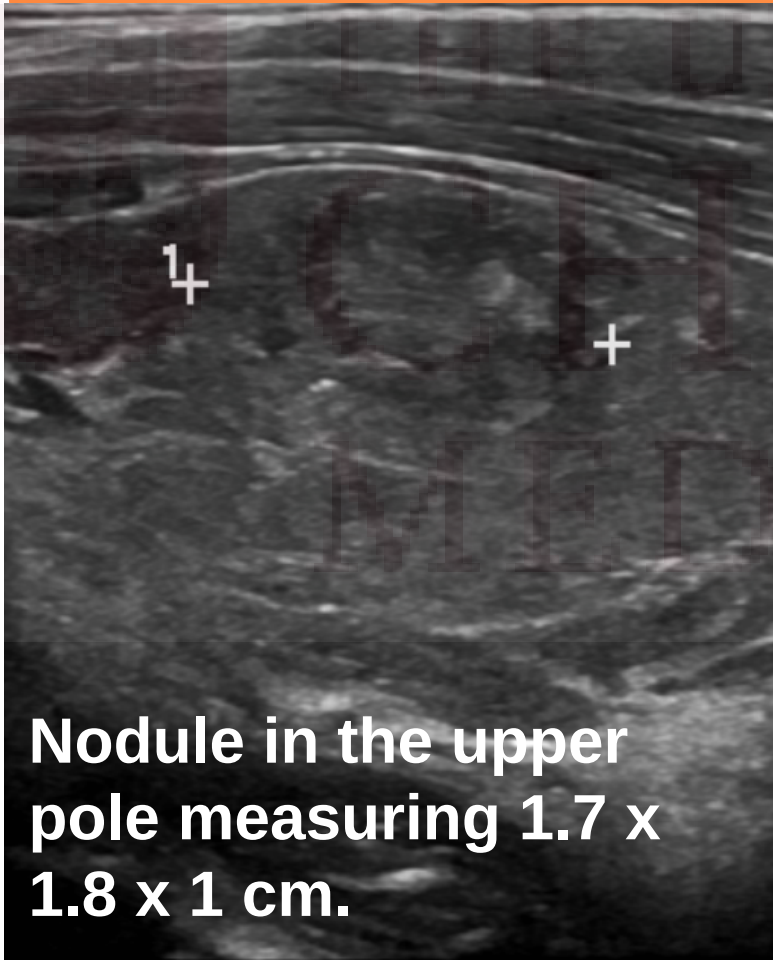


Extremely coarse texture, extreme hypervascularity

LONG LT LOBE

THYROID ULTRASOUND

Long



Trans



L THYROID NODULE FNA

- Papillary carcinoma
- Euthyroid on MMI
- Referred to Endo Surgery- Dr Grogan

TOTAL THYROIDECTOMY- 26.9 GM.

- Metastatic papillary thyroid carcinoma (TMN Staging: pT2(m), N1a) in 1/1 Level VI lymph node.
 - Unencapsulated. Margins: Uninvolved.
 - Multifocal (L lobe 2.3 cm, isthmus (0.6 cm, 0.4 cm)
 - Hyperplastic nodule (1 cm, right lobe).
- 

POST-OP COURSE

	POD #0	POD #1	POD #11	POD #14
Calcium	8.6	7.8	6.4	7.3
PTH	9	9	27	
Albumin	4.2			4.2

- Discharged home on CaCO_3 1000 mg BID
- Calcitriol added POD #7 because of symptomatic hypocalcemia
- Planning for radioactive iodine



Clinical Concepts/Questions

- Corticosteroid withdrawal syndrome vs adrenal insufficiency in IBD patients in remission
- Thyroid cancer in Graves' Disease
 - Prevalence/Prognosis
 - Pre-op optimization



CORTICOSTEROID WITHDRAWAL SYNDROME

- Symptoms + HPA suppression
- Relapse of disease for which drug was originally prescribed
- Physical/psychological dependence (no HPA suppression)
- HPA suppression but no symptoms



CORTICOSTEROID WITHDRAWAL SYNDROME IN IBD

- 2 main reasons:
 - GI sx, making it difficult for the clinician to distinguish between a flare of IBD and CWS.
 - CWS is difficult to differentiate from AI.
- By dissociating CWS (by clinical evaluation) and adrenal reserve (by cosyntropin stim), a more determined approach to weaning could be performed



CORTICOSTEROID WITHDRAWAL SYNDROME

- **AIM:** assess the effectiveness of a corticosteroid withdrawal method
- **METHODS:** 12 patients w/IBD- quiescent disease transitioned to PO dexamethasone, educated about symptoms and weaned. When patients failed a slow wean and their IBD remaining quiescent, low dose synthetic ACTH stimulation test was done
- **RESULTS:** 10 patients (83%) were successfully weaned after a median f/u from final wean of 38 months (range 5-73). Disease flares occurred in 2 patients, CWS in 5 and ACTH testing was performed in 10. Longer duration of corticosteroid use was associated with a slower wean.

								Disease duration (years)	Dependency period (years)	Average prednisone dose (mg/day)	Weaning time (months)	Follow-up duration after final steroid course (months)
Age	Gender	Year of diagnosis	IBD	Disease location	Previous Surgery	Other medications	BMI					
75	M	1954	UC	Pancolitis	Left hemi-colectomy (LGD)	Data not available	25.0	45	45	13.5	32	43
75	M	1966	CD	Jejunoeileitis, colitis	Multiple ileal and ileocolic resections	Antibiotics Infliximab	19.9	35	10	ACTH 240 units/week	26	39
59	M	1966	CD	Ileitis, perianal	Ileocolic resection ×4	MP	20.6	37	20	10.5	–	–
49	M	1971	CD	Jejunoeileitis, colitis	Ileocolic resection ×3	Antibiotics MP Methotrexate Infliximab	23.2	34	13	12.5	11	15
54	M	1976	CD	Ileitis	Ileal resection ×2	MP Infliximab Adalimumab	17.7	25	21	11	49	31
48	M	1976	CD	Ileocolitis	Ileocolic resection	MP Infliximab	21.9	26	26	15	–	–
53	M	1982	UC	Left-sided colitis	TPC and IPAA	AZA Infliximab	30.7	17	17	12.5	41	48
54	M	1986	UC	Left-sided colitis	TPC and IPAA; pouch excision and end ileostomy	Antibiotics MP	27.1	17	15	5	18	37
29	F	1997	UC	Pancolitis	–	MP Cyclosporin	28.5	6	5	5	12	43
35	F	1998	CD	Jejunoeileitis, colitis	–	Antibiotics MP	22.5	3	3	10	6	73
71	M	2002	UC	Procto sigmoiditis	–	MP Infliximab	25.3	4	4	22.5	7	5
48	M	2003	UC	Left-sided colitis	TPC and IPAA	MP Cyclosporin Infliximab	21.3	4	2	20	4	13
53.5							23.6	21	14	12.5	15	38

Prevalence of Thyroid Cancer + GD

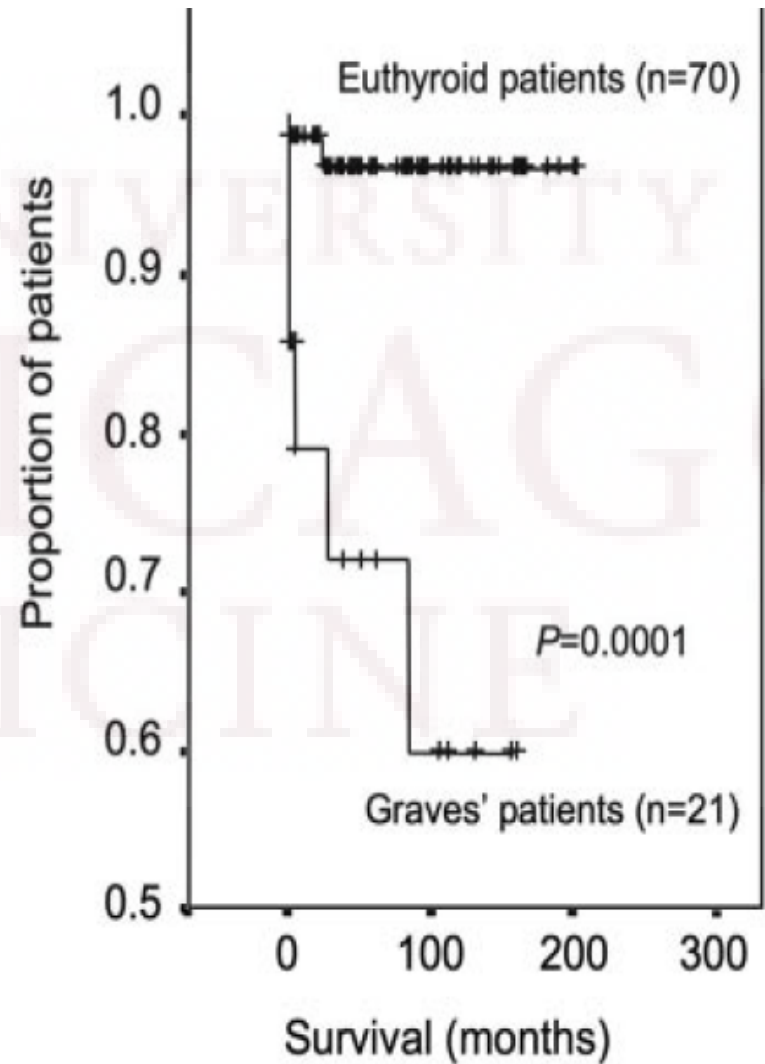
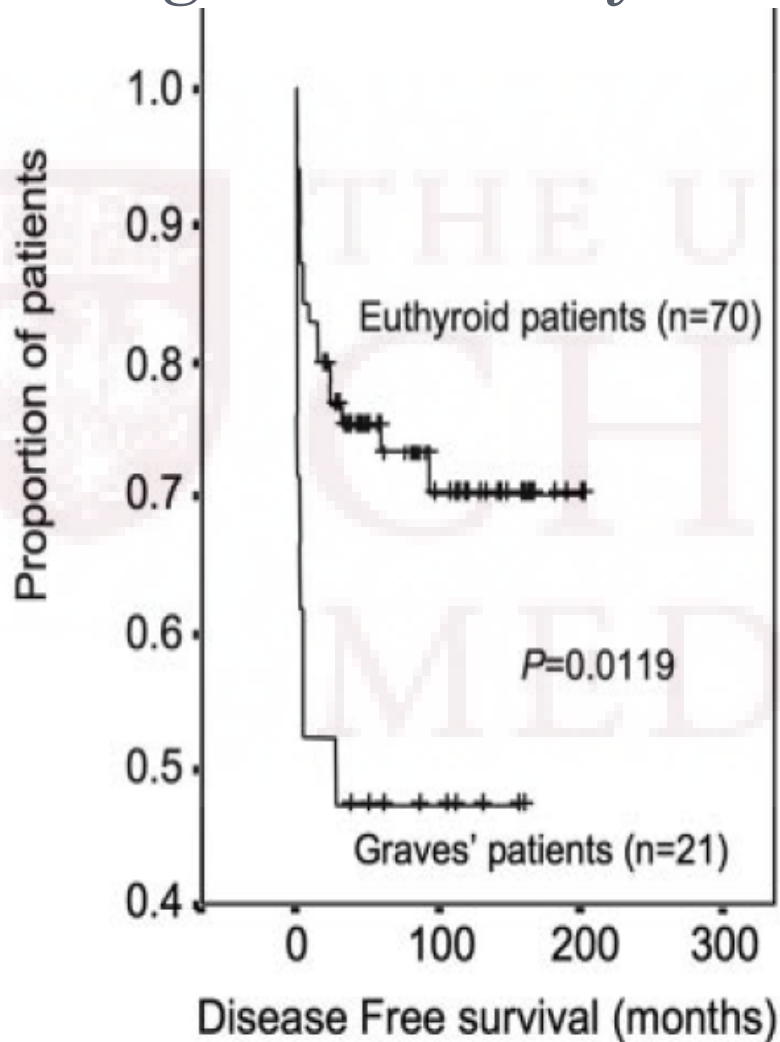
- 103 cases of thyroidectomy for GD...
 - Well-differentiated papillary carcinomas coexist w/GD in 8% cases
 - 35% occur when there is concurrent palpable nodule
 - 88% of coexisting carcinomas are microcarcinomas



Prognosis of Thyroid Cancer and GD

- **Objective:** to investigate the long-term mortality of nonoccult DTCs in GD vs matched euthyroid controls.
- **Patients and Design:** nonoccult DTCs occurring in GD (DTC-GD, n21) or matched euthyroid DTC controls (n70) after f/u (median, 165.6 m). Clinical endpoints of persistent/recurrent disease and overall survival.
- **Results:** Persistent/recurrent disease was more frequent in GD vs controls (P .0119). Disease-specific mortality was significantly higher in GD (6 of 21, 28.6%) vs controls (2 of 70, 2.9%) (P .0001). At the last visit, the % of disease-free was 57.1% (12 of 21) GD vs 87.1% (61 of 70) control (P .0025).

Prognosis of Thyroid Cancer and GD



Prognosis of Thyroid Cancer and GD

Outcome	Patients With GD (n = 21)	Euthyroid Control (n = 70)	P Value
Dead, n (%)	6 (28.6)	2 (2.9)	.002 ^a
Patients with persistent disease, (%)	3 (14.3)	7 (10)	NS
Detectable Tg	3 (14.3)	2 (2.9)	
Lymph nodes metastases		4 (5.7)	
Distant metastases		1 (1.4)	
Disease-free	12 (57.1)	61 (87.1)	.0025 ^b

Nonoccult DTCs in GD cause increased disease-specific mortality warranting early diagnosis and aggressive treatment



Pre-op optimization

- **Objective:** prospective clinical trial to evaluate thyroid blood flow and microvessel density in GD receiving Lugol solution treatment preoperatively.
- **Method:** 36 patients randomly assigned to receive (n 17)/or not receive (n 19) preop treatment with Lugol solution
- **Main Outcome Measures:** Thyroid blood flow was measured by ultrasonography. Microvessel density was assessed by through CD-34 expression in thyroid tissue. Weight and blood loss were measured.



Pre-op Optimization

	Group 1 (n = 17) (before Lugol solution treatment)	Group 1 (n = 17) Lugol solution (+)	Group 2 (n = 19) Lugol solution (-)
Age (yr)	40.7 ± 10.9	40.7 ± 10.9	42.9 ± 11
Gender (female/male)	14/3	14/3	16/3
FT ₃ (pmol/liter)	4.4 ± 0.8	4.3 ± 0.6	4.2 ± 0.6
FT ₄ (pmol/liter)	14.3 ± 1.9	13.8 ± 1.9	14.7 ± 2
TSH (mIU/liter)	2.09 ± 1.1	1.9 ± 1.06	2.4 ± 1.2
Anti-TPO (IU/ml)	243.34 ± 71	233.58 ± 64	236.52 ± 71
TRAb (IU/ml)	254.56 ± 66	276.56 ± 57	282.88 ± 53
PTU treatment (n)	9	9	11
MMI treatment (n)	7	7	9
Thyroid gland volume (ml)	49 ± 29	48.2 ± 29.4	51.5 ± 29
Blood flow (ml/min)	138.37 ± 50	74.7 ± 26 ^b	128.62 ± 42 ^a
RI (%)	0.40 ± 0.03	0.60 ± 0.02 ^b	0.40 ± 0.01 ^a
MVD (no. of vessels/×400 field)		55.38 ± 17	122.25 ± 39 ^a
CD-34 expression by Western blot analysis (U)		53.30 ± 5.8	108.31 ± 16 ^a
Intraoperative blood loss (ml)		54.4 ± 22	108.68 ± 54 ^a

2 mechanisms: decreased angiogenic stimuli and decreased blood flow

TAKE HOME POINTS

- There is a need for prospective weaning protocols for chronic glucocorticoid users
- The prevalence of PTC might be slightly higher in GD
- GD patients with PTC seem to have a worse prognosis than non-GD patients
- Before thyroidectomy, GD patients should receive SSKI to minimize bleeding



REFERENCES

- Gerenova J et al. Prevalence of Thyroid Cancer in Graves' Disease: a retrospective study of a cohort of 103 patients treated surgically. Eur J of Int Med 2003;14:321-325.
- Pellegriti G et al. Increased Mortality in Patients With Differentiated Thyroid Cancer Associated With Graves' Disease. J Clin Endocrinol Metab 2013;98:1014–1021.
- Murphy SJ. Withdrawal of Corticosteroids in Inflammatory Bowel Disease Patients after Dependency Periods Ranging from 2-45 years: a Proposed Method. Aliment Pharmacol Ther 2009 Nov 15;30(10):1078-86.
- Erbil Y et al. Effect of Lugol Solution on Thyroid Gland Blood Flow and Microvessel Density in the Patients with Graves' Disease. JCEM 2007;92:2182-2189.



ADRENAL INSUFFICIENCY IN IBD

- **OBJECTIVES:** to assess the prevalence and severity of fatigue in IBD patients in remission
- **COHORT:** 80 subjects w/ IBD and 67 healthy age-/sex-matched controls
- **METHODS:** To evaluate adrenocortical reserve in subjects with a cortisol level of 0.4 mol/L, a low dose adrenocorticotrophin hormone test was performed.
 - Disease activity -Clinical UC/CD Activity Index
 - QOL- Inflammatory Bowel Disease Questionnaire
 - Fatigue- Multidimensional Fatigue Inventory (MFI)
- **RESULTS:** >40 % of the IBD patients in remission suffered from fatigue. No correlation was found between fatigue and basal cortisol levels or other laboratory parameters.



ADRENAL INSUFFICIENCY IN IBD (IN REMISSION)

- ***Low Dose ACTH Stimulation Test:*** Of all patients participating in this study, 21 patients had a plasma cortisol level less than 0.4 mol/L.
 - 9 were excluded b/c of protocol violation (steroids administration within 12 months before the test, cortisol level taken after 9:00 AM). 2 patients were lost to f/u.
 - 9 patients (6 CD, 3UC; 2F/7M) underwent cosyntropin stim test- all showed an appropriate response to *i.v.* administration of ACTH (mean peak level 0.73 mol/L, range 0.57 mol/L to 0.87 mol/L; mean rise compared with basal plasma cortisol 0.29 mol/L, range 0.10 mol/L to 0.40 mol/L).

