Adrenal masses

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Incidentaloma

An incidentaloma is an incidentally discovered mass or lesion found on imaging or during surgery that was not clinically suspected or related to the patient's presenting complaint.

In other words — it's a "surprise finding" discovered by chance, often during scans performed for other reasons.

Incidentalomas can occur in various organs, but the most common are: adrenal gland ,thyroid , pituitary, kidney

Adrenal Incidentaloma

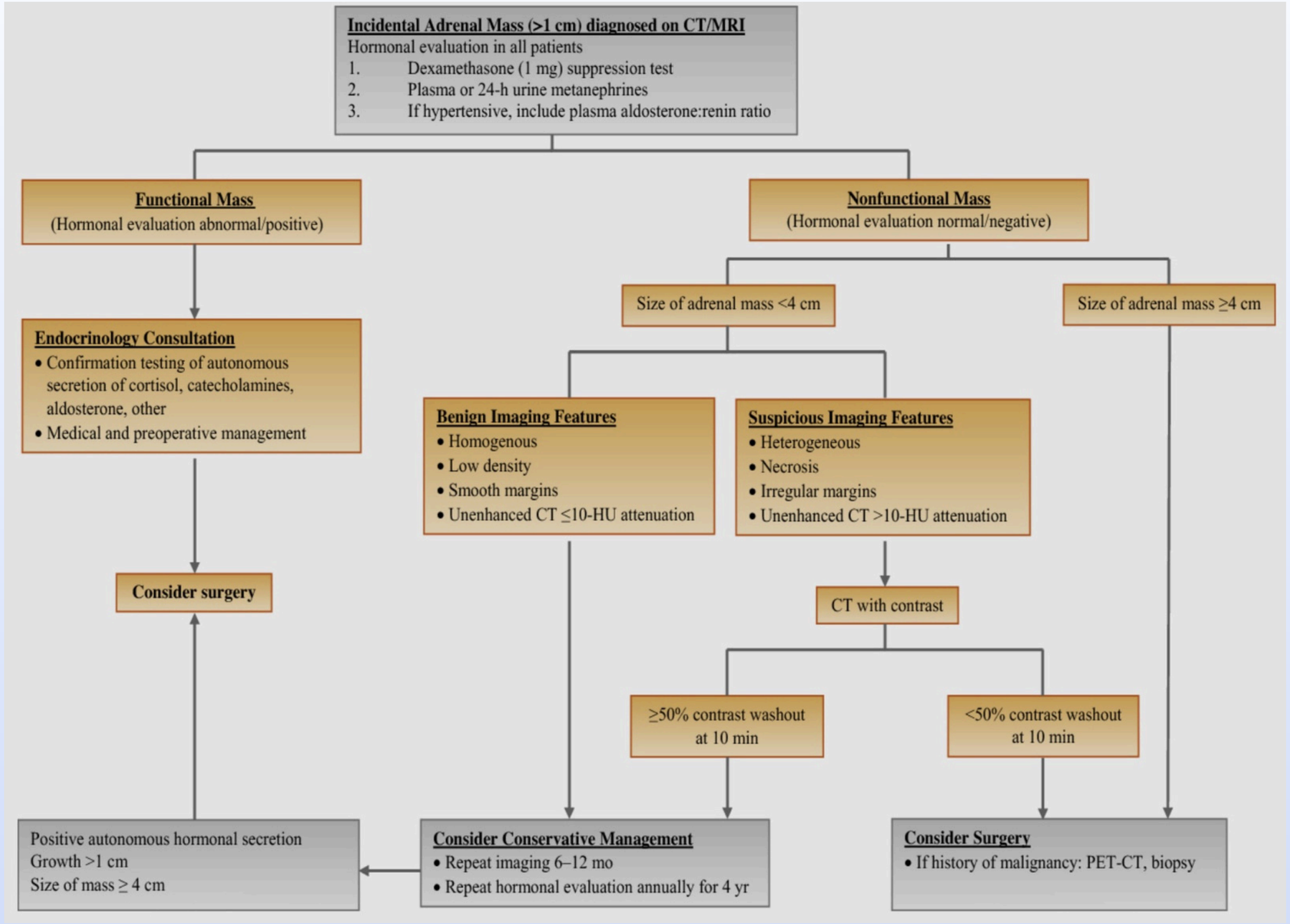
An adrenal incidentaloma is a mass in the adrenal gland >1 cm, found incidentally during imaging for unrelated reasons.

- Found in (1-7)% in abdominal CT scan
- increase with age , obesity , diabetes and HTN

Unilateral mass or bilateral in (10-15)% of cases
in some patients one adrenal mass proves to be non functioning adenoma while the contralateral mass is hormone secreating

- Causes:
- Non-functioning adenoma (most common)
- Functioning adenomas (Cushing's, Conn's, pheochromocytoma)
- Metastases
- Myelolipoma
- Adrenal carcinoma
- hyperplasia

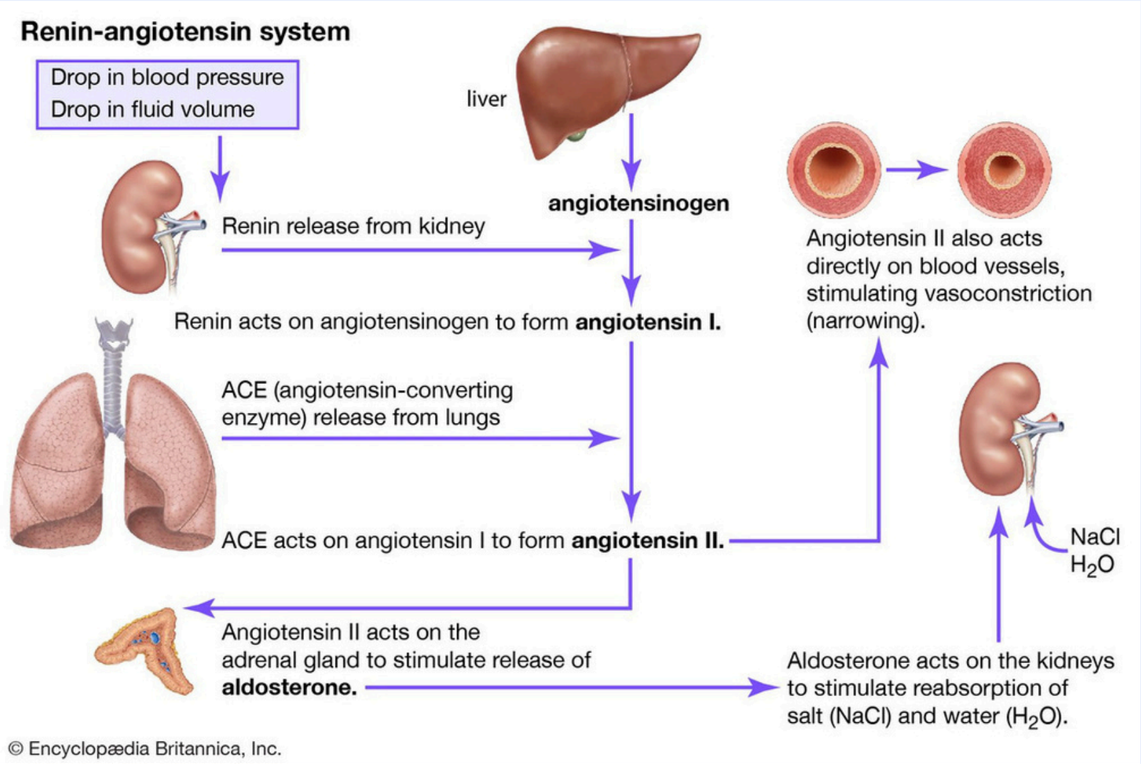
General Approach to Any Incidentaloma



2 Conn’s syndrome

Conn’s syndrome — also known as Primary Hyperaldosteronism — is a clinical condition caused by excess secretion of aldosterone from the adrenal cortex, usually due to an aldosterone-producing adenoma or bilateral adrenal hyperplasia , less commonly adrenal carcinomama

- Female to male ratio is 2:1
- most evident between ages 30-50 years old



Clinical features

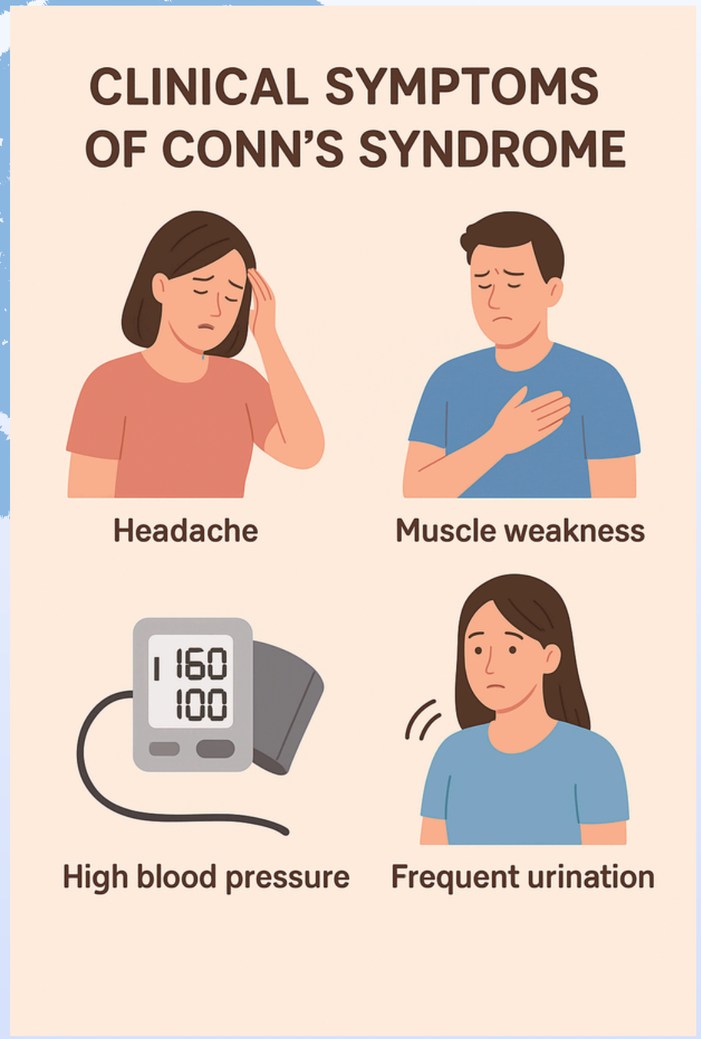
1. **Hypertension**:
   Most common feature, often moderate to severe and resistant to usual antihypertensive drugs.

   2. **Hypokalemia**:
   Leads to muscle weakness, fatigue, muscle cramps, or even periodic paralysis in severe cases.

   Can also cause constipation , polyuria, polydipsia and cardiac arrhythmias.
   ** however up to (30-40)% of patients may have normal k+ initially

   3.**Metabolic alkalosis**:
   Aldosterone promotes H^+ secretion in the kidney → loss of hydrogen ions → metabolic alkalosis.

   4. no peripheral edema



Diagnosis

1.Screening & biochemical tests
*measure plasma aldosterone concentration (PAC) + plasma renin activity (PRA)
*if PAC>15ng/dl + PRA low <1 ng/ml/hr or aldosterone to renin ratio >20-30
suggest primary hyperaldosteronism

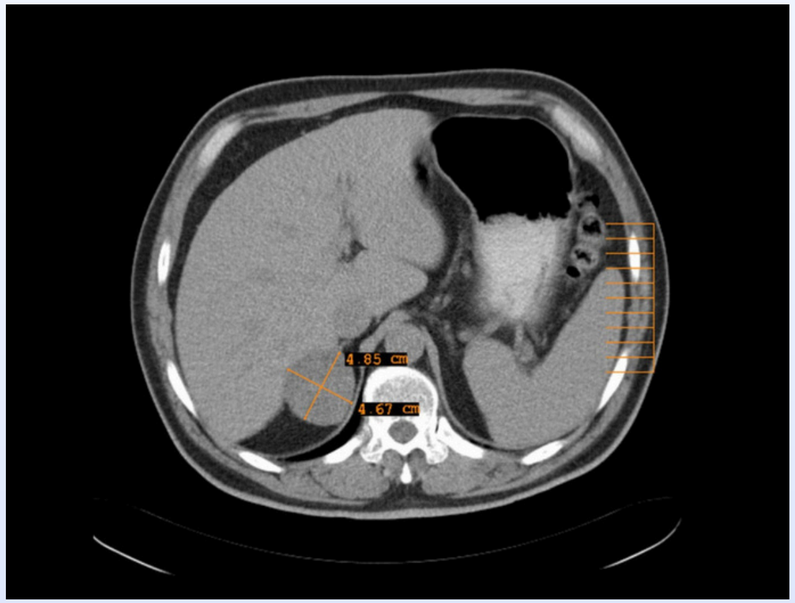
.**2. Confirmatory tests** (salt infusion test and fludrocortisone suppression test)

3.**Serum electrolytes (Na+,K+) , ECG, KFT**

3.imaging : US , CT, MRI, Iodocholesterol isotope

4.Adrenal vein sample

Diagnosis



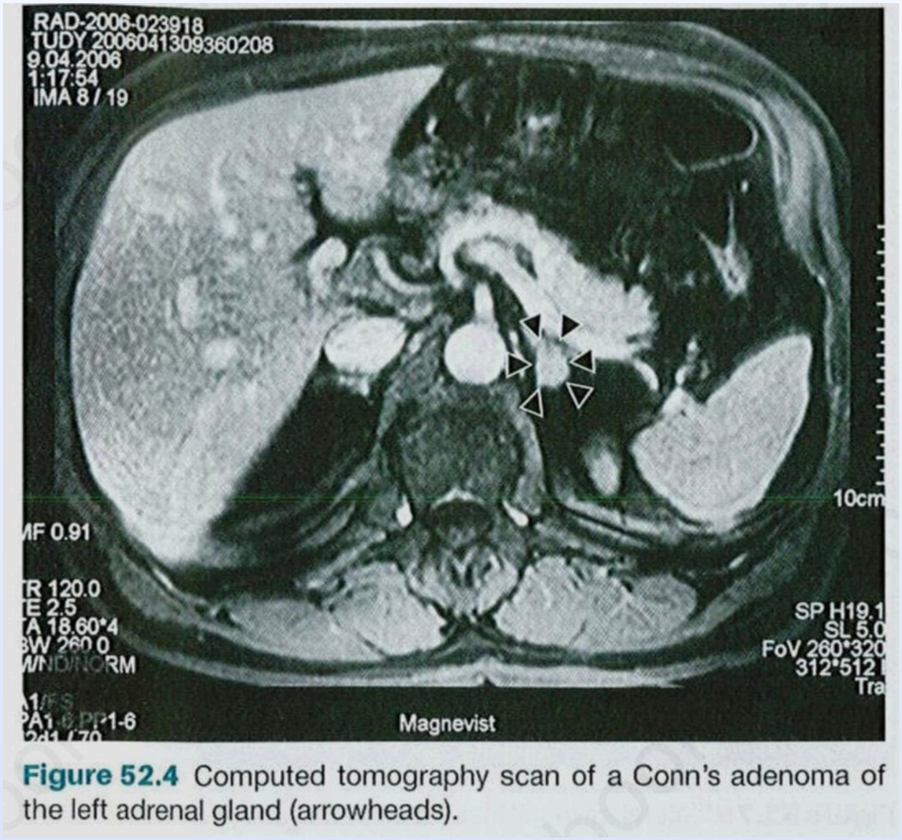
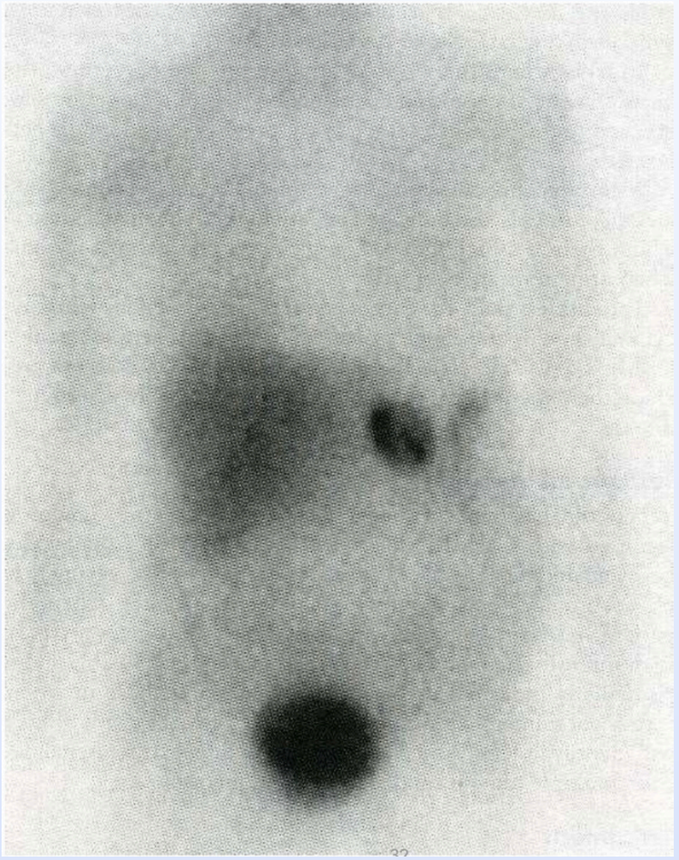


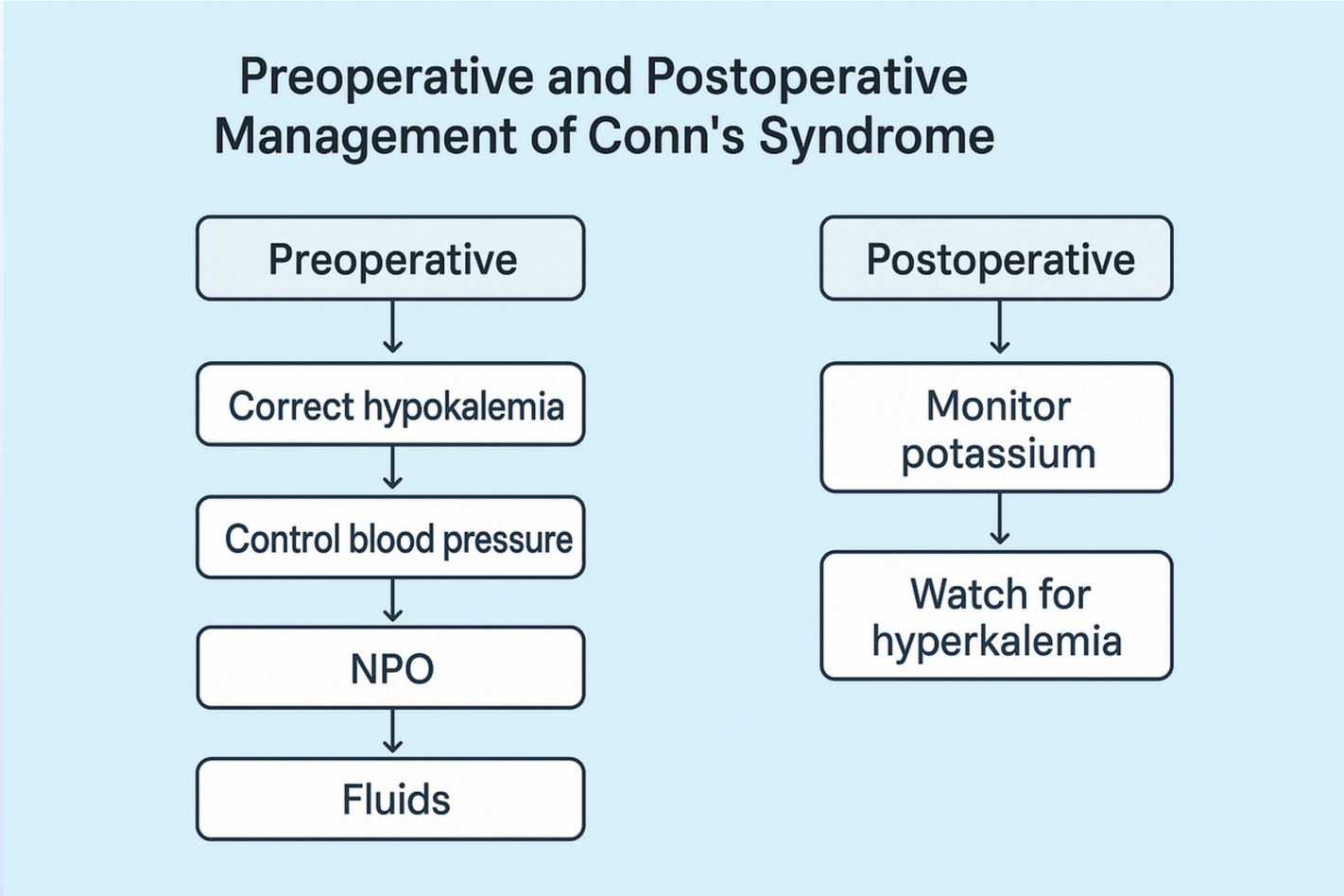
Figure 52.4 Computed tomography scan of a Conn's adenoma of the left adrenal gland (arrowheads).



Treatment

1.if unilateral mass or failed medical treatment : laparoscopic adrenalectomy

2.if bilateral: aldosterone antagonist (spironolactone) , dietry sodium restriction and BP control



Pre operative and post operative management

1) ***correct hypokalemia*** (target>4 mmol/l before surgery):
 * if mild give oral (KCL) 20-40 mol/l orally 2-3 times per day
 * if severe (K+<3mmol/l or symptomatic) , give KCL 20mmol diluted in 100ml NS over 1 hour ,reapets as needed,and always under ECG monitoring

**note*: avoid dextrose solutions because it stimulates insulin release which worsens hypoK+
 * stop K+ once you reach the target

2)***control BP***: spironolactone (100-400)mg/day start 4weeks prior to surgery

3)***keep patient NPO*** (6-8) hours prior to surgery

4)***IVfluids***: 0.9%NS (avoid glucose) & stop diuretics 1-2 dayes before surgery

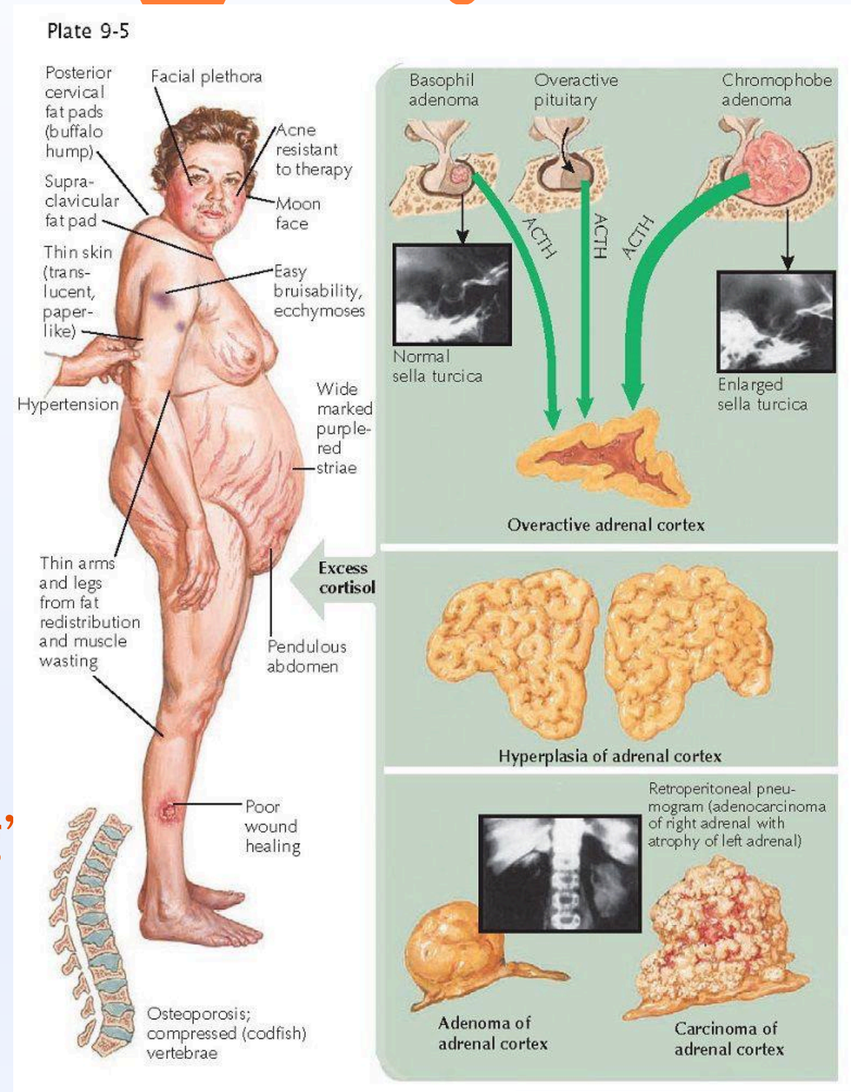
5)***post operative*** : check for serum K+ every 6-7 hours for first [24-48] hours due to risk of hyperkalemia
*BP every 4-6 hours for first 48 hours (risk for hypertension)
*urine output hourly during surgery and for 24 hours post op then every 4-6 hours (goal:>0.5ml/kg/hr)
6)***recheck aldosterone & renin*** at 4-6 weeks to confirm cure

3

Cushing’s syndrome

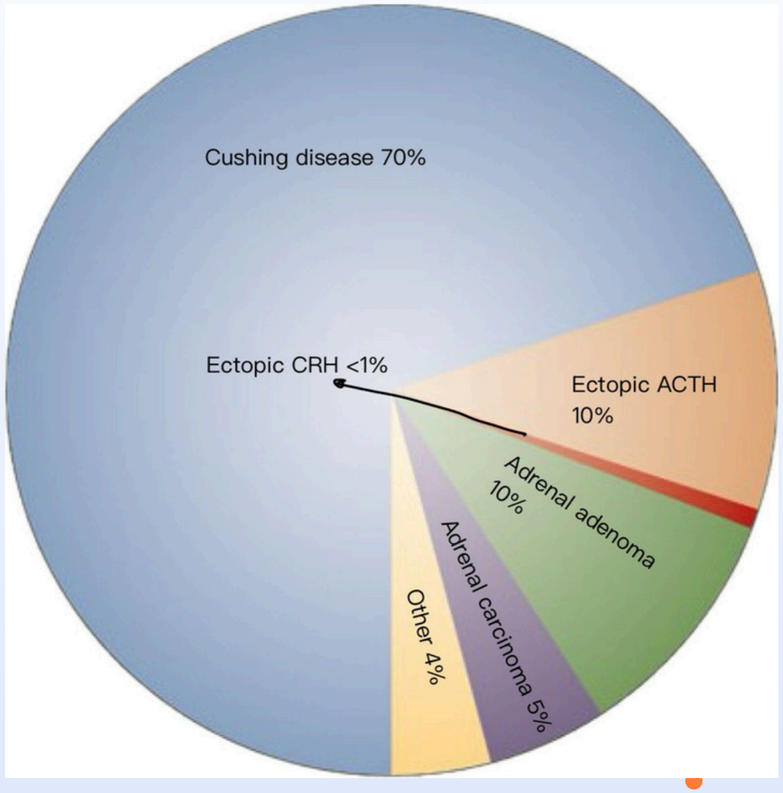
1- Hypersecretion of cortisol caused by endogenous production
of corticosteroids is known as **Cushing’s syndrome.**
due to:
Exogenous steroid medication
ACTH_ independent adrenal disease

2- Hypersecretion of cortisol caused by increased ACTH production is known as **Cushing’ disease.**



Etiology and prevalence

- Iatrogenic Cushing's syndrome (most common)
- Cushing's disease
- Ectopic ACTH
- Adrenal tumors



So the most common cause of hypercortilsolism is iatrogenic (exogenous Cushing’s syndrome).
Endogenous Cushing may be ACTH dependent (secondary) ,or ACTH independent (primary).
The most common of them is secondary due to ACTH producing pituitary micro-adenoma (Cushing's disease) .

Clinical presentation :

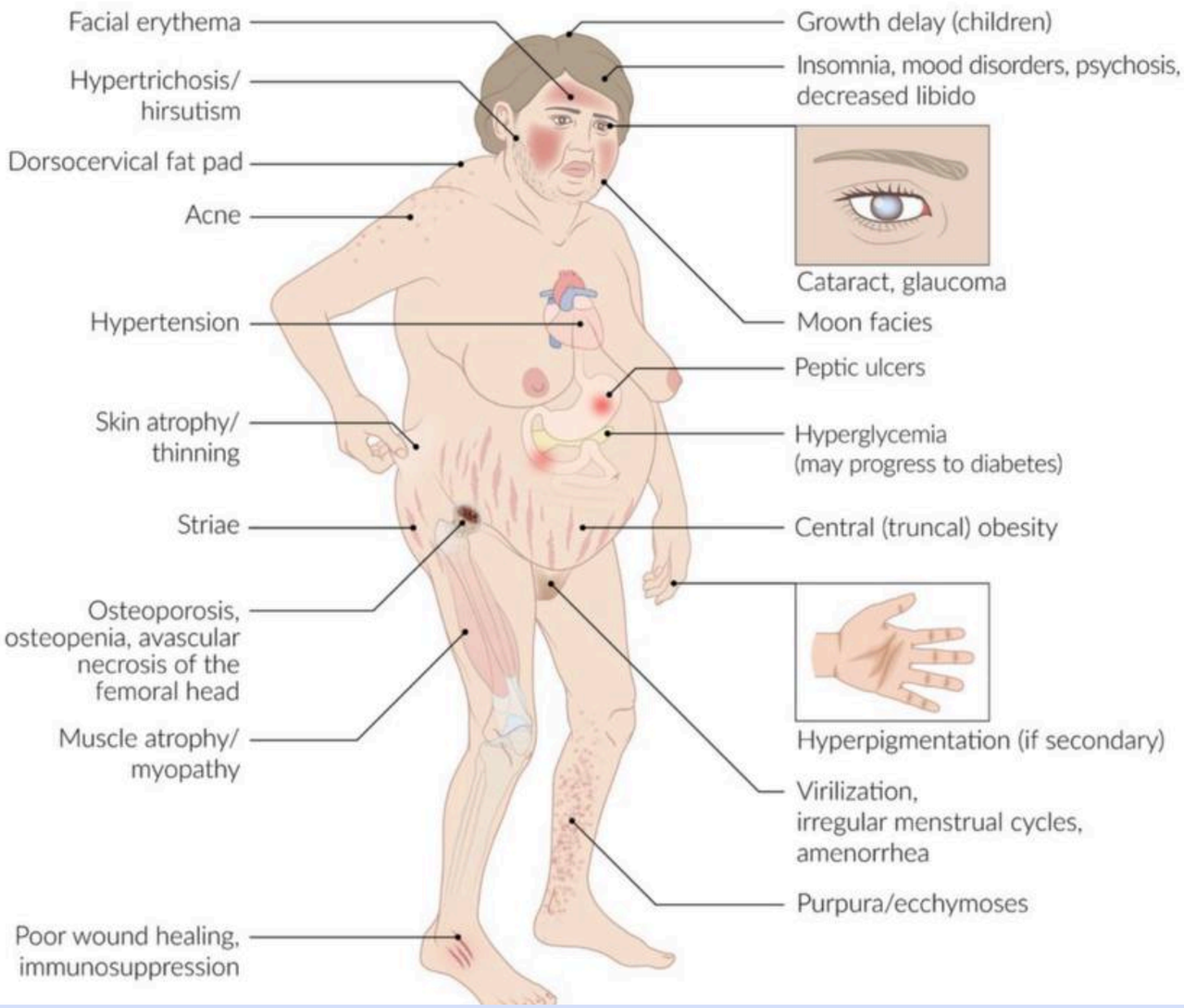
Cushing syndrome (hypercortisolism)

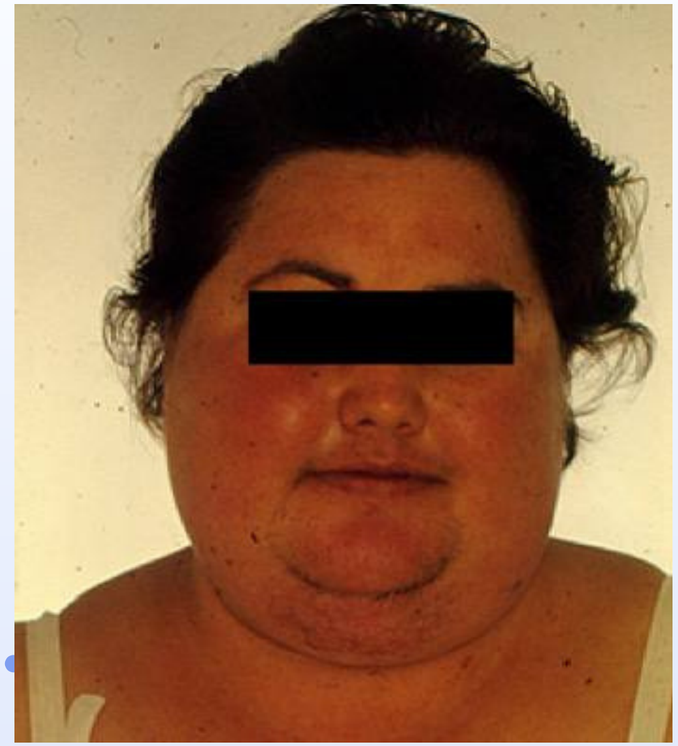
Etiology
- Exogenous (iatrogenic, most common cause of hypercortisolism): prolonged glucocorticoid therapy
- Endogenous

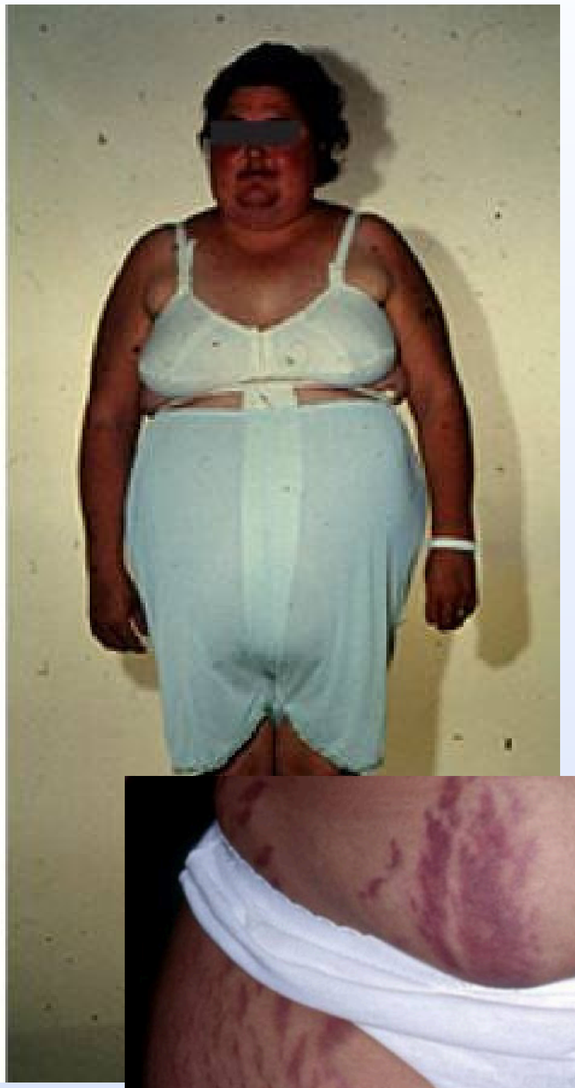
Primary: ACTH-independent (e.g., adrenal adenomas)
Secondary: pituitary ACTH production (e.g., pituitary adenomas) or ectopic ACTH production (e.g., small cell lung cancer)

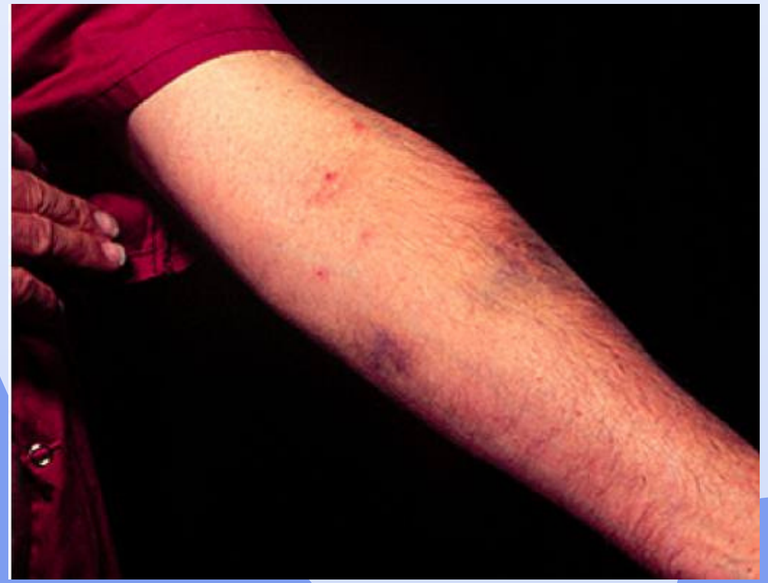
Diagnosis
Screening test (e.g., 24h urine cortisol)
Determine underlying cause: hormone analysis (e.g., serum ACTH levels), imaging to localize tumor

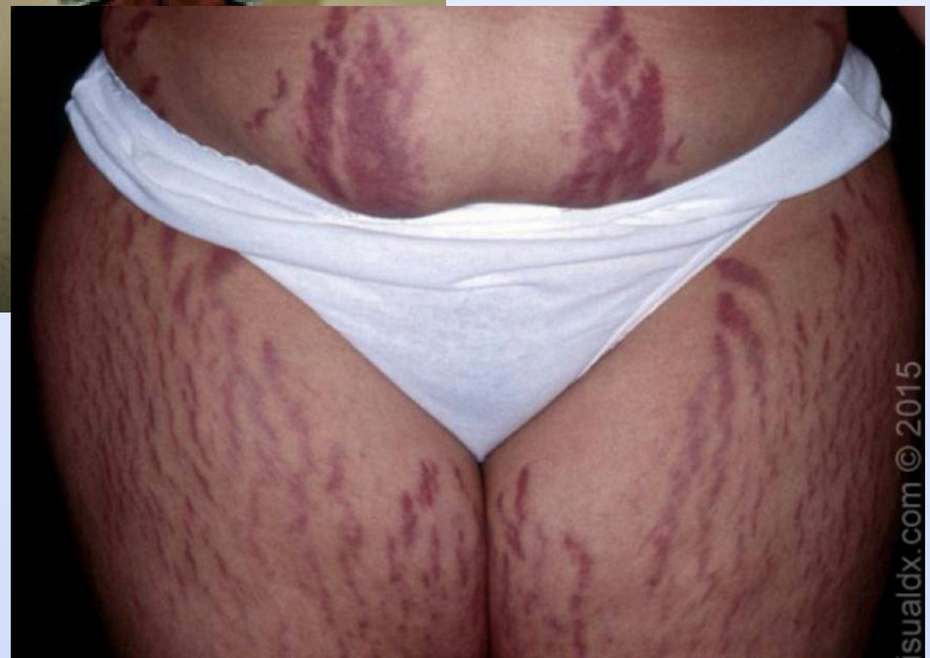
Treatment
Exogenous Cushing syndrome: reduce glucocorticoid dosage, consider alternatives
Endogenous causes: tumor resection, if inoperable drugs to suppress cortisol synthesis







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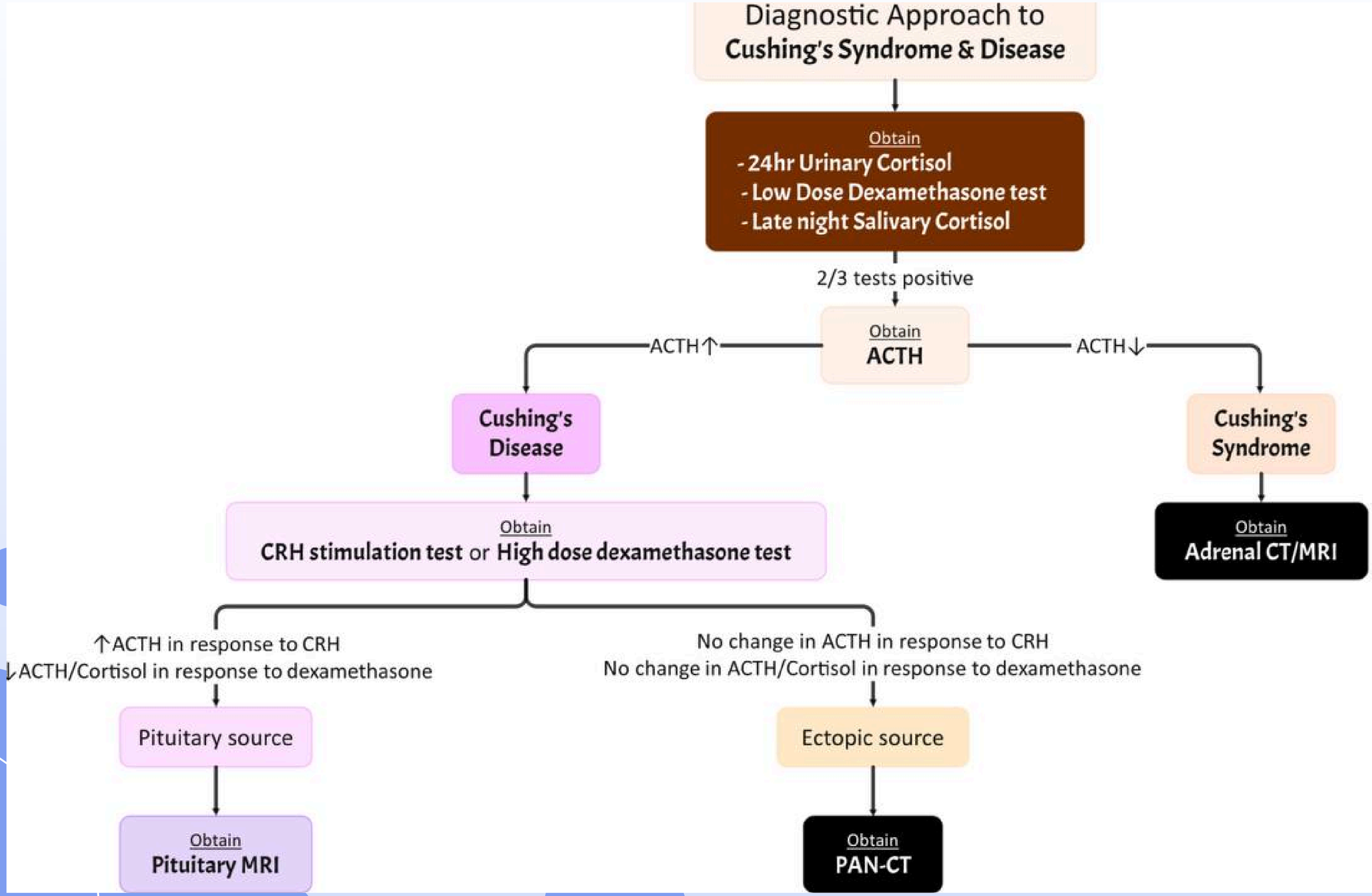
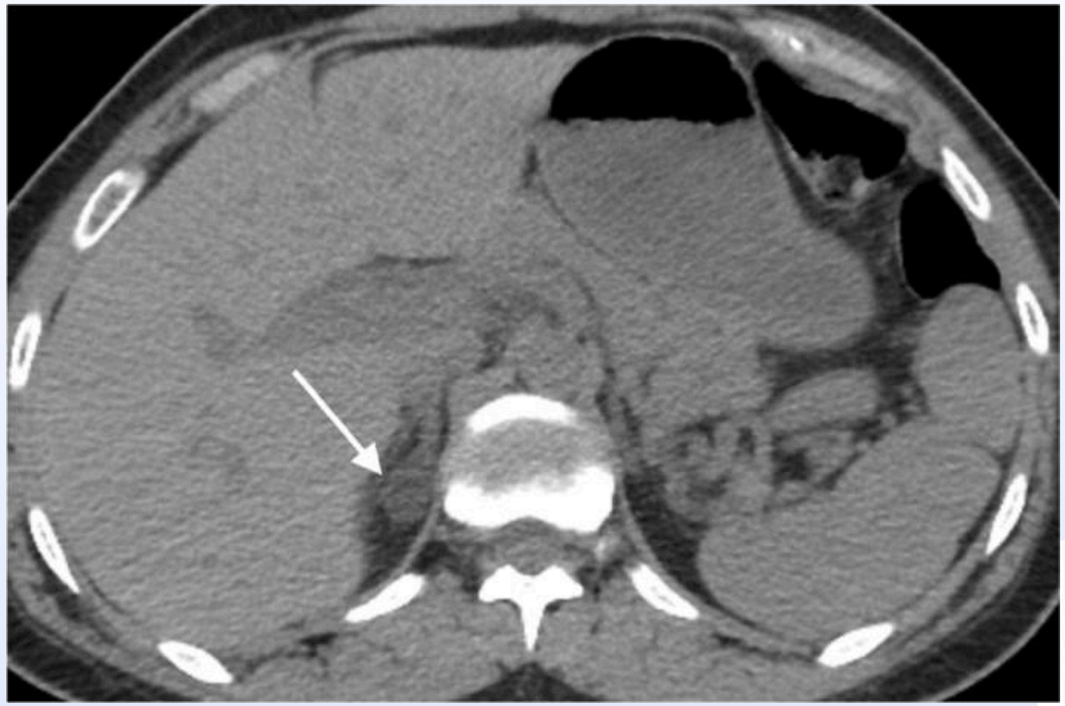
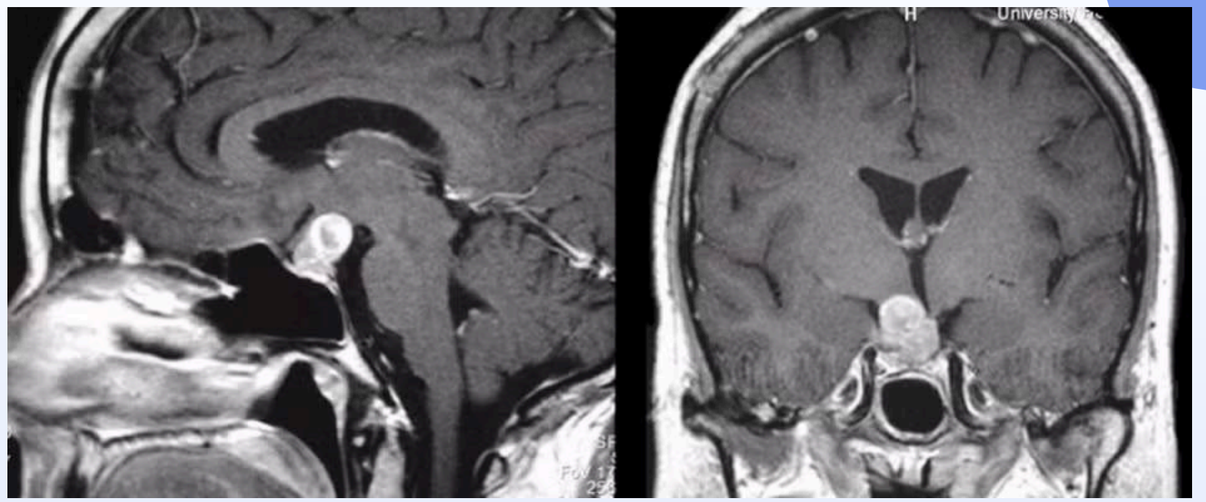
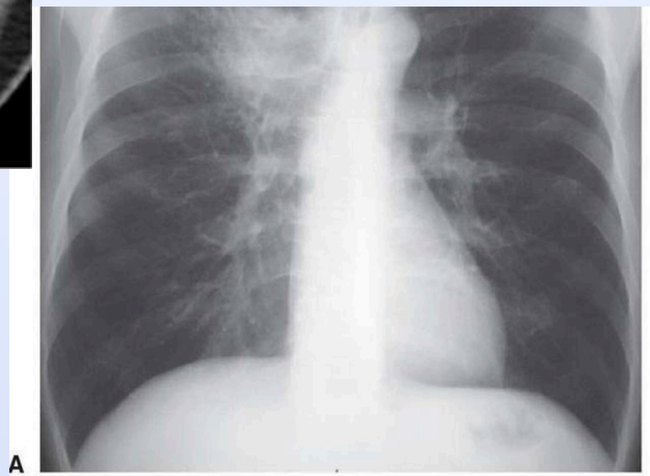
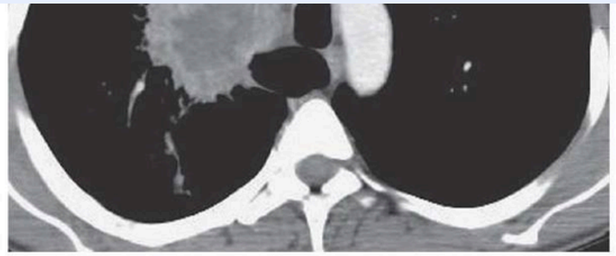
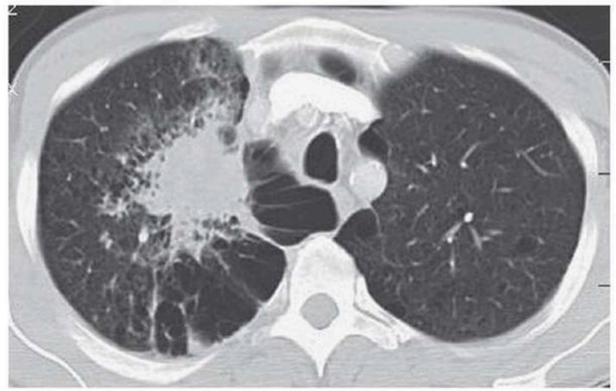

Diagnostic Approach to
Cushing's Syndrome & Disease
Obtain
- 24hr Urinary Cortisol
- Low Dose Dexamethasone test
- Late night Salivary Cortisol
2/3 tests positive
Obtain
ACTH
ACTH↑
ACTH↓
Cushing's Disease
Cushing's Syndrome
Obtain
CRH stimulation test or High dose dexamethasone test
Obtain
Adrenal CT/MRI
↑ACTH in response to CRH
↓ACTH/Cortisol in response to dexamethasone
No change in ACTH in response to CRH
No change in ACTH/Cortisol in response to dexamethasone
Pituitary source
Ectopic source
Obtain
Pituitary MRI
Obtain
PAN-CT

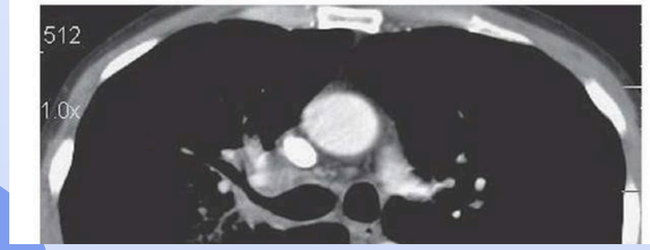












A

B

D

Diagnosis

Routine laboratory:

- CBC: leukocytosis without left shift (predominantly neutrophilic), eosinopenia.
- Electrolytes : Hypernatremia, hypokalemia.
- ABGs : metabolic alkalosis
- Hyperglycemia:

Testing for hypercortisolism :

Any of the following tests can be used. **The diagnosis is confirmed if at least two of the tests have abnormal results** :

1. 24 Urine free cortisol
2. Low-dose dexamethasone suppression test
3. Late-night salivary cortisol
4. Late-night serum cortisol

- If low ACTH : ACTH independent hypercortisolism is suspected: Obtain adrenal MRI and/or CT.
- High ACTH :Further testing in patients with ACTH-dependent hypercortisolism:

1. Obtain a pituitary MRI to evaluate for Cushing disease.
2. ectopic ACTH production is suspected:

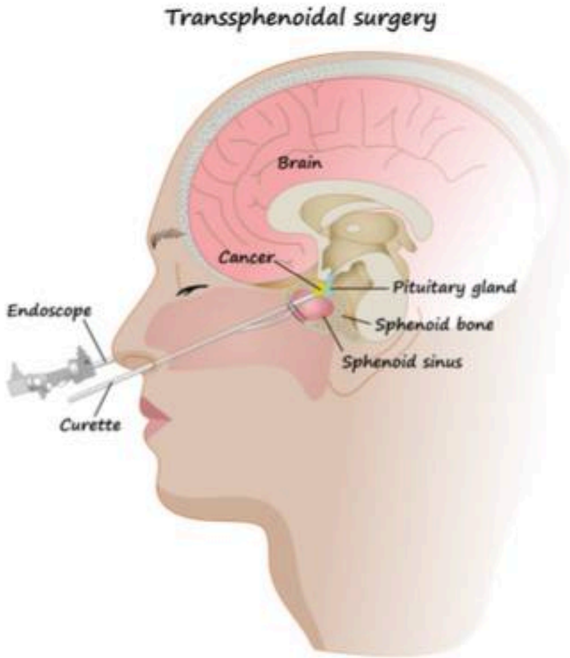
Treatment

Cushing's Syndrome and Cushing's Disease

- **Therapies:**
  - Steroid Taper
  - Ketoconazole
- **Indications:**
  - **Steroid Taper:**
    - Cushing's Syndrome secondary to chronic steroid use
  - **Ketoconazole:**
    - Cushing's Syndrome secondary to adrenal adenoma, used as a bridge to surgical removal of the adenoma
      - Can be used permanently if not a surgical candidate
    - Cushing's Disease secondary to a pituitary microadenoma used as a bridge to surgical removal of the adenoma
- **Purpose:**
  - **Steroid Taper:**
    - Gradually decrease steroid dosage → Prevents adrenal insufficiency/crisis
  - **Ketoconazole:**
    - Inhibits adrenal hormone synthesis, particularly cortisol
- **Monitoring:**
  - Monitor cortisol and ACTH levels while using ketoconazole
  - Monitor for features of Addison's Disease/Adrenal Crisis while tapering steroids

Cushing's Syndrome

- **Procedure:**
  - Adrenalectomy
  - Transsphenoidal resection of pituitary adenoma
- **Indications:**
  - **Adrenalectomy:**
    - Adrenal Adenoma with the presence of Cushing's syndrome
  - **Transsphenoidal Resection of Pituitary Adenoma:**
    - Pituitary microadenoma with the presence of Cushing's Disease
- **Purpose:**
  - **Adrenalectomy:**
    - Remove the source of ↑Cortisol production
  - **Transsphenoidal Resection of Pituitary Adenoma:**
    - Remove the source of ↑ACTH production
- **Monitoring:**
  - Monitor cortisol and ACTH levels
  - Monitor for features of Addison disease/adrenal crisis



4 Adrenocortical carcinomas

- Adrenocortical carcinomas (ACCs) are rare, often aggressive tumors that may be functional
and cause Cushing's syndrome and/or virilization, or nonfunctional and present as an abdominal mass or an incidental finding .

  - A slight female predominance is observed (1.5:1).
  - The age distribution is bimodal with a first peak in childhood and a second between the fourth and fifth decades.

Pathogenesis

Hereditary cancer syndromes

- Li-Fraumeni syndrome.
- Beckwith-Wiedemann syndrome.
- Multiple endocrine neoplasia type 1.

Sporadic ACC

Type by function :

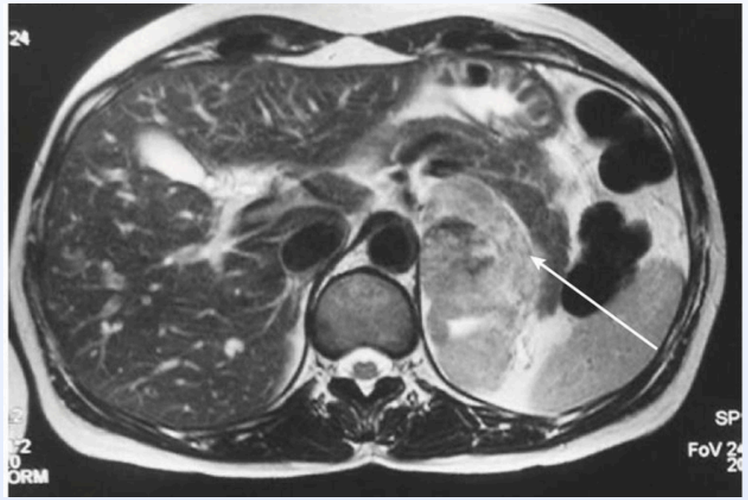
1. Functional ACC 60%
2. NON-functional ACC 40%

Clinical presentation

- Mixed Cushing's and virilization syndrome (25 percent)
- clinical symptoms associated with glucocorticoid excess, such as weight gain,

Diagnosis

- **Radiographic studies:**
- **(CT) scanning:**
  CT is usually the first imaging modality used.
  - tend to be large (>6 cm)
  - irregularly-shaped
  - central areas of necrosis and hemorrhage, resulting in variable enhancement
  - calcification is seen in up to 30% of cases
- **(MRI) is complementary** to CT, in that local invasion and involvement of the vena cava are more readily identifiable.
- **Staging :**
  McFarlane classification and defines four stages:
  - tumours <5 cm (stage I)



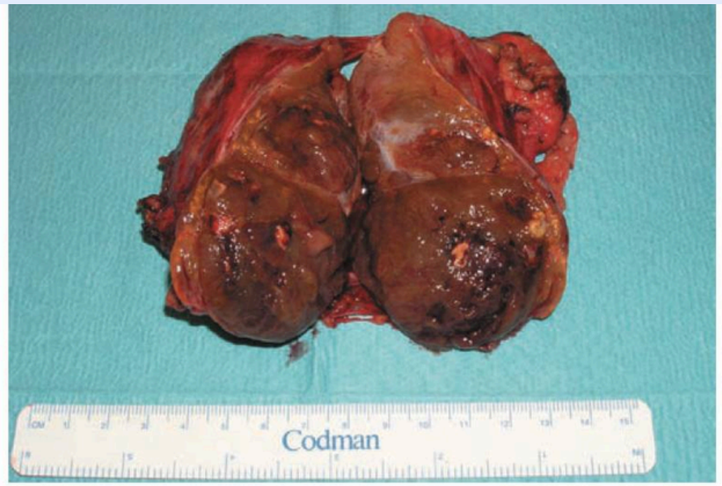


Figure 52.8 Adrenocortical carcinoma that caused Cushing's syndrome and virilisation in a female patient.

Treatment

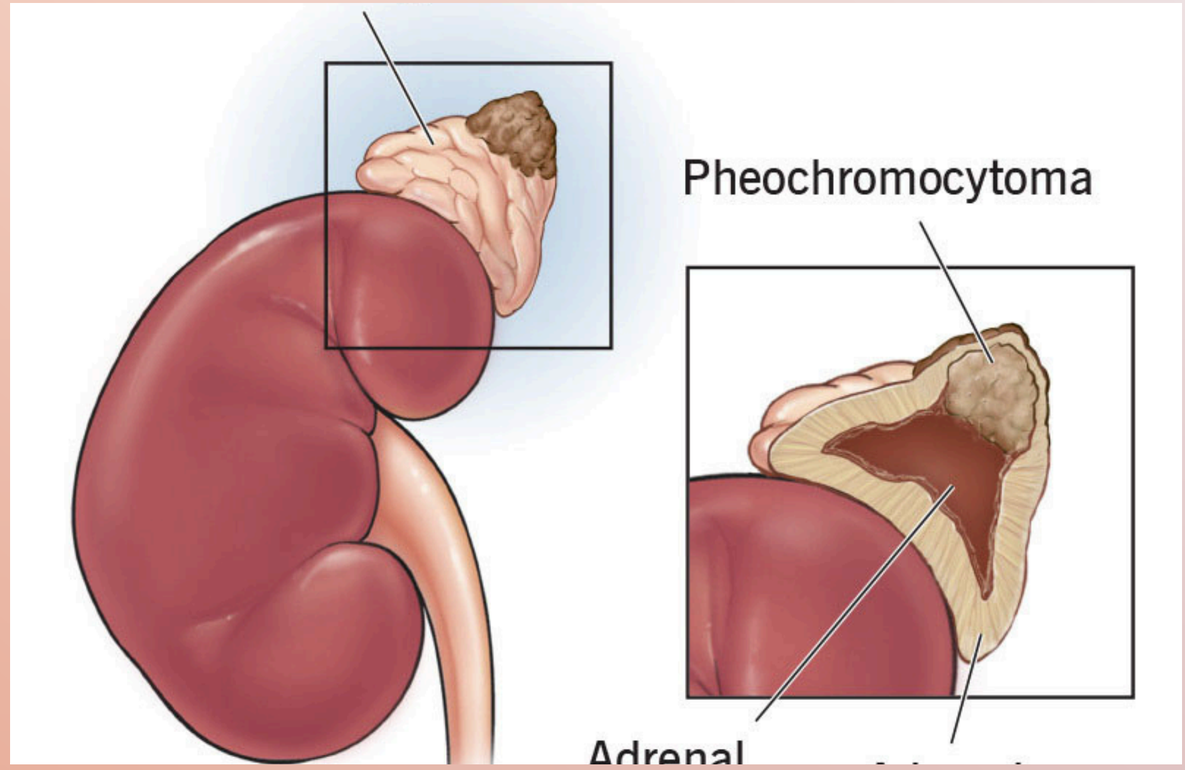
medicaltherapy preoperatively.

- **Postoperative management:**

Prognosis

- After surgery, restaging every three months is required as the risk of tumour relapse is high.
- Prognosis depends on the stage of disease and complete removal of the tumour.
- Patients with stage I or II disease have a five-year survival rate of 25 per cent
- whereas patients with stage III and stage IV disease have five-year survival rates of 6 and 0 per cent.

5 DISORDERS OF THE ADRENAL MEDULLA AND DIFFUSE NEUROENDOCRINE SYSTEM



ADRENAL MEDULLA

- It’s a part of neuroendocrine system involves neuroendocrine cells that receive nerve impulses to release neurohormones into the bloodstream.
- The adrenal medulla is the inner core that consists of a thin layer of large chromaffin cells which synthesise, store and secrete catecholamines.
- Cells of the adrenal medulla synthesise mainly adrenaline (epinephrine; 80%) but also noradrenaline (norepinephrine; 20%) and dopamine.
- Their effects, which are mediated through α and β receptors on target organs, include the cardiovascular system, resulting in an increase in blood pressure, heart rate and cardiac contractility; vasoconstriction of vessels in the splanchnic system and bronchodilatation

Extra-adrenal paraganglia

- Paraganglia are neuroendocrine cells associated with the autonomic nervous system.
- Extra-adrenal paraganglia occur throughout the sympathetic nervous system and along some branches of the parasympathetic glossopharyngeal and vagus nerves.
- There are four subgroups:
- 1. Sympathetic: the largest cluster is the organ of Zucker- kandl, which is located at the aortic bifurcation or close to the origin of the inferior mesenteric artery.
- 2. Chemoreceptor: including aortic and carotid bodies that assist in the regulation of respiration.
- 3. Visceral–autonomic: in the urinary bladder and peripheral blood vessels.
- 4. Intravagal: situated within or adjacent to the vagal trunk.

Phaeochromocytoma

- Pheochromocytomas are catecholamine-secreting tumors that arise from the chromaffin cells of the adrenal medulla.

paraganglioma

- Paragangliomas arise from the paraganglia of the autonomic nervous system outside of the adrenal medulla. Those that involve the sympathetic nervous system usually secrete catecholamines and typically are located in the lower mediastinum,abdomen and pelvis.

- Those that involve the parasympathetic nervous system are usually nonfunctional and often located in skull base,neck and upper mediastinum.

EPIDEMIOLOGY

- The incidence of PCC is about 0.6 in 100,000 and 75% are thought to be sporadic. The incidence of sporadic PGL is not known, but is less common than PCC, and the association with hereditary conditions is more common. Overall, about 70% of PPGLs are sporadic and the rest occur as part of inherited endocrine tumour syndromes, which include:
  - hereditary PPGL syndromes
  - MEN 2
  - von Hippel–Lindau disease (VHL)
  - neurofibromatosis type 1 (NF1)

Clinical association

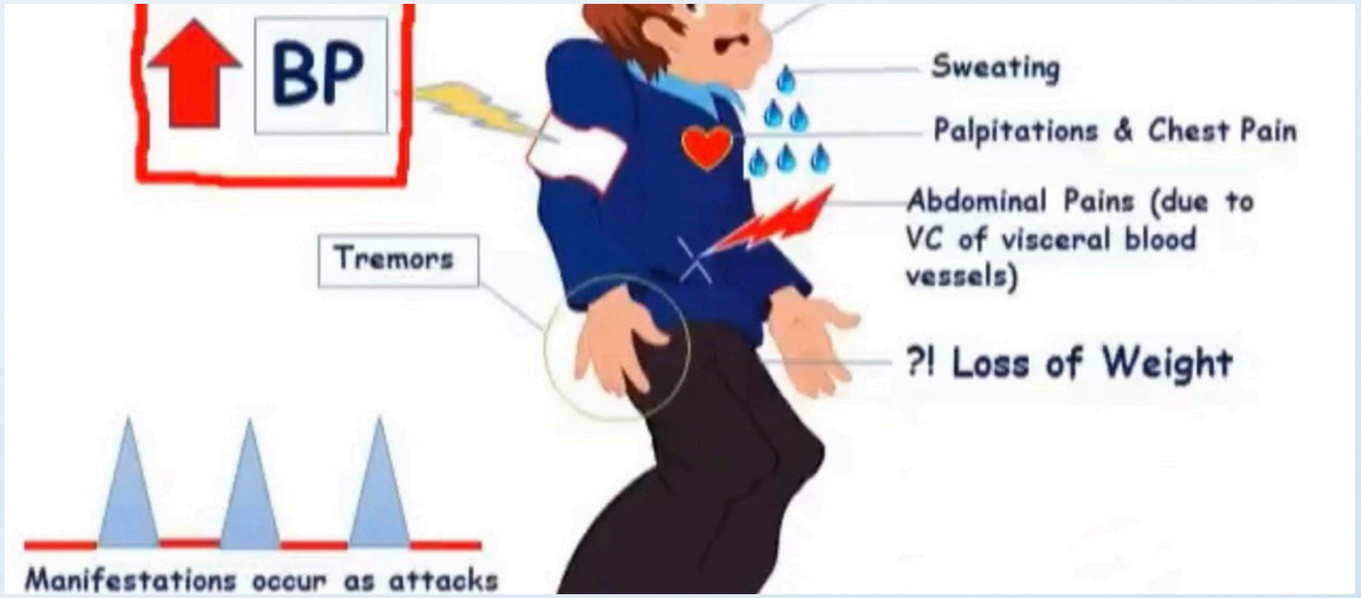
- Syndromic – Several familial syndromes are associated with pheochromocytoma, all of which have autosomal dominant inheritance:
- Von Hippel-Lindau syndrome (VHL) – Associated with pathogenic variants in the VHL tumor suppressor gene. Between 10 and 20 percent of patients with VHL have pheochromocytoma or paraganglioma.
- Multiple endocrine neoplasia type 2A or 2B (MEN2) – Associated with pathogenic variants in the RET proto-oncogene. Approximately 50 percent of cases of MEN2 include pheochromocytoma.
- Neurofibromatosis type 1 (NF1) – Due to pathogenic variants in the NF1 gene. Approximately 3 percent of patients with a disease-associated NF1 pathogenic variant develop catecholamine-secreting tumors, which may be adrenal pheochromocytomas

Malignant pheochromocytomas and paragangliomas are histologically and biochemically the same as benign tumors. The only clue to the presence of a malignant pheochromocytoma is regional invasion or distant metastases.

Approximately 10% of PCCs are malignant. The differentiation between malignant and benign tumours is difficult, except when metastases are present.

Clinical presentation

- Functioning PPGLs typically present with symptoms and signs of catecholamine excess, and these are typically intermittent.
- The classic triad of symptoms in these disorders consists of episodic headache, sweating, and tachycardia, usually accompanied by hypertension.
- Abdominal pain or distension or back pain – 30 percent in one series, these symptoms are due to mass effect of the tumor.



Hypertension	80–90
Paroxysmal	50–60
Continuous	30
Headache	60–90
Sweating	50–70
Palpitation	50–70
Pallor	40–45
Weight loss	20–40
Hyperglycaemia	40
Nausea	20–40

Diagnosis :

1. Biochemical:

The diagnosis of PPGL is confirmed by elevated catecholamine metabolites (metanephrines) in plasma and/or raised 24-hour urinary excretion of fractionated metanephrines

Metanephrines are produced as a result of intratumor conversion of catecholamines by the catecholamines O-methyltransferase enzyme

Measurement of plasma and urinary **metanephrines is more sensitive** (99% and 97% respectively) than catecholamine

Measurement of one or more of these substances that are four times greater than upper limit of the reference range are 100% diagnostic

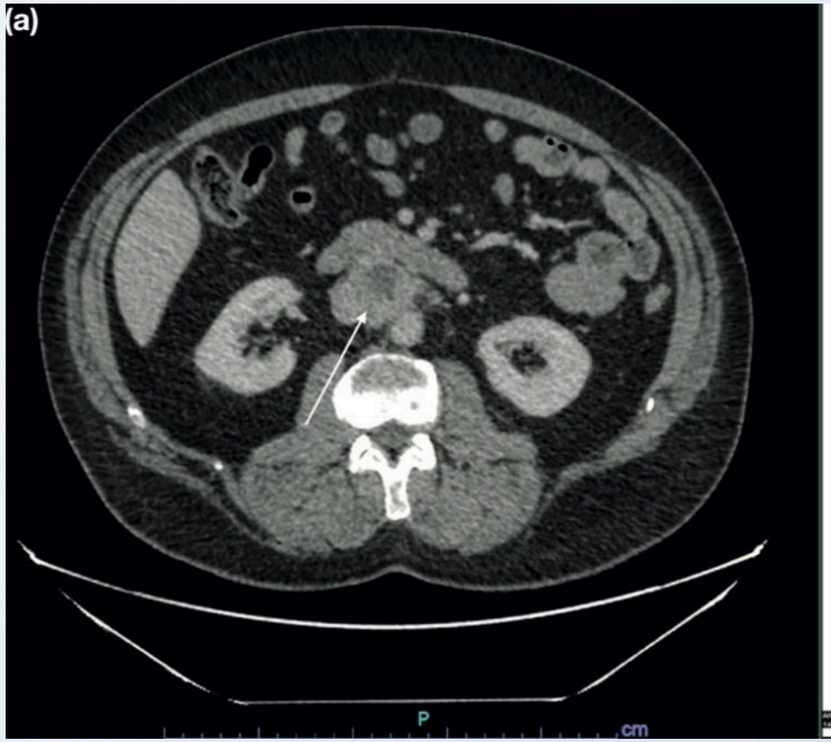
2.Radiological :

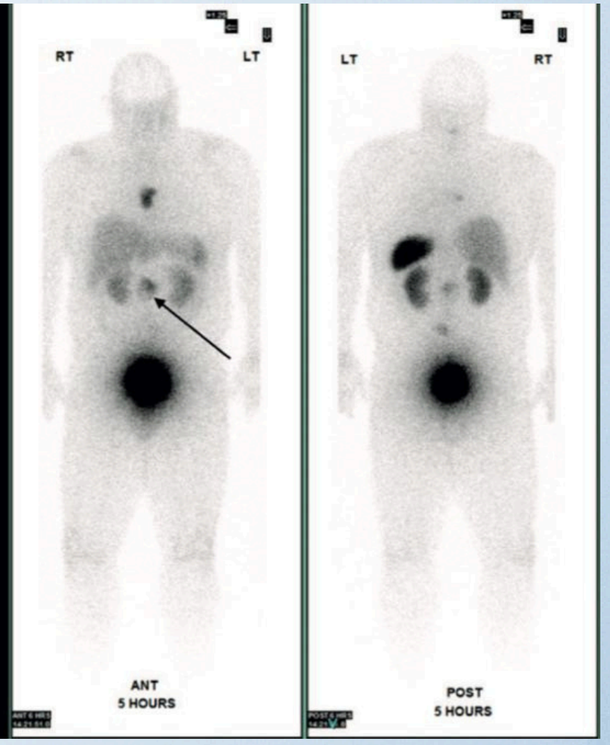
Once a biochemical diagnosis is established, imaging by CT or MRI is undertaken to determine tumour location and assess its size and risk of malignancy. Size is not a predictor of malignancy for PCC.

If initial imaging is negative or reveals extra-adrenal disease, functional investigation with I-MIBG is undertaken .

More recently,fluorodopamine PET Scanning has shown promise ,where conventional imaging and MIBG scanning are negative .

A cross-section ct scan showing a paraganglioma anterior to the abdominal aorta





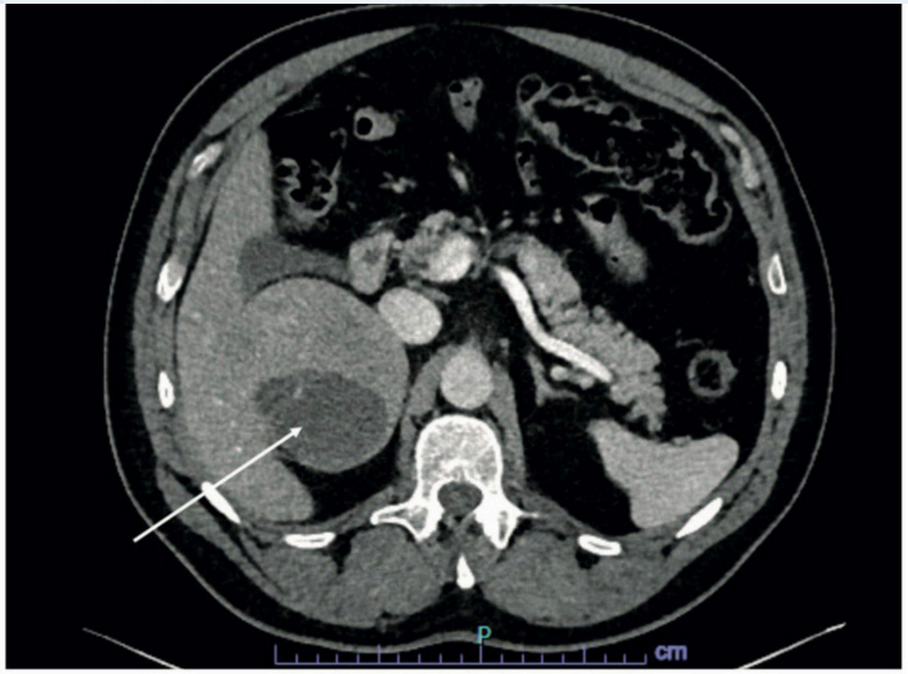
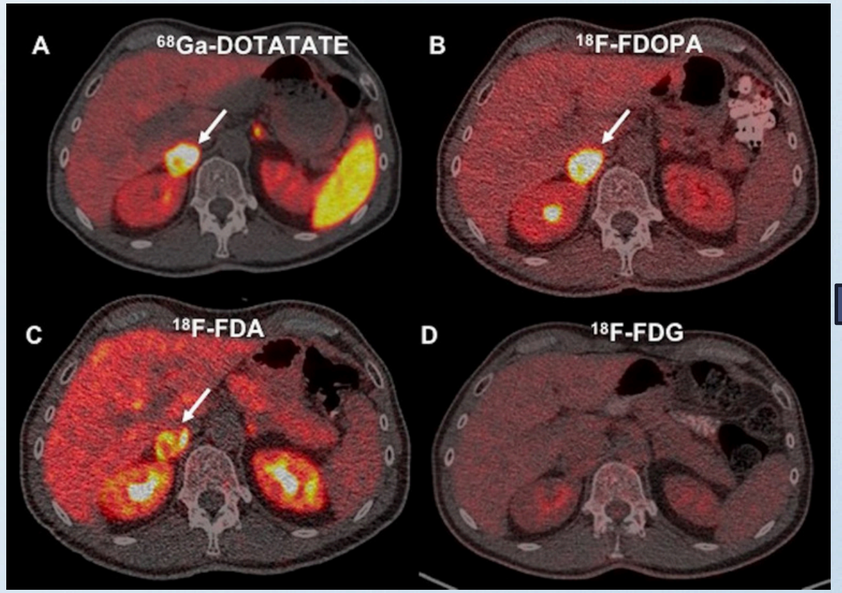


Figure 57.10 A cross-section computed tomography scan of a large phaeochromocytoma showing characteristic central necrosis (arrow).



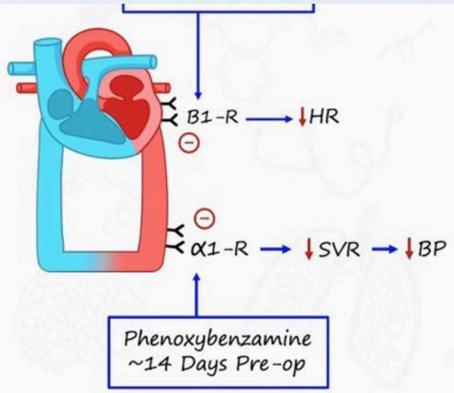
fluorodopamine PET scanning

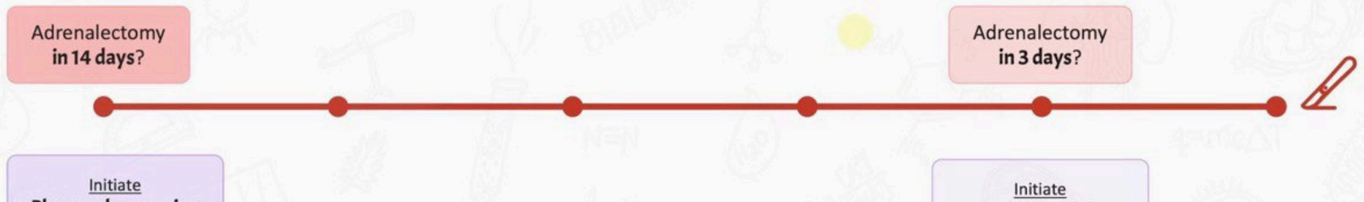
Medical management(Preoperative control of blood pressure)

Biochemical diagnosis and localisation of PPGLs should be followed by medical preparation to control blood pressure and prompt surgical excision.

Once a PCC has been diagnosed, an α-adrenoceptor blocker (phenoxybenzamine) is used to block the effects of catecholamine excess and its consequences during surgery. After adequate alpha-adrenergic blockade has been achieved, beta-adrenergic blockade is Begun.

Type	Purpose of Treatment	Treatment
Pheochromocytoma	Remove Tumor	- Adrenalectomy with venous ligation
	Prevent HTN Crisis	- Preoperative Phenoxybenzamine + Propranolol





The beta-adrenergic blocker should never be started first

Surgical treatment:

- PPGLs are excised by either laparoscopic or open surgery.
  - Adrenalectomy for phaeochromocytoma
    Laparoscopic resection is now routine in the treatment of PCC. If the tumour is larger than 10cm or radiological signs of malignancy are detected, an open approach should be considered.
  - Surgery for paraganglioma
    Tumours along the sympathetic chain can be technically challenging owing to their posterior relationship to the great vessels and visceral arterial branches, which may hide smaller lesions. Furthermore, hereditary PGLs are associated with increased risk of local recurrence. For this reason, minimally invasive surgery may not be feasible; open surgery is the preferred option.

- Malignant phaeochromocytoma.

  Surgical excision is the only chance for cure. If there is direct invasion, laparotomy and en bloc excision of involved adjacent organs offers the best chance of cure. In the presence of metastases, excision of the primary tumour is still recommended to improve symptom control.

Postoperative care

Patients should be observed for 24 hours as hypovolaemia and hypoglycaemia may occur. Lifelong yearly biochemical tests should be performed to identify recurrent and metastatic PCC.

After tumor removal, catecholamine secretion should fall to normal in approximately one week.

Neuroblastoma

Definition & Epidemiology

- Neuroblastoma is a malignant tumour arising from neural crest–derived sympathetic tissues, commonly in the adrenal medulla or sympathetic ganglia.
- It is the most frequent extracranial solid tumour in infants and children and accounts for 8% of all childhood cancers.
- Most cases present before age 5, , with a peak incidence of 2 years , 70% of patients have metastases at diagnosis.
- Also know as Clinical Enigma: Prognosis ranges from spontaneous regression without treatment to aggressive, metastatic disease resistant to therapy.
- Typical locations:
  - Adrenal Medulla (40%)
  - Paravertebral sympathetic chain (Abdomen, Chest, Neck, Pelvis)

Clinical Presentation

- **Depend on the location & size:**

Adrenal gland:
Often an asymptomatic abdominal mass; can become large and painful.

Lungs:
Breathing difficulties and abnormal breathing sounds

Spine:
Muscle weakness, sensory loss, bowel/bladder dysfunction

Neck:
Horner syndrome

Bone:
Bone pain, fractures, proptosis, periorbital ecchymosis (“raccoon eyes”)

In general:
fatigue, Sweating, Weight loss

NOTE: Rarely, Vasoactive Intestinal Peptide (VIP) secretion causes VIPoma syndrome, resulting in watery diarrhea, dehydration, and achlorhydria

Investigation

- Anemia and/or thrombocytopenia (or pancytopenia)
- **Urinary catecholamine metabolite assays**:
  - vanillylmandelic acid (VMA), homovan illic acid (HVA) are elevated in ~80% of cases.

- **Molecular markers**: MYCN amplification (poor prognosis), present in ~25% of neuroblastomas.

- **Histopathology:**
  - **Core Biopsy (Gold standard):**is the cornerstone for initial diagnosis and risk stratification.
  - **Bone marrow aspiration**: detects metastatic neuroblastoma cells; diagnosis confirmed when catecholamines are

- **Imaging**:
  - **Ultrasound :**
    Heterogeneous solid mass with hyperechoic foci and shadowing (calcifications).
  - **CT scan :**
    Calcified, irregular, heterogeneous mass crossing midline.
  - **MIBG scintigraphy** (or PET scan): for staging and detection of metastases

Staging & Risk Stratification

INRG Staging System	**Definition / Key Features**
L1	Localized tumor, no vital structure involvement (no IDRFs), confined to one body compartment
L2	Locoregional tumor with ≥1 IDRFs (vital structures involved)
M	Distant metastatic disease (any age, except MS)
MS	Metastases in children <18 months, confined to skin, liver, and bone marrow

Risk Group	**Typical Features**
Low Risk	Localized tumor (L1/L2), <18 mo, MYCN−, favorable histology
Intermediate Risk	Regional spread, <18 mo with metastasis but MYCN−, favorable histology
High Risk	MYCN amplified, metastatic disease in ≥18 mo

Treatment

- **LOW-RISK**
  - **Treatment:** Surgery alone.
  - **Prognosis :** Excellent, Surgery is often curative.
    3-Year Survival: ~90%

    Note: Some very small tumors in infants may be *observed* without surgery, but this is rare

- **INTERMEDIATE-RISK**
  - **Treatment:**
    Surgery + adjuvant Multi-agent Chemotherapy.
  - **Prognosis :** Good.
  - **3-Year Survival: 70-90%**

- **HIGH-RISK**
  - **Treatment:**
    1. **Chemotherapy** first, to shrink the tumor.
    2. **Surgery** to remove as much as possible.
    3. **Radiotherapy** to kill remaining cells.
    4. **Stem Cell Transplant** to rescue the bone marrow.

  3-Year Survival: ~30%

Ganglioneuroma

- **Definition:** Benign, well-differentiated tumor from neural crest cells
- **Histology:** Composed of mature ganglion cells and Schwann cells in a fibrous stroma.

- **Clinical Features:**
  Can occur at any age, more common <60 years.
- Common sites: Adrenal medulla (~30%) and along the paravertebral sympathetic chain.
- Typically asymptomatic; discovered incidentally on CT/MRI.
- **Key Behavioural Traits:**
  - Possible for intraspinal canal extension.
  - Rarely, causes watery diarrhea due to VIP secretion.

- **Treatment & Prognosis**
- Treatment: Complete surgical excision.

- **Prognosis:**
  - Complete resection is curative.
  - Very low risk of local recurrence.

THANK YOU

References :

Wolters Kluwer
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