PITUITARY ADENOMAS- CLINICAL, NEURO-OPTHALMIC AND RADIOLOGICAL EVALUATION

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PITUITARY GLAND – AN OVERVIEW

- WEIGHS Just 600 mg
- Cranio caudal dimensions 8-10mm
- Upper border is usually flat or concave
- EXERCISES DIRECT OR INDIRECT CONTROL ON EVERY ORGAN SYSTEM

PITUITARY GLAND – AN OVERVIEW

Sella turcica - part of body of sphenoid bone

Depth- upper limit 13mm

Length- upper limit 17mm

Width – upperlimit 15 mm

volume 1100 mm3

➢ ADENOHYPOPHYSIS

- GLANDULAR COMPONENT

  BELIEVED TO ARISE FROM STOMODEUM
- SECRETES

  GH,PRL,FSH,LH,TSH,ACTH,MSH,ENDORPHINS.

ADENOHYPOPHYSIS : DIVIDED INTO

PARS TUBERALIS

PARS INTERMEDIA

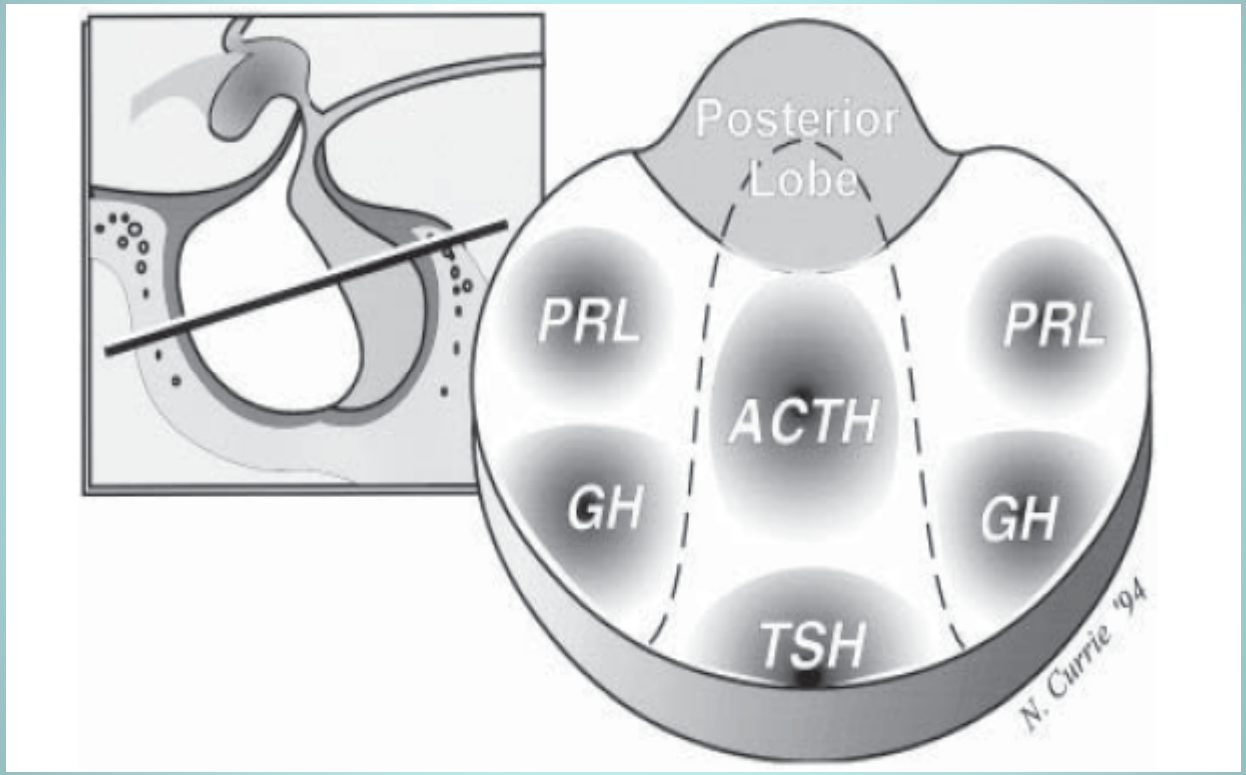
PARS DISTALIS

ADENOHYPOPHYSIS :

- DELICATE ACINAR ARCHITECTURE

- IN HORIZONTAL CROSS SECTION ,COMPOSED OF
  - TWO LATERAL WINGS
  - TRAPEZOID CENTRAL MUCOID WEDGE

SOMATOTROPHS	ANTERIOR PART OF THE LATERAL WINGS
LACTOTROPHS	POSTERIOR PART OF THE LATERAL WINGS
CORTICOTROPHS	CENTRAL WEDGE , JUST ANTERIOR TO POSTERIOR LOBE
THYROTROPHS	ANTEROMEDIAL PART OF CENTRAL WEDGE
GONADOTROPHS	THROUGH OUT PARS DISTALIS


Posterior
Lobe
PRL
PRL
ACTH
GH
GH
TSH
N. Currie '94

NEUROHYPOPHYSIS

- CONTAINS ONLY AXONS AND FENESTRATED CAPPILARIES
- DIVIDED INTO
  - MEDIAN EMINENCE
  - INFUNDIBULAR STEM
  - NEURAL LOBE

PITUITARY TUMOURS

10-15% *OF ALL PRIMARY BRAIN TUMOURS

*kovcks et al .Tumours of pituitary gland.Atlas of tumour pathology

ANNUAL INCIDENCE OF 8.2 – 14.7 CASE** / 100000 POPULATION

**annegers et al.report of increasing incidence of diagnosis in women of child bearing age. Mayo clin proc

THOUGH INCIDENCE IS EQUAL, IT IS DIAGNOSED MORE COMMONLY IN FEMALES

THIRD MOST COMMON PRIMARY BRAINTUMOURS

AUTOPSY INCIDENCE: 20-25%* OF POPULATION

molitch et al . Incidental pituitary adenomas. Am J Med Sci.1993

10%* OF ROUTINE MRI SCANS SHOW OCCULT PITUITARY MICROADENOMA.

*molitch et al . Incidental pituitary adenomas. Am J Med Sci.1993

BETWEEN 3RD – 6TH DECADE OF LIFE

PITUITARY TUMOURS

GENETICS

MEN 1

3% OF ALL PITUITARY TUMOURS

AUTOSOMAL DOMINANT DISORDER

VARIABLE PENETRANCE

OCCCURS IN 25% OF AFFECTED PATIENTS with MEN 1

PRL OR GH MACROADENOMAS

PITUITARY TUMOURS

ADENOHYPOPHYSIS

PITUITARY ADENOMAS

NEUROHYPOPHYSIS

METASTATIC TUMOURS

PRIMARY : RARE -GLIOMA' S,GRANULAR CELL TUMOURS,HEMARTOMAS

PITUITARY ADENOMAS

FUNCTIONING YOUNG ADULTS

NON FUNCTIONING WITH INCREASING AGE

Adenoma type*	Prevalence %
Prolactin cell adenoma	30
GH cell adenoma	15
ACTH cell adenoma	10
Gonadotroph adenoma	10
GH/PRL cell adenoma	7
TSH cell adenoma	1
Nonfunctioning adenoma	25

* kovcks et al .Tumours of pituitary gland.Atlas of tumour pathology .1986

PITUATARY ADENOMAS

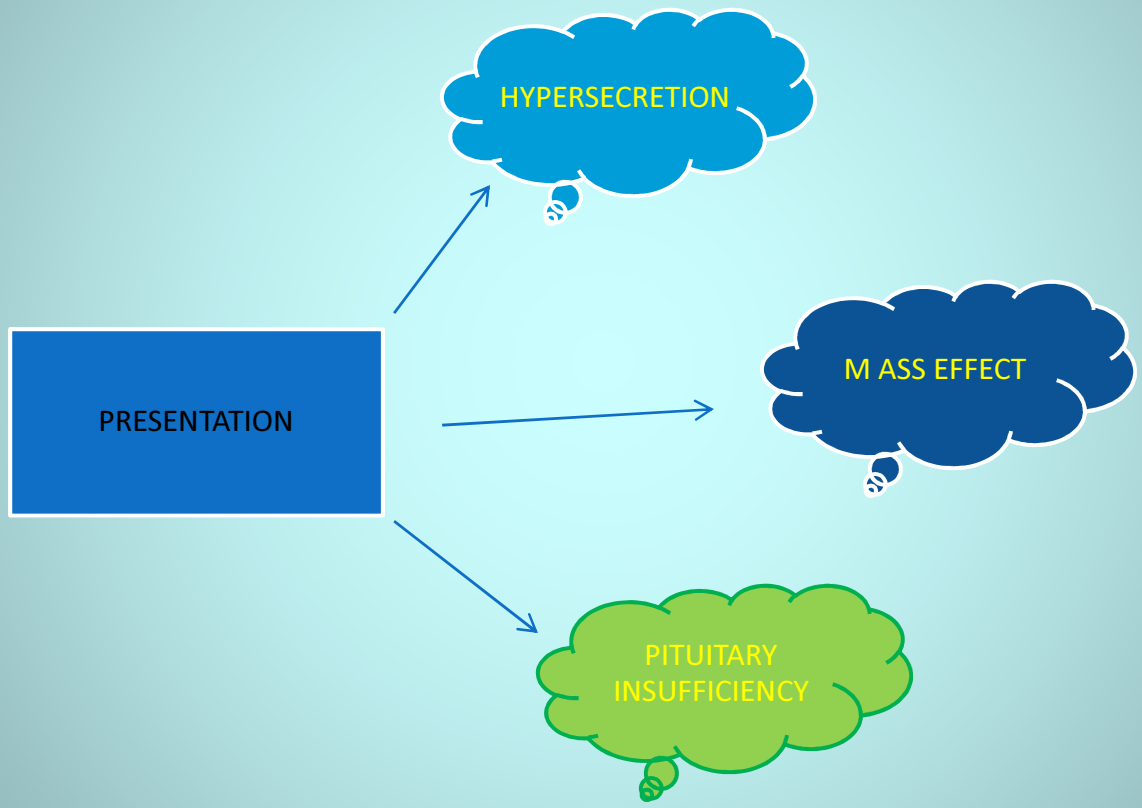
GROSS :

- **YELLOWISH GREY TO PURPLE, SOFT FLUID TO CREAMY TEXTURE**

HISTOLOGICAL:

- **CELLULAR MONOMORPHISM**
- **LACK OF ACINAR ORGANIZATION**
- **UNIFORM CYTOPLASMIC STAINING, PLEOMORPHIC CELLS , PROMINENT NUCLEOLI, MITOTIC FIGURES.**

PITUATARY ADENOMAS



HYPERSECRETION

70% OF PITUITARY ADENOMAS ARE ENDOCRINOLOGICALLY ACTIVE

MOST COMMON MODE OF PRESENTATION

PRESENTATION VARIES ACCORDING TO THE HORMONE IN EXCESS

PITUITARY INSUFFICIENCY

BY COMPRESSION OF NON TUMOUROUS PITUITARY , PITUITARY STALK,HYPOTHALAMUS.

CHRONIC PROCESS, CAN BE ACUTE AS IN PITUITARY APOPLEXY

GONADOTROPHS MOST VULNERABLE

MASS EFFECT

HEADACHE

VISUAL LOSS

HYDROCEPHALUS

INTRACAVERNOUS EXTENSION

HARDY'S Classification

- Microadenomas – Grades 0 and I
- Macroadenomas – Grades II to IV

- Grade 0 : Intrapituitary microadenoma with normal sellar floor
- Grade I : Normal-sized sella with asymmetric floor
- Grade II : Enlarged sella with an intact floor
- Grade III : Localized erosion of sellar floor
- Grade IV : Diffuse destruction of floor

Modified Hardy Wilson Classification

Type A: Tumor bulges into the chiasmatic cistern

Type B: Tumor reaches the floor of the 3rd ventricle

Type C: Tumor is more voluminous with extension into the 3rd ventricle up to the foramen of Monro

Type D: Tumor extends into temporal or frontal fossa

TYPE E : Extradural spread (extension into or out of the cavenous sinus)

Pathoologic Classification

- Chromophobic – Non-functioning
- Basophilic – Cushing's
- Acidophilic - Acromegaly
- Mixed

WHO Classification

Five-tiered system

- Clinical presentation and secretory activity
- Size and invasiveness (e.g. Hardy)
- Histology (typical vs. atypical)
- Immunohistologic profile
- Ultrasturctural subtype

PITUITARY ADENOMAS

A. PROLACTINOMA

- Most common primary tumour of pituitary
- 30% of all pituitary adenoma

  Female : male = 20: 1 for microadenoma
  1:1 for macroadenoma
- Characterized by hyperprolactinemia
- Prolactin

< 25 ng/ ml - normal

25- 150ng/ml - prolactinoma, **stalk effect**, drugs , Hypothyroid

> 150ng/ml - prolactinoma(pure or mixed)

> 1000 ng/ml - invasive prolactinomas

Causes of Hyperprolactinemia

- Medications
  - Psychotropic (e.g., haloperidol, resperidol)
  - Antidepressants (e.g., amoxapin)
  - Estrogen
  - Opiates
  - Calcium channel blocker (verapamil)
  - Antihypertensives (α methyldopa, reserpine)
  - Dopamine antagonists (domperidome, metoclopramide)
- Pituitary adenoma
  - Prolactin-secreting adenoma
  - GH-secreting adenoma
  - Secondary hyperprolactinemia, usually a macroadenoma
- Other pituitary lesion, e.g., metastatic, sarcoid, aneurysm
- Hypothalamic lesion
- Head trauma
- Pregnancy
- Spinal cord lesions
- Chest wall trauma
- Nipple stimulation

PROLACTINOMAS

CLINICAL PRESENTATION

HYPOGONADISM

Menstrual irregularities like secondary amenorrhea, delayed menarche, oligomenorrea , infertility.

Galactorrhea

Decreased libido

HEADCACHE

VISUAL DISTURBANCES

HYPOPITUITARISM

PSYCHOLOGICAL

PITUITARY ADENOMAS

B. GROWTH HORMONE SECRETING PITUITARY ADENOMAS

Growth hormone

Most abundant pituitary hormone

Secretion is pulsatile

Physiological excess seen in stress, trauma, sepsis, estrogen replacement

Exerts it's action through IGF -1

GROWTH HORMONE SECRETING PITUITARY ADENOMAS

- Equal incidence in males and females
- more than 60% are macroadenomas
- 4^{th} and 5^{th} decade
- 15% Of all pituitary tumors
- plurihormonal
- Overall mortality is increased 3 folds as compared to age matched controls

GROWTH HORMONE SECRETING PITUITARY ADENOMAS

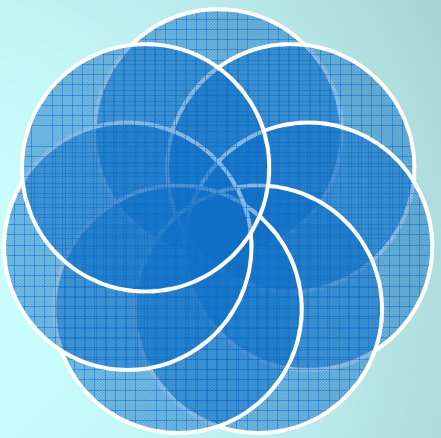
- GH excess

Before epiphyseal closure - gigantism

Beyond puberty - acromegaly

DIVERSE MANISFESTATIONS

1. BONE AND SOFT TISSUE-



Malodorous/oily perspiration

coarse facial features

Spade like enlargement of hand and feet

frontal bossing, prognathism, maxillary widening, dental malocclusion

Macroglossia

Snoring sleep apnea, low voice

2. CARDIOVASCULAR

HYPERTENSION
CARDIOMYOPATHY
ARRHYTHMIAS

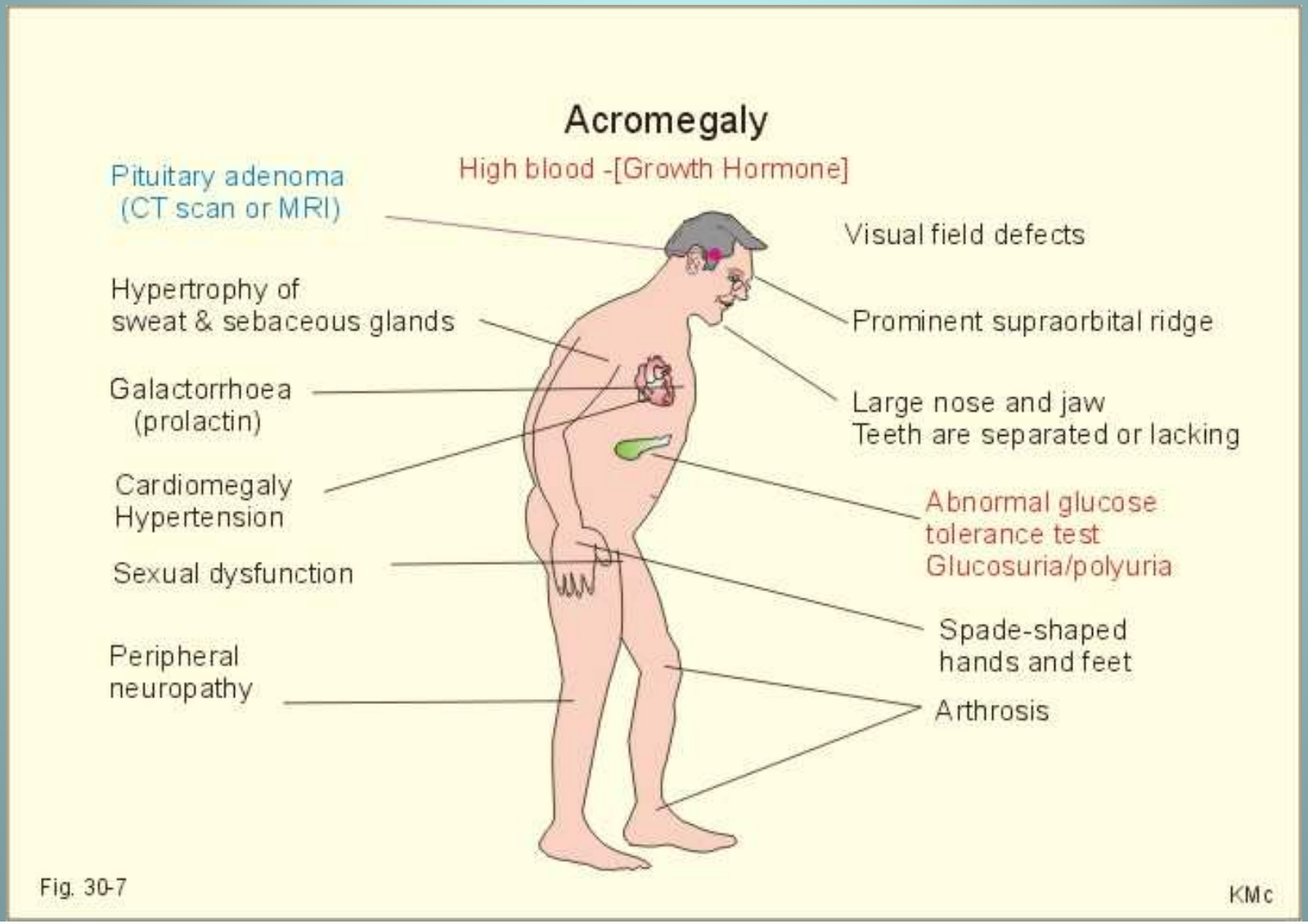
3.Musculoskeletal

Arthropathies
Kyphosis
Spinal stenosis
Barrel chest
Osteoarthritis

4. Increased incidence of premalignant polyps/ colonic cancers

5.Diabetes mellitus

Diverse manifestations




Spade like hands
normal

DIAGNOSIS

- Random GH – not useful gives false positive and false negative results
- Insulin like growth factor 1 (IGF-1) – best for screening represents average daily GH secretion
- Insufficient GH suppression on oral glucose tolerance testing – gold standard to confirm diagnosis :75 mg of glucose load normally suppresses GH< 2ng/ml RIA. GH nadir >2ng/ml RIA with adenoma confirms it

Pituitary adenomas

Cushing's disease

5 to 10 times more common in females than males

3rd and 4th decade

10-15% of all pituitary tumors

Highest morbidity of all pituitary hypersecretory disorders

Most common cause of death is cardiovascular complication

CUSHING'S DISEASE

Ch. Exposure of tissues to excessive cortisol

Moon facies

Centripetal obesity

Buffalo hump

Thin skin ,purple abdominal striae, ecchymosis

Psychological

Glucose intolerance

Hematopoietic features include leukocytosis, lymphopenia, eosinopenia

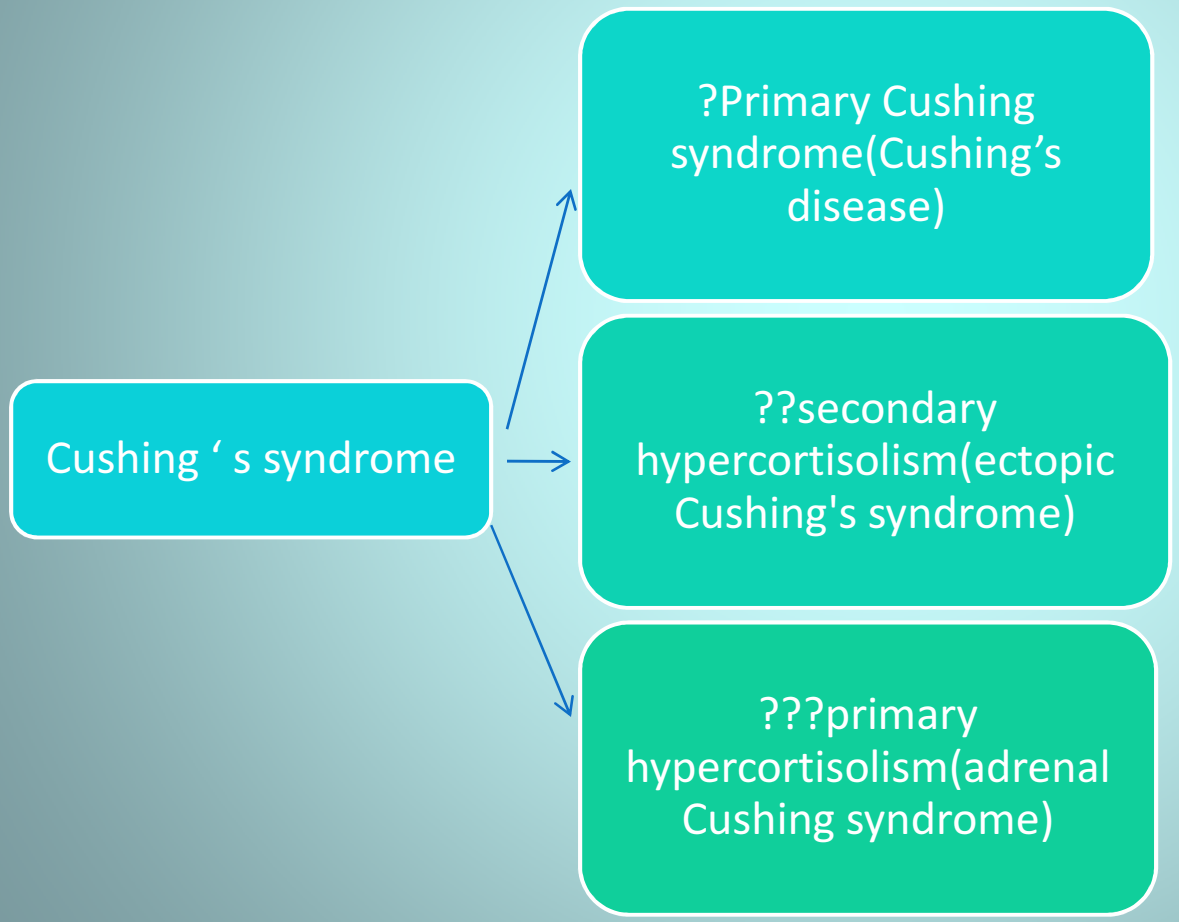
Osteoporosis, proximal myopathy,

Impaired immune function

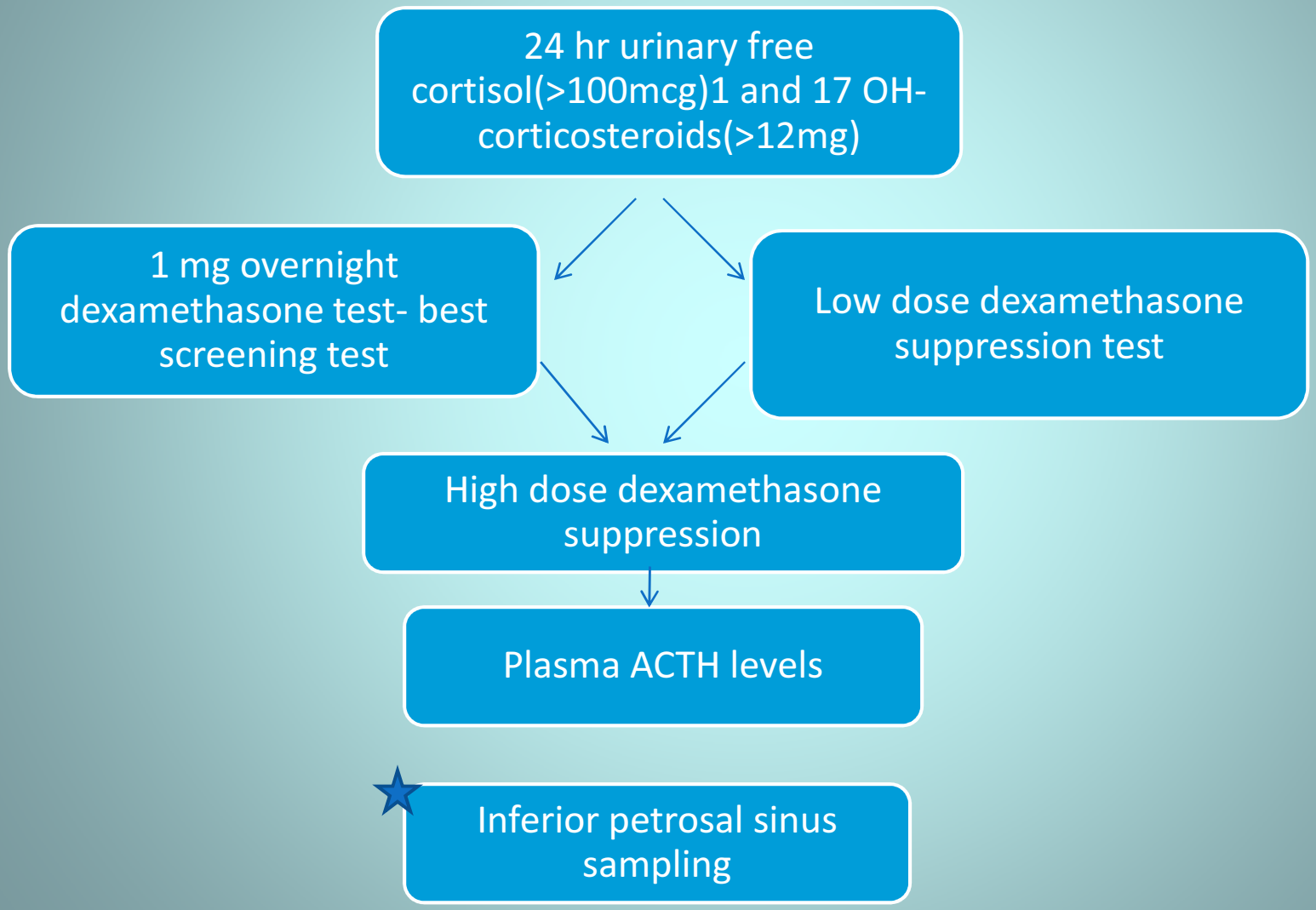
Hirsutism, acne menstrual irregularities in females

Oligospermia, impotence in males

Diagnosis


Cushing ‘ s syndrome
?Primary Cushing syndrome(Cushing’s disease)
??secondary hypercortisolism(ectopic Cushing's syndrome)
???primary hypercortisolism(adrenal Cushing syndrome)

Diagnosis


24 hr urinary free cortisol(>100mcg)1 and 17 OH-corticosteroids(>12mg)
1 mg overnight dexamethasone test- best screening test
Low dose dexamethasone suppression test
High dose dexamethasone suppression
Plasma ACTH levels
Inferior petrosal sinus sampling

INVESTIGATION PROTOCOL

- History and physical examination
- Neuro- ophthalmology:
  Acuity, field, fundus and movements

- Hormone levels basal hormone and dynamic testing
  Aim- hypersecretory state/insufficiency
- Radiology (a) X-Rays
  (b) MRI
  (c) NCCT/CECT
  (d)PET/DSA
- Routine blood investigation

NEURO OPTHALMICS OF PITUITARY ADENOMA

OPTIC NERVE consists of 1.5 million fibres.

Total length is 5 cm of which 12-16 mm is intracranial.

Both optic nerves after coming out of optic canal rise by 45 degrees and meet to form optic chiasm

NEURO OPTHALMICS OF PITUITARY ADENOMA

OPTIC CHIASM can be

Prefixed 15%

Normal 70%

Post fixed 15%

With in the chiasm

PMB lies in the middle

Temporal hemi retinal fibers pass ipsilateraly

Nasal hemi retinal fibers decussate

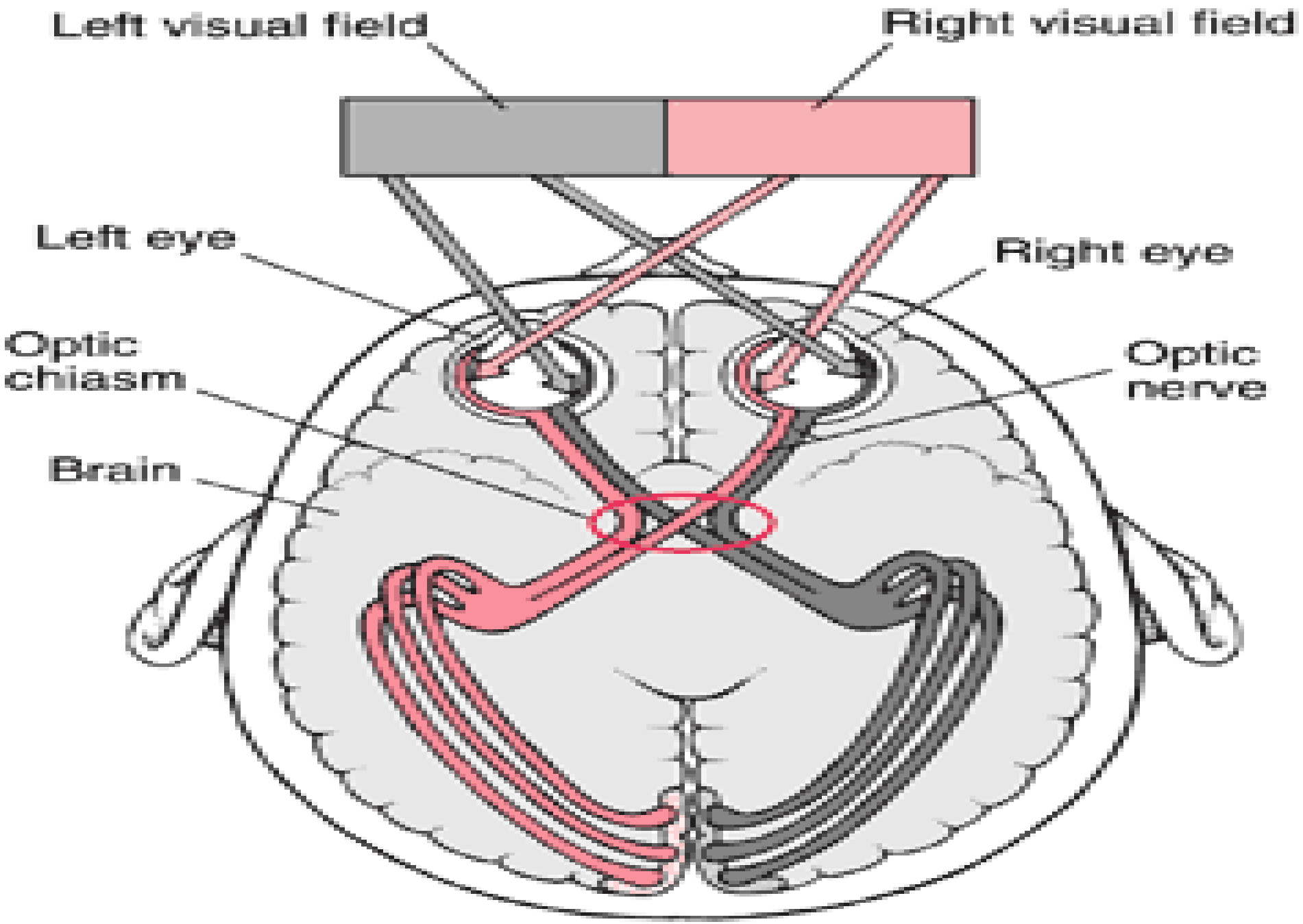
NEURO OPTHALMICS OF PITUITARY ADENOMA

Optic chiasm decussation

Inferior nasal fibers - anteroinferior

Superior nasal fibers - posterosuperior

PMB - in the middle primarily
postero superiorly

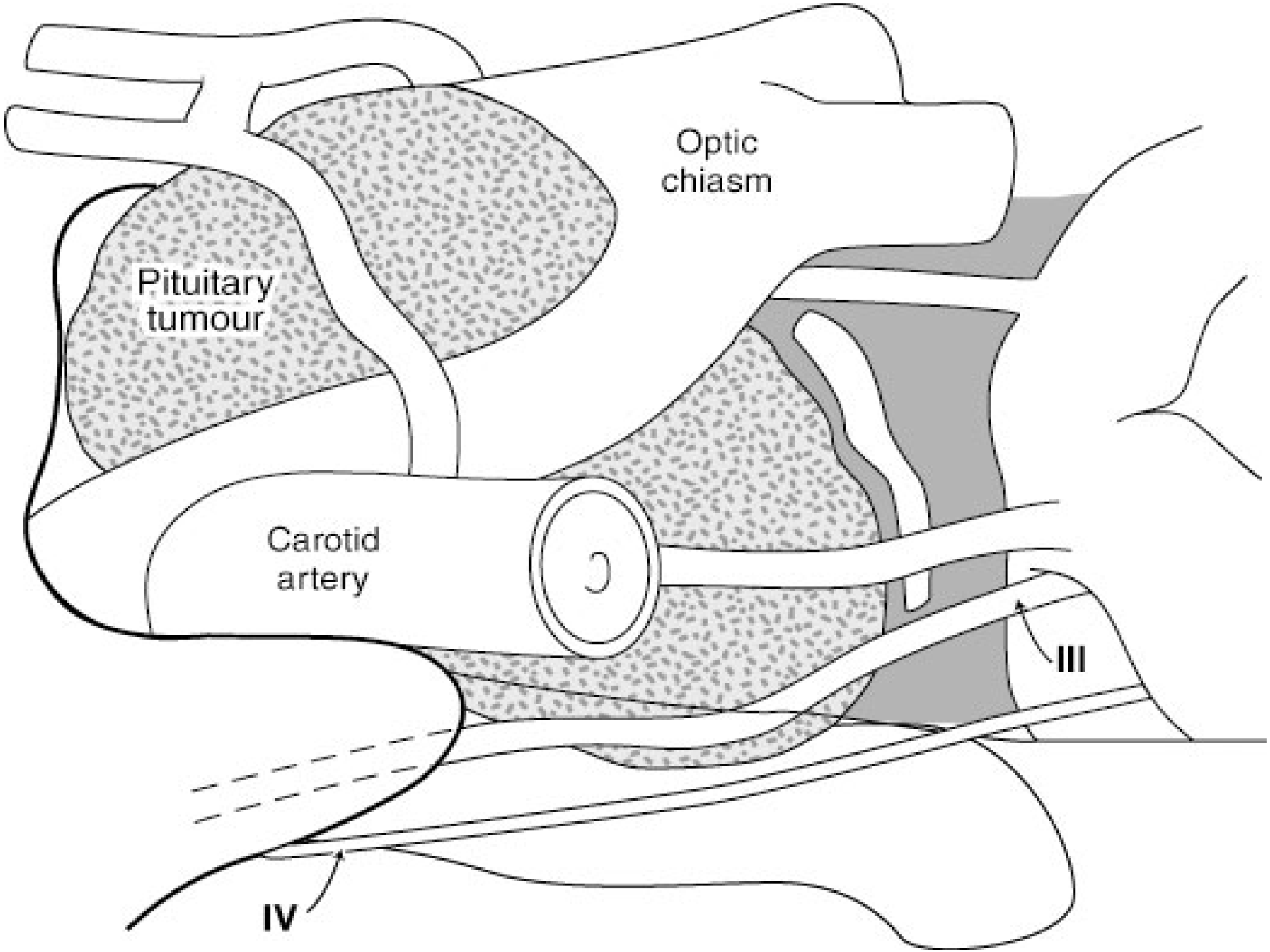

Left visual field
Right visual field
Left eye
Right eye
Optic chiasm
Optic nerve
Brain

NEURO OPTHALMICS OF PITUITARY ADENOMA

Enlarging pituitary adenoma may compress

- Optic chiasm
- Optic nerve in patients with postfixed chiasm
- Optic tracts in patients with prefixed chiasm
- 3^{rd} , 4^{th}, 6^{th} nerves with cavernous sinus extension causing diplopia
- Diplopia evaluation:: 3 principles
  - abnormal image is always peripheral
  - is always from the paretic eye
  - distance between the image increases on looking in the direction of paretic muscle

- Third ventricle leading to hydrocephalus


Optic
chiasm
Pituitary
tumour
Carotid
artery
III
IV

NEURO OPTHALMICS OF PITUITARY ADENOMA

Visual evaluation in a case of pituitary adenoma includes examination of:

- Visual acuity
- Colour vision
- Visual fields
- Opthalmoscopy
- Pupils
- Extraocular movements

NEURO OPTHALMICS OF PITUITARY ADENOMA

VISUAL ACUITY

Eye's ability to resolve details

- Neurosurgically , patients best corrected visual acuity is pertinent
- Distant vision by Snellen's chart placed at 6 m where accommodation is relaxed and light rays are parallel
- Near vision by rosenbaum's pocket chart held at a distance of 14 inches

NEURO OPTHALMICS OF PITUITARY ADENOMA

COLOUR VISION

Loss of colour vision precedes other visual deficits

In neurosurgical disease, red perception is lost first described as red desaturation or red wash outs

Ishihara/hardy ritter rand charts used

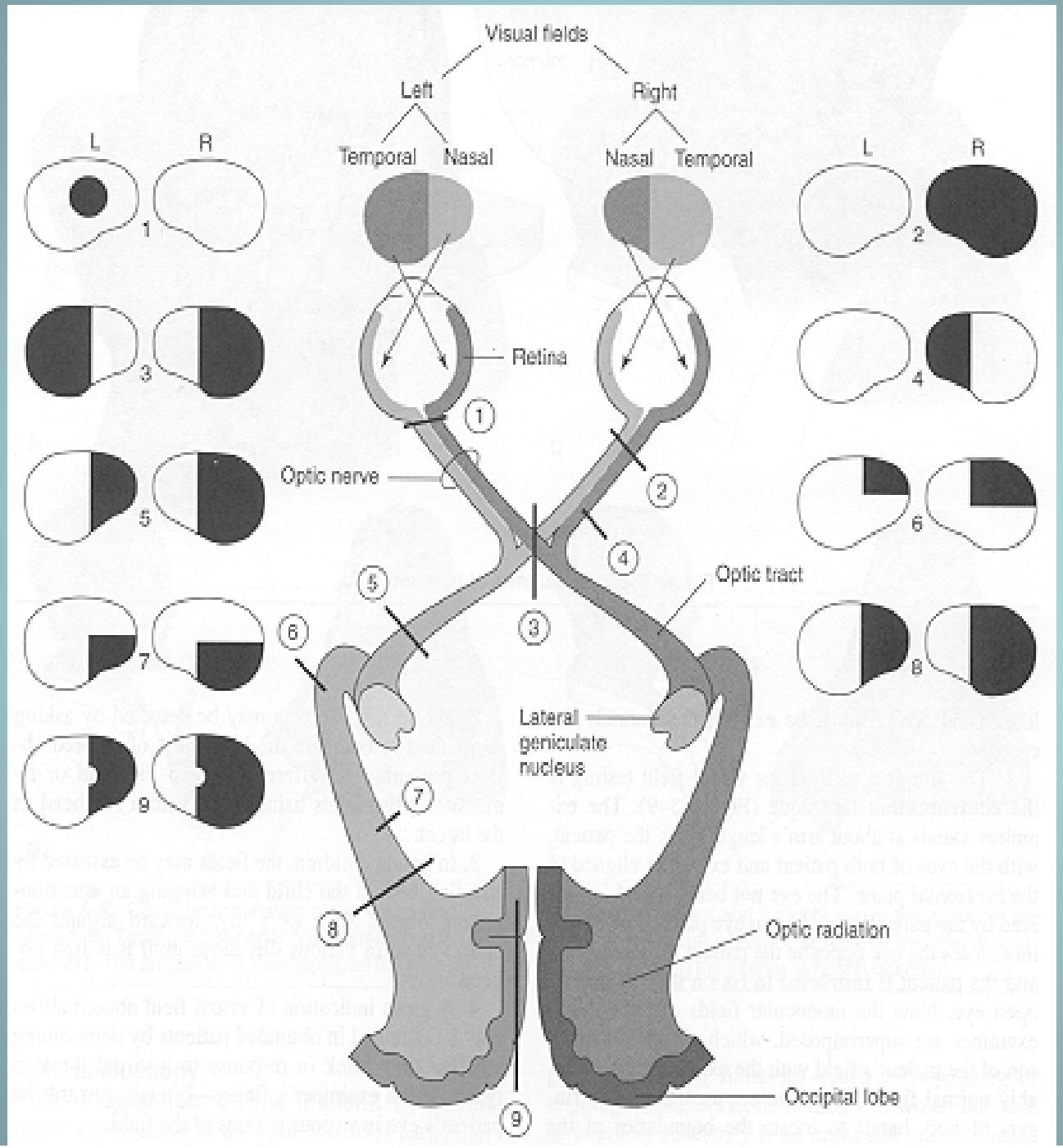
NEURO OPTHALMICS OF PITUITARY ADENOMA

Visual fields

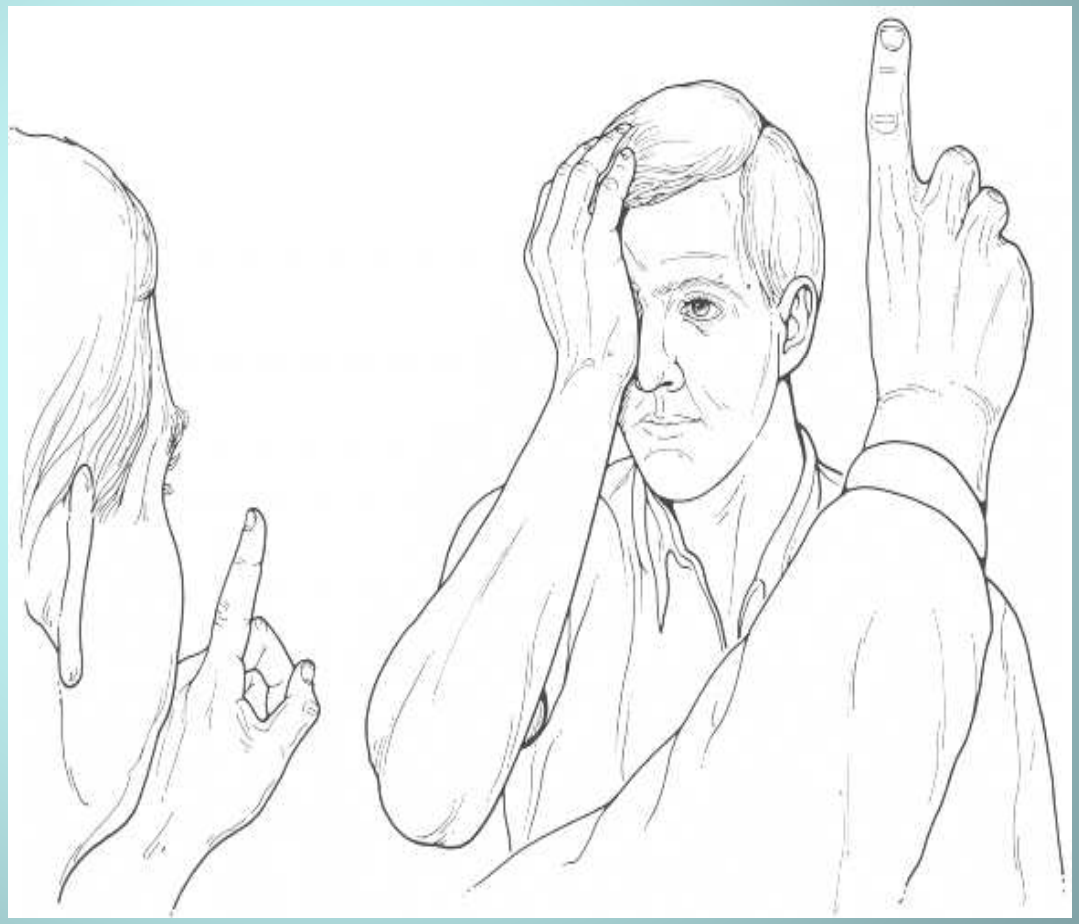
90 -100 deg	temporally
60 deg	nasally
50-60 deg	superiorly
60-75 deg	inferiorly

With binocular vision , VF of both eyes overlap

Visual fields are analyzed by
Confrontation method
Goldman's perimeter
Humphrey's field analyzer


Visual fields
Left
Right
Temporal
Nasal
Nasal
Temporal
L
R
1
2
3
4
5
6
7
8
9
Retina
Optic nerve
Optic tract
Lateral geniculate nucleus
Optic radiation
Occipital lobe

Confrontation method



NEURO OPTHALMICS OF PITUITARY ADENOMA

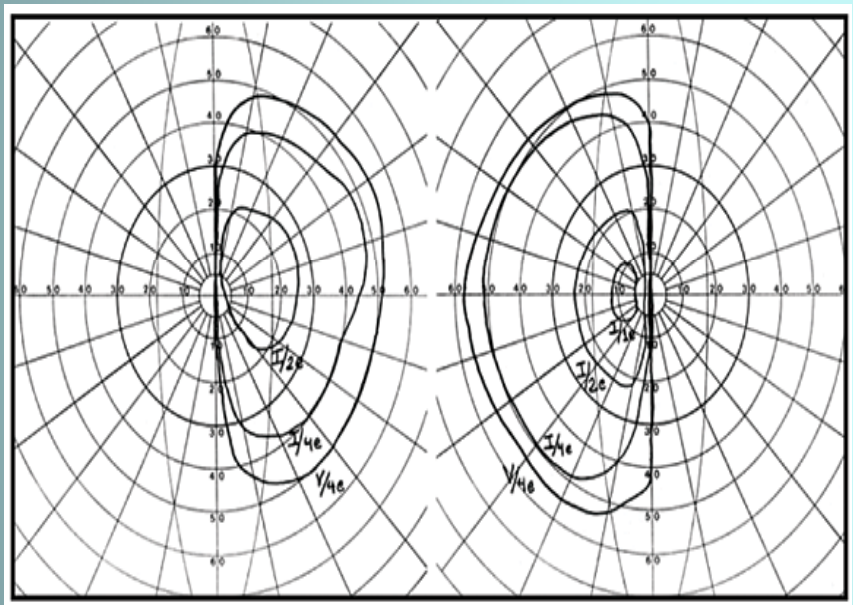
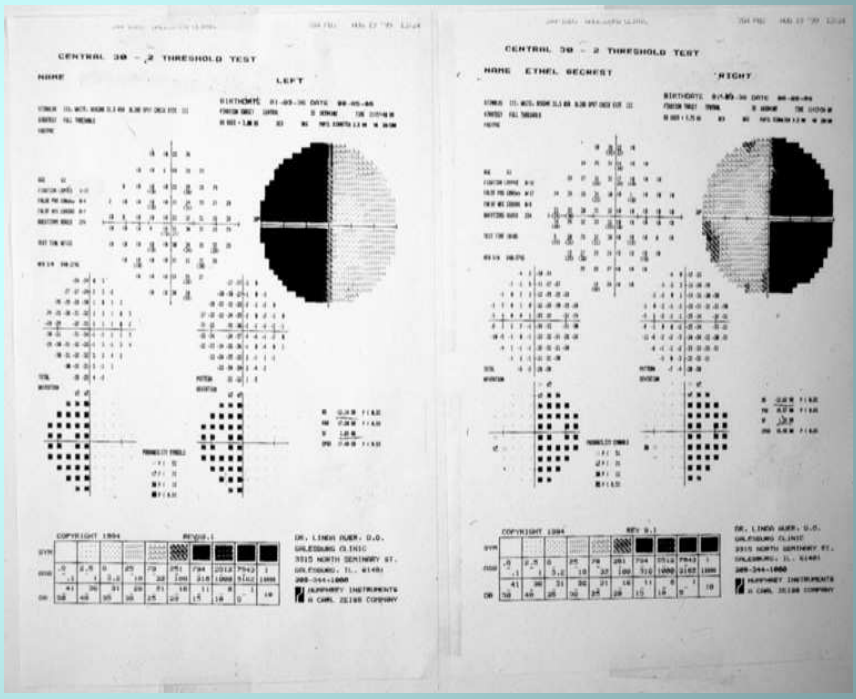


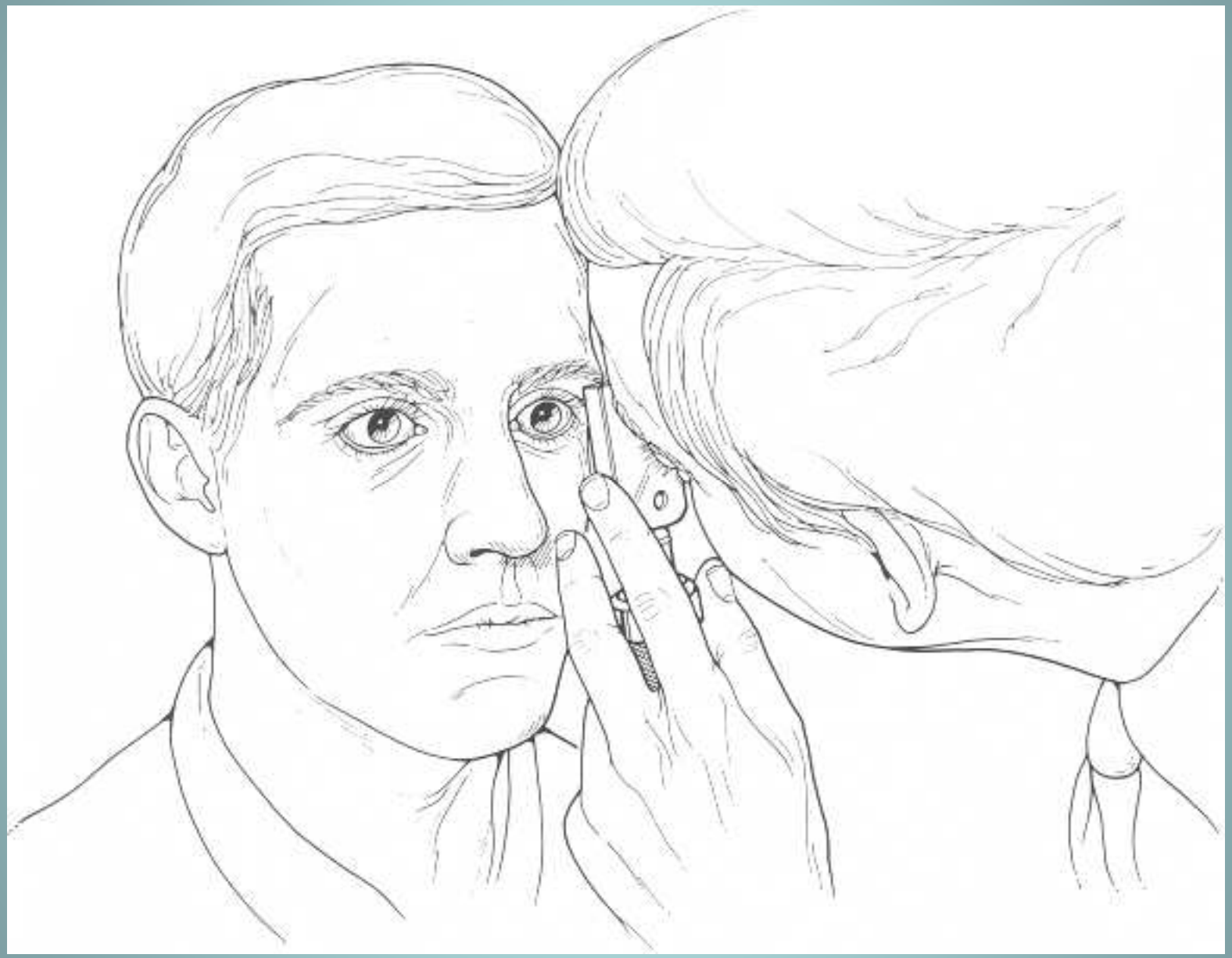
Fig 1. Goldmann perimetry, showing complete bitemporal hemianopia.

Goldman's perimeter

NEURO OPTHALMICS OF PITUITARY ADENOMA

Humphrey's field analyzer





NEURO OPTHALMICS OF PITUITARY ADENOMA

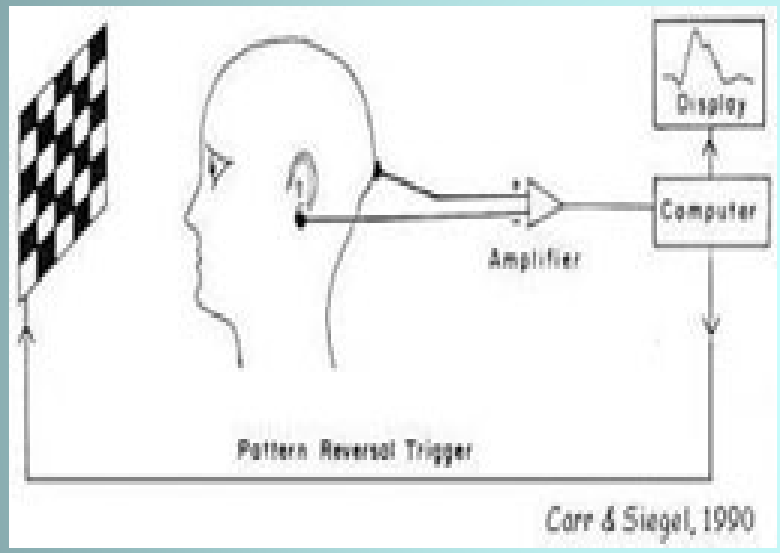
Pituitary adenoma can cause primary optic atrophy

	primary	secondary
Colour of disc	white	grey
Border of disc	Sharp	Blurred
Arteries and veins	Normal or reduced	Arteries thin, veins dilated
Distribution	May affect one sector	Entire disc affected
Causes	Optic nerve/retinal damage	Papillitis/papilledema
Lamina cribrosa	visible	Not visible

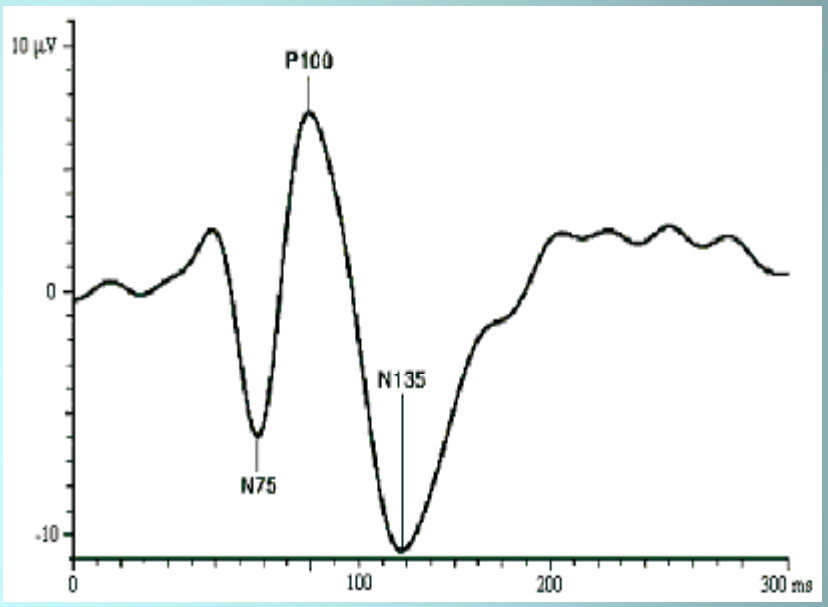
VEP

- Evoked electro physiological potential that can be extracted using signal averages from EEG activity recorded at the scalp.
- Provides diagnostic information regarding the functional integrity of visual system.
- Measures the time taken for visual stimuli to travel from eye to occipital cortex.
- Particularly useful in infants

VEP



TECHNIQUE



NORMAL TRACING

Radiology

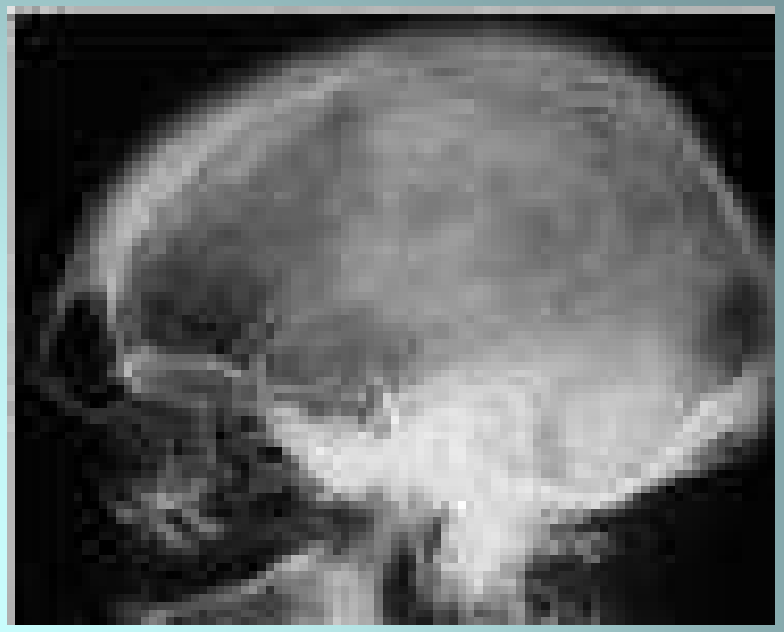
- X- Rays:
- Requires proper alignment of posterior clinoid processes

  widening of sella

  destruction of sellar floor

  relation of median sphenoidal septum

  aeration of sphenoid sinus



XRAY findings in ACROMEGALY

CT HEAD

CT HEAD is especially useful for:

- Evaluating bony structures adjacent to adenoma
- Detecting calcifications in association with macro adenoma

CT HEAD

- NCCT+ CECT head/ sella with thin coronal cuts:
  - Neck hyper extended(Reduces dental artifacts)
  - 1.5 -2.0 mm cuts from tuberculum to dorsum sella

MICROADENOMAS
- Focal hypo intensity
- Increased vertical height
- Asymmetrical convexity of superior surface

MACROADENOMAS
- Isodense or heterogenous with mixed iso and hypo areas
- intense contrast enhancement

MRI

- Better visualization of optic apparatus/carotids
- Multiplanar display

Coronal images

Examining asymmetries

Minimal volume artifacts

Sagittal images

Orientation of pituitary in relation to sphenoid sinus

Axial images

Useful in lesions with parasellar extension

Sensitivity for pituitary adenomas 90%

Sensitivity post contrast 95%

MRI

- Routine 1-2 T MRI produce 2-3 mm slices
- Newer techniques : reduce false negatives and can reduce acquisition time

I. *Volume imaging techniques(3 –D Fourier transform)*

II. Fast spin echo

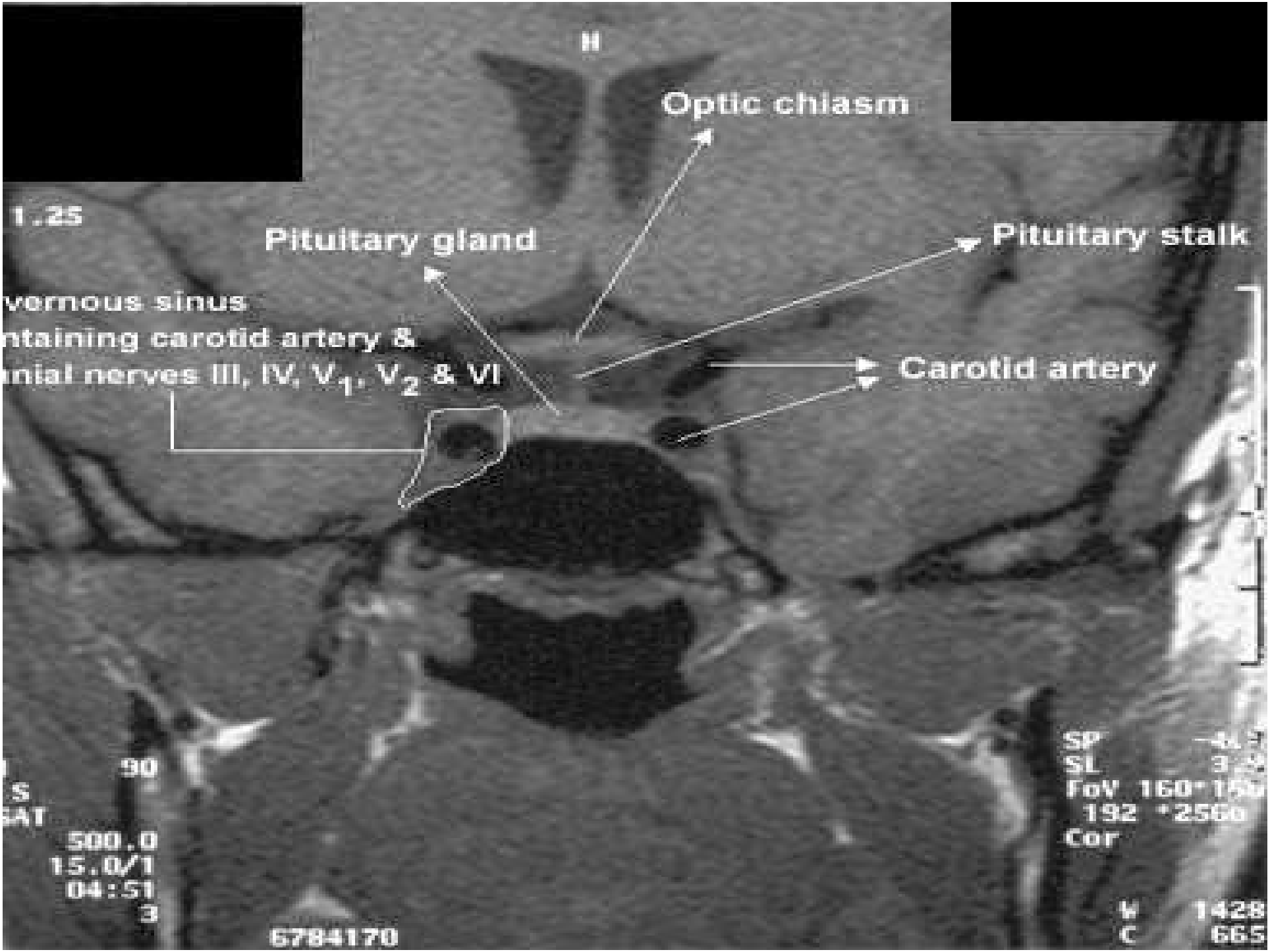
MRI

T1W

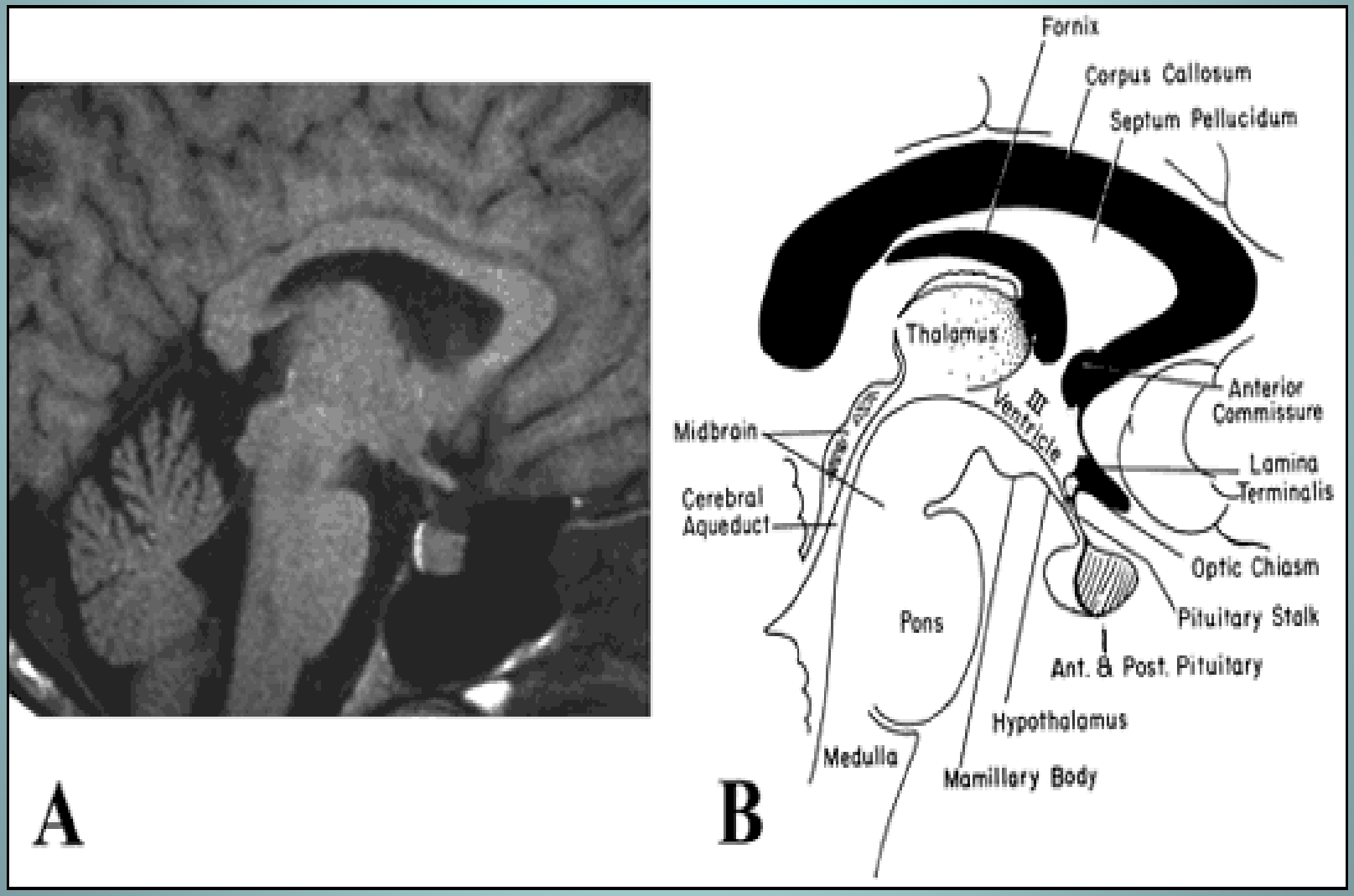
- more sensitive
- Better anatomical details of extra axial structures
- Obtained in shorter time period

  Normal anterior lobe is intermediate grey

  Posterior lobe is bright
- Paramagnetic contrast agents further improve delineation


Optic chiasm
Pituitary gland
Pituitary stalk
Carotid artery
vernous sinus
ntaining carotid artery &
nial nerves III, IV, V1, V2 & VI
1.25
90
500.0
15.0/1
04:51
3
6784170
Cor

Pituitary -normal anatomy



MRI

Microadenoma

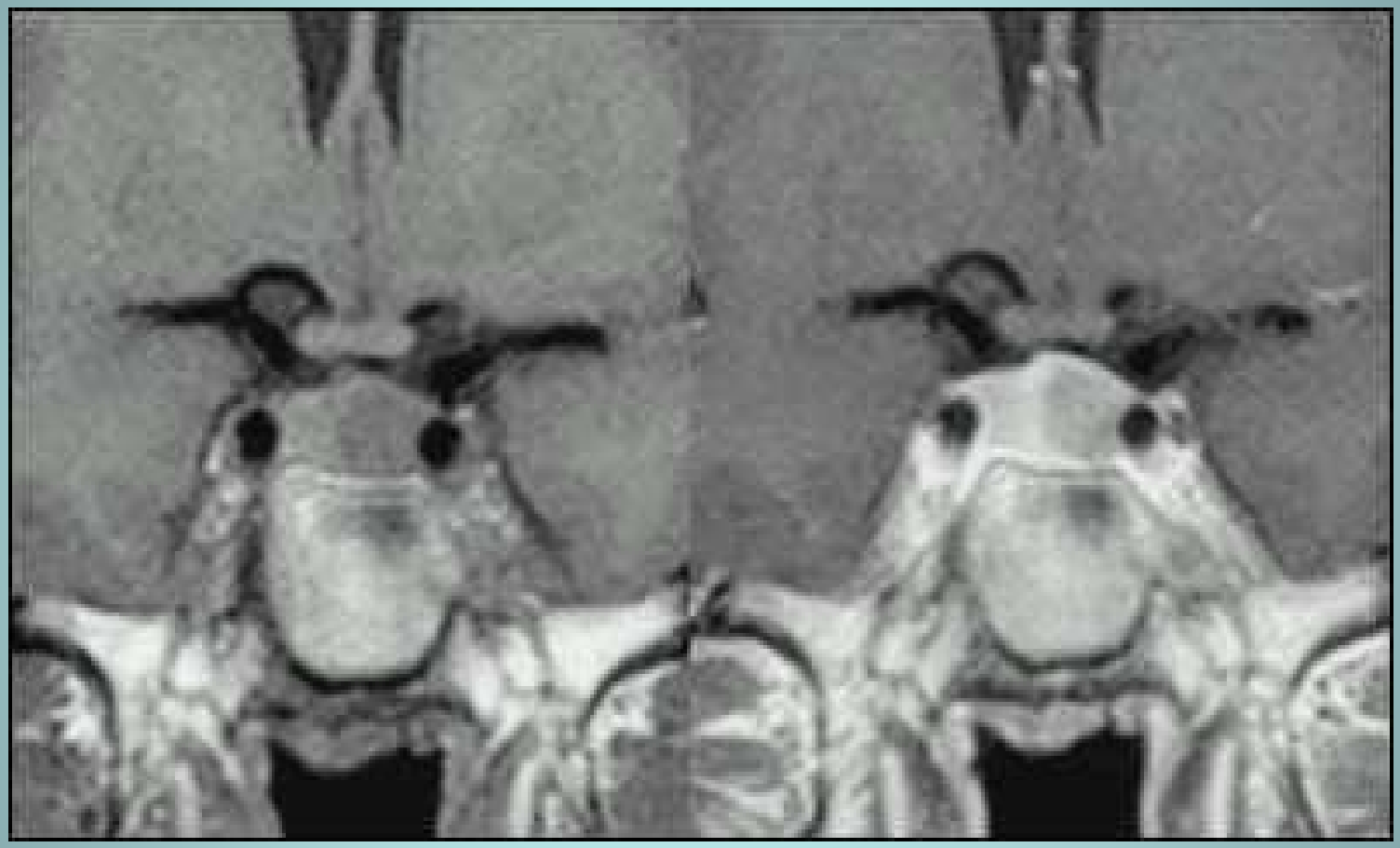
Seen as area of focal hypo intensity

Usually well defined , laterally situated

Focal convexity upward

Displacement of stalk to opposite side

Relative hypo intensity on immediate post contrast sequences



PITUITARY ADENOMA – RELATIVELY HYPOINTENSE

MRI

- Dynamic imaging

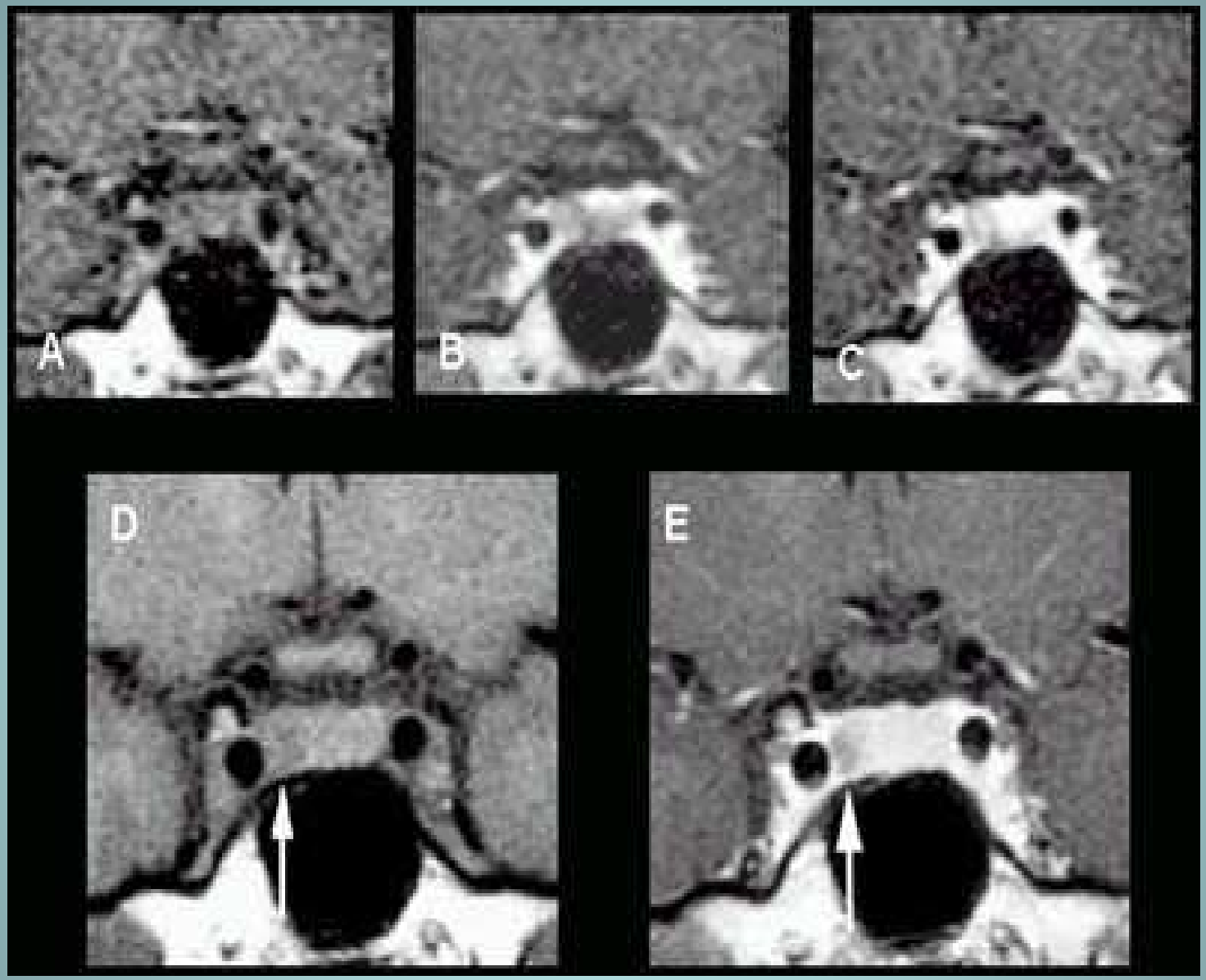
Consists of a series of images at the same location to detect temporal changes in the signal intensity

Sequential coronal images at 20- 30 sec intervals following contrast injection

Slow uptake and slow wash out of contrast by pituitary adenomas

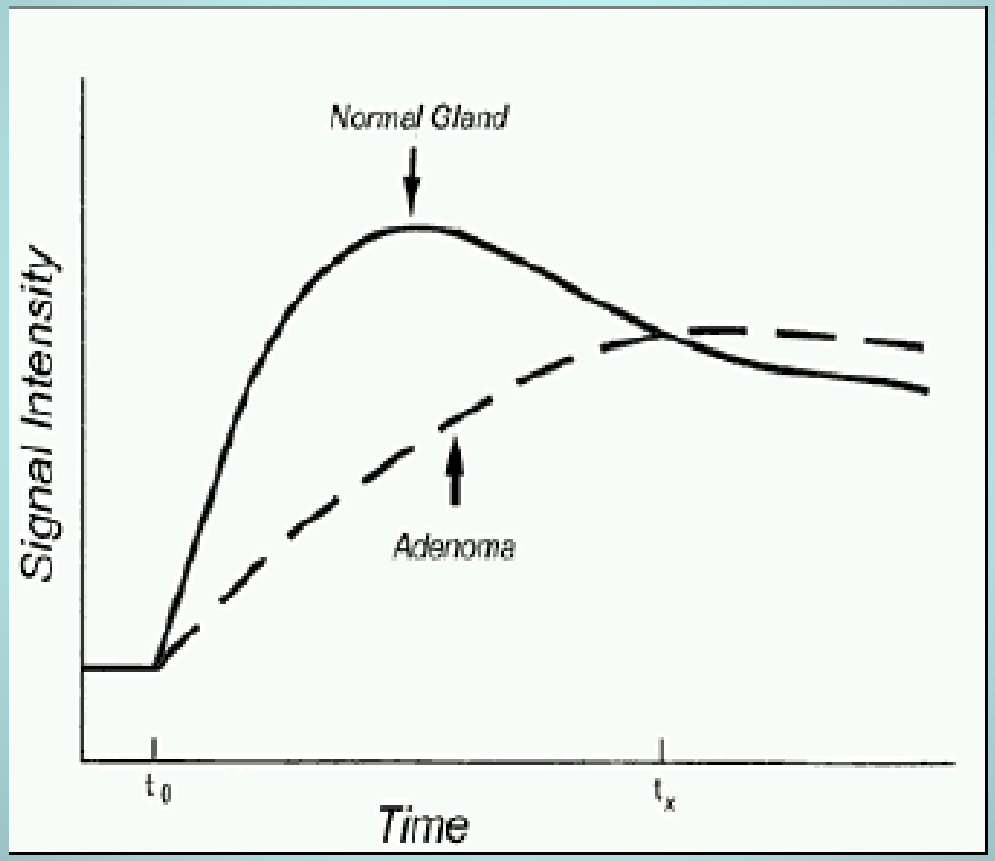
*Avg time of enhancement onset in normal pituitary	43sec
Avg time of enhancement peak in normal pituitary	112 sec
Avg time of enhancement onset in pituitary adenoma	110sec
Avg time of enhancement peak in pituitary adenoma	188sec

Indrajit et al:value of dynamic mri in imaging of pituitary adenomas;indian journal of radiology and imaging: 2001



DYNAMIC SCAN SHOWING DELAYED CONTRAST UPTAKE BY ADENOMA

Dynamic MRI



MRI

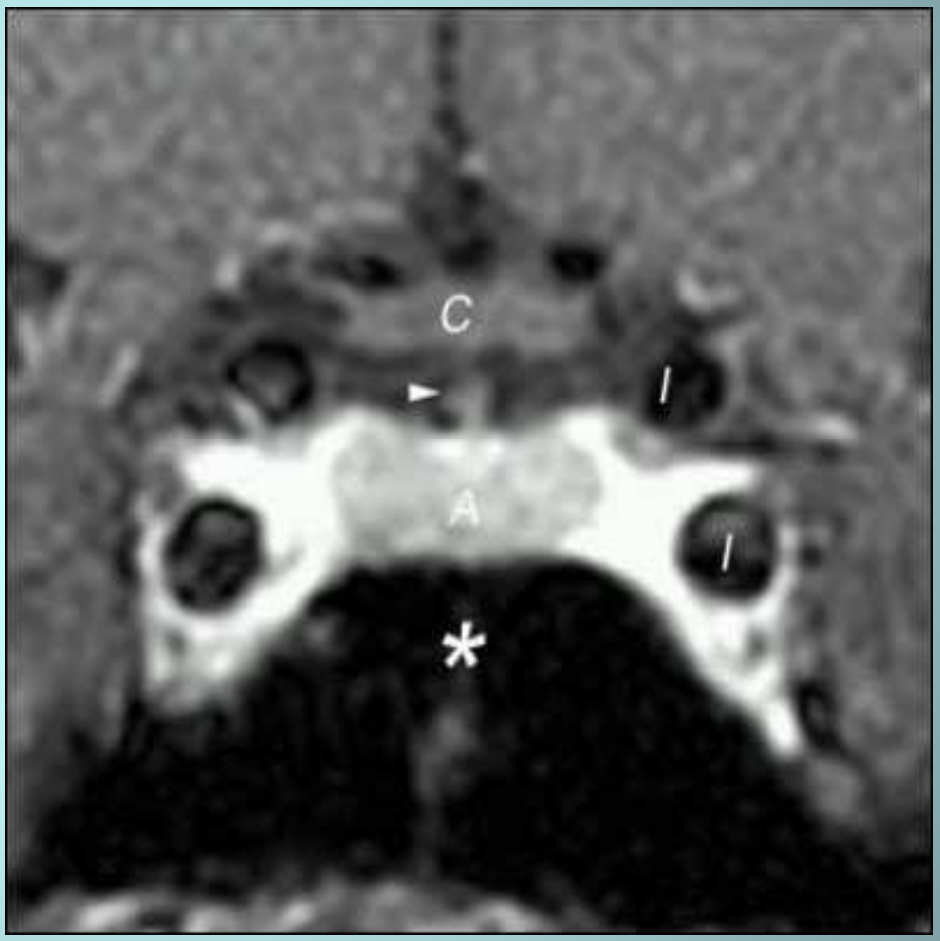
Macroadenoma

- soft tissue sellar mass of intermediate signal intensity on T1W images
- Hyperintense on T2W
- Enhancing diffusely on contrast
- Superior spread most common

(Grows through diaphragma sellae - figure of 8 image)

CONTRAST ENHANCED IMAGE SHOWING RELATIVELY LESS CONTRAST ENHANCEMENT OF PITUITARY ADENOMA

AS COMPARED TO CAVERNOUS SINUS



Pituitary adenoma showing primary infrasellar growth leading to destruction of sellar floor

DIFFERENTIALS

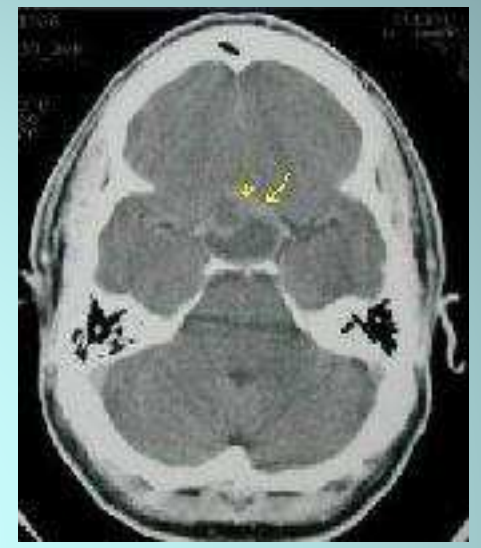
- CRANIOPHARYNGIOMA
- RATHKE'S CLEFT CYST
- MENINGIOMAS ARISING FROM TUBERCULUM SELLA, PLANUM SPHENOIDALE,ANTERIOR CLINOID,POSTERIOR CLINOID, MEDIAL SPHENOID WING
- ANEURYSMS OF CAVERNOUS/SUPRACLINOID ICA,RARELY BASILAR TOP
- EMPTY SELLA TURCICA
- CHORDOMAS
- DERMOIDS/EPIDERMOIDS
- METASTASIS ESPECIALLY IN SKULL BASE

CRANIOPHYRNGIOMAS

SUPRASELLAR LOCATION

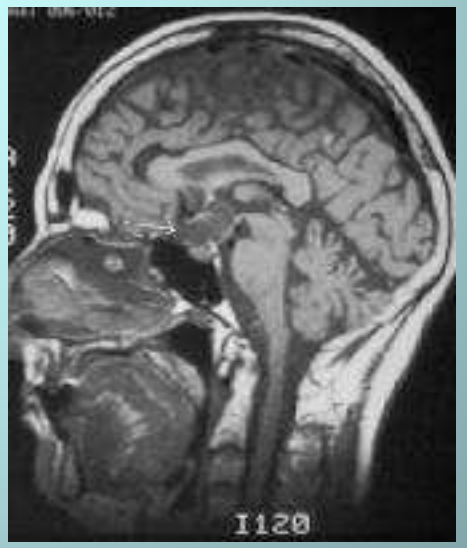
ON CT-HETEROGENOUS DENSITY MASSES WITH AREAS OF CYST FORMATION AND CALCIFICATION

SOLID TISSUE IS CONTRAST ENHANCING



ON MRI VARIABLE SIGNAL INTENSITY LESIONS

CYSTS ARE USING HIGH SIGNAL



GERMINOMAS

SEEN USUALLY IN CHILDREN

(PINEAL REGION)

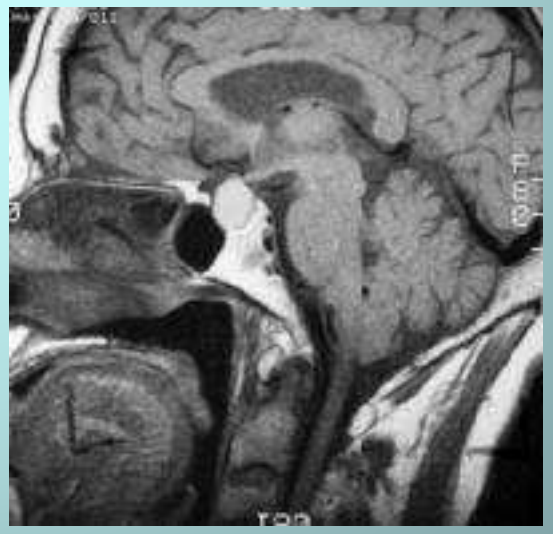
WHEN SUPRASELLAR MIDLINE IN LOCATION , BEHIND INFUNDIBULUM

HYPO ON T1W, HYPER ON T2W, CONTRAST ENHANCING

RATHKE' CLEFT CYST

ANTERIOR HALF OF SELLA TURCICA

IN FRONT OF PITUITARY STALK



PITFALLS

False negatives

Especially with Cushing's disease in conventional spin echo MRI

Pneumatized anterior clinoid process

False positives

Small pars intermedia cysts

Clinically silent infarcts

Foci of necrosis

ROLE OF PET IN PITUITARY ADENOMA

- Primarily for monitoring treatment
- 11-C- methionine and 18 – FDG for metabolic mapping.
- Highest metabolic rate with prolactinoma followed by growth hormone tumors.