**By the Name of ALLAH the Most Gracious the Most Merciful**

# Adrenal Gland


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# DISORDERS OF CORTEX

- Conn's syndrome (primary hyperaldosteronism) .
- Cushing's syndrome .
- Adrenocortical carcinoma .
- Congenital adrenal hyperplasia (adrenogenital syndrome) .

## ADRENAL INSUFFICIENCY

- Acute adrenal insufficiency (adrenal or Addisonian crisis) .
- Chronic adrenal insufficiency .

## ADRENAL HAEMORRHAGE

# Conn’s syndrome (primary hyperaldosteronism) PA

- Group of disorders characterised by hypertension , inappropriately raised plasma aldosterone concentrations and low serum potassium.
- the most common cause of endocrine hypertension.
- It is twice as common in females as in males .
- About 30–40% of cases are due to an aldosterone producing adenoma of the cortex.

# Clinical presentation

- Hypertension
- Patients may be asymptomatic unless they are hypokalaemic, in which case muscle weakness, cramps and fatigue may be present.
- It is worth noting that the following presentations might also warrant screening for PA: drug-resistant hypertension, hypertension and obstructive sleep apnoea, hypertension with incidentaloma, patients with first-degree relatives with PA, and a family history of early-onset hypertension or stroke.

# Biochemical Test

- Hypokalaemia and/or metabolic alkalosis.
- Increased potassium concentration in urine
- The diagnosis depends on the presence of non-suppressed plasma aldosterone (pmol/L) and a suppressed plasma renin activity (nmol/L/h).The two are combined to give a plasma ARR:
  - if >850 this is suggestive of PA;
  - if >1700 it is very likely to be PA

- Radiological : CT scan ( abdomen ), hypodense unilateral adrenal nodule; carcinomas are heterogenous and bilateral hyperplasia presents as bilateral bulky adrenal enlargement.
- PET scanning.
- Adrenal vein sampling (AVS) : for confirming unilateral secretion.

# Treatment

- **Medical**:
- Correction of hypertension and hypokalaemia, Prior to surgery.
- The preoperative response to aldosterone receptor antagonist (spironolactone/eplerenone) therapy is a useful .

# Treatment ( surgery ).

- Unilateral (minimally invasive adrenalectomy ).
- Bilateral disease, unless hyperplasia is marked, with dominant nodules >40 mm (indeterminate), aldosterone antagonists and other antihypertensives.
- If this is unsuccessful, lateralising investigations (side of dominant ), surgical excision of dominant side may improve medical control.

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# Hypercortisolism

I ) Excess ACTH secretion (ACTH-dependent ):(Cushing's disease)

**Endogenous :**

- Pituitary dependent; Cushing's disease)( 70-80% ).
- Ectopic ACTH secretion from a non-pituitary tumour, from foregut neuroendocrine tumours and small cell lung tumours ( 10 % )

**Exogenous** : corticosteroid therapy

II) ACTH- independent: (Cushing's syndrome )

**Endogenous :** Autonomous secretion of endogenous glucocorticoids from cortical tumours of the adrenal glands (pituitary independent; Cushing's syndrome)( 10-15 % ).

**Exogenous / (Iatrogenic)** : Corticosteroids drugs

# Cushing's syndrome

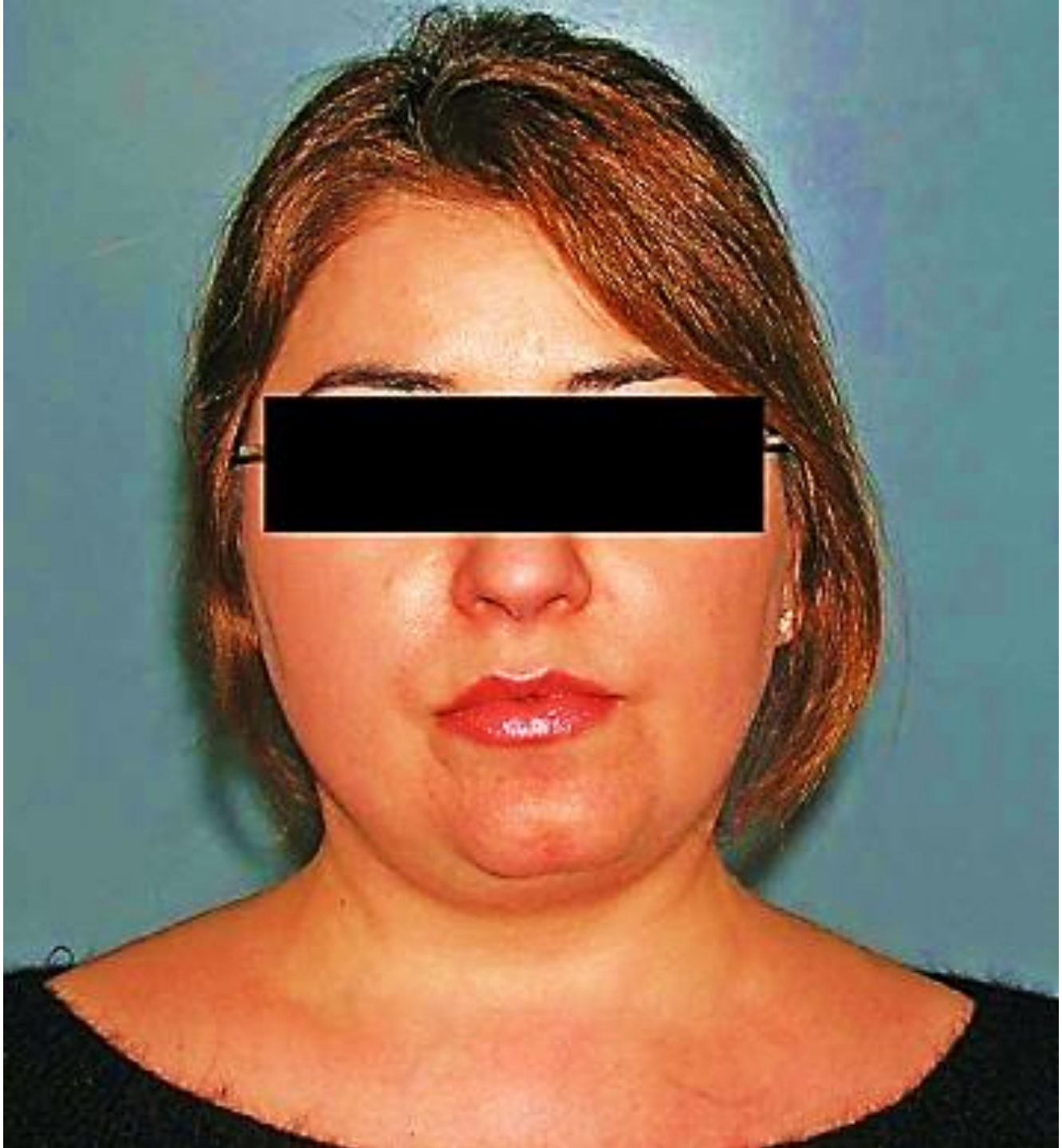
- It is an ACTH- independent disease.
- Endogenous . Similar to PA, the most common cause of adrenal

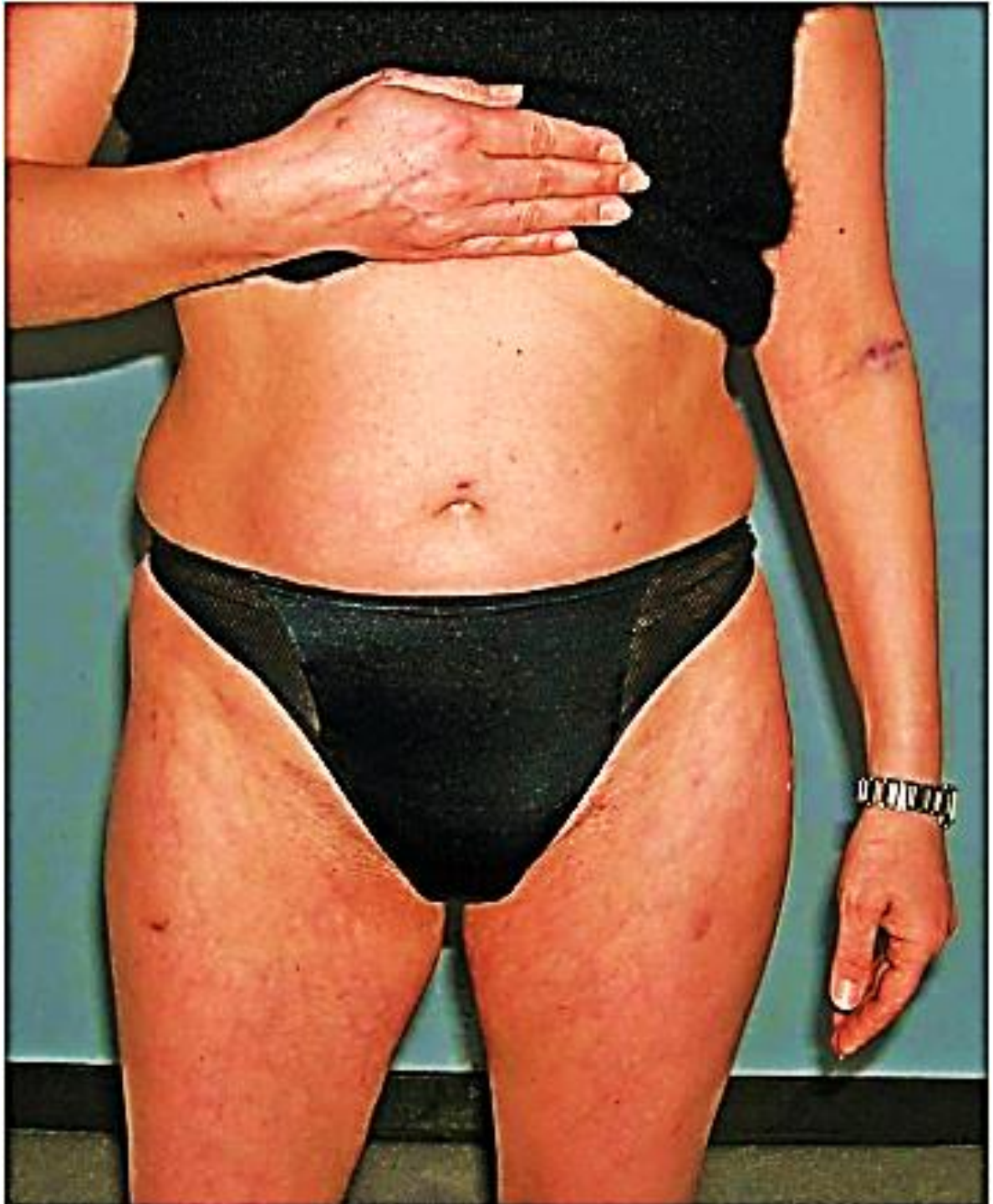
  Cushing's (syndrome) is unilateral cortisol-secreting (adrenocortical ) adenomas and occasionally bilateral nodular adrenal hyperplasia and less commonly adrenocortical carcinoma (ACCs) .
- Exogenous ( Iatrogenic ).
- Has a strong female preponderance (four to six times).
- The resulting hypercortisolism leads to suppressed ACTH, which causes atrophy of fasciculata and reticularis, not glomerulosa, in the residual or opposite adrenal gland.

- Clinical presentation
- Because of the pleiotropic actions of cortisol, the clinical features of Cushing's syndrome are broad and multisystem . The typical patient is characterised by a facial plethora, a buffalo hump and a moon face in combination with hypertension, diabetes, central obesity and proximal muscle-wasting, traditionally referred to as the 'lemon on sticks' appearance .Clinical signs can be minimal or absent in patients with subclinical Cushing's syndrome.

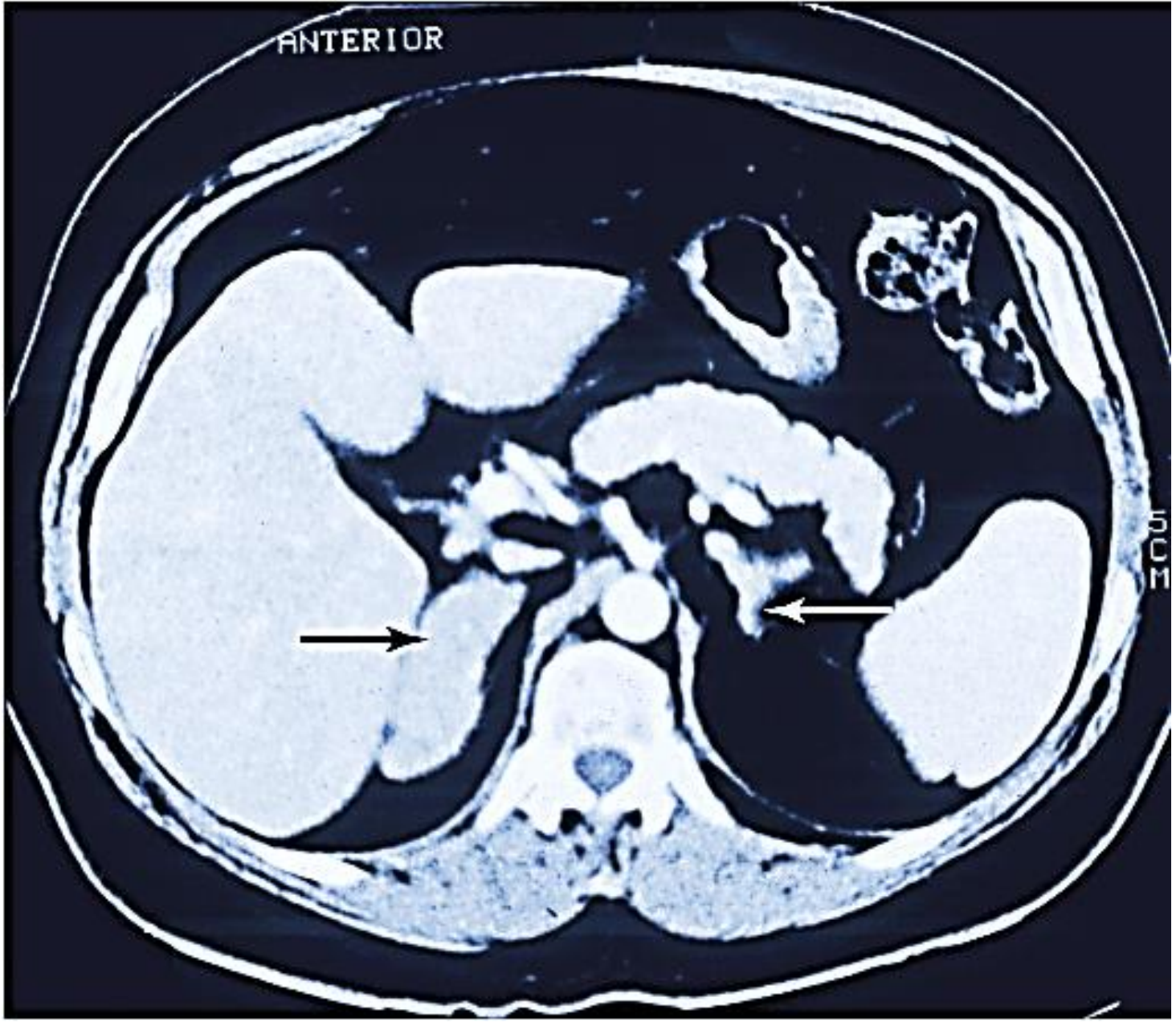
## Clinical features of Cushing's syndrome

| Clinical feature | Incidence (%) |
|---|---|
| Obesity | 90 |
| Hypertension | 85 |
| Depression/mania/psychosis | 85 |
| Decrease libido/impotence | 85 |
| Osteoporosis | 80 |
| Hirsutism | 75 |
| Glucose intolerance/diabetes | 75 |
| Facial plethora | 70 |
| Hyperlipidaemia | 70 |
| Menstrual disorders | 70 |
| Proximal myopathy | 65 |
| Abdominal striae | 50 |
| Renal stones | 50 |
| Acne | 35 |
| Easy bruising | 35 |





- Radiological imaging
- Imaging should not be pursued until the diagnosis is secure.
- These tests should determine the causative lesion. The ACTH result will determine which diagnostic pathway is taken.
- ● ACTH raised: **pituitary MRI** and inferior petrosal sinus
- sampling to exclude pituitary microadenoma. If both are negative, this suggests ectopic ACTH syndrome, which warrants CT imaging of the thorax, abdomen and pelvis. Functional imaging with 68Ga-SSTR **PET-CT is** a useful adjunct and is 75–80% sensitive in confirming the source of ectopic ACTH.
- ● **ACTH suppressed: dedicated adrenal CT or MRI**
- to determine if unilateral adenoma or bilateral nodular hyperplasia (or rarely adrenocortical cancer) are present. Benign lesions are typically hypodense and <10 HU on non-contrast CT.




Bilateral asymmetrical hyperplasia of the adrenal glands (arrows) in a patient with Cushing's syndrome.

# Treatment

- The principal aim therefore is to determine and treat the underlying cause, while avoiding, if possible, long-term hormonal deficiency or dependence on medication.

- **Medical therapy**
- **Metyrapone or ketoconazole therapy** reduces steroid synthesis and secretion by CYP11B1 inhibition and can be used to prepare patients with severe hypercortisolism preoperatively or as primary therapy if surgery is not possible.
- In patients who are critically ill with Cushing's syndrome, intravenous **etomidate** infusion (even at non-hypnotic doses) can reduce serum cortisol levels to normal within 24 hours, providing a suitable window for surgery. This requires monitoring in an intensive care unit setting.

- Surgical treatment
- ACTH-producing pituitary tumours are treated by transsphenoidal resection and/or radiotherapy. Resection of ectopic ACTH-secreting tumours will also correct hypercortisolism.
- Patients who have undergone failed pituitary surgery or those with an unresectable or unlocalised ectopic ACTH-secreting tumour may require bilateral adrenalectomy to control hormone excess. This will render them steroid dependent.
- Unilateral adenoma should be treated by minimally invasive adrenalectomy provided adrenocortical cancer is not suspected.

- In cases of bilateral ACTH-independent disease , the extent of adrenalectomy is contentious; bilateral adrenalectomy should be employed in severe Cushing’s and equally enlarged adrenals.
- In asymmetric disease, excision of the larger gland may be curative with a low risk of recurrence. In cases of subclinical Cushing’s syndrome and a unilateral adenoma, unilateral adrenalectomy is indicated if the tumour is >4 cm or <4 cm with features of the metabolic syndrome.

- **Preoperative management**
- Chemical and mechanical thromboprophylaxis .
- Perioperative broad-spectrum antibiotics.
- Accompanying diabetes should also be adequately controlled.
- As unilateral or bilateral adrenalectomy in the setting of Cushing's syndrome will result in steroid deficiency in the postoperative period, patients should receive **intraoperative corticosteroids** (50–100 mg intravenous hydrocortisone) and close liaison with the endocrinology team is strongly advised to guide postoperative management.

- Postoperative management.
- After unilateral adrenalectomy the contralateral gland will be suppressed and so all patients should be commenced on 15–25 mg daily of hydrocortisone. In total, 15 mg/h is required parenterally for the first 12 hours followed by a daily dose of 100 mg for 3 days, which is gradually reduced thereafter. After unilateral adrenalectomy, the contralateral suppressed gland may need up to a year to recover adequate function.
- A synacthen test is used to confirm adequate adrenal function prior to stopping hydrocortisone supplementation.
- In 10% of patients with Cushing's disease who undergo a bilateral adrenalectomy after failed pituitary surgery, the pituitary adenoma causes Nelson's syndrome owing to continued ACTH secretion at high levels, resulting in hyperpigmentation due to uncontrolled secretion of pro-opiomelanocortin (POMC). POMC is cleaved to produce ACTH and melanocyte-stimulating hormone, excess of the latter resulting in hyperpigmentation.

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## ADRENAL HAEMORRHAGE

# Adrenocortical carcinoma

- Is a rare aggressive malignancy. that arises from the adrenal cortex.
- The prognosis is  generally poor(present at a late stage).
- Although most ACCs are sporadic, a minority occur as part of genetic tumour syndromes such as  type 1 (MEN 1), familial adenomatous polyposis and the Li–Fraumeni and Lynch syndromes.
- Optimal surgery remains the best way of curing the patient  .
- ACCs can occur at any age but the peak incidence is in the fourth and fifth decades.

- Pathology
- Malignant adrenocortical tumours ( local invasion or distant metastasis .
- Modified Weiss histopathological system may be used to guide management. It comprises five criteria:
  - >6 mitoses/50 high-power fields. ( 2 )
  - ≤25% clear tumour cells in cytoplasm. ( 2 )
  - abnormal mitoses.( 1 )
  - necrosis .( 1 )
  - capsular invasion.( 1 )
- If a total score ≥3 is suggestive of malignant behaviour.
- Ki-67 proliferation index is suggesting poorer prognosis.

# Clinical presentation

- Around one in six incidentalomas.
- (50–60%) Hormonal excess.Those that are hormonally active usually cause Cushing's syndrome or a mixed picture of Cushing's and virilisation in women. Mineralocorticoid excess is rare, as is feminisation in male patients.
- (30–40%) abdominal mass such as abdominal or back pain.

## Diagnosis

Although radiological investigations are critical in diagnosis, the presence of autonomous secretion of glucocorticoids, sex hormones and steroid precursors should also be carefully evaluated. Exclusion of phaeochromocytoma.

- adrenal biopsy is discouraged and fine-needle aspiration cannot distinguish benign from malignant tumours. Biopsy may have a role in patients with widespread metastatic disease at presentation to guide palliative systemic treatment.

# Biochemistry

- Glucocorticoid excess should be excluded by careful history and examination, followed by low-dose overnight DST.
- Serum levels of adrenal androgens (DHEAS, androstenedione, testosterone, 17-hydroxyprogesterone) and serum oestradiol in men and postmenopausal women should also be measured.
- In patients who are hypertensive, the aldosterone–renin ratio should be measured along with the serum potassium.
- Steroid precursors can be measured in 24-hour urine collections.
- A 24-hour urine or plasma metanephrines should be measured in all patients to exclude PCC.

# Radiology

- CT or MRI , where size (>6 cm), heterogeneous appearance and presence of necrosis are suggestive and local invasion and metastatic disease are diagnostic.
- Common sites of metastases are the lungs and liver, so staging should include the thorax.
- FDG-PET scanning is complementary and is advised to exclude occult metastatic disease in suspicious lesions.

- **Treatment**
- **Surgery**
- Successful R0 resection of the tumour should be the aim of surgery .
- Preoperative assessment should therefore focus on determining whether any adrenal tumour is potentially malignant as this will guide the operative strategy.
- Treatment should take  place in a multidisciplinary setting in a unit with experience of treating this rare disease.
- Patients with cortisol excess should be given perioperative hydrocortisone.

# At presentation, there are three common scenarios

- Indeterminate or probably malignant tumour
- <6 cm: laparoscopic adrenalectomy may be feasible in this situation, but if there is evidence of local invasion on imaging or suspicion of it at laparoscopy open surgery is mandated.
- Indeterminate or probably malignant tumour
- >6 cm: open radical resection must be undertaken, if necessary en bloc with involved adjacent organs .
- Indeterminate or probably malignant tumour
- <6 cm with synchronous metastatic disease.

- For limited metastatic disease, open resection of the tumour and intra-abdominal metastases is advised.
- For distant disease, resection of the primary followed by adjuvant systemic or surgical treatment of metastases is appropriate.
- For widespread metastatic disease, initial palliative treatment with mitotane with or without chemotherapy should be pursued. If there is significant disease regression after 3–6 months, surgery may then become an option.
- More rarely, patients present with locally advanced disease with tumour extension into the great vessels. In this situation, it is recommended that such patients are referred to centres with experience of treating these cases.

- **Oncological treatment**
- Patients at high risk of recurrence and those with metastatic disease should commence **mitotane** therapy as soon as possible (for up to 5 years) .
- Palliative chemotherapy EDP (etoposide– doxorubicin–cisplatin) if there is disease progression despite mitotane therapy.
- Unless there is ongoing steroid excess, all patients treated with mitotane should receive oral hydrocortisone replacement therapy.

# Adrenal Metastases

- They are not uncommon and often portend disseminated incurable disease. Primary tumours that commonly spread to the adrenals include lung, renal, gastric, breast and colorectal cancers.
- **Diagnosis**
- Screening for catecholamine and cortisol excess to exclude a coincident hormonally active tumour.
- Careful diagnostic work-up to determine whether it is an isolated adrenal metastasis (seen most often with renal, lung and colorectal primaries) or a more widespread metastatic picture.
- Patients should therefore undergo CT thorax, abdomen and pelvis and PET-CT to exclude disease at other sites.

- **Treatment**
- If disease is widespread, metastasectomy will not usually be appropriate and systemic or palliative treatment should be the norm.
- Adrenal metastasis diagnosed at presentation (synchronous disease) should be removed if ipsilateral to a renal cell cancer (radical nephrectomy). In the case of other primary tumours, it should be observed with interval scanning at 3–6 months; if the lesion remains stable and isolated, resection should be considered. If adrenal metastasis arises more than 6 months after initial treatment (metachronous), PET-CT should be performed to exclude widespread disease; if the lesion is solitary, excision can be considered.

- **Surgery**
- Laparoscopic adrenalectomy is the preferred surgical option.
- Local invasion, but the surgery is likely to improve survival, open surgery and en bloc excision may be appropriate.
- Note that, in the setting of previous nephrectomy with adrenalectomy, excision of an affected contralateral adrenal gland will render the patient steroid dependent.

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## ADRENAL HAEMORRHAGE

# Congenital adrenal hyperplasia (adrenogenital syndrome)

- This is an autosomal recessive disorder leading to a variety of enzymatic defects in the synthetic pathway of cortisol and other steroids from cholesterol. E.g. (95%) is the 21-hydroxylase deficiency, leading to secondary ACTH secretion leads to an increase in androgenic cortisol precursors and to CAH.
- **Virilisation** and adrenal insufficiency in children (pathognomonic). It may present in girls at birth with ambiguous genitalia or as late-onset disease at puberty. **Hypertension** and **short stature (**premature epiphyseal plate closure), are common signs.
- Treatment (adrenal insufficiency ) is replacement of hydrocortisone and fludrocortisone. Large hyperplastic adrenals may need to be removed if symptomatic.

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## ADRENAL HAEMORRHAGE

# Acute adrenal insufficiency (adrenal / Addisonian crisis)

- This is a medical emergency.  (shock with some or all of the following: fever, nausea, vomiting, abdominal pain, hypoglycaemia and electrolyte imbalance), it can be difficult to diagnose. It is also rapidly fatal unless prompt and appropriate treatment is instituted early in its course.
- Typically there is a precipitating illness that may unmask longstanding adrenal insufficiency or a history of trauma or severe sepsis that result in adrenal haemorrhage or infarction (Waterhouse–Friderichsen syndrome), respectively.
- Because intestinal symptoms and fever are frequent, Addisonian crisis may often **be misdiagnosed as an acute abdominal emergency**

- Diagnosis
- Cortisol deficiency and then determining whether this is ACTH dependent or independent by performing an ACTH stimulation test (synacthen test).
- Blood is drawn for basal ACTH and cortisol. If both are low, the diagnosis is secondary or tertiary adrenal insufficiency. If the ACTH is high and the cortisol is low, the cause is adrenal disease (primary adrenal insufficiency).
- Synacthen testing is used because it is the quickest way to determine if there is any adrenal function; adrenal function is present for some after the onset of pituitary or hypothalamic disease, whereas there will be no response when the adrenal glands are diseased.

# Treatment

- The treatment must be commenced immediately while the results of confirmatory testing are awaited.
- Plasma ACTH, serum cortisol, plasma renin activity and aldosterone and therapy with intravenous saline and hydrocortisone should be commenced.
- A typical regime would consist of a 100-mg bolus of IV hydrocortisone followed by 50 mg IV hydrocortisone 6-hourly and 2–3 litres of 0.9% saline in 6 hours, with careful cardiovascular monitoring to prevent fluid overload. Concomitant infections, which are frequently present, should also be treated. Fluids and steroids are then tapered as the patient stabilises.
- To prevent an Addisonian crisis, patients must be aware of the need to double the dose in cases of illness or stress (‘sickness day rules’). If patients with adrenal insufficiency are scheduled for surgery, appropriate steroid cover must be administered.

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## ADRENAL HAEMORRHAGE

# Chronic Adrenal Insufficiency .

- Patients with chronic adrenal insufficiency may also be difficult to diagnose because symptoms appear insidiously over time.
- They may experience anorexia, weakness and nausea and, in the case of primary adrenal insufficiency, hyperpigmentation of the skin and oral mucosa because of the loss of negative feedback on secretion of ACTH and POMC.
- Hypotension, hyponatraemia, hyperkalaemia and hypoglycaemia are commonly observed due to the deficiency of mineralocorticoids.

**Diagnosis**：as for acute adrenal insufficiency

## **Treatment** ( chronic )

- Replacement therapy : daily oral hydrocortisone (15–25 mg orally in two or three divided doses) and fludrocortisone (0.05–0.2 mg each morning orally).
- Patients must be advised about the need to take lifelong glucocorticoid and mineralocorticoid replacement therapy.

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# ADRENAL HAEMORRHAGE

- It is a serious condition that can result in adrenal insufficiency (bilateral haemorrhage) , shock, acute adrenal crisis and mortality if not managed with adequate treatment.
- It is one of the most vascular tissues in the body.
- The predisposing factors include { infection (sepsis), myocardial infarction, anticoagulants, trauma, surgery and antiphospholipid syndrome}.
- Clinical presentation can vary from non-specific abdominal pain to adrenal insufficiency or hypovolaemic shock.

- Investigation
- Abdominal C.T. scan angiography is the most common way to diagnose the condition (left retroperitoneal haematoma ) .
- Management
- Most of the cases are successfully managed conservatively.
- Stop anticoagulation therapy temporarily.
- Rarely, interventional radiology may be necessary to staunch the bleed ( T.A.E. by injection of gel foam and coils.
- If bilateral haemorrhage,the possibility of adrenal insufficiency should be considered.

# DISORDERS OF THE ADRENAL MEDULLA AND DIFFUSE NEUROENDOCRINE SYSTEM

- **Phaeochromocytoma and paraganglioma (PPGL)**
- Neuroblastoma.
- Ganglioneuroma .

# Phaeochromocytoma

- **Phaeochromocytoma** (PCCs) **(**arise from the neuroectodermal tissue of the adrenal medulla )
- **Paragangliomas** (PGLs) ( arise from the extra-adrenal parasympathetic and sympathetic ganglia .
- PGLs are either :

  - **Parasympathetic PGLs** are sited mainly in the head and neck (HNPGLs) and 95% do not secrete catecholamines or other hormones. The commonly ( carotid body, vagal and jugulotympanic) .

  - **Sympathetic PGLs** usually secrete catecholamines.

- The incidence of PCC is about 0.6 in 100 000 and 75% are thought to be sporadic. The incidence of sporadic PGL 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)

- Hereditary PPGL syndromes
- These are associated with germline mutations in genes, including succinate dehydrogenase (SDH) subunits, Mycassociated protein X (MAX) and transmembrane protein 127 (TMEM127) .Loss-of-function mutations in SDH lead to accumulation of Krebs cycle precursors, which act as oncometabolites.
- Loss-of-function TMEM127 and MAX mutations result in PPGL development through cell death escape and enhanced survival. SDHB gene variants account for the majority of secreting PGLs whereas SDHD mutations account for the majority of non-secreting HNPGLs. A□cted individuals are regularly surveilled with annual blood tests and 3-yearly MRI (neck and or abdomen).

- Von Hippel–Lindau disease
- An autosomal dominant disease characterised by central nervous system and retinal haemangiomas (60–80%), renal cysts (50–70%), clear cell renal cell carcinoma (30%), pancreatic neuroendocrine tumours (P-NETs) (8–17%), PPGL (20%), endolymphatic sac tumours (6–15%) and epididymal/broad ligament cyst adenoma (50%). VHL is defined by its genotype as type I (deletions) without PPGL and type II (missense mutations), which is associated with PPGL. Patients develop PCC much more frequently than PGL. VHL tumours overproduce only noradrenaline.

- Neurofibromatosis type 1
- This is a syndrome characterised by the development of café- au-lait spots (100%), axillary freckling (90%), neurofibromas (84%), Lisch nodules of the iris (70%), typical osseous lesions (14%) and optic glioma (4%). PPGL (PCC 96%) are found in 7% of a□ected patients. NF-1 is a tumour-suppressor gene and loss-of-function mutations lead to cell proliferation and cancer development.

- **Pathology**
- PCCs are greyish-pink on the cut surface and are usually highly vascularised. Areas of haemorrhage or necrosis are often observed. Microscopically, tumour cells are polygonal but the configuration varies considerably.
- Approximately 10% of PCCs are malignant. The differentiation between malignant and benign tumours is difficult, except when metastases are present. An increased PASS (phaeochromocytoma of the adrenal gland scale score), a high number of **Ki-67**-positive cells, **vascular invasion** or a breached capsule all lean more towards malignant rather than benign.
- PCCs may also **produce calcitonin**, ACTH, vasoactive intestinal polypeptide (VIP) and parathyroid hormone-related protein (PTHrP). In patients with MEN 2, the onset of PCC is preceded by adrenomedullary hyperplasia, sometimes bilateral.
-

- Clinical presentation
- Functioning PPGLs typically present with symptoms and signs of catecholamine excess, and these are typically intermittent .In total, 90% of patients with the combination of headache, palpitations and sweating in the presence of an adrenal tumour have a PCC. Paroxysms may be precipitated by physical training, induction of general anaesthesia and numerous drugs and agents (contrast medium, tricyclic antidepressant drugs, metoclopramide and opiates). Hypertension may occur continuously, be intermittent or absent.
- HNPGLs present with the side effects arising from their local mass effect (e.g. neck mass, dysphonia or tinnitus).

- **Diagnosis**
- Biochemical
- The diagnosis of PPGL is confirmed by elevated catecholamine metabolites (metanephrines) in plasma and/or raised 24-hour urinary excretion of fractionated metanephrines.
- Plasma and urinary metanephrines is more sensitive (99% and 97%, respectively) than plasma and urinary catecholamine measurement ( VMA) (86% and 84%, respectively).
- Measurements of one or more of these substances that are four times greater than the upper limit of the reference range are 100% diagnostic.
- Plasma dopamine can be regarded as a marker of tumour burden in malignant PPGL.

| Range and incidence of symptoms from PPGL. | |
|---|---|
| **Symptoms** | **Prevalence (%** |
| **Hypertension** | **80–90** |
| **Paroxysmal** | **50–60** |
| **Continuous** | **30** |
| **Headache** | **60–90** |
| **Headache** | **60–90** |
| **Sweating** | **50–70** |
| **Palpitation** | **50–70** |
| **Pallor** | **40–45** |
| **Weight loss** | **20–40** |
| **Hyperglycaemia** | **40** |
| **Nausea** | **20–40** |
| **Psychological** | **20–40** |

## Radiological ( localization )

- Imaging by CT or MRI to determine tumour location, size and risk of malignancy.
- Size is not a predictor of malignancy for PCC. Malignant PPGLs are diagnosed by the presence of local invasion or metastatic disease.
- Tumours appear vascular and frequently possess cystic areas or central necrosis .If initial imaging is negative or reveals extra-adrenal disease, **functional investigation with 123I-MIBG** (meta-iodobenzylguanidine; 80–90% sensitive) or **111In-octretide scanning** (50–70% sensitive) is undertaken.

- Routine use is not advocated in well-localised adrenal lesions.
- Recently, **6-[18F]fluorodopamine PET scanning** has shown promise, particularly in the setting of PGLs, where conventional imaging and MIBG scanning are negative.

- **Medical management**
- **Preoperative control of blood pressure**
- Once a PCC has been diagnosed, an α-adrenoceptor blocker (phenoxybenzamine) ( 10 mg / daily till 100–160 mg postural hypotension may be reported ) to block the effects of catecholamine excess and its consequences during surgery. This will decrease mortality rate from 20–45% to less than 3%.
- Additional β-blockade is required if tachycardia or arrhythmias develop; this should not be introduced until the patient is α-blocked.
- Other regimens , e.g. α-blockade with doxazosin or prazosin, with and without β-blockade, using calcium channel blockers alone and using the catecholamine synthesis blocker metyrosine in the setting of cardiac failure.

- With adequate α-blockade preoperatively, anaesthesia should not be more hazardous than in patients with a nonfunctioning adrenal tumour; however, in some patients, dramatic changes in heart rate and blood pressure may occur and require sudden administration of pressor or vasodilator agents.
- A central venous catheter and invasive arterial monitoring are used. Special attention is required when the **adrenal vein is ligated** as a sudden drop in blood pressure may occur. **The infusion of large volumes of fluid** or **administration of noradrenaline** can be necessary to correct postoperative hypotension in the presence of unopposed α-blockade.
- **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, metastatic or metachronous PCC.

# 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 > 10 cm or malignanant radiological signs 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**.

# Special circumstances

- **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 to improve symptom control and improve the efficacy of adjuvant radiolabelled MIBG and octreotide therapy, a 5-year survival rate of less than 50%.

# Phaeochromocytoma in pregnancy.

- It may be silent and present as a hypertensive emergency or it may mimic an amnion infection syndrome or pre-eclampsia.
- Without adequate α-blockade, mother and unborn child are threatened by a hypertensive crisis during delivery.
- In the first and second trimesters the mother should be scheduled for laparoscopic adrenalectomy after adequate α-blockade; the risk of a miscarriage during surgery is high.
- In the third trimester, elective caesarean with delayed consecutive adrenalectomy 6 weeks later should be performed.
- The maternal mortality rate is 50% when a PCC remains undiagnosed.

# DISORDERS OF THE ADRENAL MEDULLA AND DIFFUSE NEUROENDOCRINE SYSTEM

- Phaeochromocytoma and paraganglioma.
- **Neuroblastoma.**
- Ganglioneuroma .

- **Neuroblastoma** is the most common and deadliest solid extracranial malignancy in children. It is derived from the primitive nerve cells (neuroblasts) of the sympathetic nervous system, derived from the neural crest. It is often termed the ‘clinical enigma’ as the prognosis ranges from spontaneous regression to treatment resistance, metastasis and death.
- 7% of all childhood cancers, $10/10^6$ under the age of 15 years.
- It arises from neuroblasts populating the adrenal medulla ( 40 % ) and sympathetic ganglia in other sites.

- **Clinical presentation**
- (40%) > 1 year, 35% between (1 and 2 years) and 25% older than 2 years.
- Is related to tumour growth pressure or incidentally at ultrasonographic findings.
- Presenting symptoms include malaise and/or pain or obstruction of veins or lymphatics or hydronephrosis. Acute or subacute paraplegia can develop from spinal cord or nerve root involvement.
- Many children (70%) have metastases at the time of presentation. Rarely secretes VIP, which results in diarrhoea, dehydration and hypokalaemia.

- **Diagnosis**
- 24-hour urinary metanephrines (elevated ).
- Serum lactate dehydrogenase ( tumour marker).
- Tissue biopsy either the tumour or bone marrow aspirate.

  - The **histopathological diagnosis** is established from immunohistochemistry (neurofilaments, synaptophysin and neurone-specific enolase).

  - The **genetic analysis** .Genomic amplification of MYCN is reported in 25% of tumours and is the strongest predictor of poor prognosis, other chromosome arm-level alterations, notably deletion of 1p and 11q and gain of 17q.

- Staging the disease using CT or MRI and MIBG .
- In children with regional or metastatic disease, biopsy is necessary for diagnosis and prognostication.
- Prognosis can be predicted by the tumour stage and the age at diagnosis.

## Treatment

- Surgical excision with adjuvant multiagent chemotherapy.

# DISORDERS OF THE ADRENAL MEDULLA AND DIFFUSE NEUROENDOCRINE SYSTEM

- Phaeochromocytoma and paraganglioma.
- Neuroblastoma.
- **Ganglioneuroma .**

- Ganglioneuroma is a Benign differentiated tumours of neural crest-derived cells in the autonomic nerves.
- Incidence : GNs are rare, affecting one per million of the population. Most are sporadic but they can be associated with neurofibromatosis type II and MEN 2B.
- **Pathology**
- Are most often located in the mediastinum (20%), retroperitoneum (10%) and adrenal gland (30%). However, GNs can arise anywhere sympathetic nervous tissue is found, such as tongue, bladder, uterus, bone and skin. They are composed of an admixture of ganglion cells and Schwannian stroma/cells.

- **Clinical presentation**
- GNs develop in childhood but typically present later as they are **non-secreting and slow growing.**
- Two-thirds of patients are under the age of 20 years. They are usually asymptomatic and are identified incidentally. When large, GNs may cause **local pressure symptoms** such as abdominal pain or bloating. Occasional reports of elevated metanephrines exist and the differential diagnosis is PCC.
- **Diagnosis**
- Once a mass is discovered CT and MRI are usually performed to characterise the lesion. They are well defined with a capsule and calcification may be present. GN has a low T1- and a high T2-weighted signal on MRI. Radiology cannot definitively diagnose a GN; **histology is required** and so preoperative diagnosis can be challenging.
- **Treatment**
- Excision is the treatment of choice. A laparoscopic approach is preferred. The prognosis is excellent as recurrences are rare.

# SURGERY OF THE ADRENAL GLANDS

1) Minimally invasive adrenalectomy

- **Transperitoneal laparoscopic adrenalectomy**
  - **Right transperitoneal laparoscopic adrenalectomy**
  - **Left transperitoneal laparoscopic adrenalectomy**
- **Posterior retroperitoneoscopic adrenalectomy**

2) Open adrenalectomy


# PRAISE BE TO ALLAH