Thyroid Disorders

Michael B. Harper, M.D.
Professor of Family Medicine
LSUHSC Shreveport

Thyroid Disorders
Introduction

- Common
- Serious
- Chronic
- Lifelong monitoring

Thyroid Disorders
Introduction

- Hyperthyroidism
- Hypothyroidism
- Thyroid Nodules
- Thyroid Cancer

Thyroid Disorders
Introduction

- Clinical presentation
- Diagnosis
- Treatment
- Long-term management

Thyrotoxicosis

- Excess thyroid hormone
- Prevalence of adults in the US - 2%
- 2/3 on replacement treatment

Thyrotoxicosis

- Graves' Disease
  - 90% of cases
- Thyrotoxic Nodules
- Thyroiditis

Thyrotoxicosis

- Women more often affected
- Ratio F:M
  - 4:1
  - 10:1

Thyrotoxicosis-Health Risks

- Atrial fibrillation
- Stroke
- Cardiac failure
- Angina
- Myocardial infarction

Thyrotoxicosis-Health Risks

- Thyroid storm
- Osteoporosis
- Periodic paralysis

Thyrotoxicosis
Clinical Presentation

Symptoms

Nervousness	88%
Weight loss	83%
Heat intolerance	75%
Dyspnea	70%
Palpitation	69%
Increased sweating	62%

Thyrotoxicosis
Clinical Presentation

Symptoms

Fatigue	58%
Tachycardia	51%
Eye complaints	49%
Weakness	47%
Increased appetite	45%
Vomiting	44%

Thyrotoxicosis
Clinical Presentation

Symptoms

Swelling of legs	38%
Chest pain	36%
History of fever	36%
Nausea	28%
Diarrhea	26%
Frequent BM's	21%

Thyrotoxicosis
Clinical Presentation

Symptoms

- Abdominal pain 20%
- Swelling in neck 16%
- Anorexia 13%
- Constipation 12%
- Dysphagia 12%
- Hair loss 4%

Thyrotoxicosis
Clinical Presentation

Symptoms

- Weight loss
  - even with increased appetite
- Heat intolerance
  - prefer room temperatures cooler
  - prefer winter to summer
- Weakness
  - proximal muscles
  - difficulty climbing stairs

Thyrotoxicosis
Clinical Presentation

Abdominal symptoms

- Vomiting and abdominal pain
  - relatively common
  - higher risk of missed diagnosis
- Vomiting
  - can occur without nausea
  - tends to be postprandial

Thyrotoxicosis
Clinical Presentation

Abdominal pain

- Epigastric
- Left upper quadrant
  - unrelated to meals
  - sharp or cramping

Thyrotoxicosis
Clinical Presentation

Signs

- Goiter 96%
- Skin changes
  - smooth,moist 85%
- Tremor 79%
- Tachycardia
  - heart rate >100 76%
  - heart rate >80 100%

Thyrotoxicosis
Clinical Presentation

Signs

- Systolic murmur 76%
- Ocular signs
  - lid lag 60%
- Brisk DTR's 56%

Thyrotoxicosis
Clinical Presentation

Signs

- Pulse pressure
  - > 70 mm Hg 52%
- Bruit over thyroid 47%
- Atrial fibrillation 8%
  - 15% in patients age 70-79 yr
- Gynecomastia 7%

Thyrotoxicosis
Clinical Presentation

Signs

- Goiter
  - enlargement may be only mild
  - difficult to appreciate
  - especially when substernal
- Tremor is fine
  - outstretched hands

Thyrotoxicosis
Clinical Presentation

Signs

- Brisk DTR's
  - rapid relaxation phase
- Lid lag may be present with any cause of thyrotoxicosis
- Exophthalmos is specific to Graves' disease

Thyrotoxicosis
Clinical Presentation

Signs

- Onycholysis
  - typically of the ring fingers
  - Plummer's nails
- Hair is often thin from excess hair loss

Thyrotoxicosis
Clinical Presentation
In older patients

- Cardiopulmonary symptoms may predominate
  - tachycardia (or atrial fibrillation)
  - dyspnea on exertion
  - edema
- They also tend to have more weight loss and less of an increase in appetite
- May have no symptoms except for weakness and asthenia **(generalized weakness)**
  - "apathetic thyrotoxicosis"

Thyrotoxicosis
Diagnosis

- Thyroid-stimulating hormone (TSH) (thyrotropin)
  - highly sensitive assay
- Thyroid function tests

Thyrotoxicosis
Diagnosis

Thyroid function tests

- L-thyroxine (total T_4)
  - radioimmunoassay
- Euthyroid patients may have an elevated total T_4

Thyrotoxicosis
Diagnosis

Thyroid function tests

- Excess thyroid-binding proteins
  - during pregnancy
  - use of estrogens
  - some inherited disorders
- Causes a high total T_4

Thyrotoxicosis
Diagnosis

Thyroid function tests

- Free T_4 measured directly
- Free T_3 measured directly
- Free thyroxine index (FTI)
  - calculated from THBR and the T_4

Thyrotoxicosis
Diagnosis

Thyroid function tests

- T_3 resin uptake
- Indirect measure of thyroid-binding proteins
- Thyroid hormone binding ratio (THBR)

Thyrotoxicosis
Diagnosis

- TSH level changes first
- More sensitive than free T_4 or FTI
- May remain supressed for months after free T4 normalized

Thyrotoxicosis

- Patients with low TSH and normal free T_4
- Subclinical hyperthyroidism

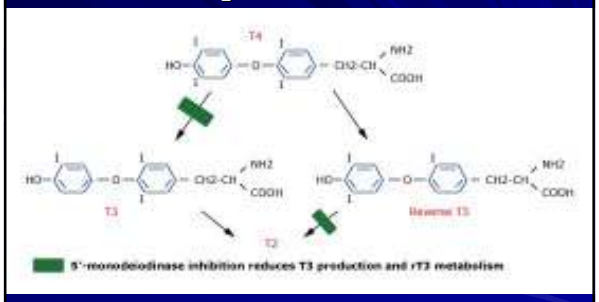
Increased risk of

- Atrial fibrillation
- Osteoporosis

Thyrotoxicosis
Diagnosis

- TSH can be moderately low
  - nonthyroidal illness
  - medications
    - glucocorticoids and dopamine
  - occasionally in healthy people
  - particularly the elderly
- TSH level is usually not less than 0.05 mU/L

Nonthyroidal Illness



The inhibition of 5'- monodeiodinase in nonthyroidal illness leads to decreased conversion of T4 to T3 and reduced metabolism of reverse T3

Thyrotoxicosis
Diagnosis
Nonthyroidal Illness

- TSH can be moderately low
  - usually not less than 0.05 mU/L
- Low T3
- Elevated reverse T3
- May have Low T4 and free T4
- Probably best to not screen for thyroid disease in critically ill patients unless it is strongly suspected

Amiodarone

- May cause either hypo- or hyperthyroidism
- Has direct effects on the thyroid gland and it contains iodine
- Inhibits extrathyroidal conversion of T4 to T3
  - Low T3
  - Elevated reverse T3

Thyrotoxicosis
Diagnosis

- If TSH level is < 0.01 mU/L
  - thyrotoxicosis is usually present
- Confirmed with free T4 and T3
- TSH-secreting adenoma (rare)
  - hyperthyroidism with an elevated TSH

Thyrotoxicosis
Diagnosis

Nuclear medicine scans

- Thyroid size
- Thyroid function
  - thyroid uptake
- Thyroid nodules
  - functioning (hot)
  - nonfunctioning (cold)

Graves' Disease

- Described by Robert Graves in 1835
- Etiology is autoimmune
- May follow some physical or psychological stress
- Family history of thyroid disease is often present

Graves' Disease

- All the clinical findings of thyrotoxicosis plus
- Ophthalmopathy
  - >50% of patients
- Dermopathy
  - 1% to 2% of patients

Graves' Disease

- A diffuse goiter occurs in most patients
- Thyroid gland is nontender and somewhat soft

Graves' Disease

- Eye problems
  - pressure sensation, irritation
  - gritty feeling, lacrimation
  - a change in appearance
  - blurred vision or diplopia
- Exophthalmos can cause
  - marked eye irritation
  - even blindness

Graves' Disease

- Dermopathy
  - raised, firm, nontender, intradermal nodules
  - on the anterior surfaces of the lower legs
- Clubbing of the nails (acropachy) is rare

Graves' Disease
Diagnosis

- Hyperthyroidism on thyroid function tests
  - FTI or free T_4
- Along with eye or skin findings specific to Graves'

Graves' Disease
Diagnosis

- If exophthalmos or dermopathy absent
- Distinguish from
  - subacute painless thyroiditis
  - postpartum thyroiditis

Graves' Disease
Diagnosis

- Hx of chronic symptoms strongly suggests Graves'
- Thyroid scan with elevated thyroid uptake confirms Dx

Graves' Disease
Diagnosis

- Thyroid-stimulating antibodies are present
- Not usually necessary or helpful diagnostically
- May prove useful to identify those likely to relapse

Graves' Disease
Treatment

- Control the effects of excess thyroid hormone
- Reduce the production of additional hormone

Graves' Disease
Treatment – control effects

- ß-blockers for
  - tachycardia
  - tremor
  - other symptoms of excess hormone
- Atenolol 25-50mg/d
- Propranolol
  - 20 to 40 mg BID or QID
  - increase every few days until the heart rate is <100
- If ß-blockers contraindicated
  - diltiazem or clonidine

Graves' Disease
Treatment

- Controlling hormone production
  - antithyroid medications
  - radioiodine ablation
  - surgery
- Radioiodine most common in USA
- Antithyroid medications most common in Europe and Asia

Graves' Disease
Treatment

- Radioiodine is the therapy of choice in the United States
  - selected by 69% of thyroid specialists
- It is less popular in other countries
  - Europe (22 percent)
  - Japan (11 percent)

Graves' Disease
Treatment

- The only randomized prospective trial of these three therapies, each was equally effective in 179 patients in normalizing serum thyroid hormone concentrations within six weeks
- After treatment, 95 percent or more of the patients were satisfied with their therapy
  - Graves' hyperthyroidism: treatment with antithyroid drugs, surgery, or radioiodine--a prospective, randomized study. Thyroid Study Group. J Clin Endocrinol Metab 1996 Aug;81(8):2986-93.

Graves' Disease
Treatment

- Choice of treatment
  - clinical presentation
  - age of the patient
  - ability and willingness to comply with treatment

Graves' Disease
Antithyroid medications

Methimazole & propylthiouracil

- Block production of thyroid hormone
- May alter the course of the disease via their immunosuppressive effects

Graves' Disease
Antithyroid medications

- Initial dosage

  methimazole 10-30 mg/day

  propylthiouracil 100 to 600 mg/day given as tid
- Maintenance after free T3&T4 normalized (usually 4-6 weeks)

  methimazole 5 to 20 mg/day once daily

  propylthiouracil 50 to 150 mg/day given as tid

Graves' Disease
Antithyroid medications

- Methimazole usually the preferred drug

  lower risk of agranulocytosis

  once-a-day schedule

  more rapid return to euthyroid status
- Propylthiouracil

  preferred during pregnancy

  or thyroid storm

  Blocks peripheral conversion of T_4 to T_3

Graves' Disease
Antithyroid medications

- Initial dosage methimazole with mild hyperthyroidism and small goiter
  - methimazole 10mg/day in a single dose
- With more severe hyperthyroidism and large goiter
  - Methimazole 20-30mg/day in two divided doses to avoid GI side effects
  - Change to once daily dosing for maintenance
- Smaller initial dosage supported by *Cochrane Systematic Review* 2005

Graves' Disease
Antithyroid medications

- Duration of treatment
  - 6 months to 2 years
  - Remission higher with longer treatment
    - 12-18 months, based on four studies *Cochrane Systematic Review* 2005
- Remission rate reported as high as 60%
  - But generally lower in the US
- Failure to achieve remission after 2 years
  - indication for alternate therapy

Graves' Disease
Antithyroid medications

- Remission probably higher in patients with
  - less severe hyperthyroidism
  - short duration of illness
  - small goiter
  - Females over age 40
  - Smoking cessation

Graves' Disease
Antithyroid medications

Concomitant administration of thyroxine 100 to 200 µg/day

- May avoid frequent adjustments in antithyroid dosage
- One study: reduced recurrence of hyperthyroidism.
- Several subsequent studies failed to demonstrate this benefit
- Not currently recommended

Graves' Disease
Treatment

Iodine 131 ablation

- Used to destroy thyroid tissue & reduce hormone production
- May be used as initial therapy for Graves' disease
- Major disadvantage
  - high prevalence of hypothyroidism (> 90%)
  - continues to increase with time

Graves' Disease
Treatment

Subtotal thyroidectomy

- Indicated when
  - the goiter is large
  - if obstructive symptoms present
  - children who fail antithyroid medication trial
- Disadvantages
  - cost
  - risk of surgical complications
- Following surgery for Graves' disease
  - hypothyroidism in 53%
  - recurrence in 3.4%

Graves' Disease

Requires lifelong monitoring

- Patients in remission must be followed for
  - relapses
  - late hypothyroidism
- After ^{131}I ablation or surgery
  - require chronic periodic monitoring for hypothyroidism
- Hypothyroidism requires
  - lifelong hormone replacement

Thyrotoxic Nodule

- Autonomously functioning thyroid nodule
- Typical hyperthyroid symptoms and signs
- P E - thyroid nodule
- Graves' specific findings absent

Thyrotoxic Nodules

Diagnosis

- Elevated free T_4 or FTI
- Low TSH
- Hot nodule on radioiodine scan

Thyrotoxic Nodules

Treatment

- ^{131}I ablation
  - hypothyroidism less common
- Surgery
  - very large nodule
  - progressively enlarging
  - other signs of thyroid cancer
- Antithyroid medications

Thyrotoxic Nodules

- Nodule may persist after ablation treatment
- Monitor for any increase in size
  - evaluate for cancer
- Monitor for hypothyroidism

Thyroiditis

- Thyrotoxicosis
  - release of thyroid hormone
  - from an injured gland
- ^{123}I thyroid uptake
  - decreased

Thyroiditis

Subacute painful thyroiditis granulomatous

- Viral infection
- Symptoms
  - neck pain, flu-like
  - thyrotoxicosis
- Physical exam
  - tender, firm,
  - asymmetric nodular thyroid

Thyroiditis

Subacute painful thyroiditis

- Sed rate is elevated
- Antithyroid antibodies are absent

Thyroiditis

Subacute painful thyroiditis

- Thyrotoxic - 3 to 6 weeks
- Euthyroid state - few weeks
- Hypothyroid - weeks to months
- Euthyroid state

Thyroiditis

Subacute painful thyroiditis

- Treatment of inflammation
  - aspirin
  - other NSAID's
  - corticosteroids (2-4 weeks)
- May need ß-blocker therapy
- Usually no long-term sequelae

Thyroiditis

Subacute painless thyroiditis lymphocytic

- Autoimmune process
- Mildly enlarged thyroid gland
  - firm and nontender
- Antithyroid antibodies
  - about 50% of patients

Thyroiditis

Subacute painless thyroiditis lymphocytic

- May go through the same four phases
- Some patients remain hypothyroid

Thyroiditis

- Hashimoto's thyroiditis
- Postpartum thyroiditis
- Usually cause hypothyroidism

Hypothyroidism

- Deficiency of thyroid hormone
- Most common causes:
- Autoimmune thyroid disease
  Hashimoto's thyroiditis
- Previously treated Graves' disease

Hypothyroidism

Uncommon causes

- Other types of thyroiditis
- Congenital hypothyroidism
- Central hypothyroidism

Hypothyroidism

- More common with age
- 7% of patients over age 55
- Congenital hypothyroidism
  1/3500 live births

Hypothyroidism

Health Risks

- Coma and death
- Hearing impairment
- Carpal tunnel syndrome
- Hypercholesterolemia
- Dementia
- Depression and suicide

Hypothyroidism

Symptoms

- Generalized weakness
- Fatigue
- Memory loss or slowed thinking
- Intolerance to cold
- Dry skin, hair loss
- Hoarseness, dyspnea
- Anorexia, deafness

Hypothyroidism
Symptoms

- Chest pain
- Edema
- Weight gain
  - 10 pounds is typical
- Weight loss
- Constipation
- Depression
- Heavy, prolonged menses

Hypothyroidism
Physical findings

- Periorbital edema
- Peripheral edema
- Pale, thick, dry skin
- Hyperkeratosis
- Diastolic hypertension
- DTR's
  - delayed relaxation phase

Hypothyroidism
Physical findings

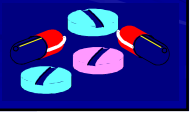
- Myxedema
- Pleural and pericardial effusions
- Cardiomegaly
- Bradycardia
- Prolonged QT interval

Hypothyroidism
Laboratory Evaluation

- Elevated TSH (>10mU/L) and
- Low free T_4 or FTI
- Subclinical hypothyroidism
  - high TSH with normal free T_4

Hypothyroidism
Treatment

- L-thyroxine – several brands available
- Start at low dose (12.5-25Ug) if patient is older or any coronary artery disease
- Check TSH after 6 weeks
- Adjust dosage to maintain normal TSH



Hypothyroidism
Treatment

- After steady state reached usually need to check only once every year
- Requirement may slowly decrease with age
- If TSH is too high, check compliance and other medications before increasing dose

Hypothyroidism Treatment

- L-thyroxine should be taken on an empty stomach
- Decreased absorption if on vitamins, iron, calcium, or antacids
- Give thyroid tab 1 hour before or 4 hours after these
- Also interactions with digoxin, anticonvulsants, and warfarin

Hypothyroidism Treatment

- Addition of triiodothyronine
- Study in NEJM '99
- Double-blind cross-over
- May improve quality of life
- Increased sex hormone binding protein

Hypothyroidism Treatment

- Small study
  - Brief duration of trial
  - Dose of T-3 too high
- A meta-analysis of all 11 published randomized studies concluded that there was no benefit of combined therapy
- Thyroxin is standard of care

Hypothyroidism Treatment

- Consider adding 10*u*g of T-3 to replace 50*u*g of T-4
  - pts who are depressed
  - pts intolerant to switching from desiccated thyroid

Hypothyroidism Treatment

- No current physiologic combination available
- Could use T-3 (Cytomel) 5*u*g bid
- Or T-4/T-3 combination of 50*u*g/12.5*u*g (Thyrolar)

Subclinical Hypothyroidism

- Patients often feel better with therapy
- Treatment is usually indicated
- Especially patients with depression

Subclinical Hypothyroidism

Treatment can be deferred

- Asymptomatic patients
- Mild TSH elevation
  (< 14 mU/L)
- Negative antithyroid antibodies
- No goiter

Hashimoto's Thyroiditis

- Most common cause of adult hypothyroidism
- Etiology is autoimmune
- Antithyroid antibodies
- Genetic predisposition
- Most common in women (8:1)
- Age of onset - 30 to 50

Hashimoto's Thyroiditis

Presentation

- Painless, diffuse, firm goiter
- Hypothyroidism
- Antibodies to thyroid peroxidase in 90%
- Antithyroglobulin antibodies in 70%

Thyroid Nodules and Thyroid Cancer

- Thyroid nodules are common
  - occur in 4% to 8% of adults
- Clinically significant thyroid cancer is uncommon
  - only 1% of all malignancies
  - 35th among causes of cancer death

Factors suggesting high probability of malignancy

- Rapid growth of nodule
- Vocal cord paralysis
- Fixation to adjacent tissue
- Enlarged regional lymph node(s)
- Very firm nodule
- Family history of MEN-II or medullary carcinoma
- Distant metastases

Factors suggesting moderate probability of malignancy

- Age < 15 years
- Age > 70 years
- History of neck irradiation
- Diameter of nodule > 4 cm
- Male sex and solitary nodule

Thyroid Nodule

Workup of a solitary nontoxic thyroid nodule

- TSH
- Fine-needle aspiration cytology (FNAC)
  - Usually first step if TSH normal
- Nuclear medicine scans
- Ultrasonography
- Surgery

Thyroid Nodule

Results of FNAC

- Positive - malignant cells
- Negative - adequate benign glandular tissue
- Indeterminate - tissue is present but criteria for above not met
- Inadequate - insufficient tissue

Thyroid Nodule

Surgery indicated for

- Patients with one or more high risk clinical factors
- Or FNAC yielding positive or indeterminate results

Thyroid Nodule

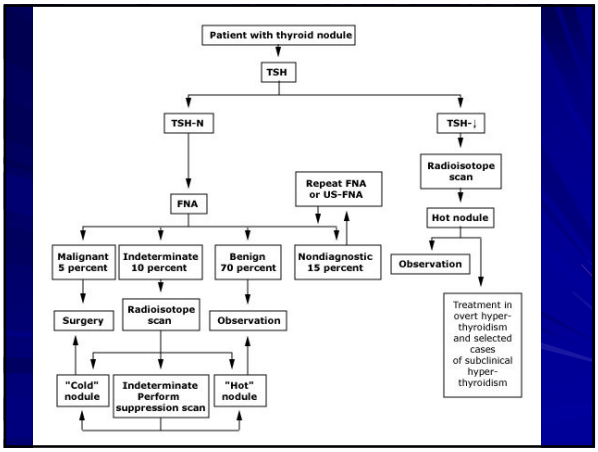
- Observation for benign FNAC
- If nodule increases in size
  - repeat FNAC or surgery

Thyroid Nodule

- If the initial results are inadequate repeat the FNAC
- Consider surgery if second FNAC is inadequate

Thyroid Nodule

- For a persistent nodule after aspiration of a cyst
- Consider surgery or repeat the FNAC



Thyroid Cancer

- Four cell types of thyroid cancer are possible
- Each with a different natural course and prognosis

Papillary carcinoma

- 70% to 75% of thyroid cancer
- Slow-growing
- Good long-term survival if surgical removal is early
- Spreads by lymphatics

Follicular carcinoma

- 10% to 15% of thyroid cancers
- Slightly more aggressive than papillary
- Spreads by hematogenous route
- Subcategory is the Hürthle cell type, which is more aggressive

Medullary carcinoma

- 2% to 5% of thyroid cancers
- Most are sporadic but some are familial
- 20% are part of the MEN-II syndrome
- Elevated calcitonin levels and genetic testing
- If palpable mass at diagnosis, cure rate < 50%

Anaplastic carcinoma

- Most aggressive type
- But only 2% to 5% of cases
- Older patients, mean age 65yr
- Many patients have history of
  - Multinodular goiter
  - Coexisting differentiated carcinoma
- Worst prognosis of any thyroid cancer
  - Median survival time of 3 to 7 months
  - 5-year survival only 5 to 14%

Summary

- Thyroid disease requires lifelong monitoring
- Obtain TSH when suspected
- Free T3 & Free T4 to confirm diagnosis
- Consider antithyroid medications first for Graves' Disease
- Treat hypothyroidism to normal TSH
- FNAC for thyroid nodules