

DISORDERS OF THE THYROID GLAND

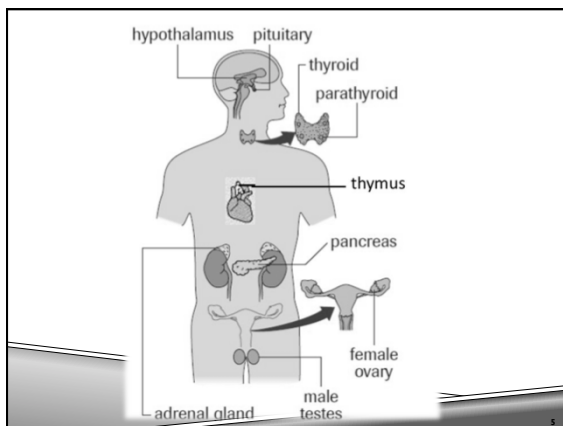
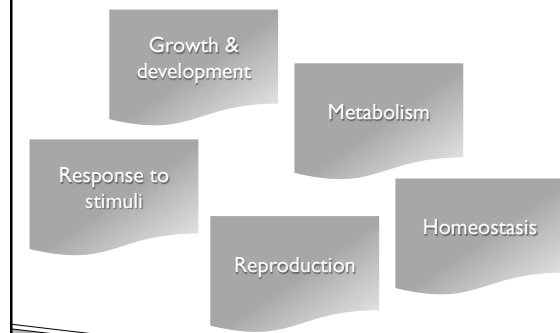
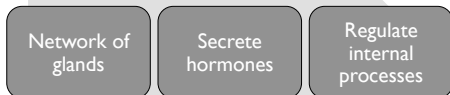
SIGNS, SYMPTOMS, & TREATMENT

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OBJECTIVES

- ▶ Discuss the synthesis and action of thyroid hormones.
- ▶ Differentiate various thyroid abnormalities.
- ▶ Assess symptoms, lab values, and treatment associated with various thyroid conditions.

ENDOCRINE SYSTEM AT A GLANCE



ANATOMY OF THE THYROID

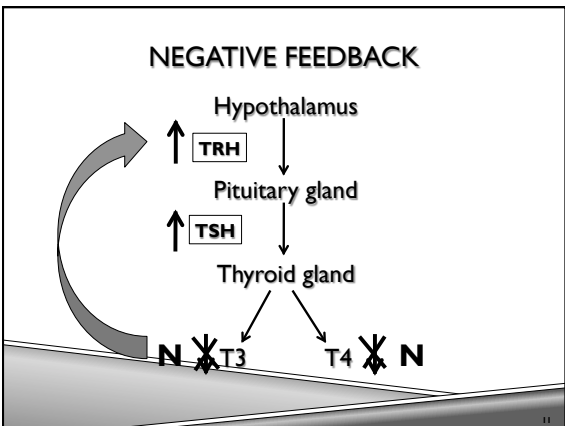
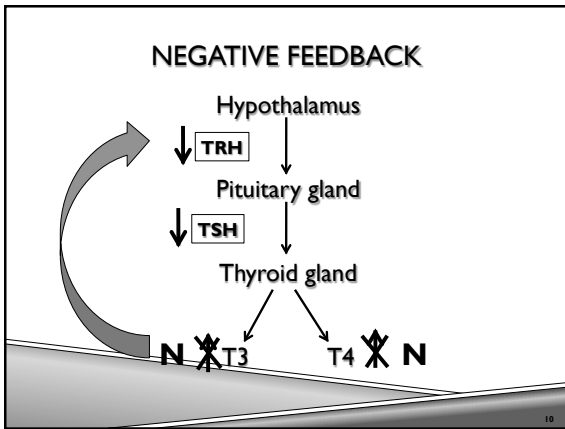
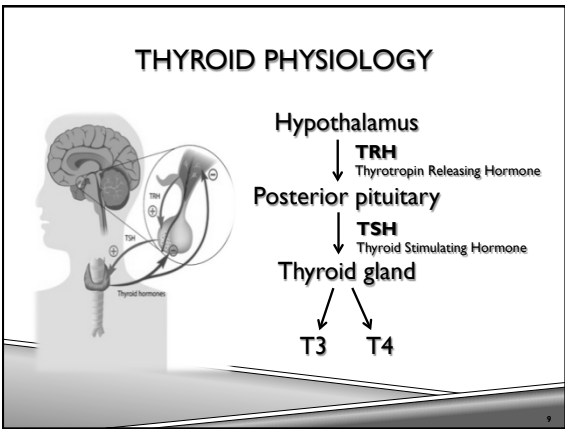
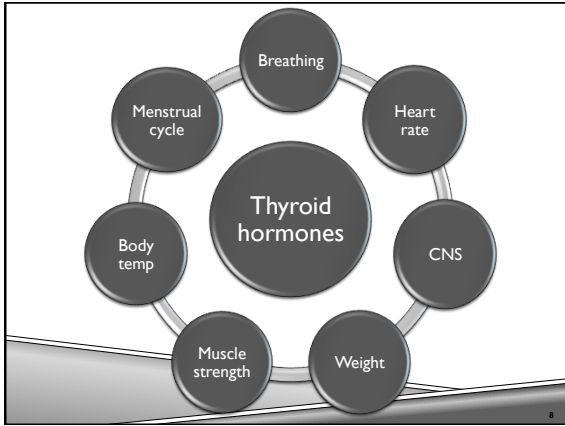
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- ▶ Butterfly-shaped gland
 - ▶ Lies in front of trachea, below larynx
 - ▶ Two lobes connected by isthmus

The thyroid releases hormones that control metabolism – the way the body uses energy

Hypothalamus
Pituitary gland
Thyroid gland

The hypothalamus and the pituitary in the brain control the normal secretion of thyroid hormones which in turn controls metabolism

#ADAM

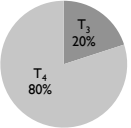


SYNTHESIS OF T₃ AND T₄

- ▶ Dietary iodine
 - ▶ Critical first step in synthesis
 - ▶ Absorbed by thyroid cells → (in presence of TPO) → THYROID HORMONES produced
- ▶ Iodine deficiency leads to hypothyroidism & cretinism
- ▶ Recommended intake:
 - ▶ 150 µg/dl adults
 - ▶ 90-120 µg/dl children

THYROID HORMONES

- ▶ T_4 → thyroxine
 - ▶ Deiodination of T_4 to form T_3
- ▶ T_3 → triiodothyronine
 - ▶ Strongest & most potent



A pie chart illustrating the relative concentrations of thyroid hormones. The chart is divided into two segments: a larger segment representing T_4 at 80% and a smaller segment representing T_3 at 20%.

THYROID HORMONES




- ▶ T_3 (99.6%) and T_4 (99.97%) bound to proteins in circulation
 - ▶ Thyroid binding globulin (TBG)
 - ▶ Thyroid-binding pre-albumin (TBPA)
 - ▶ Transthyretin (TTR)
 - ▶ Albumin
- ▶ Only free T_3 and T_4 (FT_3 , FT_4) are metabolically active

LAB EVALUATION

- ▶ **TSH** – first assessed
 - ▶ Normal 0.5-5 μ U/ml
- ▶ If TSH is abnormal...
 - ▶ **Free T_4**
 - ▶ Normal 0.8-2.8 ng/dl

THYROID SCANNING

- ▶ Nuclear imaging
 - ▶ Inject radioactive iodine
 - ▶ Checks thyroid function or abnormalities (lumps, inflammation, cancer)
- ▶ Ultrasound
 - ▶ Detects thyroid nodules, cysts, or tumors
 - ▶ Useful to evaluate recurrent thyroid cancer






Two side-by-side thyroid scans. The left scan, labeled 'A. Normal', shows a uniform, dark uptake of radioactive iodine. The right scan, labeled 'B. Graves' disease', shows a significantly increased and uneven uptake of radioactive iodine across the thyroid gland.

THYROID DISEASE

THYROID DISEASE

- ▶ Affects more than 12% of U.S. population
 - ▶ ~20 million Americans
 - ▶ ~60% unaware
 - ▶ Affects 1 in 8 women
 - ▶ Women 5x more likely to be affected than men



A row of eight female icons and one male icon, representing the statistic that 1 in 8 women are affected by thyroid disease.

THYROID DISEASE

- ▶ Often traced to one of the following:
 - ▶ Too much thyroid hormone
 - ▶ Too little thyroid hormone
 - ▶ Abnormal growth of thyroid
 - ▶ Nodules within the thyroid
 - ▶ Thyroid cancer

THYROID DISORDERS

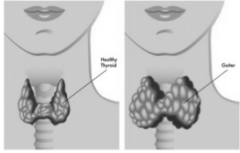
Goiters	Thyroid nodules	Thyroiditis
Thyroid cancer	Hypo-thyroidism	Hyper-thyroidism

THYROID DISORDERS

Goiters	Thyroid nodules	Thyroiditis
Thyroid cancer	Hypo-thyroidism	Hyper-thyroidism

GOITER

- ▶ Enlarged thyroid gland
 - Entire gland
 - OR
 - Multiple nodules




- ▶ Non-toxic goiter
 - ▶ Not associated with overproduction of thyroid hormones or malignancy

CAUSES OF GOITERS:

- ▶ Iodine deficiency
 - ▶ Rare in U.S.
- ▶ Increased thyroid stimulating hormone (TSH)
 - ▶ Enlargement takes several years
- ▶ Grave's disease & Hashimoto's disease
- ▶ Thyroid nodules
- ▶ Thyroiditis
- ▶ Thyroid cancer

GOITER



- ▶ Swollen neck
- ▶ Mass may compress trachea & esophagus
 - ▶ Coughing
 - ▶ Wake up with feeling of inability to breathe
 - ▶ Sensation that food is stuck in throat

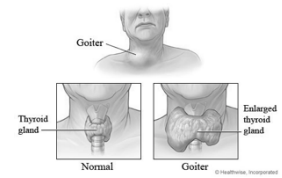
TREATMENT FOR GOITERS

- ▶ Depends on cause of goiter
- ▶ Asymptomatic → no treatment
- ▶ Hashimoto's → treat with thyroid hormone
- ▶ Grave's → treat with radioactive iodine
- ▶ If very large or therapy fails → surgical removal necessary

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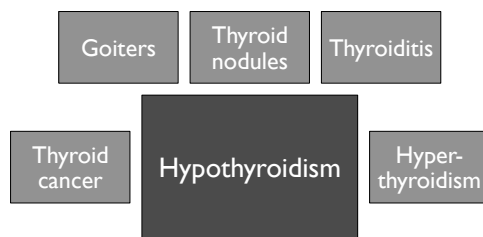
INDICATIONS FOR SURGERY

- ▶ Compression of trachea or esophagus
- ▶ Malignancy
- ▶ Cosmetic purposes



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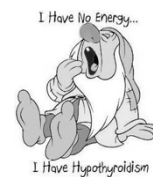
THYROID DISORDERS



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HYPOTHYROIDISM

- ▶ Insufficient levels thyroid hormone



- ▶ PRIMARY hypothyroidism
 - ▶ SECONDARY hypothyroidism
 - ▶ TERTIARY hypothyroidism
- } Rare

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PRIMARY HYPOTHYROIDISM

- ▶ ~10% women have some degree of hypothyroidism
- ▶ Women 4x more likely than men
- ▶ Prevalence increases with age
 - ▶ Mean age at diagnosis is 60 yr
- ▶ Millions are asymptomatic

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CAUSES - PRIMARY HYPOTHYROIDISM

- ▶ Iodine deficiency (most common worldwide)
- ▶ Autoimmune disease
 - ▶ Hashimoto's
- ▶ Iatrogenic
 - ▶ Treatment for hyperthyroidism
- ▶ Congenital
- ▶ Trauma
- ▶ Radiation exposure
- ▶ Infections
- ▶ Drugs

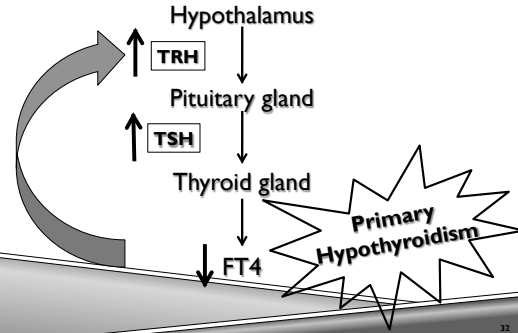
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SYMPTOMS – PRIMARY HYPOTHYROIDISM

- ▶ Fatigue
- ▶ Weakness
- ▶ Weight gain
- ▶ Coarse, dry hair
- ▶ Hair loss
- ▶ Dry, rough skin
- ▶ Cold intolerance
- ▶ Muscle cramps
- ▶ Constipation
- ▶ Depression
- ▶ Irritability
- ▶ Memory loss
- ▶ Abnormal menstrual cycle
- ▶ Decreased libido

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LAB EVALUATION



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CRETINISM

- ▶ Congenital hypothyroidism
- ▶ 1 in 4000 live births
- ▶ Hypoplasia of thyroid gland
- ▶ Failure of gland to move to normal location
- ▶ Ineffective hormone (enzyme deficiency)

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CRETINISM

- ▶ Abnormal bone formation → stunted growth
- ▶ Mental retardation
- ▶ Pale, gray, cool skin
- ▶ Constipation
- ▶ Large tongue
- ▶ Poor muscle tone

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CRETINISM - TREATMENT

- ▶ Thyroid hormone replacement
- ▶ Prevention:
 - ▶ Screen at birth
 - ▶ Improved prognosis is treatment started in first 2 months of life

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HASHIMOTO'S DISEASE

- ▶ Most common thyroid disorder in U.S.
- ▶ Chronic lymphocytic thyroiditis or chronic autoimmune thyroiditis
- ▶ Affect 14 million people in U.S.
 - ▶ Women more likely than men
 - ▶ Middle-aged

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HASHIMOTO'S DISEASE - CAUSES

- ▶ Autoimmune disease
- ▶ Antibodies attack healthy thyroid tissue
 - ▶ Leads to inflammation
 - ▶ Decreased FT3 and FT4
- ▶ Autoantibodies to TPO
 - ▶ Decreased FT3 and FT4

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COMPLICATIONS OF HASHIMOTO'S

- ▶ Goiter (due to increased TSH)
- ▶ Increased risk of heart disease
- ▶ Depression
- ▶ Myxedema coma
 - ▶ Severest form of hypothyroidism
 - ▶ Mental slowing, profound lethargy, ultimately coma → life threatening

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TREATMENT FOR HASHIMOTO'S

- ▶ Hormone replacement
 - ▶ Levothyroxine (Synthroid)
 - ▶ Dosage depends on degree of thyroid failure (range 50-150 µg daily) and age
 - ▶ Repeat TSH in ~6 weeks
 - ▶ Change dosage (25-50 µg) as needed
 - ▶ Take same time each day
 - ▶ Takes 2-3 months for improvement in symptoms



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TREATMENT FOR HASHIMOTO'S

- ▶ Adults older than 50 yr or those with heart disease:
 - ▶ Start Levothyroxine 25 µg daily
 - ▶ Adjust 25 µg every four weeks according to response, TSH levels, and angina symptoms

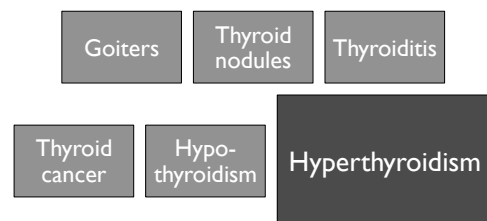
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TREATMENT FOR HASHIMOTO'S

- ▶ Some patients do not feel completely well, despite normal TSH levels
 - ▶ Need to bring TSH levels down to lower end of normal range
- ▶ Erratic TSH levels, despite constant dose of Levothyroxine
 - ▶ Poor adherence
 - ▶ Rule out malabsorption

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THYROID DISORDERS



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HYPERTHYROIDISM



CAUSES - PRIMARY HYPERTHYROIDISM

- ▶ Grave's disease – most common
- ▶ Toxic nodular or multinodular goiter
- ▶ Thyroiditis

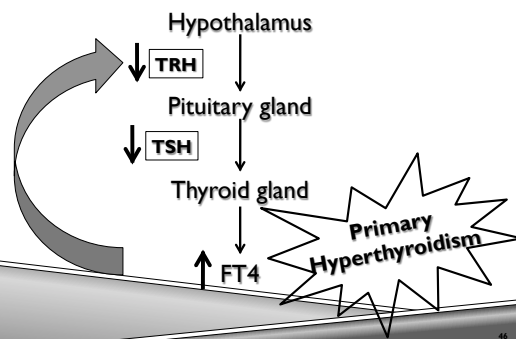
- ▶ Pituitary tumor
 - ▶ Secretes TSH
 - ▶ Secondary hyperthyroidism

SYMPTOMS - HYPERTHYROIDISM

- ▶ Fatigue
- ▶ Muscle weakness
- ▶ Weight loss
- ▶ Hand tremors
- ▶ Mood swings
- ▶ Anxiety
- ▶ Rapid heartbeat

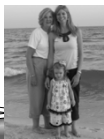
- ▶ Irregular heartbeat or hear palpitations
- ▶ Dry skin
- ▶ Trouble sleeping
- ▶ Light menstrual flow or irregular cycle
- ▶ Increased bowel movements

LAB EVALUATION



GRAVE'S DISEASE

- ▶ Accounts for ~75% hyperthyroidism
- ▶ Females 8x more likely than males
- ▶ Typically occurs between ages of 20-40 yr.
- ▶ Familial tendency

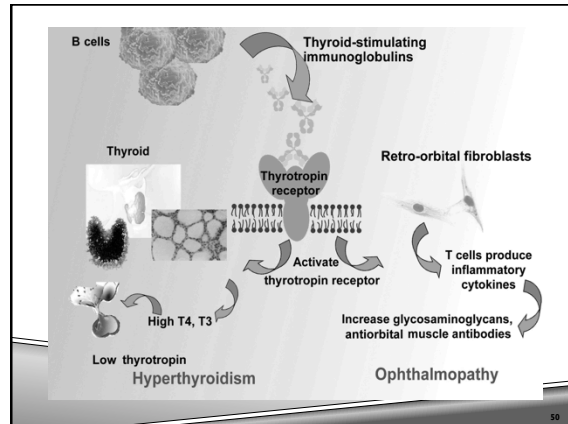


GRAVE'S DISEASE

- ▶ Autoimmune disease
- ▶ Presence of thyroid stimulating immunoglobulin
 - ▶ Binds to TSH receptors on thyroid gland
 - ▶ Increased T3 and T4
- ▶ Autoantibodies to TPO
 - ▶ Decreased FT3 and FT4

GRAVE'S DISEASE

- ▶ Inflammation of tissues around eyes causing swelling
- ▶ Thickening of skin over lower legs
- ▶ Goiter sometimes present



TREATMENT FOR GRAVE'S

- ▶ Beta-blockers (propranolol) treats symptoms in early treatment
- ▶ Anti-thyroid drugs
 - ▶ Propylthiouracil (PTU) or methimazole
 - ▶ Often add levothyroxine after 4 weeks of treatment to maintain euthyroidism
 - ▶ 2/3 patients relapse one year after treatment stops
 - ▶ Younger patients less likely to enter remission
 - ▶ Symptoms resolve slowly after treatment started

TREATMENT FOR GRAVE'S

- ▶ Treat with radioiodine
 - ▶ Thyroid cell destruction
 - ▶ ~90% patients with Grave's disease treated with single dose
 - ▶ May cause hypothyroidism (40-60% patients within one year)
- ▶ Thyroidectomy
 - ▶ Last resort if no response to treatment

THYROID STORM

- ▶ **Life threatening emergency**
- ▶ Rare
- ▶ Extremely high thyroid hormones
- ▶ Marked elevation in body temperature
- ▶ High mortality rate (30%)

THYROID STORM

- Usually caused by stress: Symptoms:
- ▶ Infection
 - ▶ Trauma
 - ▶ Surgery
 - ▶ Delivery
 - ▶ High fever
 - ▶ Rapid heartbeat
 - ▶ Disorientation
 - ▶ Chest pain
 - ▶ Shortness of breath
 - ▶ Inc sweating
 - ▶ weakness

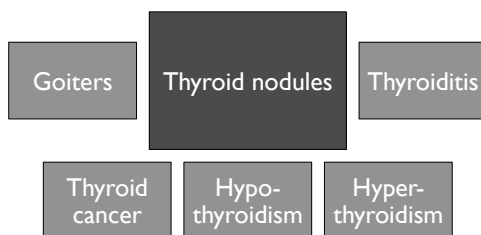
THYROID STORM

- ▶ Prevention → Early treatment for hyperthyroidism
- ▶ Recognize warning signs & get treated immediately
 - ▶ Highly elevated T3 & T4
 - ▶ Tachycardia

TREATMENT FOR THYROID STORM

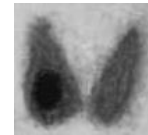
- ▶ Propylthiouracil – large doses
- ▶ If heart failure → propranolol
- ▶ Glucocorticoids → inhibits conversion of T4 to T3

THYROID DISORDERS



“HOT” NODULE

- ▶ Toxic nodular goiter or toxic adenoma
- ▶ Benign lumps on thyroid gland
 - ▶ Excessive thyroid hormones
 - ▶ Single “hot” nodule contains thyroid cells which have lost their regulatory mechanism that dictates amount of hormone to produce



THYROID NODULES

- ▶ Nodule = abnormal overgrowth of tissue in thyroid gland
 - ▶ May be solid or fluid filled
- ▶ Up to 50% of adults have at least one thyroid nodule
 - ▶ Asymptomatic
 - ▶ More common as people age
 - ▶ Typically benign



SYMPTOMS – THYROID NODULES

- ▶ Rapidly growing lump on neck
- ▶ Lump felt in throat
- ▶ Difficulty swallowing
- ▶ Hoarseness
- ▶ Enlarged lymph nodes
- ▶ May have symptoms of hyperthyroidism

THYROID NODULES

- ▶ Elevated T3 and T4
- ▶ Decreased TSH
- ▶ Treatment:
 - ▶ Careful monitoring with ultrasound
 - ▶ Anti-thyroid drugs in combination with beta blockers
 - ▶ Radioiodine
 - ▶ If malignant → surgical removal

THYROID DISORDERS

THYROIDITIS

- ▶ Inflammation of thyroid gland
- ▶ Can lead to excessive thyroid hormones
- ▶ Acute thyroiditis
 - ▶ Caused by infection
- ▶ Postpartum thyroiditis
 - ▶ 1 in 20 women
 - ▶ Few months following delivery

ACUTE THYROIDITIS

- ▶ Rare
- ▶ Typically affects children or young adults
- ▶ Lab results:
 - ▶ ↑ ESR
 - ▶ ↑ WBC
 - ▶ Normal thyroid function
- ▶ Symptoms:
 - ▶ Thyroid pain
 - ▶ Small goiter
 - ▶ Fever, dysphagia, erythema over thyroid
- ▶ Treatment:
 - ▶ Antibiotics

THYROID DISORDERS

THYROID CANCER

- ▶ 56,000 new cases/year in U.S.
- ▶ Females 3x more likely than males
- ▶ Most commonly occurs after age of 30 yr.
- ▶ More aggressive in older patients

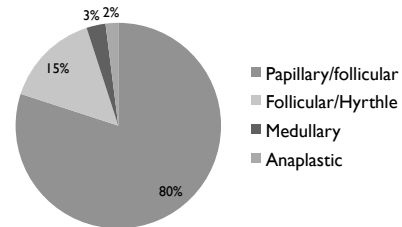
THYROID CANCER - SYMPTOMS

- ▶ Hoarse voice
- ▶ Neck pain
- ▶ Enlarged lymph nodes



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TYPES OF THYROID CANCER



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THYROID CANCER - PROGNOSIS

- ▶ Most are curable
- ▶ 97% cure rate if treated appropriately
 - ▶ Papillary & follicular
 - ▶ Remove portion of thyroid gland that harbors cancer

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THYROID CANCER - PROGNOSIS

- ▶ Medullary thyroid cancer
 - ▶ Tends to spread to lymph nodes
 - ▶ More aggressive treatment needed
 - ▶ Complete thyroid removal (plus local lymph nodes)
- ▶ Anaplastic thyroid cancer
 - ▶ Incurable
 - ▶ Very aggressive

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TREATMENT – THYROID CANCER

- ▶ Radioactive iodine given after removal of thyroid
 - ▶ Destroys any remaining thyroid cells
- ▶ Medullary cancer – cant absorb iodine
 - ▶ Treat only with surgery

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PITUITARY ADENOMA

PITUITARY ADENOMA

- ▶ Benign, slow-growing tumor on pituitary gland
- ▶ Relatively common
 - ▶ 1 in 1000 adults
- ▶ Usually occurs spontaneously

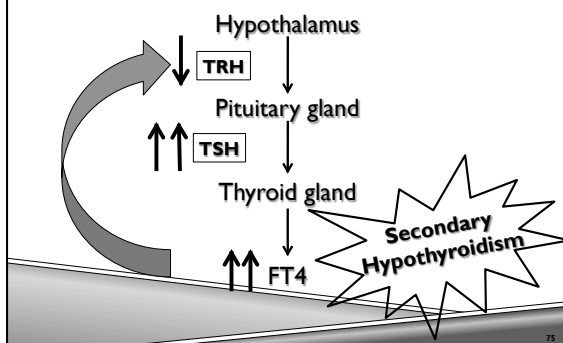
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PITUITARY ADENOMA

- ▶ Either hormone-producing or hormone-inactivating tumors
- ▶ Hormone-producing adenomas:
 - ▶ TSH-secreting pituitary adenoma
 - ▶ Prolactin-secreting pituitary adenoma
 - ▶ Growth hormone-secreting pituitary adenoma
 - ▶ ACTH-secreting pituitary adenoma

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LAB EVALUATION



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CONFIRMATION OF THYROID DISEASE

WHAT IS GOING ON?

- ▶ Is the patient symptomatic?
- ▶ Does patient need treatment?
- ▶ Is the patient euthyroid?

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THYROID STIMULATING HORMONE

- ▶ Single most useful test in diagnosis of thyroid disease
- ▶ **hsTSH**
 - ▶ Detects TSH <0.001 mU/L
 - ▶ Differentiates euthyroid, hyperthyroid, & hypothyroid

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hsTSH	<0.1 mU/L	0.1 – 0.49 mU/L	0.5 – 4.8 mU/L	>4.8 mU/L
Presumptive diagnosis	Hyperthyroid suspected	Borderline thyroid status	No thyroid dysfunction	Hypothyroid suspected
Confirmatory testing	Confirm with FT4 or FT3	Do FT4, FT3, or TRH stimulation	No further testing	Confirm with FT4

TOTAL THYROXINE (TT₄)

- ▶ In circulation, 99.7% bound to proteins
- ▶ Detection of TT₄:
 - ▶ Bound T₄ released from protein in vitro and measured using chemiluminescence
- ▶ TT₄ may change depending on changes in TBG concentration
 - ▶ Estrogen!!
- ▶ Replaced with FT₄

TRIIODOTHYRONINE (T₃)

- ▶ Most active thyroid hormone
- ▶ Detection of TT₃:
 - ▶ Bound T₃ released from protein in vitro
- ▶ Helpful in confirmation of hyperthyroidism
- ▶ Often normal in hypothyroidism

REVERSE T₃ (rT₃)

- ▶ Metabolite with minimal metabolic activity produced by T₄
- ▶ Patient with NTI:
 - ▶ ↓ T₃ ↑ rT₃
 - ▶ Serum T3 dec because enzyme that converts T4 to T3 is blocked
- ▶ Patient with hypothyroidism:
 - ▶ ↓ T₃ ↓ rT₃

Clinical condition	T4	T3	rT3	FT4	TSH
Graves' disease	I	I	NA	I	D,U
Multinodular goiter	I	I	NA	I	D,U
Toxic adenoma	I	I	NA	I	D,U
Primary hypothyroidism	D	D,N	NA	D	I
Nonthyroid disease	N,D	N,D	N,I	N,I	N

I=increase, D=decrease,
U=undetectable, NA=not applicable,
N=normal

THYROID SCANNING

- ▶ Nuclear imaging
 - ▶ Inject radioactive iodine
 - ▶ Checks thyroid function or abnormalities (lumps, inflammation, cancer)
 - ▶ Increased uptake → hyperthyroidism
 - ▶ Decreased uptake → hypothyroidism

