ADRENAL Cortex

And

its Pathology

Prof. Dr Arun Jamkar

MS. Ph D(Surgical Oncology),

FICS, FIAGES, FMAS, FAIMER fellow

Director,

Post graduate programme, Research and Development,

MIT Group of Medical colleges Pune

Ex Vice Chancellor, Maharashtra university of Health sciences, Nashik

Consultant , Persistent system pvt. ltd

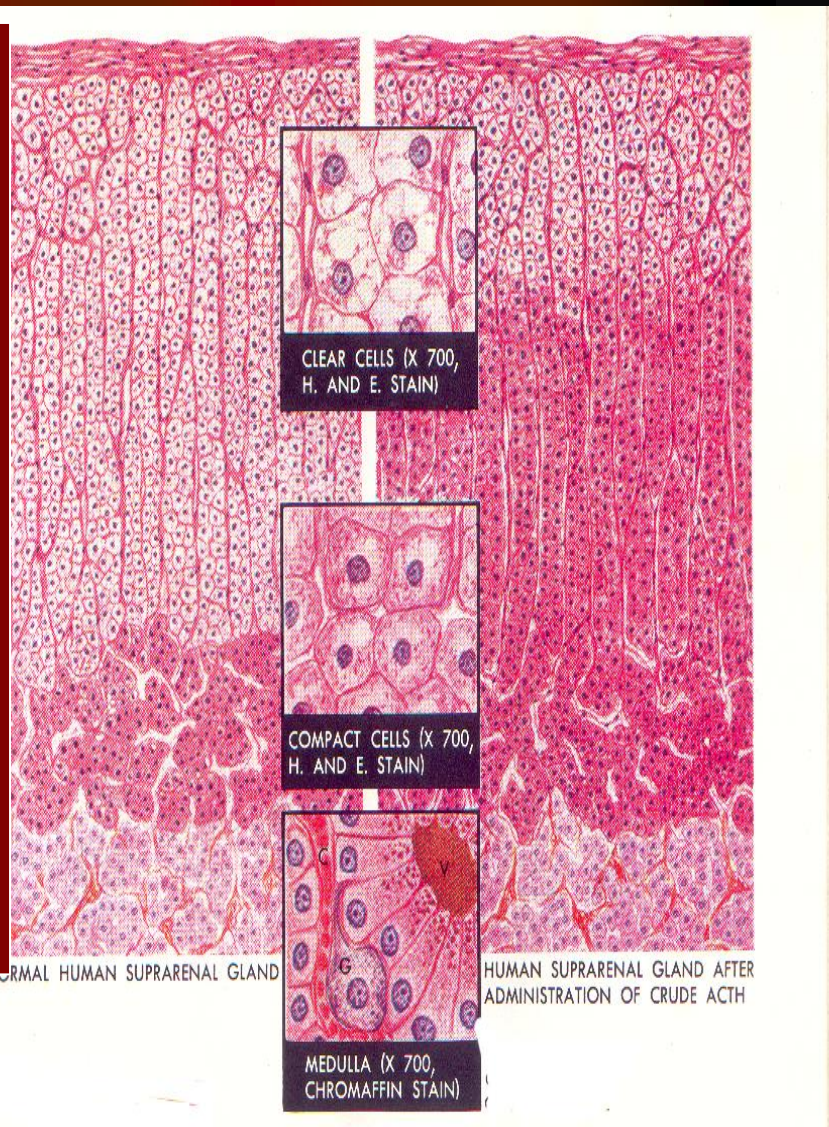
Embryology

- Adrenal Cortex:
- Coelomic mesoderm
- Cluster of cells between root of mesentery and genital ridge
- Androgenic and Oestrogenic Tumor

- Adrenal Medulla:
- Develops as special portion chromafin system
- from neuro ectoderm
- Sympathoblast
- Sympathogonia
- Mature Ganglion cells

Histology:

- Adrenal Cortex:
  - Zona Glomerulosa
    - Aldosterone
  - Zona fasciculate
    - Store house for cholesterol
  - Zona reticularis
    - Rest of hormones.
- Adrenal Medulla
  - Adrenaline, Noradrenaline



The Adrenal gland,

- Suprarenal gland
- Enclosed, together with the kidney, within the renal fascia but a lamina of fibroareolar tissue separates the two structures, so that they occupy separate compartments.
- Right adrenal is triangular in shape and the left is semilunar

Tests for Adrenal Cortical Function:

A. By measuring the blood level of the hormone directly:-

1.Plasma cortisol (hydrocortisone) level.

- Normally 8 to 28 micrograms per 100 ml.

2.Other cortical hormones- Using Immunoassay

Aldosterone

B. By measuring the urinary output (24 hours) of the metabolites

- 17- Hydroxycorticoid (for hydrocortisone)
- 17ketosteroid (for androgens and Oestrogens)
- Free urinary cortisols

- A.C.T.H. stimulation tests
- A.C.T.H. suppression test

Hypercorticism:

- Infantile
- Pre pubertal
- Adult Type
  - Cushing Syndrome
  - Adreno-Genital syndrome
- Post menopausal
- Primary Aldosteronism.

Hypercorticism/ Hypercorisolism

- Hypercorisolism Cushing Syndrome
  - High plasma cortisol levels
- Adreno genital syndrome
  - high 17 ketosteroid levels
- hyper aldosteronism
  - High aldosterone levels
- One and two might overlap

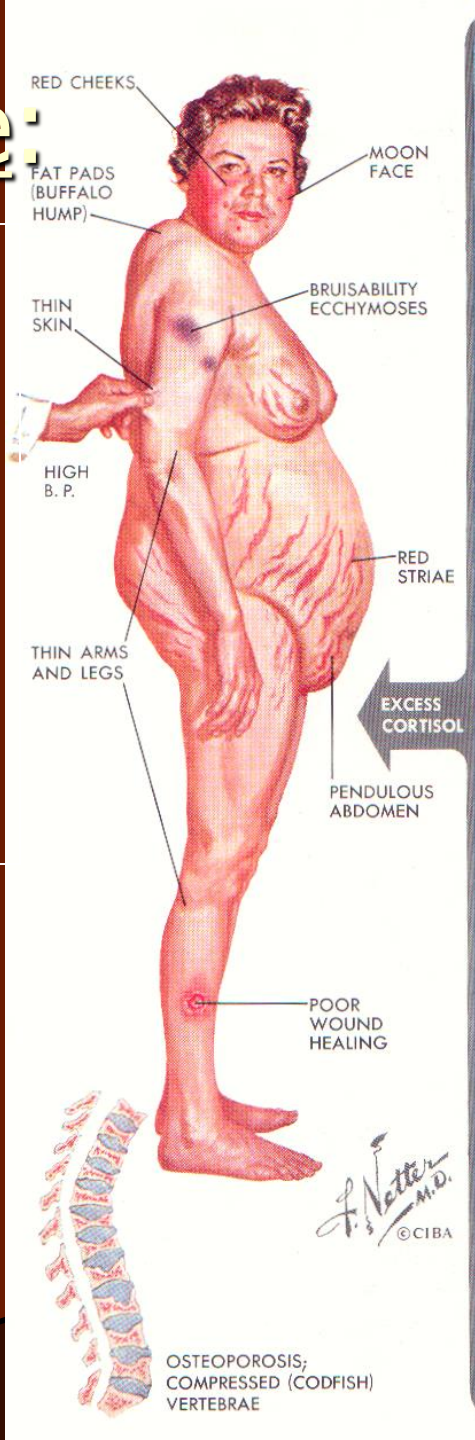
Infantile

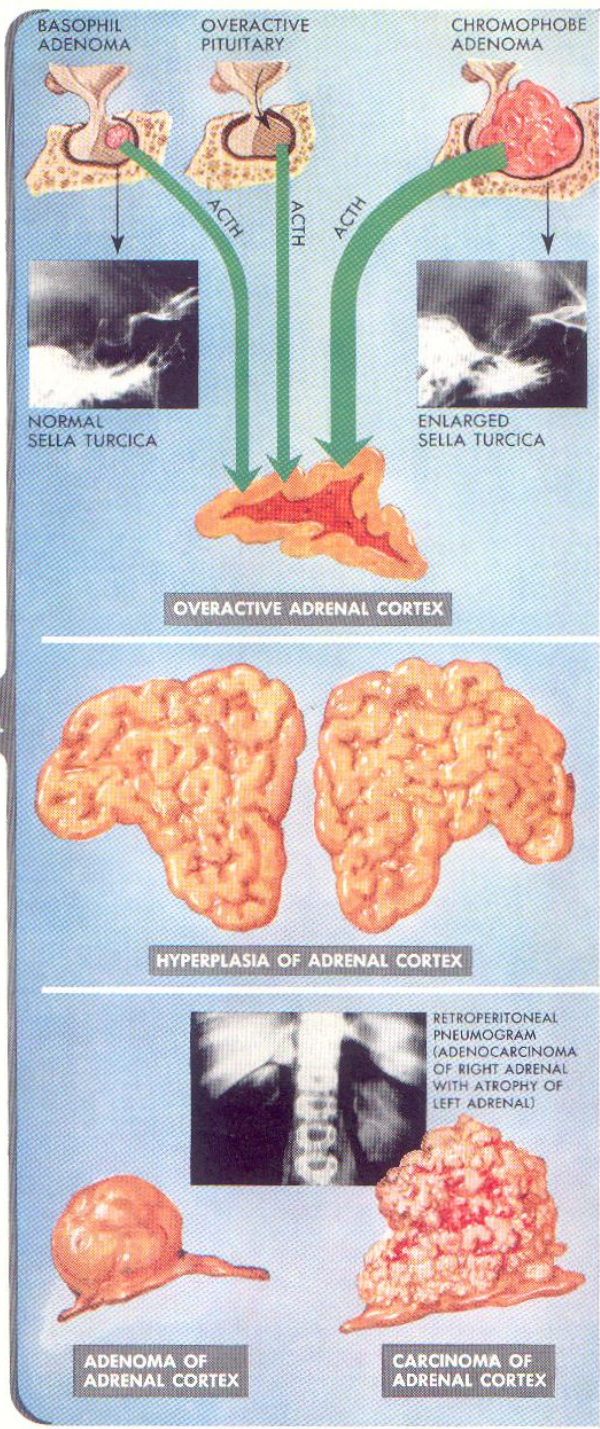
- Due to androgenic excess, during intrauterine life.
- Pseudo hermaphrodite
- Presents at birth
- Enlarged clitoris, Hypospaedias,
- Difficult to determine Test.

Cushing Syndrome:

- Primary:
- Cushing disease: Pituitary Tumors : 30%
- Ectopic ACTH producing Tumour
- Hyperplasia of adrenal gland: 60%
- Tumor of adrenal cortex
  - Adenoma
  - Carcinoma
- Tumours of: pineal gland, thymus.

- Secondary:
- Excessive steroid Therapy
  - Rheumatoid arthritis
  - Transplants Patients receiving Steroid therapy
  - Auto immune disorders





Cushing syndrome

- Female Male Ratio: 3:1
- Age 15 to 50 years
- Highly characteristic features
  - Obesity,
  - Hypertension,
  - Diabetes
  - Abdominal striae,
  - Hirsutism,
  - Menstrual disorder.

clinical features

- May be divided into 5 broad groups:-
  1. Those due to metabolic disorders.
  2. Those due to fluid and electrolyte disturbances.
  3. Sexual disorders.
  4. Mental changes
  5. Other features.

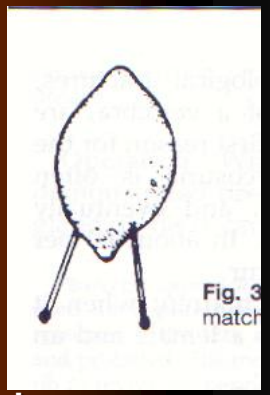
Those due to Metabolic Disturbances

Disturbances releted to fat, protein, sugar and calcium metabolism: -

1.Obesity: Although overall weight is not increased

Deposition of fat in certain areas There is an excessive deposit of fat over

- Protuberant abdomen
- Buffalo lump (fatty pads over the scapulae)
- Moon face with pursed lips
- Obliteration of supraclavicular fossae.



2.Protein breakdown::

- Thinning of arms and legs due to muscle breakdown
- (the swollen abdomen with the thinned-out legs may be compared to 'a lemon on the match-sticks').
- Increasing muscular weakness.

3.Atrophy of the dermis and inhibitory effect on fibrous tissue:

- Skin gets inelastic and assumes a tissue-paper consistency; on the abdomen : striae gravidarum.
- Purpura and bruising to minimal trauma

4. Diabetes, due to increased neoglucogenesis.

5. Negative calcium balance causing gross osteoporosis and, sometimes, pathological fractures (particularly of the vertebrae)

Those due to Fluid and Electrolyte Imbalance

- Hydrocortisone has a weak Aldosterone effect.
- Retention of sodium and water with excessive loss of potassium.
- This results in:
  - Hypertension, may lead to cardiac hypertrophy, myocardial ischaemia, cerebro-vascular accidents, and congestive heart failure.
  - Hypokalaemic alkalosis

Sexual Disorders

1)Common types:

- Sterility and impotency in the males.
- Sterility and menstrual disorders in the females (oligomenorrhoea, amenorrhoea or menorrhagia).

(2)Uncommon type i.e. Adreno-genital Syndrome:

sexual disorders are more predominant than the metabolic disorders:

- Due to excessive secretion of androsterone.

Oligomenorrhoea, atrophy of the breasts, enlargement of the clitoris, deepening of the voice, and a change of body structure to a manly build.

- Young males ---- excessive seceretion of Oestrogens.

Gynaecomastia, atrophy of the testes, change in voice

- **Mental Changes:**
  Various types of psychosis may set in (more than half of the cases).

- **Other Features:**

(1)Increased growth of lanugo hairs,
sometimes frank hirsutims.
(2) Acne and skin infections
(due to suppressed inflammatory reaction).
(3) Recurrent intercurrent infections
(4) Excessive pigmentation of the skin
(Due to increased A.C.T.H.)

Special Investigations

(1) Blood Count – Polycythemia and leucocytosis (with lymphopaenia and eosinopaenia).

(2) Urine Examination (a)Glycosuria (b) Hypercalciuria

(3) Blood Biochemistry: (a)Hyperglycaemia
(b) Hypercholesterolaemia.

(4) B.M.R. – Low.

(5) X -Ray:

- Skeleton- Gross osteoporosis, particularly in the vertebrae and pelvis.
- Pituitary fossa (sella turcica)- An enlargement may sometimes be seen if the condition is due to a pituitary tumour.
- IVP will show displacement of kidney

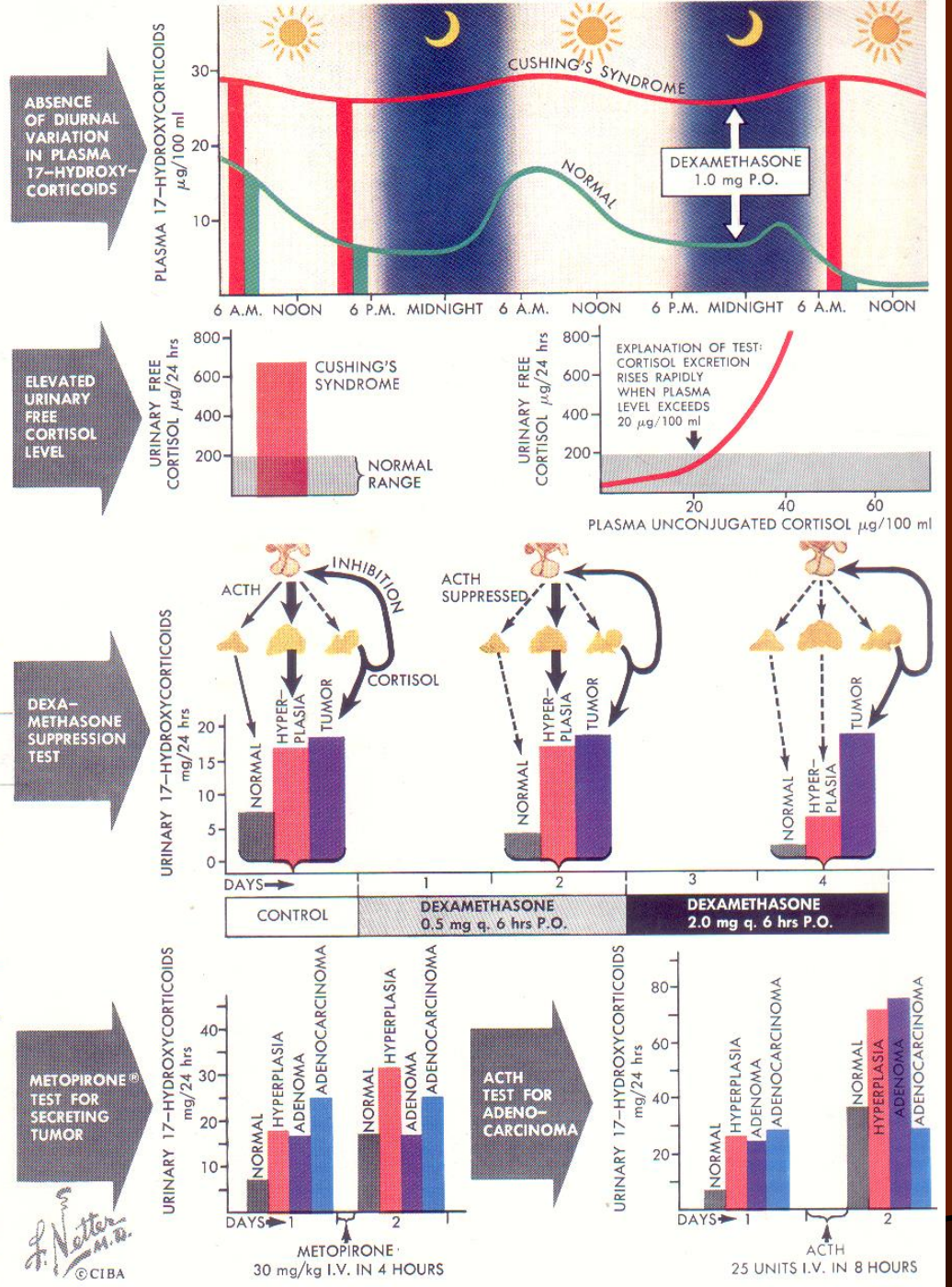
Cortisol Function Test

- Plasma Cortisol Levels:
  - Cushing Syndrome 8 to 28 mg /100 ml (220-780 nmol/liter)
- Plasma ACTH levels
- 24 hours output of urinary steroids: cortisol product
  - 17 ketosteroid: Principle metabolite from
    Testosterone, androsterone etiocholanolong from Testes
    Dehydroepiandrosterone, from cortex.
    2/3 of cortex 1/3 Testes in males
    All of it from Cortex in Females
    9- 25mg /24 hrs in males
    8-12mg/24 hrs. in Females
    Test for adreno-cortical function + Testicular
  - 17 Hydroxy Steroid
    - All urinary steroids are oxidized
    - Converted steroids are mead
    - 80 to 90% cortisol metabolites can be measured.
    - 8 to 13 mgs/24 hrs.
  - 24 hours Free urinary cortisol level
    - > 100 micro gm /24 hours +

Localization of cause of Cushing Syndrome

- Pituitary Cushing Disease:
  ACTH high, Both are stimulated
  17 Keto + 17 Ketogenic
- Cortical adenoma,
  A.C.T.H. low, Androgens low
  17 Keto (Normal) + Ketogenic (2 to 4 times)
- Cortical Carcinoma
  Aberrant sterodogenesis
  Very high 17 Ketosteroids (40 – 100 mgs)
- Ectopic ACTH producing tumour
  Ketogenic high 4 times of Ketosteroids

- A.C.T.H. suppression tests
  High dose dexamethasone Test
  2mg dexamethasone 6 hrly for 4 days
  Plasma Cortisol ,Urinary free Cortisol
  and 17 hydroxy Cortisol levels decrease
  by 50 % in Pituitary adenoma
  Adrenal hyperplasia,A.C.T.H. Producing Tumour
  Ectopic ACTH producing tumour No effect
- A.C.T.H stimulation. test Metyrapone Test
  11 deoxy cortisol ⇓ cortisol
  30mg/kg 750mg every four hours for six doses
  Pitutory adenaoma patients increase in ACTH secreation and increase in urinary
  17 hydroxy steroid
  No effect in others
- CRH test Pituitary Cushing disease from ectopic ACTH tumour: 1micgm/kg---- Plasma ACTH levels go up


ABSENCE OF DIURNAL VARIATION IN PLASMA 17-HYDROXY-CORTICOIDS
PLASMA 17-HYDROXYCORTICOIDS μg/100 ml
30
20
10
CUSHING'S SYNDROME
NORMAL
DEXAMETHASONE 1.0 mg P.O.
6 A.M. NOON 6 P.M. MIDNIGHT 6 A.M. NOON 6 P.M. MIDNIGHT 6 A.M. NOON
ELEVATED URINARY FREE CORTISOL LEVEL
URINARY FREE CORTISOL μg/24 hrs
800
600
400
200
CUSHING'S SYNDROME
NORMAL RANGE
EXPLANATION OF TEST: CORTISOL EXCRETION RISES RAPIDLY WHEN PLASMA LEVEL EXCEEDS 20 μg/100 ml
20 40 60
PLASMA UNCONJUGATED CORTISOL μg/100 ml
DEXA-METHASONE SUPPRESSION TEST
URINARY 17-HYDROXYCORTICOIDS mg/24 hrs
ACTH
INHIBITION
CORTISOL
ACTH SUPPRESSED
NORMAL
HYPER-PLASIA
TUMOR
20
15
10
5
0
DAYS 1 2 3 4
CONTROL
DEXAMETHASONE 0.5 mg q. 6 hrs P.O.
DEXAMETHASONE 2.0 mg q. 6 hrs P.O.
METOPIRONE® TEST FOR SECRETING TUMOR
URINARY 17-HYDROXYCORTICOIDS mg/24 hrs
NORMAL
HYPERPLASIA
ADENOMA
ADENOCARCINOMA
40
30
20
10
DAYS 1 2
METOPIRONE 30 mg/kg I.V. IN 4 HOURS
ACTH TEST FOR ADENO-CARCINOMA
URINARY 17-HYDROXYCORTICOIDS mg/24 hrs
80
60
40
20
DAYS 1 2
ACTH 25 UNITS I.V. IN 8 HOURS
F. Netter M.D.
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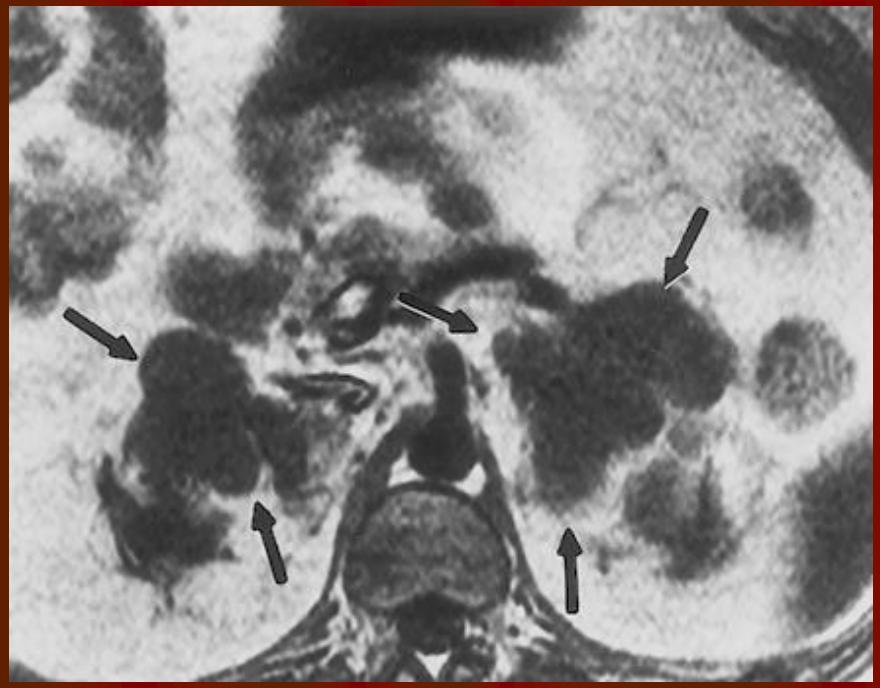
CAT scan in Cushing Syndrome

- For Pitutory tumours of size 5-10 mm can be diagnosed
- 95% Sensitivity for Adrenal localisation
- Adenoma can mimic Pheochromocytoma
- Hyperplasia on one side and hypoplasia on opposite side
- Cannot dignose micronodular hyperplasia

MRI scan in Cushing Syndrome

- Better modality for Pitutory tumours
- Gadolinium MRI is still better
- Does not diagnose Micro adenoma
- Better modality for adrenal pathology as on T1 weighted image both Primary and mets appear darker than Liver
- Pheochromocytoma appears 3times brighter

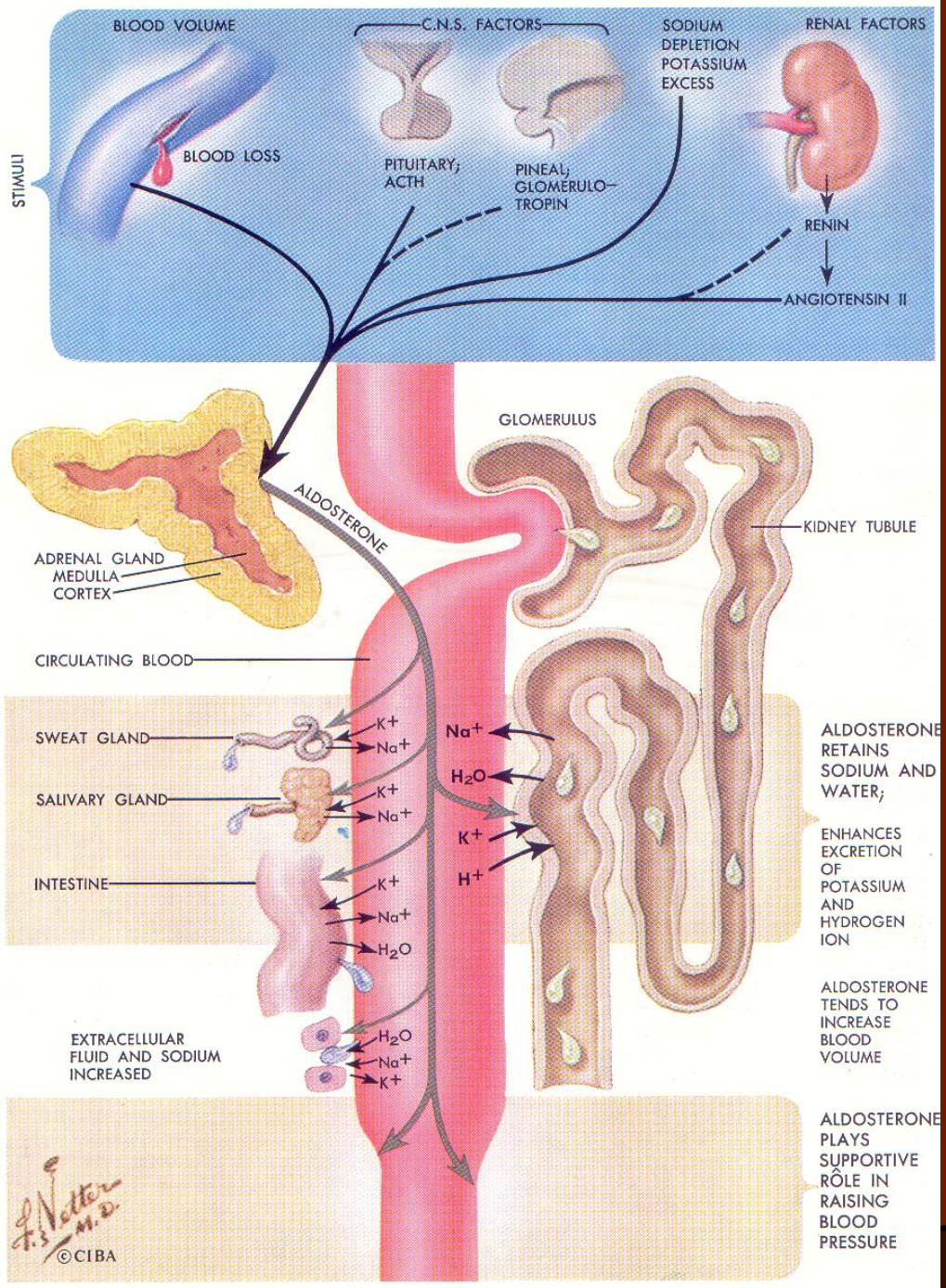


Nuclear scan in Cushing Syndrome

- I 131 iodomethyl norcholesterol scan
- Selective for hypercorticism
- Differentiate adenoma ,Carcinoma and hyperplasia

LOCALIZATION OF THE ETIOLOGY OF HYPERCORTISOLISM[1]

TEST	PITUITARY	ECTOPIC TUMOR	ADRENAL TUMOR	MICRONODULAR HYPERPLASIA
Adrenal CT or MR	Normal or bilateral hyperplasia	Normal or bilateral hyperplasia	Unilateral mass	Normal
Plasma ACTH level	Normal or mildly increased	Normal to greatly increased	Low or undetectable	Low or undetectable
High-dose dexamethasone test	Suppression	No suppression	No suppression	No suppression
Petrosal sinus sampling petrosal:peripheral ACTH ratio	>3.0	<3.0	<3.0	<3.0
CRH test plasma ACTH:cortisol ratio	Increased	No increase	No increase	No increase



Actions of Aldosterone

- Primary aldosteronism:CONN's syndrome
  - Tumour of Zona glomerulosa
    - Small Tumour 0.5 cm to 2 cm , Golden yellow in colour,
    - APA May project from surface of gland.
  - Bilateral hyperplasia of adrenal :
    Idiopathic Hyperaldosteronism.
- Secondary Aldosteronism
  - Rennin angiotensin activity ↑ PRA plasma Rennin Activity ↑
  - Edema Blood Volume
  - Cirrhosis , Oral contraceptive
  - CCF , Renal artery stenosis
  - Nephrotic Syndrome ,Barter syndrome
  - Renin producing Tumour.

Clinical Picture

- Hypertension, frontal headache, dizziness
- Muscle weakness due to low K
- Nocturia, Polyurea, Polydypsia
- Hypertension with Hypokalaemic acidosis
- Postural hypotension

Rx:

Salt loading 2 gm KCl TDS
Spiranolactone 400 mg/day

APA
Aldosterone producing adenoma

- Gross: Small tumour 8 to 20 mm in diameter
- Usually has distinct Golden yellow colour
- They may project from Gland but they can be intraglandular

- Histology: Large lipid laden or clear cells arranged in cords or lines separated by fine fibroins tissue trabeculae

Clinical. – Usually between ages of 30 to 50
Twice: common in women than men.

Investigations of Aldosteronism:

Clinical Triad to Suggest

- High B.P.
- Low Serum K in a patient not on diuretics
- High CO_2 content

- Serum Aldosterone
- Excretion of Urinary Metabolites
- Aldosterone suppression Test : Spironolactone

Localistion like Adrenal Cushing Syndrome

Adreno-genital Syndrome

- Adreno-genital Syndrome:
- Excessive production of adrenal androgen ⟶ virilism
- Due to deficiency of 21 hydroxylase , hydroxy progesterone cannot be converted into cortisol so through different pathways adrenal androgens are produced.
  - Adreno-cortisol hyperplasia
  - Tumour of cortex

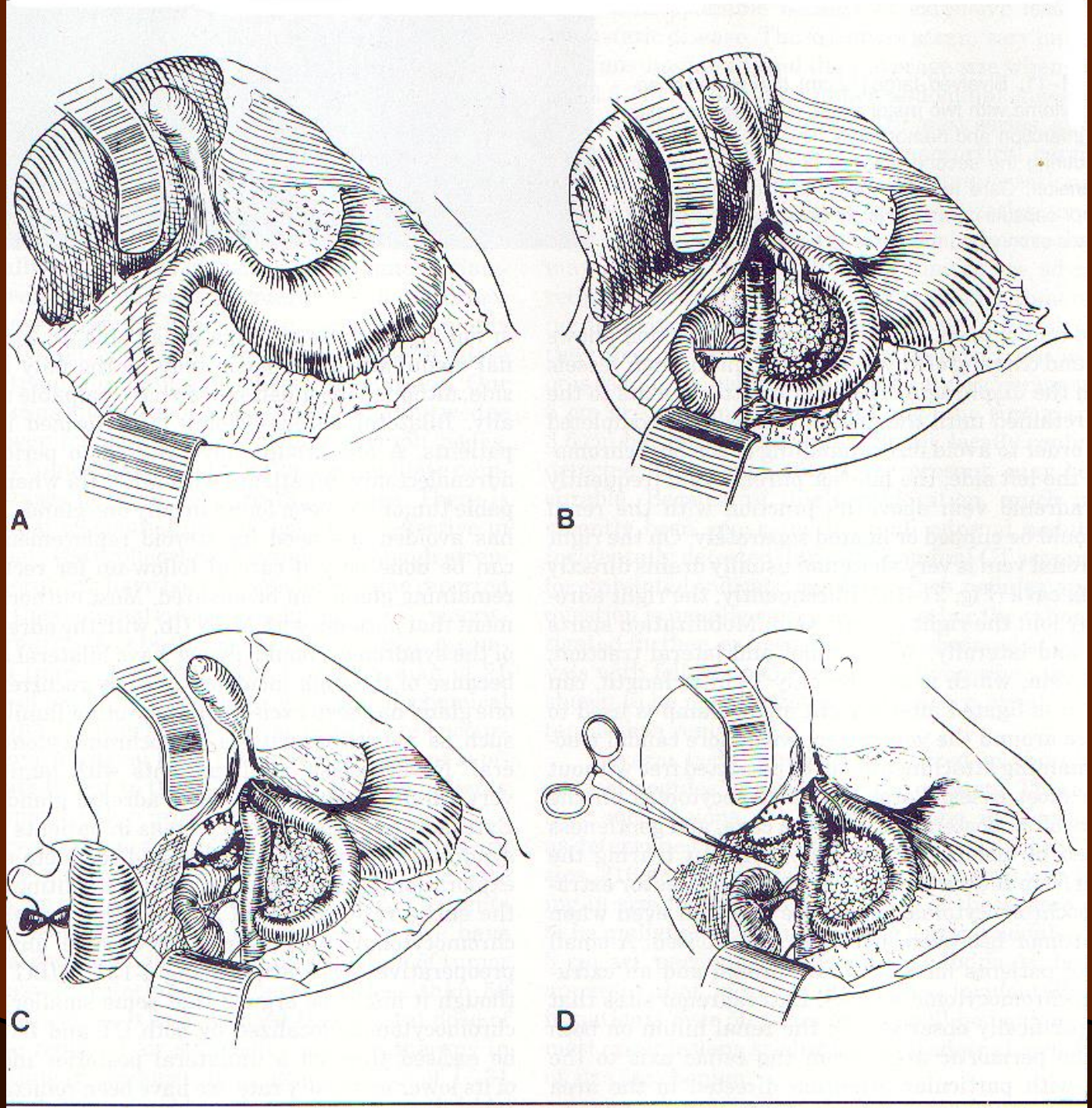
1) Infantile
2) Pre pubertal
3) Adult

INDICATIONS FOR ADRENALECTOMY

UNILATERAL ADRENALECTOMY	APPROACH
Cortical adenoma causing Cushing's syndrome	Posterior or laparoscopic
Aldosteronoma	Posterior or laparoscopic
Pheochromocytoma, sporadic	Anterior
Pheochromocytoma, MEN IIa or MEN IIb*	Anterior or laparoscopic
Adrenocortical carcinoma	Anterior or thoracoabdominal
Virilizing or feminizing tumor	Anterior
Incidental solid mass >6 cm	Anterior or thoracoabdominal

BILATERAL ADRENALECTOMY	APPROACH
Pheochromocytoma involving both adrenals	Anterior
Primary pigmented micronodular adrenal hyperplasia	Posterior or laparoscopic
Massive macronodular adrenal hyperplasia	Posterior or laparoscopic
Severe Cushing's syndrome caused by an occult ACTH producing tumor which is unresponsive to medical management	Posterior or laparoscopic

*Bilateral adrenalectomy is required if tumors are identified in both adrenals.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