EMERGENCY CARE IN ENDOCRINOLOGY. DIABETIC AND HYPOGLYCEMIC COMA. SEIZURES. DIFFERENTIAL DIAGNOSTICS. EMERGENCY AID.

Endocrine Emergencies

- Adrenal
  - Addisonian Crisis
  - Pheochromocytoma
- Thyroid
  - Thyroid Storm
  - Myxedema Coma
- Miscellaneous
  - Hypoglycemia
  - Diabetes Insipidus

General Mechanisms of Endocrine Pathophysiology

- Deficient hormone action
- Excess hormone production or action
- Neoplasia

Mechanisms of Endocrine Pathophysiology

- 1. Deficient hormone action
  - –Primary glandular failure
    - Congenital
    - Acquired (atrophy, surgery, tumor, drug-induced, autoimmune, infectious)
  - –Secondary glandular failure
  - –Disordered hormone release or activation
  - –Accelerated hormone metabolism
  - –Target tissue resistance

Mechanisms of Endocrine Pathophysiology (cont.)

- 2. Excess hormone production or action
  - Gland autonomy (neoplasia, hyperplasia)
  - Abnormal stimulation
  - Ectopic hormone production
  - Altered hormone metabolism
  - Target tissue increased sensitivity to hormone action

Mechanisms of Endocrine Pathophysiology (cont.)

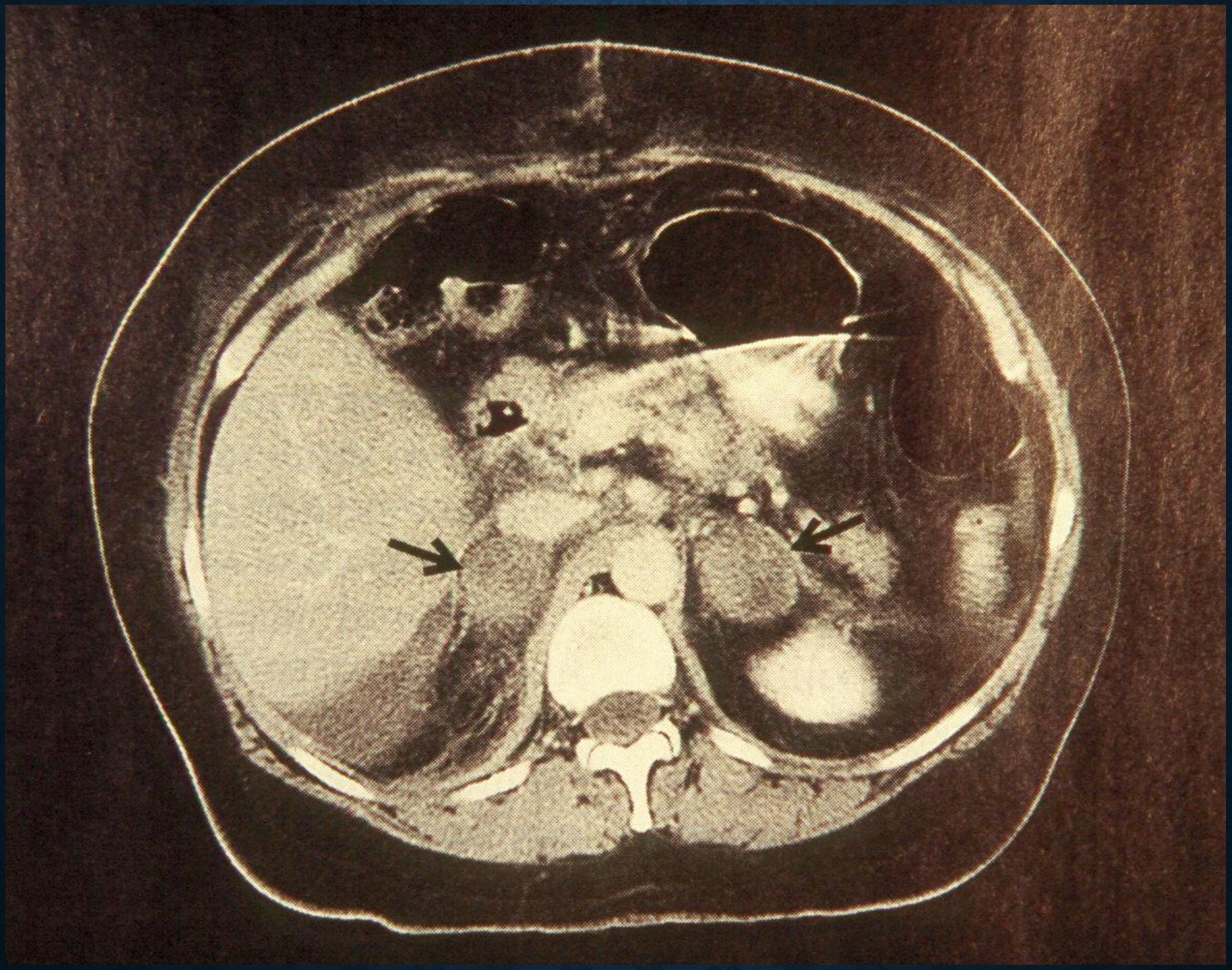
- 3. Neoplasia
  - Benign vs. malignant
  - Functional vs. nonfunctional
  - Ectopic hormone production
  - Sporadic vs. familial syndromes

Diseases of the Adrenals

- Adrenocortical insufficiency
  - Addison's
  - Hypopituitarism
  - Iatrogenic ACTH deficiency
- Cushing's Syndrome
  - Cushing's Disease (cortical hyperplasia)
  - Pituitary tumor
- Adrenal adenoma or carcinoma
  - Ectopic ACTH syndrome (from tumors)
- Virilization
  - Adrenal adenoma or carcinoma
  - Congenital adrenal hyperplasia (CAH)
- Adrenal-mediated hypertension syndromes
  - Primary hyperaldosteronism (adenoma vs. hyperplasia), Cushing's syndrome, Pheochromocytomas

Etiologies of Primary Adrenal Insufficiency

- Iatrogenic suppression
- Autoimmune adrenalitis (idiopathic)
- Infections (mycobacteria, fungal, CMV, HIV)
- Sarcoidosis
- Hemorrhage (anticoagulants, meningococcemia, trauma, toxemia, emboli)
- Collagen vascular disease
- Amyloidosis
- Hemochromatosis
- Metastatic malignancy
- Congenital (hypoplasia, adrenogenital syndrome, adrenoleucodystrophy)



CT scan showing bilateral adrenal hemorrhages in a 57 year old female with breast cancer

Etiologies of Secondary Adrenal Insufficiency

- Pituitary insufficiency
  - Congenital, tumor, infarction, sarcoid, autoimmune
- Hypothalamic dysfunction
  - Tumor
  - Vascular malformation

Symptoms of Adrenal Insufficiency

- Weakness, fatigue, lethargy
- Nausea, vomiting
- +/- diarrhea
- Anorexia, weight loss
- Mental sluggishness
- +/- syncope
- Addisonian Crisis:
  - Shock
  - Cardiovascular collapse

Signs of Adrenal Insufficiency

- Hypotension
- Other signs of dehydration
- Hyperpigmentation / vitiligo
- Skin atrophy
- Muscle wasting
- Loss of axillary & pubic hair
- +/- fever

Lab Findings in Adrenal Insufficiency

- Hyponatremia
- Hyperkalemia
- Hypoglycemia
- Azotemia (prerenal)
- +/- eosinophilia
- +/- anemia

Precipitating Factors for Addisonian Crisis

- Acute infection, esp. pneumonia
- Acute MI
- Pulmonary embolus
- Trauma / burns
- Surgery
- Heat exposure
- Vomiting / diarrhea
- Dehydration
- Blood loss
- Rapid cessation or reduction of chronic steroid therapy

Acute Adrenal Crisis
Caveats

- Suspect this diagnisis when:
  - Sudden hypotension in response to procedure or stress, and does not correct with initial IV fluids +/- raising legs
- Patients previously maintained on chronic glucocorticoid Rx may not exhibit severe dehydration or hypotension until preterminal since mineralocorticoid function is usually maintained

Addisonian Crisis treatment

1. High flow oxygen
2. Aggressive fluid / electrolyte replacement

   Initially IV infusion - usually need 4 to 6 liters

   Switch to when K+ decreases
3. IV hydrocortisone

   100 to 250 mg IV bolus

   10 to 20 mg per hour IV infusion
4. +/- cortisone acetate 50 mg IM (in case infusion stops)
5. Search for precipitating cause

Further treatment of Addisonian Crisis

Once the patient's condition improves:

- **Decrease hydrocortisone to 100 mg bid**
- **Halve dose daily till maintenance dose achieved (usually 20 mg hydrocortisone per day)**
- **Add fludrocortisone 0.1 mg per day when dose of cortisone < 100 mg / day**

Prevention of Acute Adrenal Crisis

- For patients on chronic steroid treatment:
  - Double their normal daily dose before and for at least 2 - 3 days after a stressful procedure or when an active infection is present
- For severe stress:
  - Consider tripling steroid dose

Dosing Comparisons for Adrenocortical Steroids

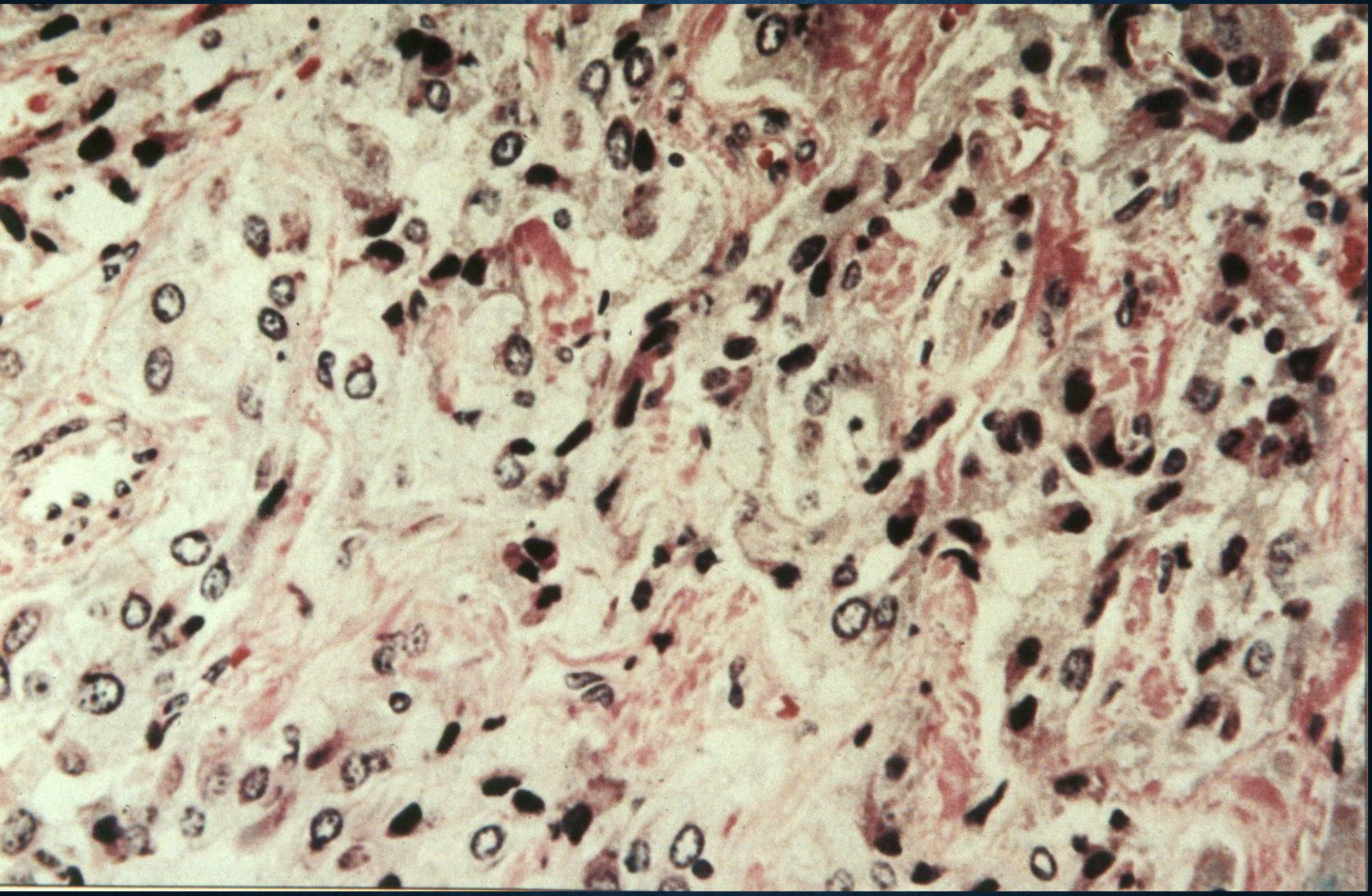
STEROID	t1/2 (hrs.)	Relative potency	Equivalent dose
Cortisone	**8 - 12**	**0.8**	**25**
Cortisol	**8 - 12**	**1.0**	**20**
Prednisone	**12 - 36**	**4.0**	**5**
Methylpred-nisolone	**12 - 36**	**5.0**	**4**
Dexameth-asone	**36 - 72**	**25**	**0.75**

Pheochromocytoma

- Tumor of chromaffin cells
- Chromaffin cells produce, store, & secrete catecholamines
- Clinical features of these tumors are due to excessive catechol release (not usually due to direct tissue extension effects of tumor)
- Cause only 0.1% of cases of hypertension but represent a curable cause of hypertension

Fig 2. Surgical specimen showing areas of hemorrhagic necrosis of the adrenal gland. The mass was freely movable, suggesting a benign tumor.

Excised pheochromocytoma



High power microscopy view of stained pheochromocytoma cells

Pheochromocytoma Locations

- Adrenal medulla : 90 %
- Abdomen : 8 %
- Neck or thorax : 2 %
- Multiple sites : 10 %
- Malignant : 10 %
- Associated with familial syndromes : 5 %

Pheochromocytoma Catechol Secretion

- Most secrete both norepinephrine and epinephrine (generally norepi > epi)
- Most extrarenal tumors secrete only norepi
- Malignant tumors secrete more dopamine and HVA
- Predominant catechol secreted cannot be predicted by clinical presentation

Most Common Symptoms of Pheochromocytoma

- Hypertension > 90 %
  - Sustained 30 %
  - Sustained with crises 30 %
  - Paroxysmal 30 %
- Headache 80 %
- Sweating 70 %
- Palpitations 65 %

Additional Symptoms of Pheochromocytoma

- Pallor 45 %
- Nausea +/- emesis 40 %
- Nervousness 35 %
- Fundoscopic changes 30 %
- Weight loss 25 %
- Epigastric or chest pain 20 %

Indications to Screen Patients for Pheos

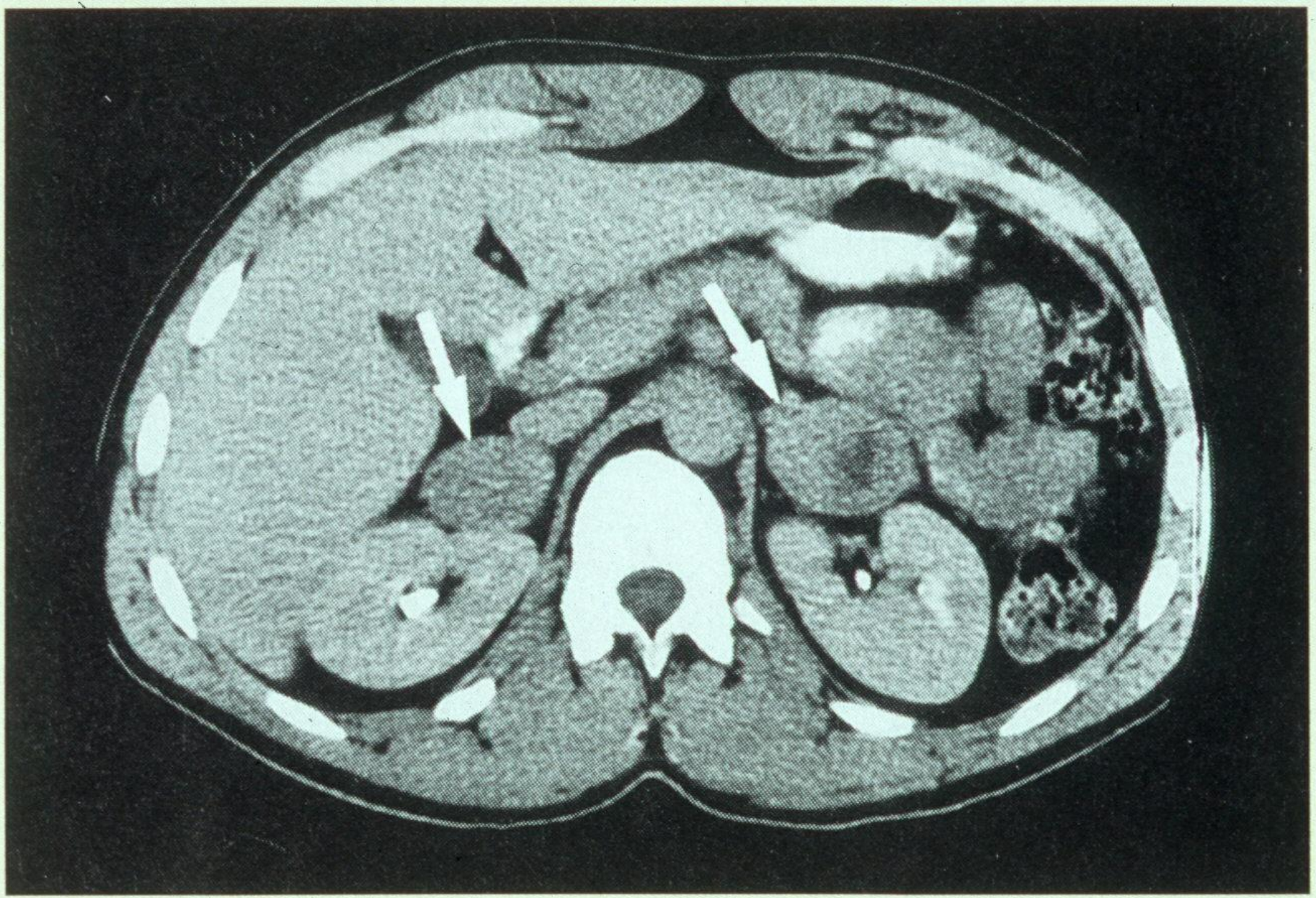
- Hypertension with:
  - Grade 3 or 4 retinopathy of uncertain cause
  - Weight loss
  - Hyperglycemia
  - Hypermetabolism with nl. thyroid profile
  - Cardiomyopathy
  - Resistance to 2 or 3 drug Rx
  - Orthostatic hypotension (not due to drug Rx)
  - Unexplained fever
- Marked hyperlability of BP
- Recurrent attacks of sx of pheos

More Indications to Screen Patients for Pheos

- Severe pressor response during or induced by:
  - Anesthesia or intubation
  - Surgery
  - Angiography
  - Parturition
- Unexplained circulatory shock during:
  - Anesthesia
  - Pregnancy, delivery, or puerperium
  - Surgery (or after surgery)
  - Use of phenothiazines
- Family history of pheos
- Hyperlabile BP or severe hypertension with pregnancy
- X ray evidence of suprarenal mass

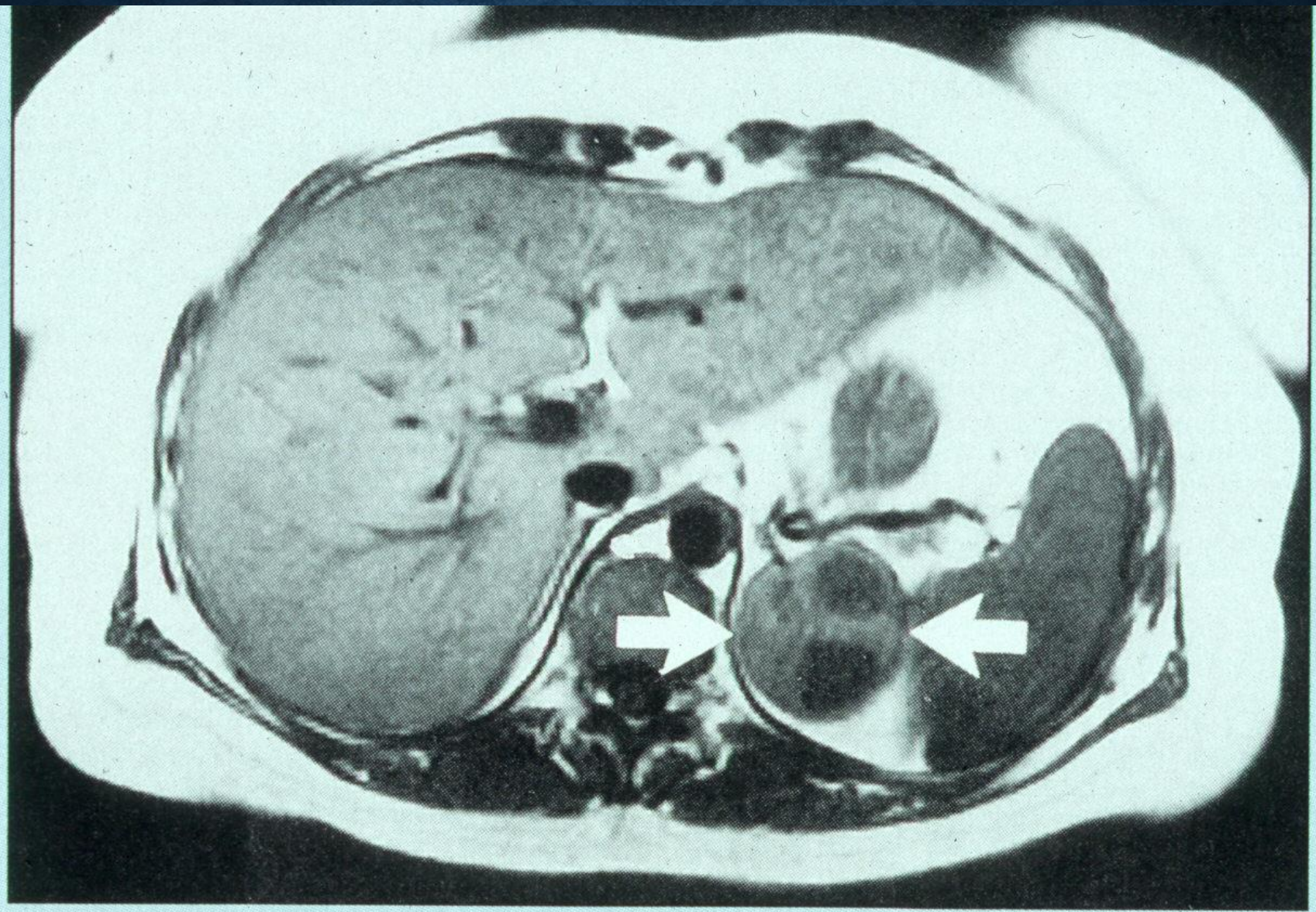
Localization Techniques for Pheos

- Abdominal CT : most useful
  - Cannot confirm tissue dx
- Iodine 131 metaiodobenzylguanidine nuclear medicine scanning
  - Helpful for non-abdominal tumors and to confirm function
- Angiography
  - Requires medication prep for safety



CT scan demonstrates a 5-cm-diameter mass in the left adrenal and a 4-cm-diameter mass in the right adrenal (arrows). A small central area

Bilateral pheochromocytomas (the one on the left has a small area of central hemorrhage)



MRI scan with T_1-weighted partial saturation sequences demonstrates a 4.5-cm left adrenal mass (arrows). The areas of cystic necrosis within the tumor are typical of pheochromocytoma.

Treatment: Acute Symptom Control for Pheos (also for pre-angio or preop prep)

- Phentolamine 2 to 5 mg IV (alpha block)
- Then propranolol 1 to 2 mg IV (beta block) or labetolol 20 to 40 mg IV (alpha & beta block)
- Use nitroprusside or phentolamine infusion for hypertensive crisis (50 to 100 mg in 250 cc D5W)
- For hypotension : norepi infusion
- For arrhythmias : lidocaine bolus & infusion

Meds for Nonemergent or Chronic Sx Control for Pheos

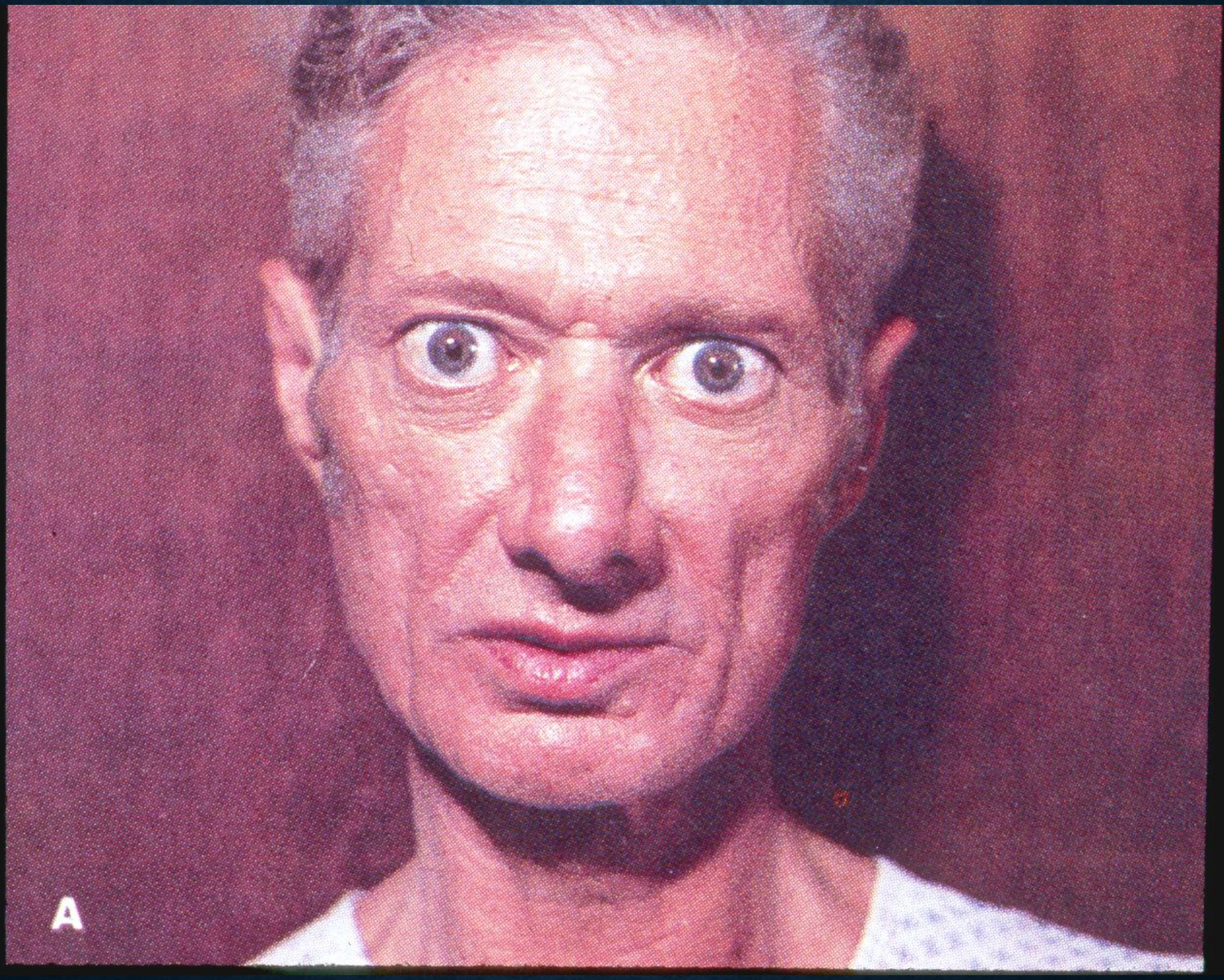
- Phenoxybenzamine 10 to 20 mg tid-qid (alpha block)
- Prazosin 1 to 5 mg bid
- Propranolol 10 to 40 mg qid or labetolol 200 to 600 mg bid (beta block)
- Alpha-methyl-p-tyrosine (metyrosine) 250 mg to 1 gram bid (synthesis inhibitor)

Thyroid Storm
Definitions

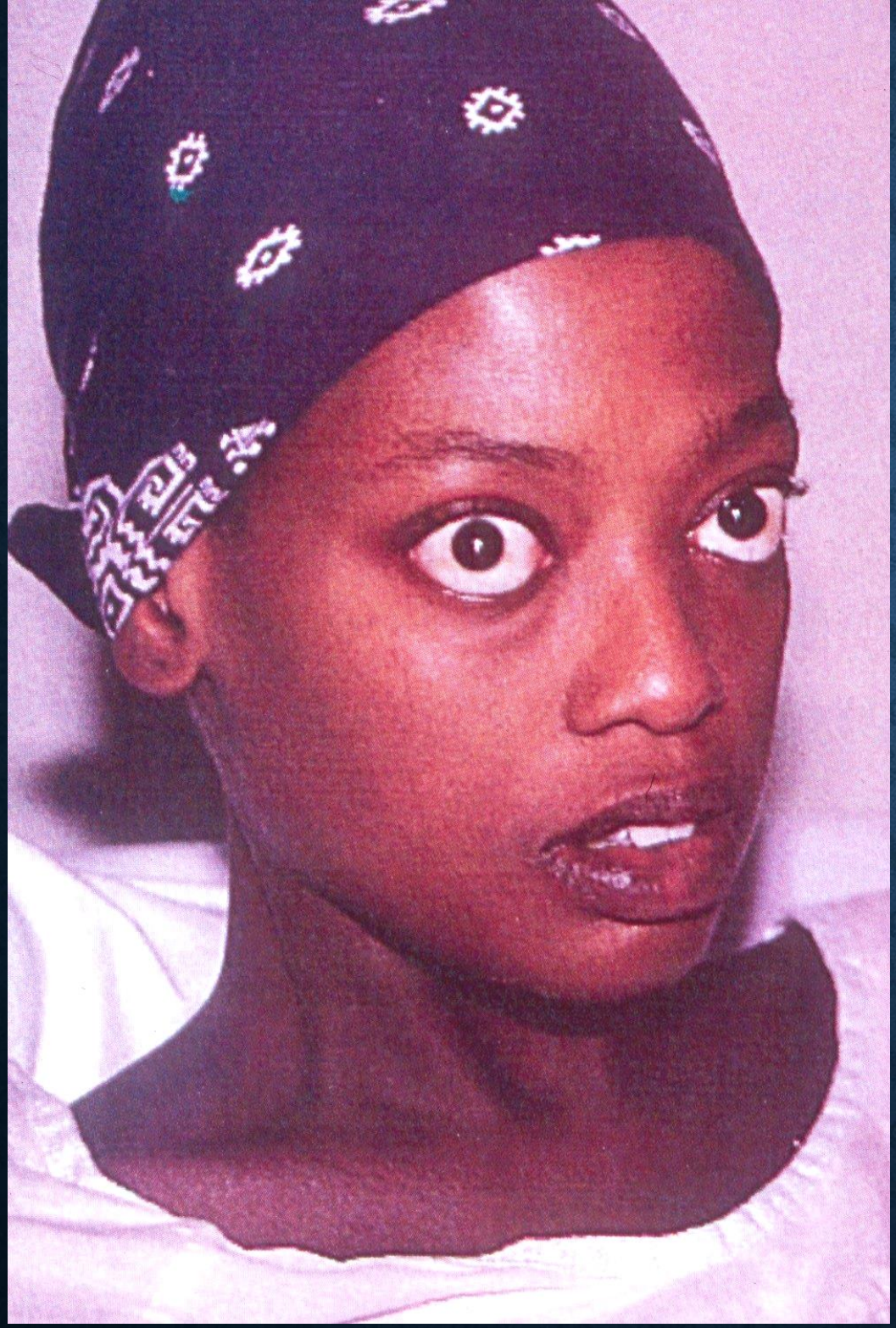
- "Exaggerated or florid state of thyrotoxicosis"
- Life threatening, sudden onset of thyroid hyperactivity"
- May represent end stage of the continuum:
  - hyperthyroidism to thyrotoxicosis to thyrotoxic crisis to thyroid storm
- "Probably reflects the addition of adrenergic hyperactivity, induced by a nonspecific stress, into the setting of untreated or undertreated hyperthyroidism"

Thyroid Storm
Epidemiology

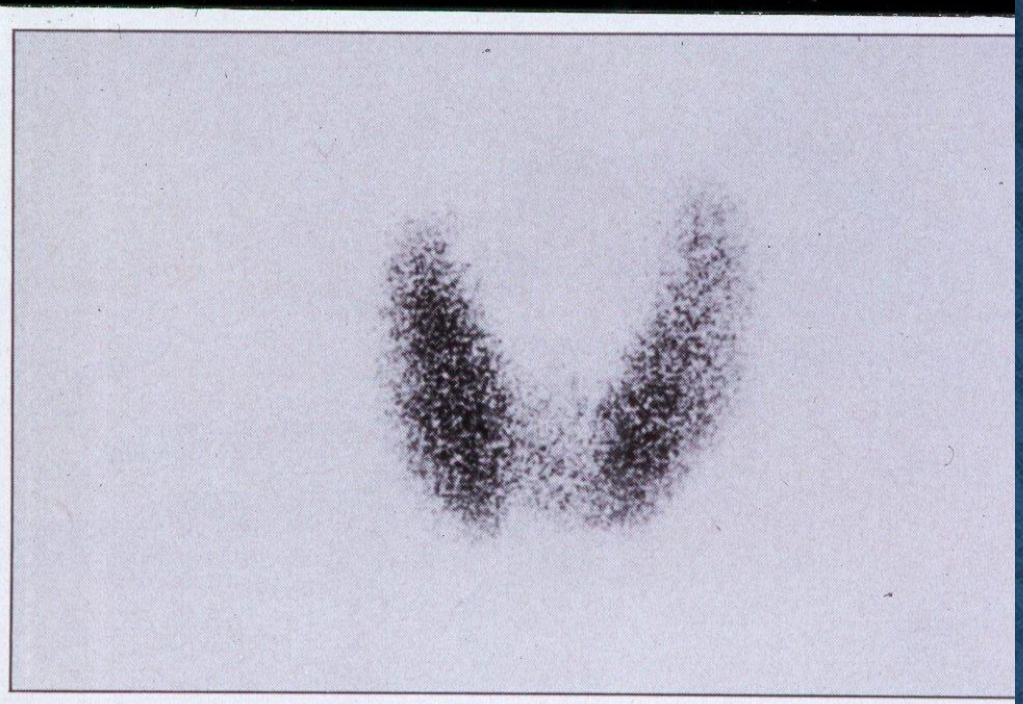
- Most cases secondary to toxic diffuse goiter (Grave's Disease)
  - Mostly in women in 3rd to 4th decades
- Some cases due to toxic multinodular goiter
  - Mostly in women in 4th to 7th decades
- Very rarely due to :
  - Factitious
  - Thyroiditis
  - Malignancies
- Very rare in children



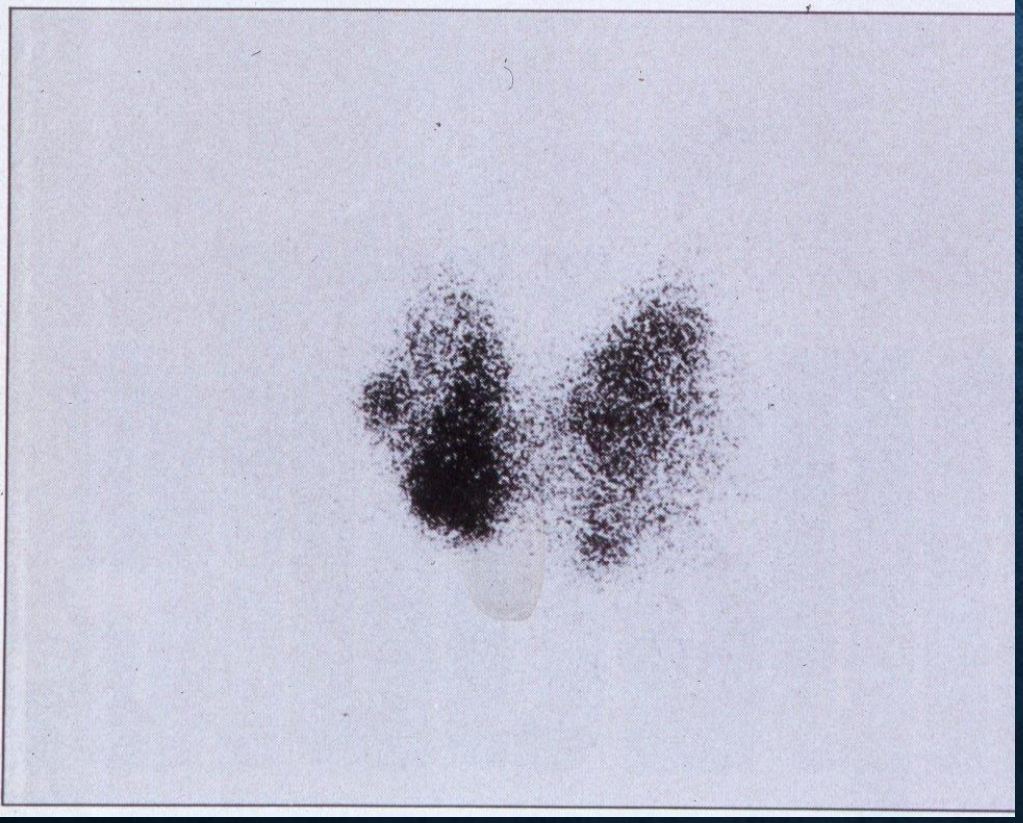
51 year old male with Graves Disease who presented with urine retention



Patient with Graves Disease



Thyroid scan of patient with Graves Disease



Scan of patient with toxic multinodular goiter with hot nodule

Thyroid Storm
Clinical Presentation

- Most important:
  - Fever
  - Abnormal mental status (agitation confusion, coma)
- Tachycardia
- Vomiting / diarrhea
- +/- jaundice
- +/- goiter
- +/- exopthalmos

Thyroid Storm
CNS Manifestations

- With increasing severity of storm:
  - Hyperkinesis
  - Restlessness
  - Emotional lability
  - Confusion
  - Psychosis
  - Apathy
  - Somnolence
  - Obtundation
  - Coma

Thyroid Storm
Cardiovascular Manifestations

- Increased heart rate
  - Sinus tachycardia or atrial fibrillation
- Increased irritability
  - First degree AV block
- Wide pulse pressure
- Apical systolic murmur
- Loud S1, S2
- May develop CHF

"Apathetic" or "Nonactivated" Thyrotoxicosis

- Represents dangerous hyperthyroidism masked by preexistent sx
- Usually age > 70
- Recent weight loss > 40 lbs.
- May present as seemingly isolated sx:
  - CHF
  - Atrial fib
  - CNS sx
    - Somnolence, apathy, coma

Thyroid Storm Precipitating Factors

- Infection, esp. pneumonia
- Pulmonary embolus
- Parturition / toxemia
- Trauma
- Surgery
- I 131 R-x
- Iodinated contrast agents
- Withdrawl of antithyroid drugs

Thyroid Storm
Initial Lab Studies Needed

- clinical blood count, BUN, glucose
- T4, T3, T3 RU, thyroid stimulating hormone
- Urine test
- Arterial Blood Gas
- +/- Liver function tests
- +/- serum cortisol

Thyroid Storm
Usual Lab Results

- Lab studies do NOT distinguish thyrotoxicosis from thyroid storm
- Usually T4 & T3 elevated, but may be only increased T3
- Usually plasma cortisol low for degree of physiologic stress present
- Hyperglycemia common

Thyroid Storm
Emergent Rx

- High flow O2
- Rapid cooling if markedly hyperthermic
  - Ice packs, cooling blanket, mist / fans, NG lavage, acetominophen (ASA contraindicated)
- IV +/- IV fluid bolus if dehydrated
  - May need inotropes if already have CHF)
- Propranolol 1 to 2 mg IV & repeat or labetolol 20 to 40 mg IV & repeat prn
- +/- digoxin, Ca channel blockers for rate control for atrial fib; +/- diuretics for CHF
- Find & treat precipitating cause

Myxedema Coma

- Represents end stage of improperly treated, neglected, or undiagnosed primary hypothyroidism
- Occurs in 0.1% or less of cases of hypothyroidism
- Very rare under age 50
- 50% of cases become evident after hospital admission
- Mortality 100% untreated, 30 to 60% treated
- Most cases present in the winter

General Causes of Thyroid Failure

- Diseases of the:
  - Thyroid (primary hypothyroidism) : 95 %
  - Pituitary (secondary hypothyroidism) : 4 %
    - Pituitary tumor or sarcoid infiltration
  - Hypothalamus (tertiary hypothyroidism) : < 1 %

Etiologies of Primary Hypothyroidism

- Autoimmune : most common
- Post thyroidectomy
- External radiation
- I 131 Rx
- Severe prolonged iodine deficiency
- Antithyroid drugs (including lithium)
- Inherited enzymatic defect
- Idiopathic

Symptoms of Hypothyroidism

- Cold intolerance
- Dyspnea
- Anorexia
- Constipation
- Menorrhagia or amenorrhea
- Arthralgias / myalgias
- Fatigue
- Depression
- Irritability
- Decreased attention +/- memory
- Paresthesias

Signs Related to Hypothyroidism

- Dry, yellow (carotenemic) skin
- Weight gain (41% of cases)
- Thinning, coarse hair
- "Myxedema signs“ :
  - Puffy eyelids
  - Hoarse voice
  - Dependent edema
  - Carpal tunnel syndrome
- Anemia


CHARACTERISTIC FACIES
IN MYXEDEMA:
COARSE FEATURES;
THICK LIPS; DRY SKIN;
PUFFY EYELIDS;
DULL, LETHARGIC EXPRESSION;
COARSE HAIR
MEGALOGLOSSIA,
SHOWING DENTAL IMPRESSIONS
F. Netter M.D.
©CIBA
PUDGY HANDS; CHIPPED NAILS;
DRY, WRINKLED SKIN;
HYPERKERATOSIS OF ELBOW

Patient with myxedema coma

Hypothyroidism and Myxedema Coma
Cardiac Signs

- Hypotension
- Bradycardia
- Pericardial effusion
- Low voltage EKG
- Prolonged QT
- Inverted or flattened T waves

Myxedema Coma
Typical Presentation

- Usual signs & sx of hypothyroidism plus:
  - Hypothermia (80 % of cases)
    If temp. normal, consider infection present
  - Hypotension / bradycardia
  - Hypoventilation / resp. failure
  - Ileus
  - Depressed mental status / coma

Lab Studies to Order for Suspected Myxedema Coma

- Clinical blood count
- ElectroLytes, BUN, glucose, calcium
- T3, T4, TSH
- Serum cortisol
- Arterial Blood Gas
- Liver function tests
- +/- drug levels

Precipitants of Myxedema Coma

- Cold exposure
- Infection
  - Pneumonia
  - Urinary Tract Infection
- Trauma
- Central nervous system depressants:
  - Narcotics
  - Barbiturates
  - Tranquilizers
  - General anesthetics
- Cerebral vascular accident
- Congestive heart failure

Contributing Factors to Coma in Myxedema Coma

- Hypothyroidism itself
- Hypercapnia
- Hypoxia
- Hypothermia
- Hypotension
- Hypoglycemia
- Hyponatremia
- Drug (sedative) side effect
- +/- sepsis

Emergency Treatment of Myxedema Coma

- O2 +/- intubation / ventilation (if resp. failure)
- Rapid blood glucose check +/- IV D50 +/- Naloxone
- Hydrocortisone 100 to 250 mg IVP
- Cautious slow rewarming (warm O2, scalp/groin/axilla warm packs, NG lavage)
- Thyroxine (T4) 500 micrograms IV, then 50 mcg qd IV
- Add 25 mcg triiodothyronine (T3) PO or by NG q 12h if T4 to T3 peripheral conversion possibly impaired
- Careful IV fluid rehydration ; watch for CHF
- Follow TSH levels ; should decrease in 24 hrs. & normalize in 7 days of Rx

Causes of Hypoglycemia

- **Fasting**
  - –Insulinoma or extrapancreatic tumors
  - –Extensive hepatic dysfunction
  - –Starvation
  - –Sepsis
  - –Chronic renal failure
  - –Glycogen storage diseases
  - –Diseases with antibodies to insulin or receptor
  - –Hormonal deficiency (steroids, growth hormone, epi)
  - –Drugs (on next slide)
- **Postprandial (Alimentary, Reactive, Genetic - galactosemia or fructose intolerance)**
- **Artifactual (leukemia, polycythemia)**

Drugs Causing Hypoglycemia

- Insulin
- Oral hypoglycemics
- Ethanol
- Salicylates
- Beta blockers
- Pentamidine
- Diisopyramide
- Quinine
- Isoniazid
- MAO inhibitors
- Various drugs causing decreased liver metabolism of oral hypoglycemic agents

Symptoms and Signs of Hypoglycemia

- Symptoms
  - Diaphoresis
  - Palpitations
  - Headache
  - Hunger
  - Trembling
  - Faintness
- Signs
  - Hypothermia
  - Confusion
  - Amnesia
  - Seizures
  - Coma
  - ANY FOCAL Central Nervous System SIGN

Diagnostic Approach to Fasting Hypoglycemia

- Prove that hypoglycemia is directly responsible for sx during attacks by showing:
  - typical sx
  - plasma glucose < 50 mg%
  - prompt relief of sx by glucose ingestion or IV
- Consider checking:
  - Serum insulin level
  - Insulin antibodies
  - Sulfonylurea levels
  - C-peptide levels
  - Proinsulin levels

Causes of Polyuria

- Urinary tract infection
- Osmotic diuresis (e.g., diabetes mellitus)
- Primary (psychogenic) polydipsia (Compulsive water drinking)
- Nephrogenic diabetes insipidus
- Central diabetes insipidus

Causes of Diabetes Insipidus

- Central
  - Head trauma
  - Craniopharyngioma
  - Infiltrative (sarcoid)
  - Post neurosurgery
  - Familial
  - Vascular
  - Infectious
  - Idiopathic
- Nephrogenic
  - Drugs
    - Demeclocycline
    - Lithium carbonate
  - Acquired
    - Sickle cell anemia
    - K+ deficiency
    - Hypercalcemia
    - Amyloidosis
    - Sjogren Syndrome
    - Multiple myeloma
  - Familial