

Autoimmune Endocrine Disorders

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The Spectrum

- Thyroid: Hashimotos: Goiter
 - Hypothyroidism
 - Hashitoxicosis
 - Postpartum thyroiditis
- Graves disease: Hyperthyroidism
 - Thyroid ophthalmopathy
- Islet cells: Type 1 DM
- Adrenal: Addisons

- Parathyroid: Hypoparathyroidism
- Pituitary: Autoimmune hypophysitis (postpartum 2nd adrenal insufficiency)
 - Diabetes insipidus
- Gonads: Premature ovarian failure
 - Male hypogonadism



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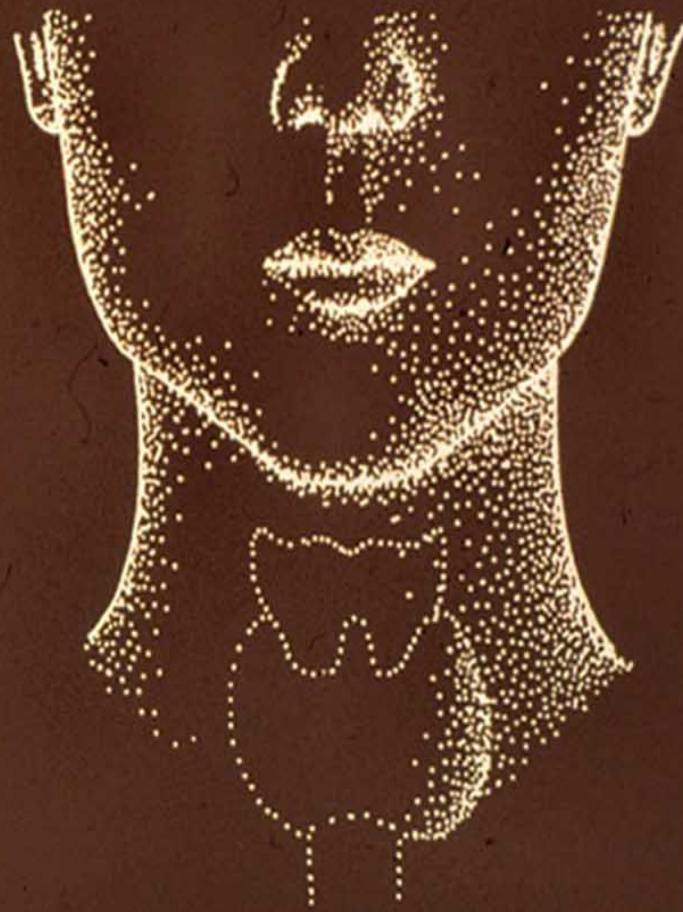
Autoimmune Disorders Hang Out Together

- Vitiligo
- Alopecia areata
- Pernicious anemia/atrophic gastritis
- Celiac disease (15% Type 1 DM)
- Lupus, RA, Sjogrens
- MS, Myasthenia
- ITP
- Autoimmune hepatitis, pancreatitis

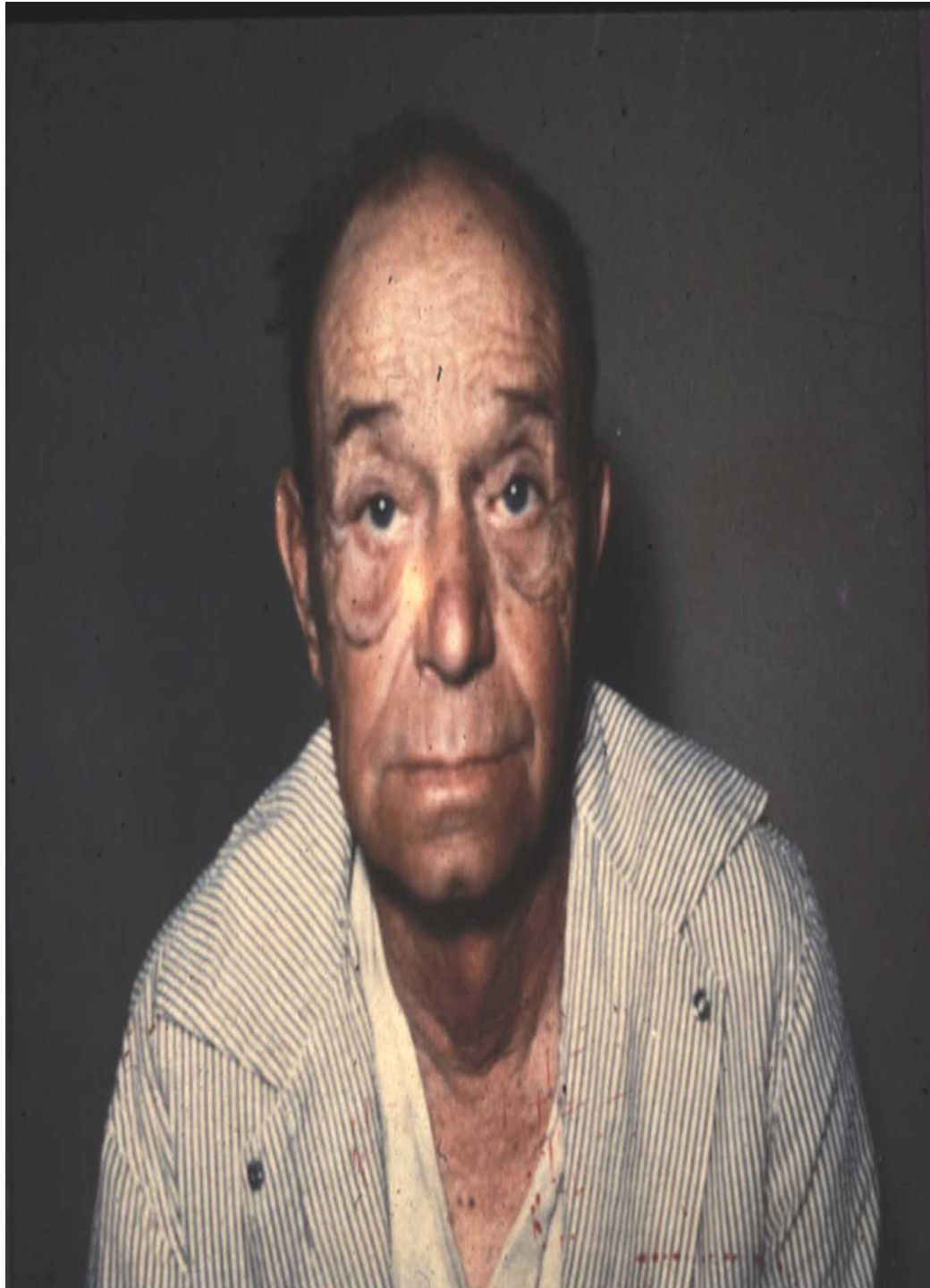


- TSH 92
- FREE T4 .7
- + Anti-TPO and Anti-thyroglobulin antibodies

- DTRs: delayed relaxation
- Thyroid enlarged



**Note shadow after
patient swallows**



THYROID REPLACEMENT

- AVERAGE REPLACEMENT : .7ug/lb.
- 150 lbs. : $150 \times .7 = 100\text{ug}$ or .1mg.
- ELDERLY REQUIRE LESS (25-50 ug. less)

Which of the following interferes with thyroid absorption?

- Food
- Iron
- Calcium
- Coffee
- All of the above



**Unstable
elderly patient
beginning daily
levothyroxine
dose:**



25 μg

or



12.5 μg

What about T3 Rx.?

- Subset of patients may not be able to convert T4 to T3 efficiently (deiodinase deficiency)
- Can give trial T3 5mcg qd -5 mcg bid(10 mcg T3 = 50mcg T4)
- ? Armour thyroid – cannot use T4 assay to follow but can titrate dose with TSH levels

Prefer not to use in the elderly

30 yo woman on thyroid
replacement calls to inform you she
is 6 weeks pregnant.

TSH 6 months prior: 2.5

.137 mg. T4

Pregnancy: Estrogen increases TBG (Thyroid binding globulin)

- Fetus needs adequate T4 from mom
- Goal: TSH < 2.5
- Increase dose by 30 %-2 extra pills/week or increase dose from .137 to .175/d

78 yo woman

- TSH 6.8 (nl.: .4-4)
 - Less energy compared to when she was 50
 - Normal exam; no goiter.
-
- 1. Rx with low dose T4?
or
 - 2. Observe-repeat TSH in 1 year.

Subclinical Hypothyroidism

- **10-20% of the population 60 and above have subclinical hypothyroidism. (TSH 4-10)**

Of Those:

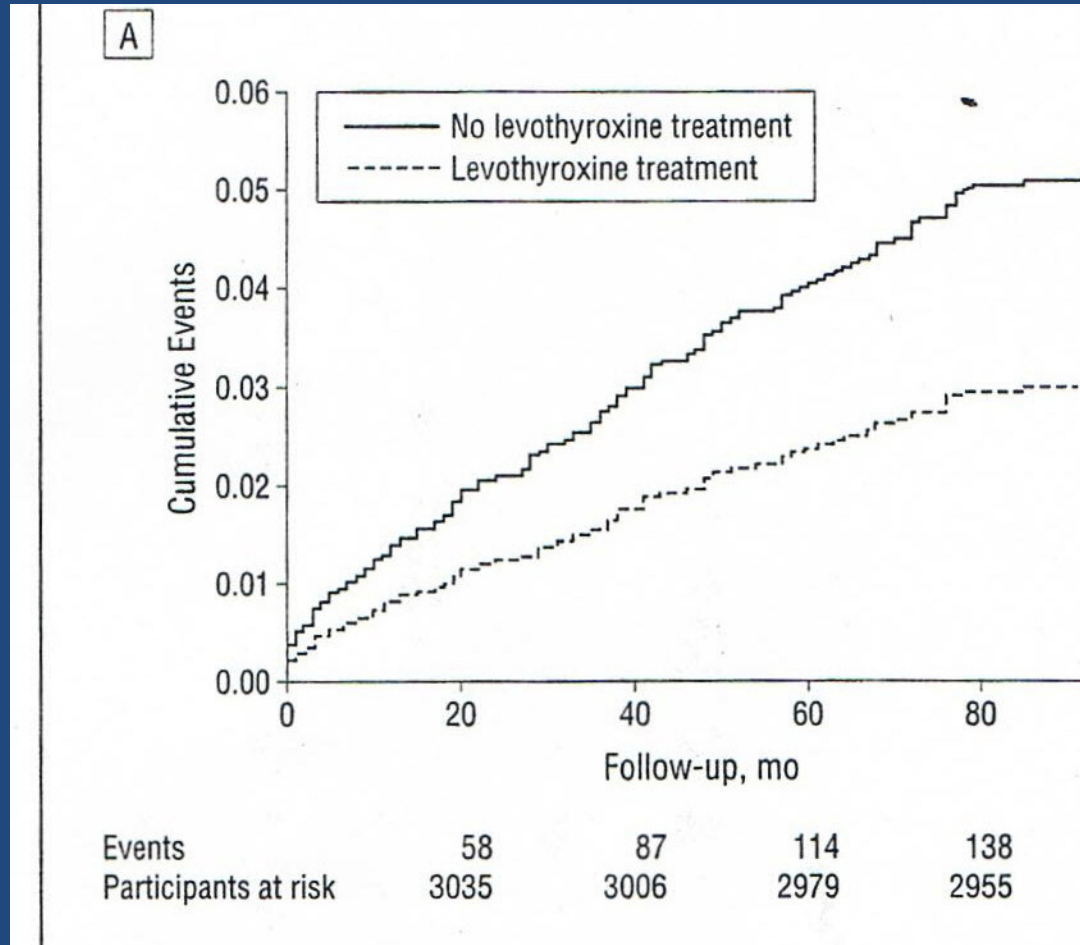
- **5% per year progress to overt hypothyroidism (more commonly if antibody +)**
- **In 20-50%, the TSH returns to normal**
- **The rest stay the same**

Subclinical Hypothyroidism – Development of Ischemic Heart Events on Rx

Young Patients 40 - 70 years

Older Patients >70

Subclinical Hypothyroidism - Age Under 70



No T4

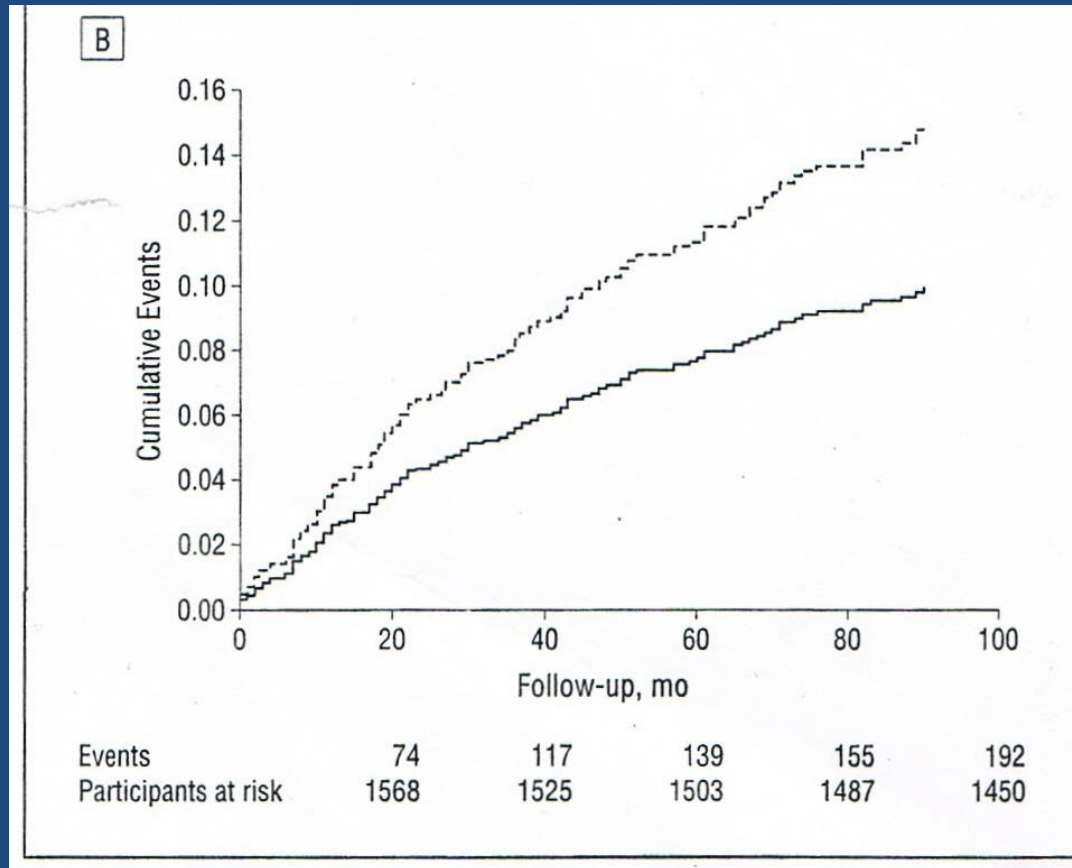
T4

Subclinical Hypothyroidism – Development of Ischemic Heart Events

Older Patients over 70 years

- 104 of 819 patients treated with thyroxine
- 88 of 823 untreated patients

Subclinical Hypothyroidism - Age Over 70



T4

No T4

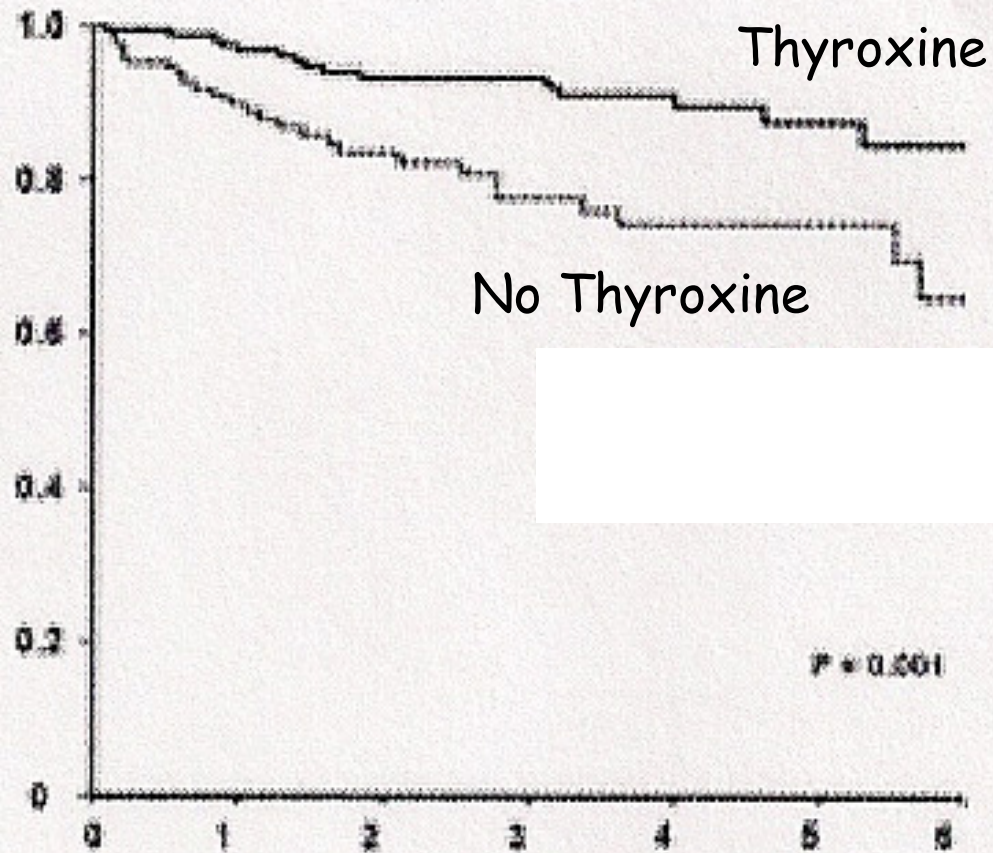
- Elderly women (> age 85) with mild TSH elevation correlates with longevity - in the municipality of Leiden the Netherlands mild TSH elevation was associated with lower cardiovascular and all cause mortality over 4 years (JAMA 2004 Dec1;292(21):2591-9)

Subclinical Hypothyroidism – Effects of Treatment on GFR

- Decrease in GFR 50% or progression to ESRD
- 180 patients treated with thyroxine and 129 patients without thyroxine
- Follow-up 34 +/- 24 months

HR for treatment = .28

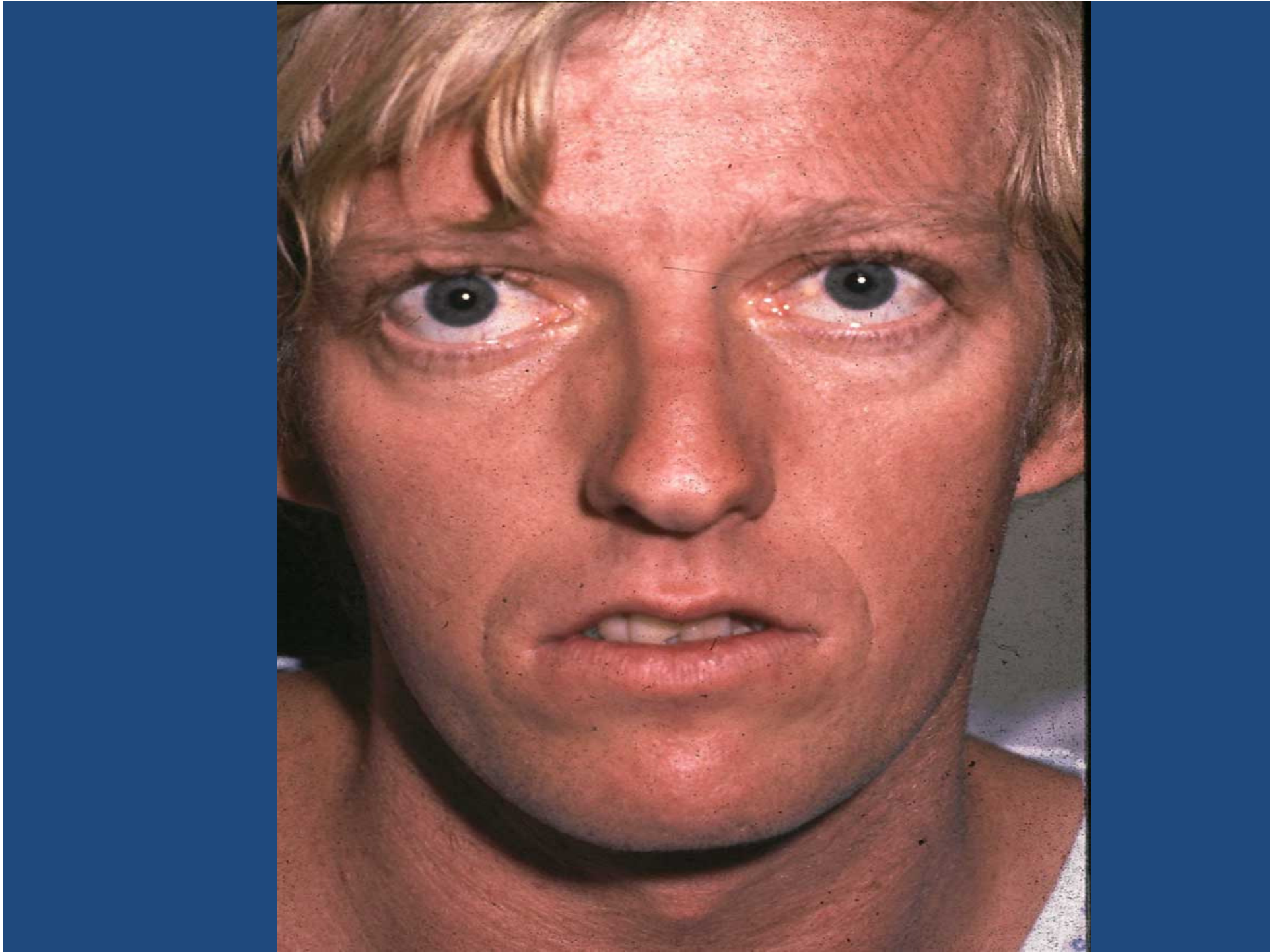
Renal event - free survival

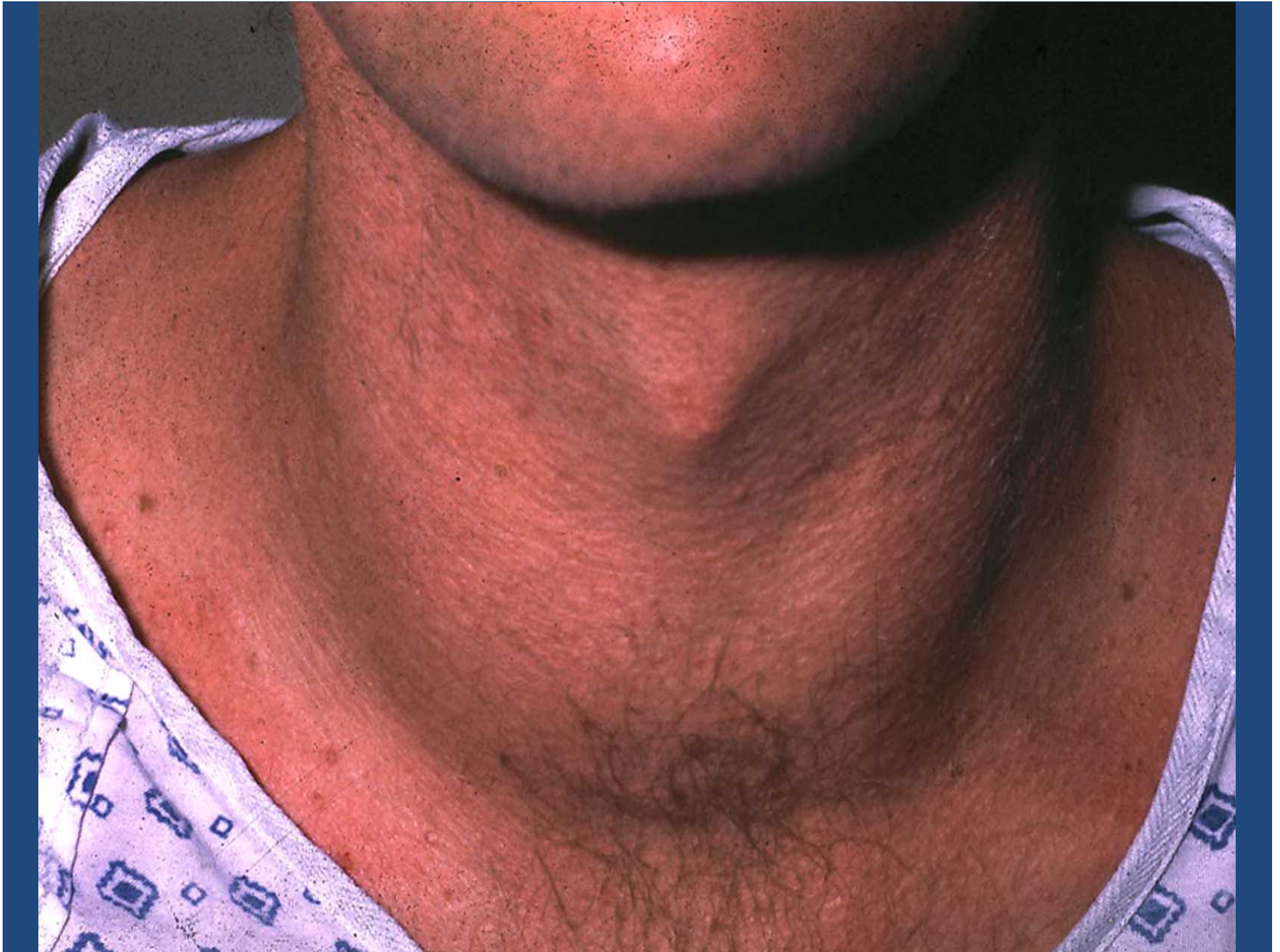


Duration (years)

Subclinical hypothyroidism: TSH 4-10

- Rx if younger and symptomatic, +antibodies
- T4 may exert a cardio protective effect in younger folks (<70)
- T4 may protect renal function in individuals with subclinical hypothyroidism and renal impairment
- Observation best in elderly









CARDINAL FEATURES OF GRAVES DISEASE

- HYPERTHYROIDISM WITH DIFFUSE HYPERPLASIA OF GLAND
- OPHTHALMOPATHY
- DERMOPATHY (PRETIBIAL MYXEDEMA)

Thyroid Stimulating Hormone

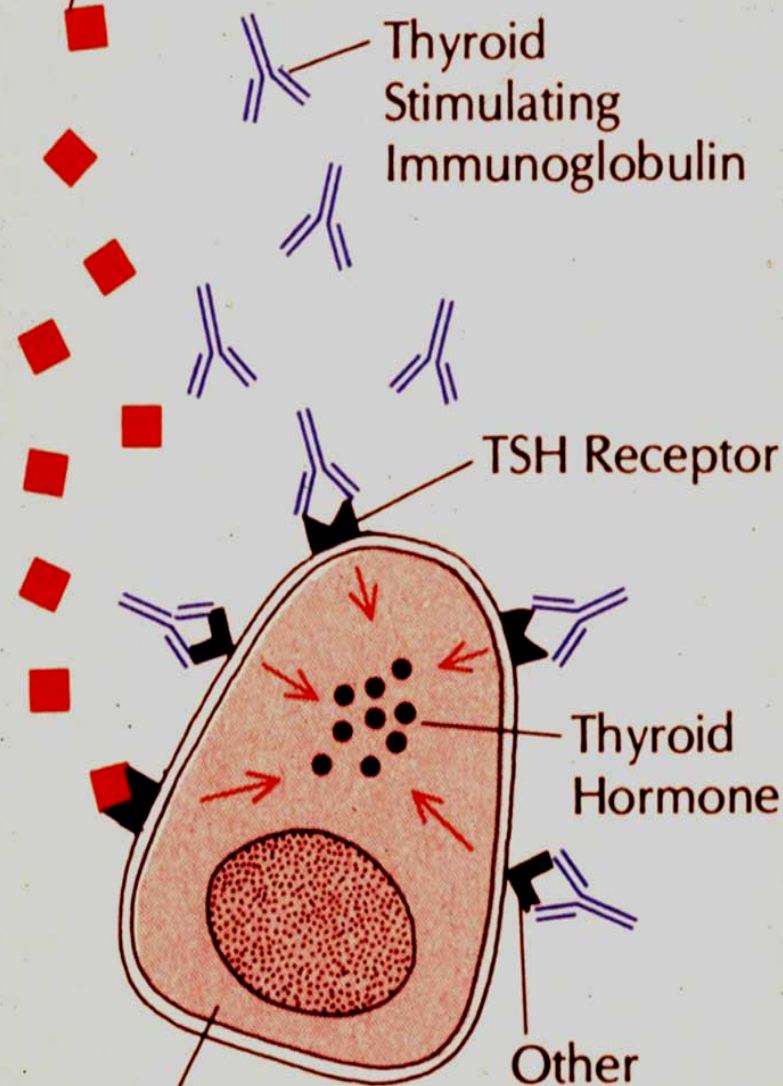
Thyroid Stimulating Immunoglobulin

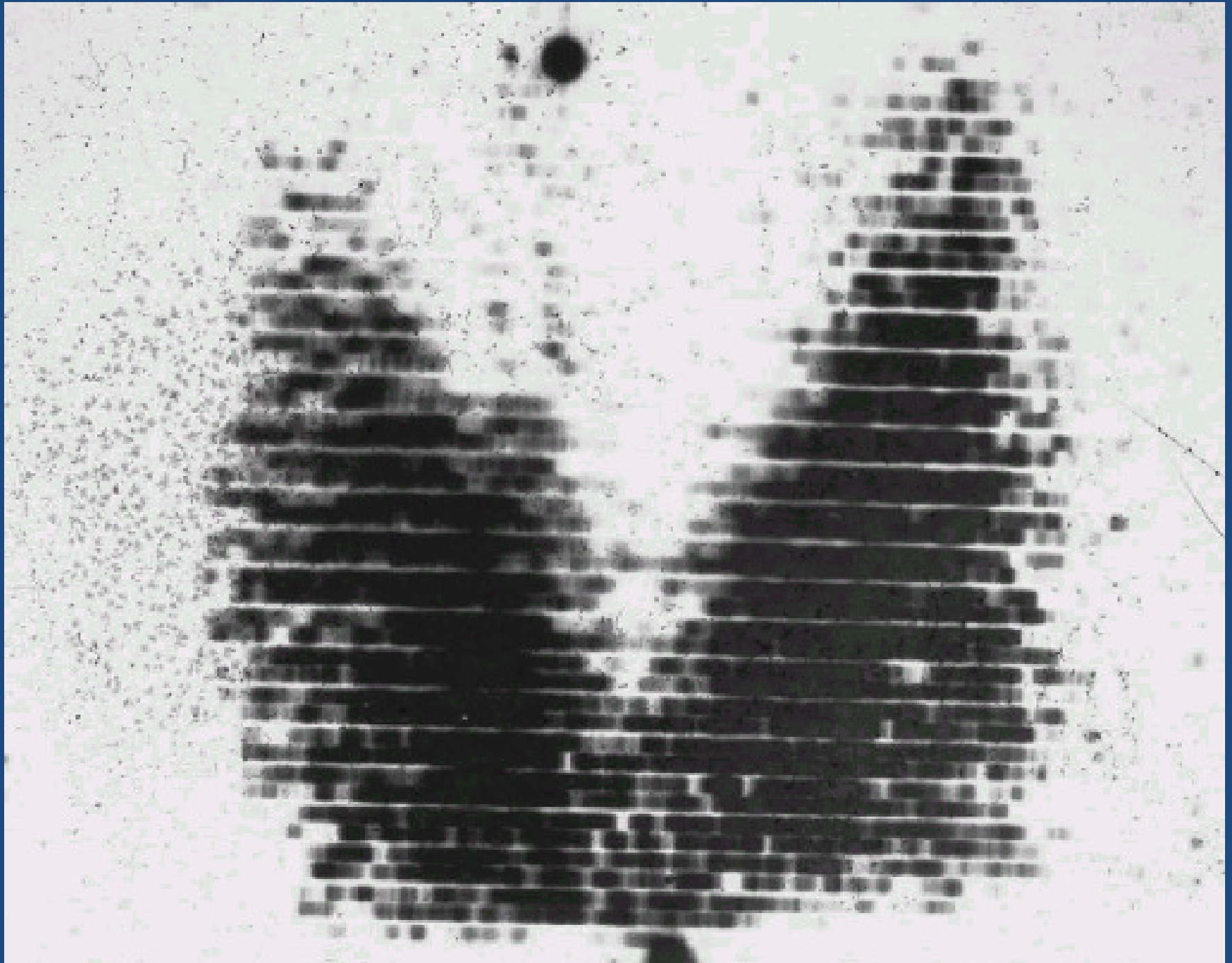
TSH Receptor

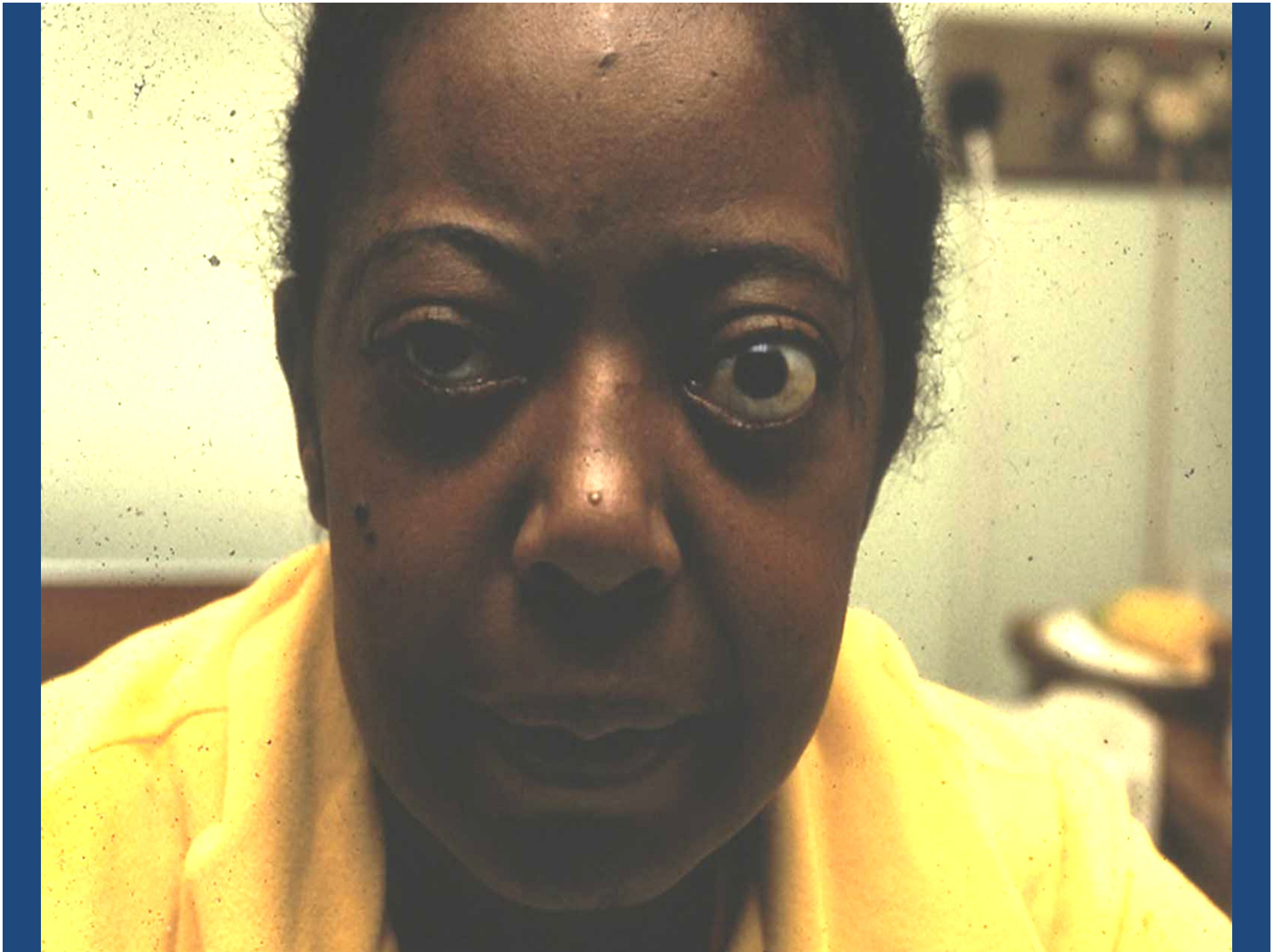
Thyroid Hormone

Other Receptor

Thyroid Cell









Diagnosing Graves

Clinical

Confirm: FT4, FT3, TSH

TSI (Thyroid stimulating immunoglobulin)

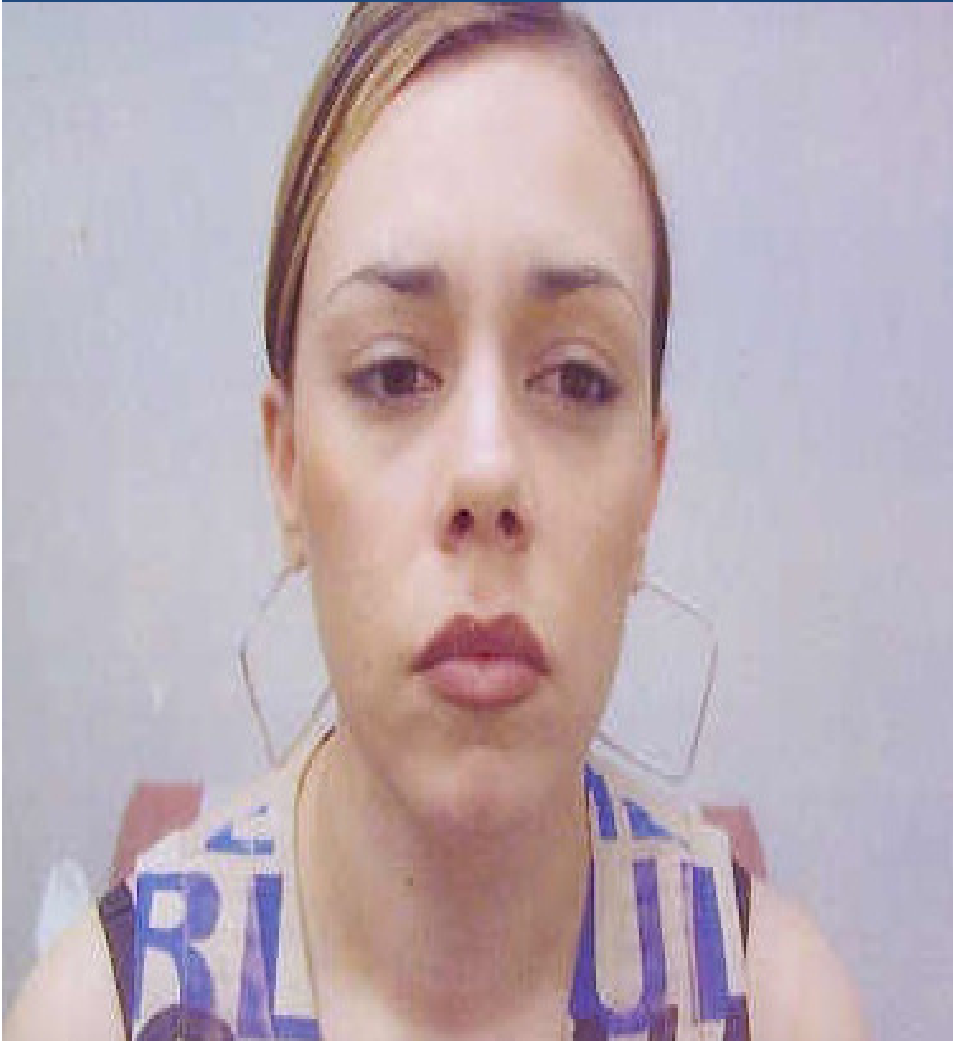
Usually do not need scan/uptake till I-131 RX

Treatment of Graves

- Methimazole/PTU (prefer methimazole except during pregnancy)
- I-131 Rx. except:
 - Pregnancy-always screen before I-131
 - Severely toxic/elderly
 - Active ophthalmopathy
- I-131: inform patient that it will destroy the thyroid and need for long term replacement; suspend antithyroid med prior but continue beta blocker; expect 6-8 weeks to work
- Methimazole : advise patient to call if rash/fever/severe sore throat/joint pains and document



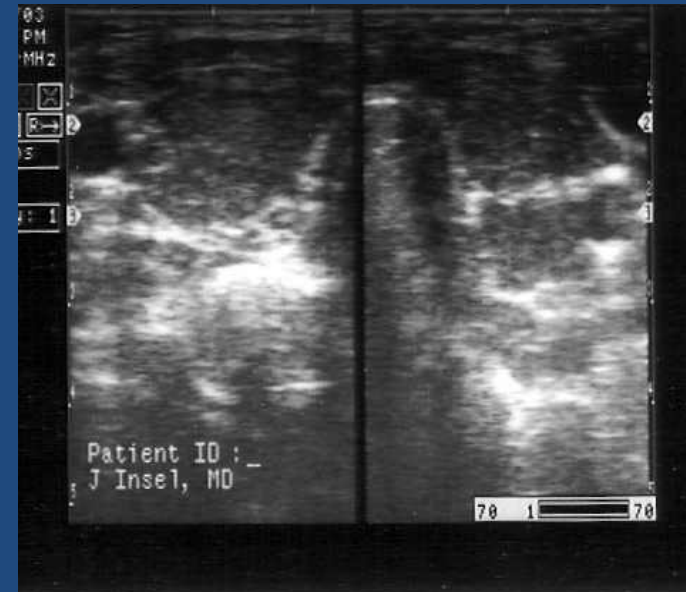
R.B.



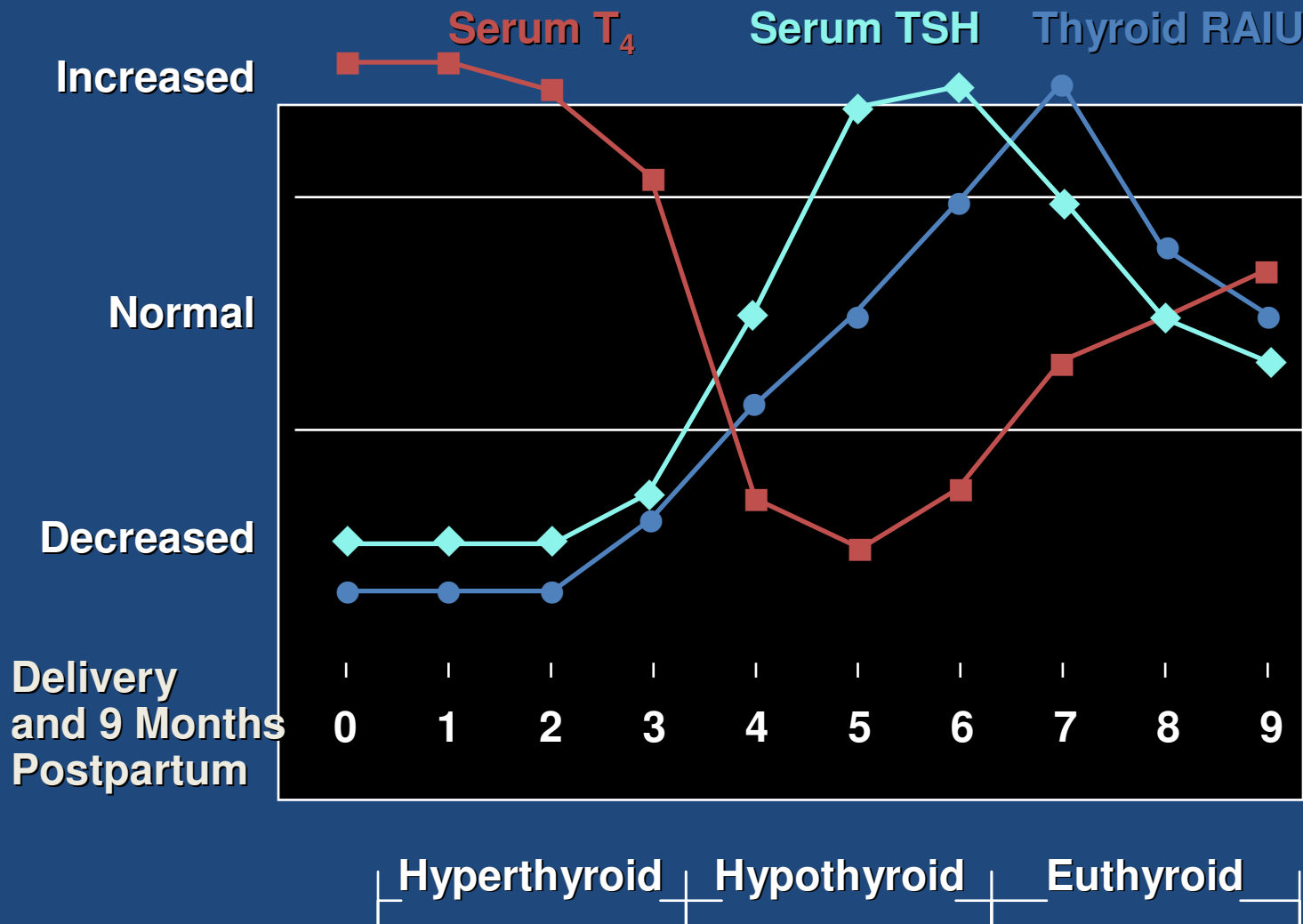
- 22 yo , 3 mos.old daughter
- “out of it”
- Rapid pulse, wt. loss, hyperventilation, shakiness
- 1/16: Free T4 3.4(.6-1.7)
- TSH .013
- 2/21: P 68
- Thyromegaly

RB

- Free T4 .37
- TSH 30.8
- ANTI-TPO 6681
- I-131 UPTAKE .6%



Clinical Course of Silent, Postpartum, and Subacute Thyroiditis



Subclinical hyperthyroidism:
usually multinodular goiter in
elderly

TSH < .1, nl FT4/FT3

Risk Atrial Fibrillation 3xs normal
(From 11% to 28%)

Risk of bone loss

Rx:Antithyroid Rx,Beta blockers,I-131

Type 1 DM: Autoimmune destruction of islet cells

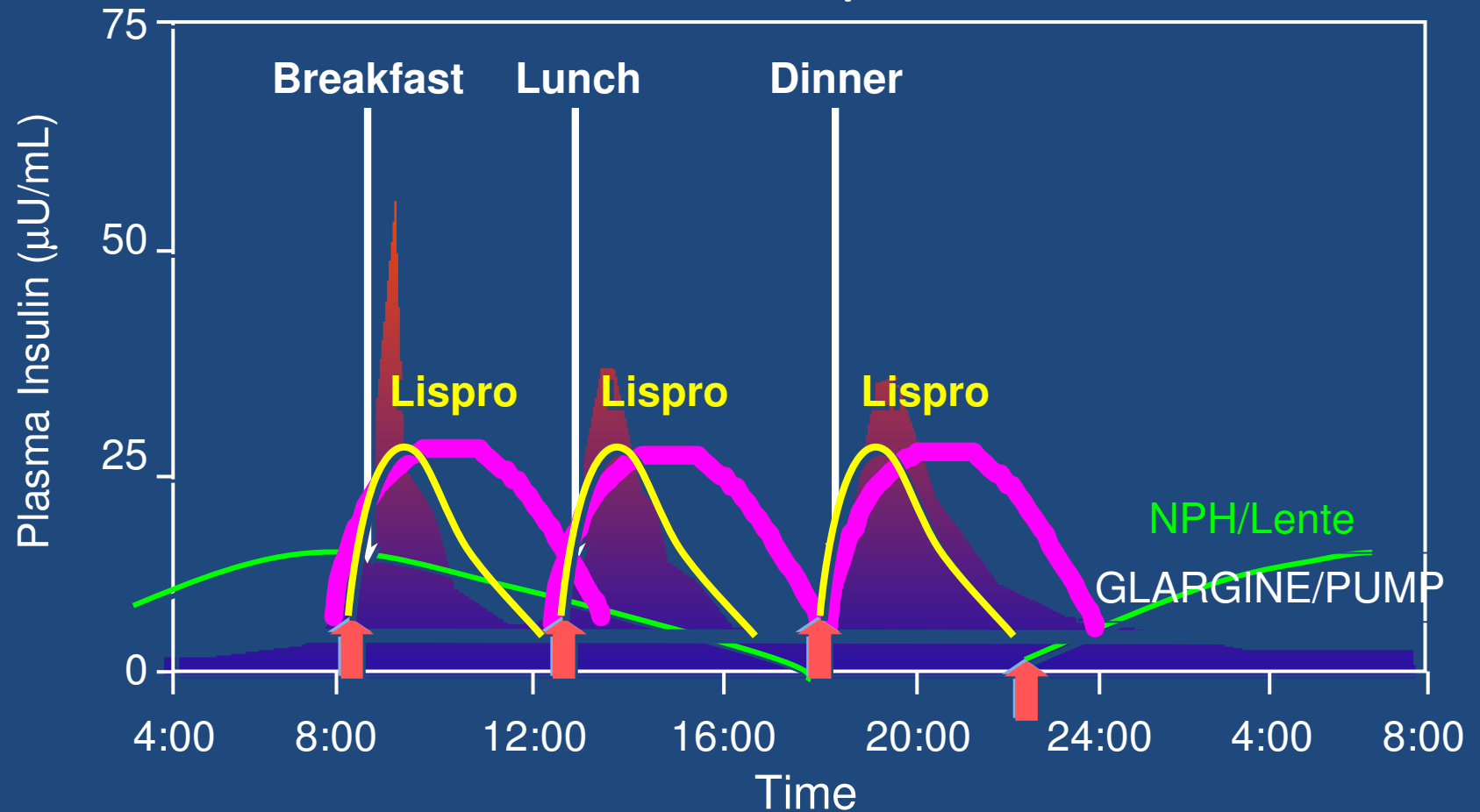
- Clinically: Polys, weight loss, visual blurring,
- Ketones- + urine/risk DKA
- Confirm by measuring C-peptide and antibodies:
- Anti-GAD (glutamic acid decarboxylase)
- Anti-insulin
- Anti-islet cell

- Can come on anytime in life-LADA-Latent autoimmune diabetes of adults

Rx DM1

- MDI- Basal: Glargine or Detemir
- Premeals: Aspart, Glulisine, Lispro
- Insulin pumps
- Continuous glucose monitoring
- Dexcom- G4
- Medtronic- Veo-suspends infusion for 2 hours at a low BS threshold

Basal/Bolus Insulin Absorption Pattern With Standard Insulin Preparations

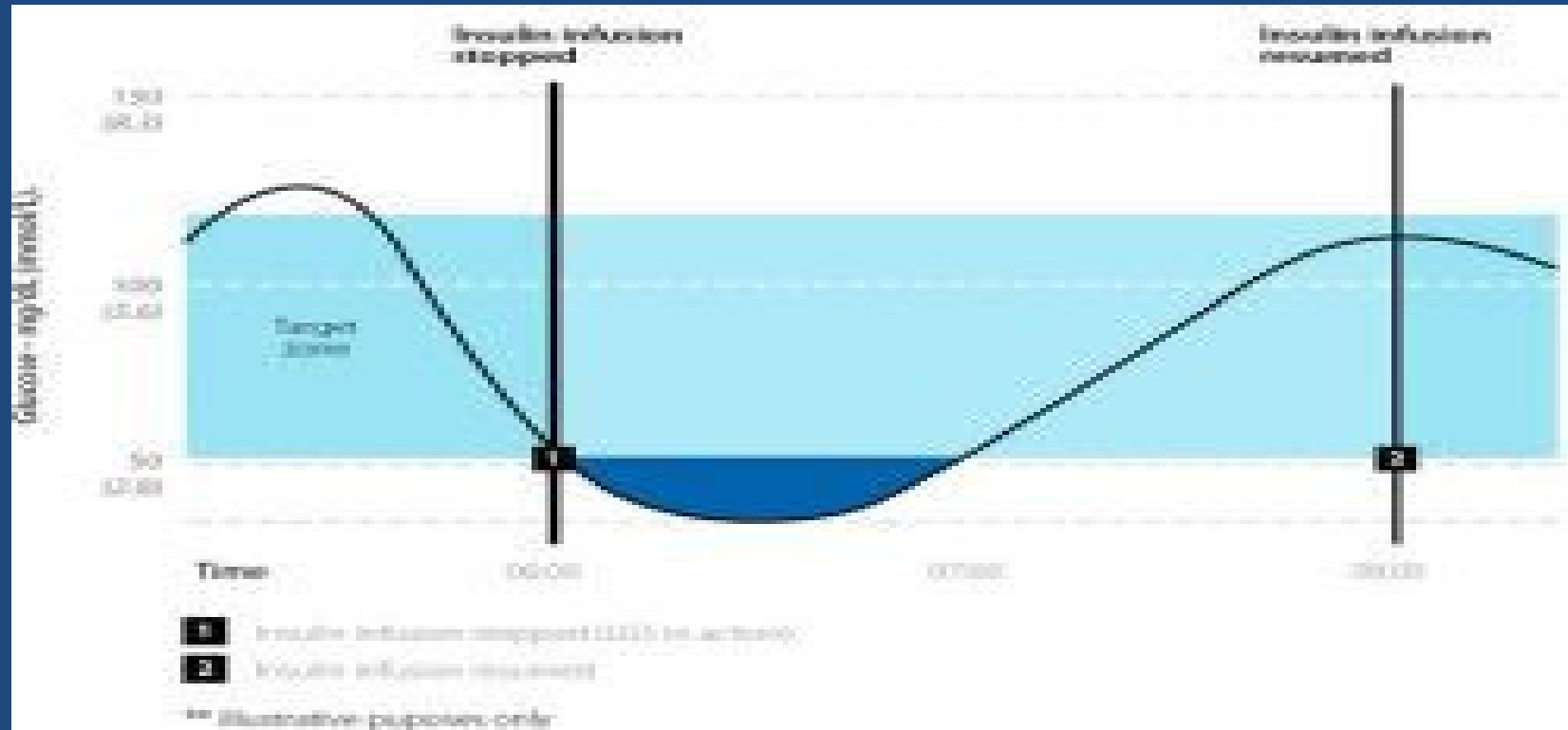


Skyler J. Kelley's Textbook of Intern Med. 2000.

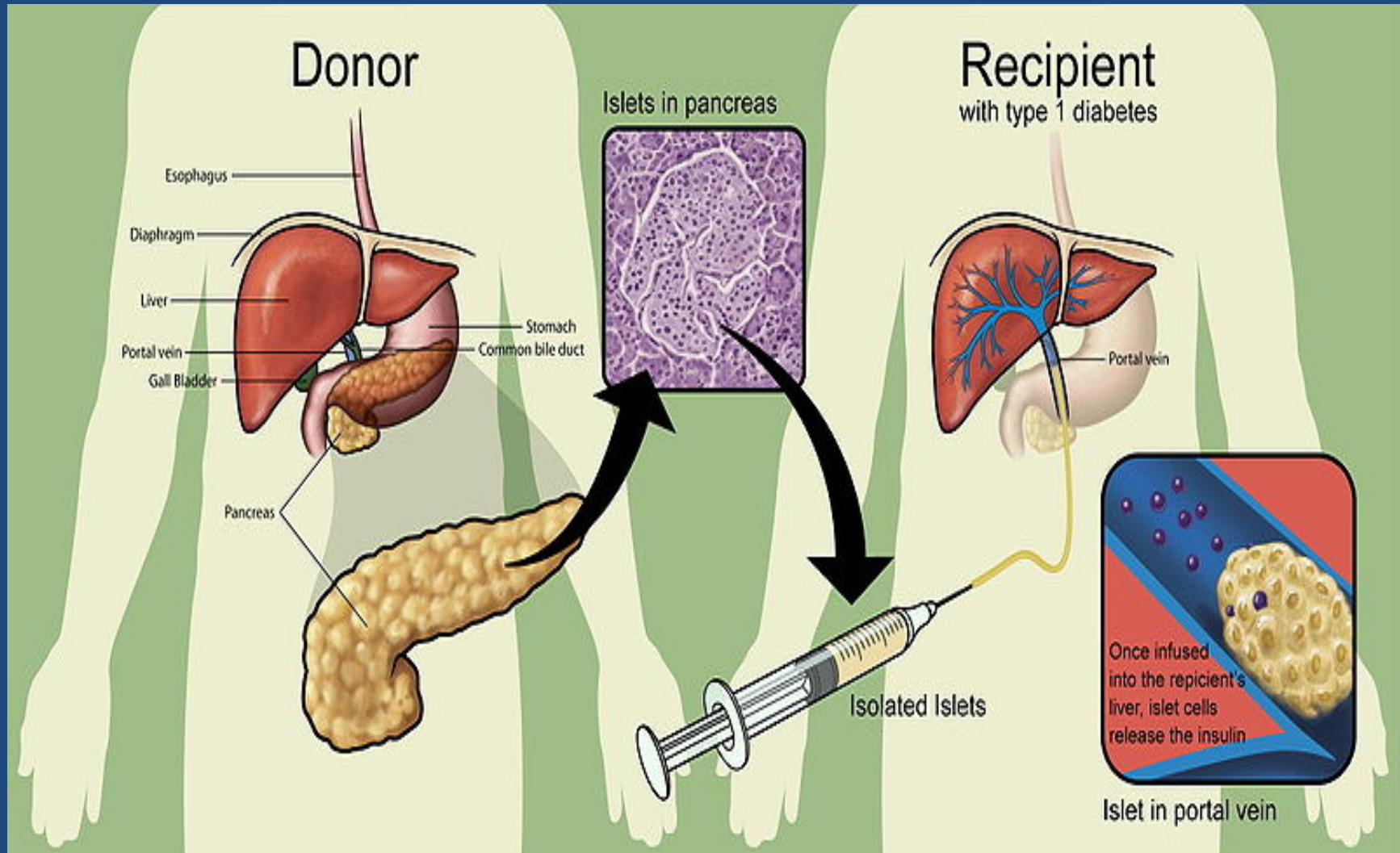


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VEO



Islet cell transplant

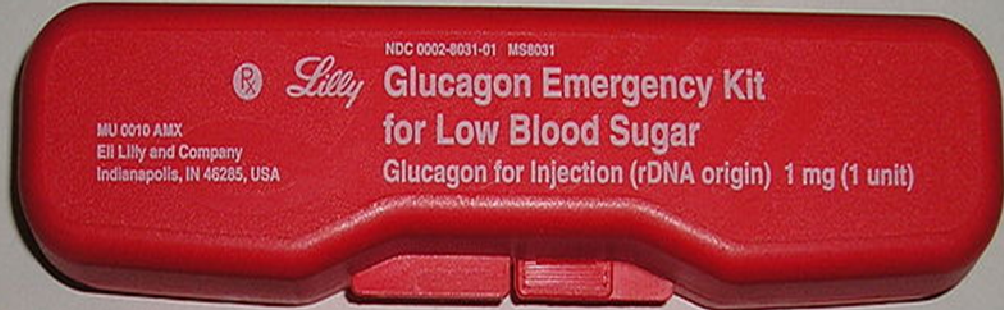


35 yo physician

- AGE 12 TYPE 1 DM
- 18 MOS AGO: BLOATING/DIARRHEA-
Rxed FLAGYL
- 1 MOS PRIOR: INCREASE BLOATING/
DIARRHEA ;HYPOGLYCEMIA









50 yo woman C/O fatigue

- Since 1999 spells of extreme dizziness, fuzziness, and nausea
- Dxed: anxiety-Valium, Compazine
- Dxed: Menieres, Vestibular migraine
- Past year bedridden
- Cannot stand for any interval; lightheaded when she walks
- Weight loss: 147-124 now at 130 lbs
- Amenorrhea past 2 months

DT

- BP 108/80 supine and 78/60 standing
- Thyroid:mild firmness







Addisons

- Fatigue, weight loss, orthostatic lightheadedness, salt craving, hyperpigmentation, nausea & vomiting, failure to thrive, hypoglycemia
- Dx: Lytes (low Na and elevated K) ,
- AM cortisol , ACTH, +anti-adrenal antibodies
- Cortrosyn stimulation test:
250 mcg Cortrosyn: 0,30 and 60 minute Cortisols
Failure to stimulate >20 mcg/dl
-

Rx of Addisons

- Hydrocortisone 15-25 mg/d in split dosages

Alternatives: Prednisone: 5-7.5 mg/d

Dexamethasone : .25-.5 mg/d

Fludrocortisone:.05-.1 mg/d

? DHEA in women

Patient with Addisons calls with fever and myalgias

- Double the glucocorticoid dose
- If N/V or signs of crisis-100 mg Solu-cortef or
- 4 mg Dexamethasone IM; always have injectable steroid available



Patient with Addisons undergoing surgery

Solucortef: 50-100 mg pre and post op



55 yo

- DM1: 8yrs ago-insulin
- Hx thyroidectomy for benign nodules-T4
- Cholecystectomy 6 month prior-since N/V;
60 lb wt. loss, weakness
BS 600 , non ketotic, K 6.0

LB: Autoimmune Polyglandular Syndrome Type 2 (Schmidt's syndrome)

- Addison's - + anti-adrenal antibodies
- Hypothyroidism –prior thyroidectomy for benign goiter- +anti-thyroid peroxidase
- Type 1 DM- + anti-GAD
- + anti –parietal cell antibody

B-12: 885

KM

- Addison's
- Hypothyroidism
- Alopecia totalis
- Vitiligo
- Psoriasis



The Holy Grail

- Immune tolerance : neutralizing the immune assault to self antigens-reprogramming the immune response to accept ourselves
- Understanding the triggers