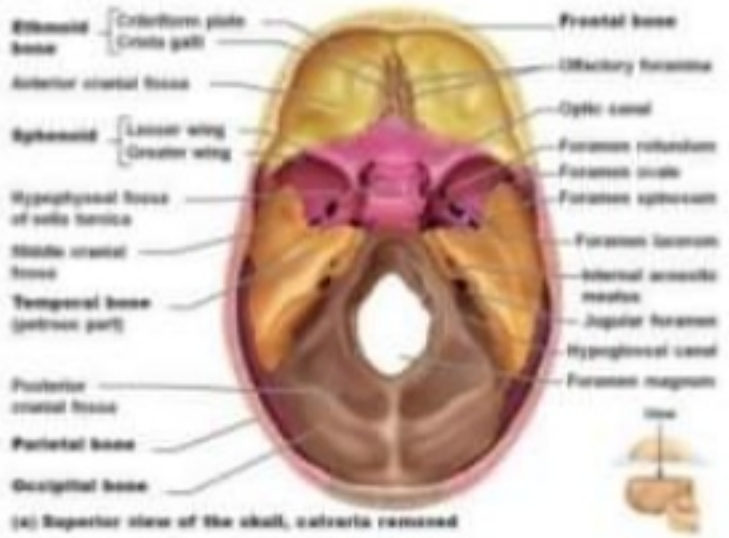
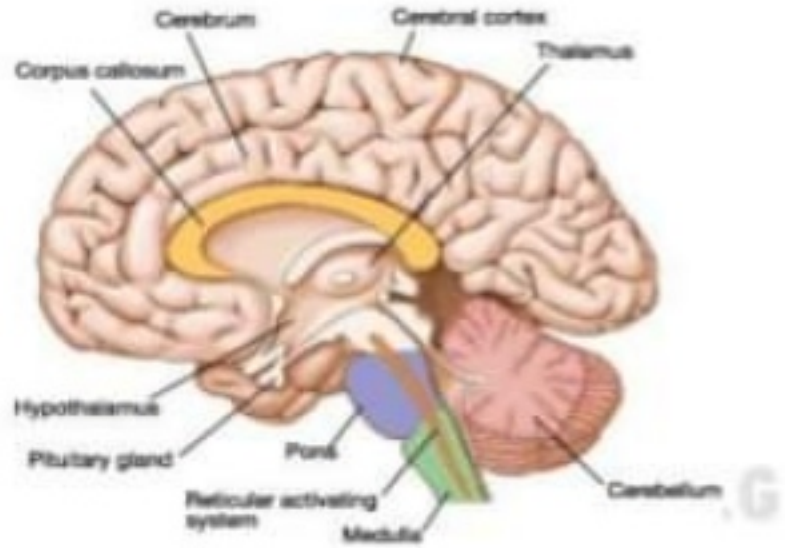
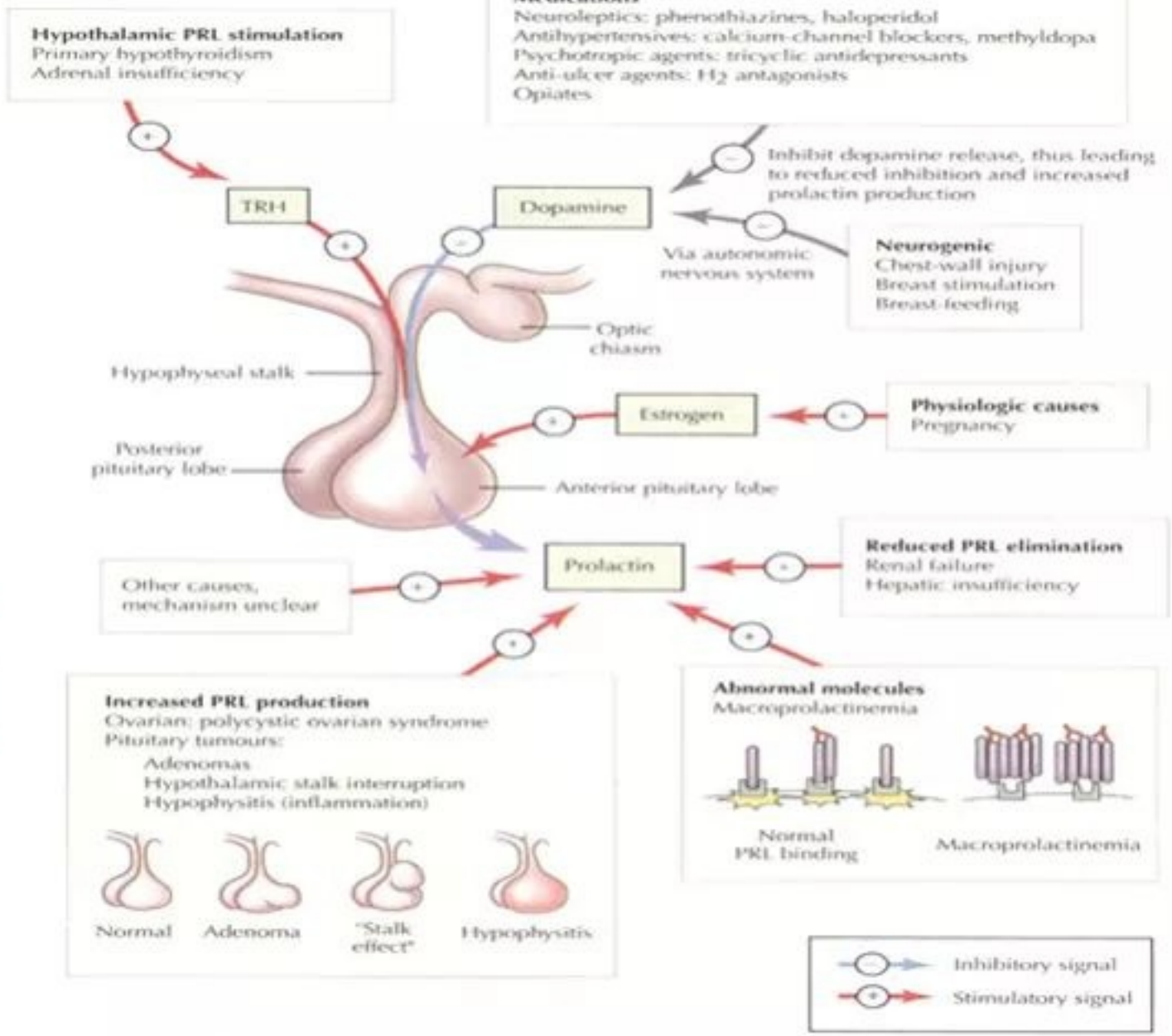
Hyperpituitarism

Pituitary gland

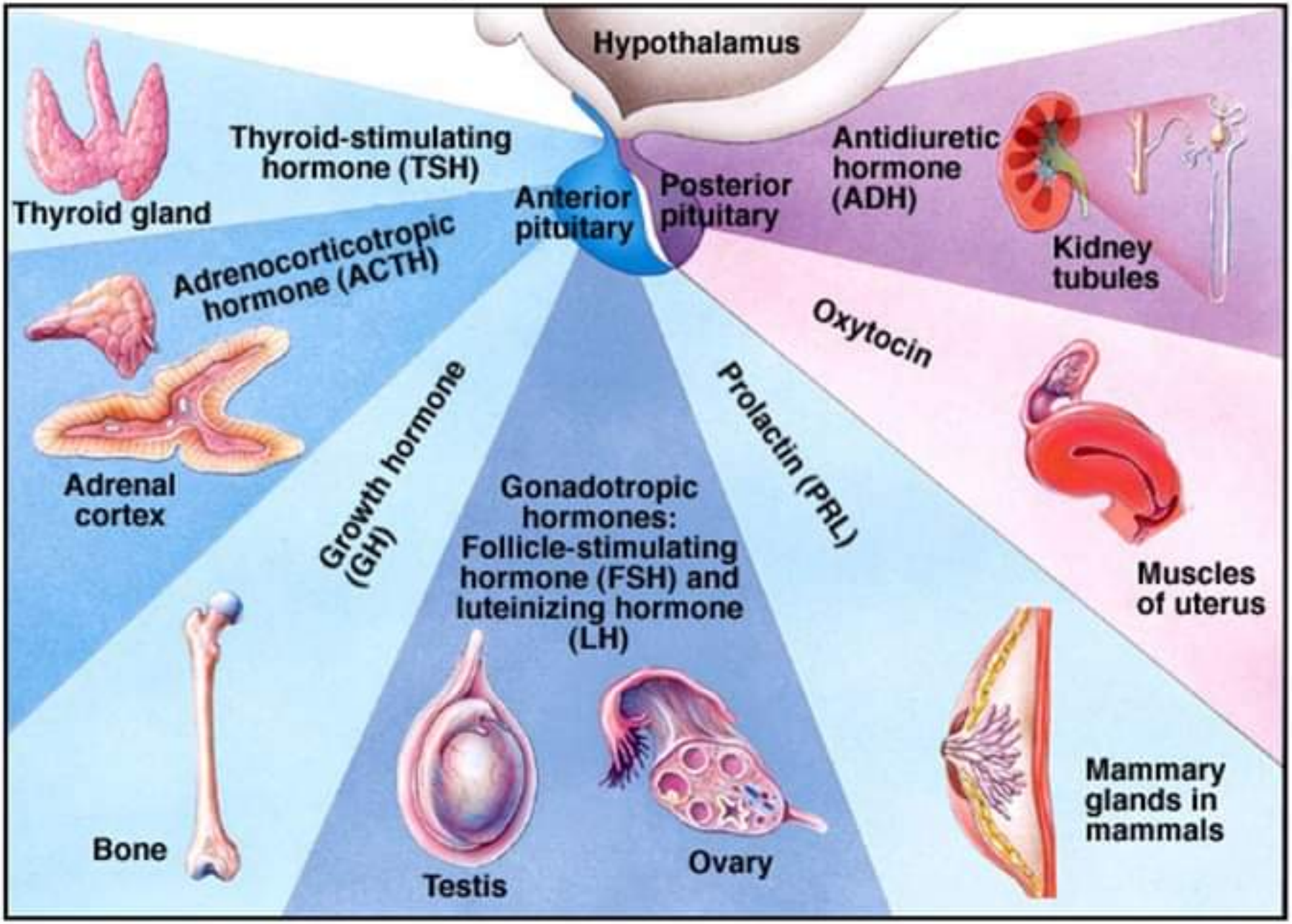
- Pituitary gland (master gland) is situated in pituitary fossa in the middle cranial fossa
- The gland consists of two lobes
  - **Anterior lobe (adenohypophysis)**
  - **Posterior lobe (neurohypophysis)**







Pituitary Gland Hormones



Hypothalamic hormone	Pituitary hormone	Target-gland hormone
Corticotropin-releasing hormone (CRH)	ACTH (LPH, MSH, endorphins)	Cortisone
Thyrotropin-releasing hormone (TRH)	TSH	T_3, T_4
Gonadotropin-releasing hormone (GnRH)	LH, FSH	Androgens, estrogens, progestins
Growth hormone-releasing hormone (GHRH)	GH	IGF-1
Growth hormone-release inhibiting hormone (GHRIH)	GH (TSH, FSH, ACTH)	IGF-1, T_3, T_4 others (?)
Prolactin-release inhibiting hormone (dopamine and GAP)	PRL	Neurohormones (?)

Symptoms and signs at presentation	Overall prevalence (%)
Facial change, acral enlargement, and soft-tissue swelling	100
Excessive sweating	83
Acroparesthesiae/ carpal tunnel syndrome	68
Tiredness and lethargy	53
Headaches	53
Oligo- or amenorrhea, infertility	55*
Erectile dysfunction and/or decreased libido	42#
Arthropathy	37
Impaired glucose tolerance/ diabetes	37
Goiter	35
Ear, nose throat and dental problems	32
Congestive cardiac failure/ arrythmia	25
Hypertension	23
Visual field defects	17

* percentage of female patients
# percentage of male patients

Hormones of anterior pituitary

- Growth Hormone(GH)
  - Regulation of body growth via liver by secreting growth factors which help in chondrogenesis, skeletal growth, protein synthesis & cell proliferation
- Prolactin
  - Helps in milk production during lactation
- ACTH
  - Regulates secretion from adrenal cortex of its corticosteroids
- TSH(Thyroid Stimulating Hormone)
  - Regulates secretion of thyroid hormones from thyroid
- FSH & LH(ICSH)
  - Also known as gonadotropic hormones
  - Regulate production of estrogens and progesterone & induce ovulation from ovaries
  - Regulate production of testosterone from testis by acting on interstitial cells of Leydig and help in maturation of sperms

Hormones of posterior pituitary

- ADH(Anti diuretic hormone)
  - Causes reabsorption of water from the renal tubules & maintains the osmolality of plasma
- Oxytocin
  - Acts on myoepithelial cells of breast helping propulsion of milk during lactation
  - Contraction of uterine muscles during delivery

Endocrine Diseases

Hormone Excess

Hormone Deficiency

Hormone Resistance

Pituitary Gland Diseases

- Hyperpituitarism
  - Hypersecretion of growth hormone (GH) by the pituitary
- Gigantism
  - GH hypersecretion during puberty and growth years
    - Person is very tall, proportioned normally
- Acromegaly
  - GH hypersecretion during adulthood
  - Disfiguring overgrowth of bones & soft tissues

Hyperpituitarism

- Other aspects:
  - Gigantism:
    - Fairly abrupt onset
    - Non-life threatening
    - Growth up to 6 inches/yr
  - Agromegaly:
    - Gradual onset
    - Decreases life expectancy
    - Headache, sinus problems, skin changes, paresthesias, joint pain, visual disorders

Hyperpituitarism

- Excess hormone production by the anterior pituitary gland
  - Caused most often by a benign tumor (pituitary adenoma) that produces growth hormone
  - Giantism results if it occurs before the closure of long bones.
  - Acromegaly results when hypersecretion occurs during adult life.

Hyperpituitarism

- GH (Growth Hormones)
  - Adult
    - Acromegaly
    - abnormal growth of the hands, feet, and face, caused by overproduction of growth hormone by the pituitary gland.
  - Child
    - Gigantism
- ADH (Antidiuretic Hormones)
  - Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Hyperpituitarism

- For all practical purposes, hyper function of anterior pituitary is due to a hormone secreting adenoma or rarely a carcinoma
- Heperfunction of anterior pituitary
  - Gigantism and Acromegaly
  - Hyperprolactinemia
  - Cushing's syndrome

Hyperpituitarism

The increase secretion of pituitary

* What two hormones are affected with hyperpituitarism?
  * GH
  * ADH

Hyperpituitarism

- Acromegaly
- Gigantism
- Itsenko-Cushing's syndrome
- Hyperprolactinaemia

Pituitary Gland

Hyperpituitarism – pituitary adenoma

- Most common cause is adenoma arising in the anterior pituitary
- Classified based on the hormone produced
- Functional or nonfunctional
- Microadenoma < 1 cm
- Macroadenoma > 1 cm
- Usually soft, well-circumscribed
- 30% invasive adenomas – no capsule
- Cellular monomorphism and the absence of a significant reticulin network distinguish pituitary adenomas from non-neoplastic anterior pituitary parenchyma
- Atypical adenomas – p53 mutations, aggressive

PITUITARY ADENOMA

CATEGORIES

MICROADENOMA

- Diameter = / < 10 mm
- Intrasellar
- Presents usually with hormonal hypersecration syndrome

MACROADENOMA

- Diameter > 10 mm
- Extends outside the sella
- Presents often with chiasmal compression syndrome

Clinical Features and Oral Manifestations of Hyperpituitarism

- Affects both men and women, most commonly during the fourth decade of life
  - Patients experience poor vision, light sensitivity, enlargement of hands and feet, and an increase in rib size.
- Facial changes
  - Enlargement of maxilla and mandible may cause separation of teeth and malocclusion.
  - Frontal bossing and an enlargement of nasal bones may lead to deepening of voice.
- Mucosal changes
  - May have thickened lips and macroglossia

Causes of acromegaly

SOMATOTROPH ADENOMAS

- ***Eosinophilic pituitary adenoma***
- ***Pituitary tumors:*** microadenomas (pituitary tumors less than 1 cm in size); macroadenomas (pituitary tumors greater than 1cm)
- ***Nonpituitary tumors:*** by tumors of the pancreas, lungs, and other parts of the brain

Gigantism and Acromegaly

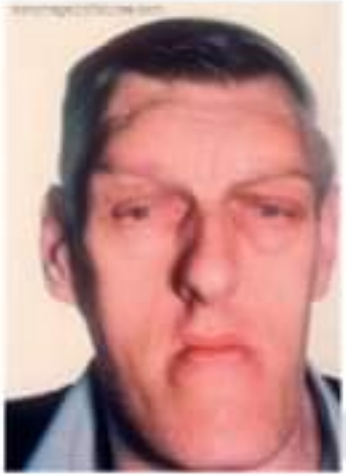
- Occur because of sustained excess of growth hormone

Gigantism occurs prior to closure of epiphysis in pre-pubertal boys and girls

- Excessive and proportionate growth of child
- Considerable increase in height and thickening of bone

Acromegaly occurs in adults following cessation of bone growth

- Enlargement of hands and feet
- Coarseness of facial features
- Prominent supraorbital ridges
- Prominent lower jaw producing prognathism

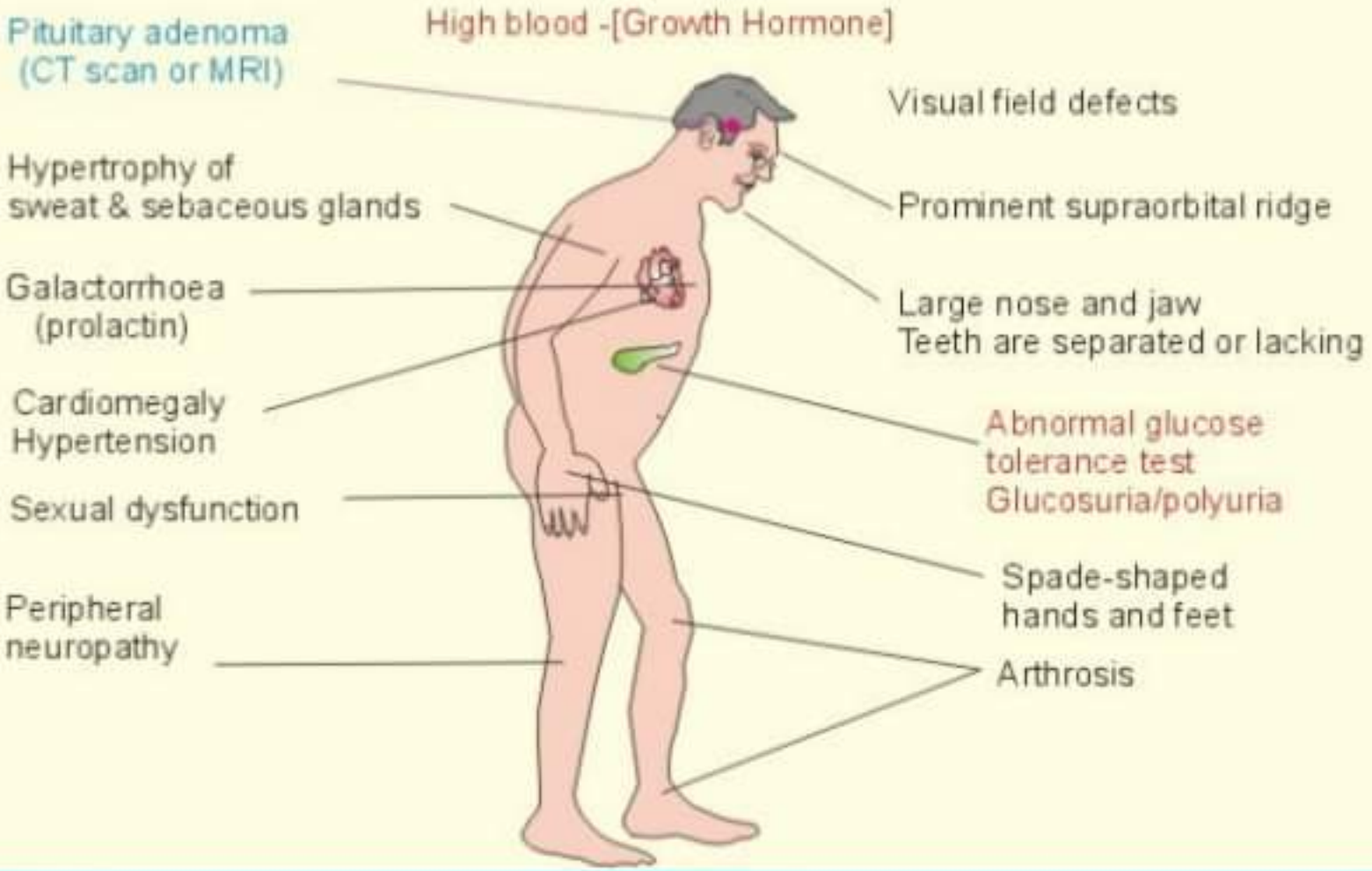


Symptoms of acromegaly

Facial change, acral enlargement, and soft-tissue swelling
Excessive sweating
Acroparesthesiae/ carpal tunnel syndrome
Tiredness and lethargy
Headaches
Oligo- or amenorrhea, infertility
Erectile dysfunction and/or decreased libido
Arthropathy
Impaired glucose tolerance/ diabetes
Goiter
Ear, nose throat and dental problems
Congestive cardiac failure/ arrythmia
Hypertension
Visual field defects

A – Arthralgias/ Arthritis
B – BP raised
C – Carpal Tunnel
D – Diabetes
E – Enlarged Organs
F – Field defect

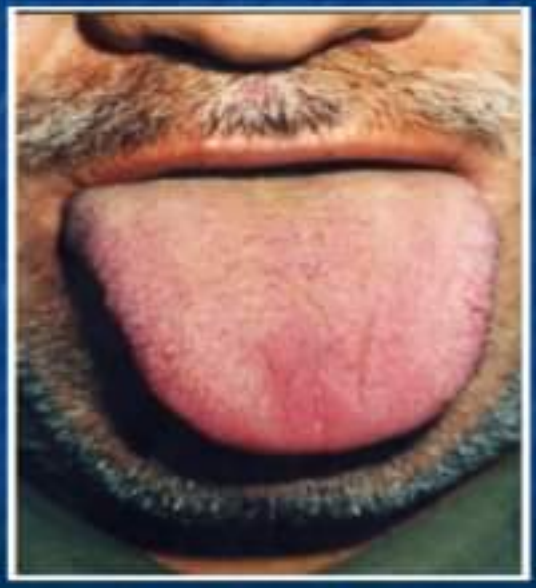
Acromegaly


Pituitary adenoma
(CT scan or MRI)
High blood -[Growth Hormone]
Visual field defects
Hypertrophy of
sweat & sebaceous glands
Prominent supraorbital ridge
Galactorrhoea
(prolactin)
Large nose and jaw
Teeth are separated or lacking
Cardiomegaly
Hypertension
Abnormal glucose
tolerance test
Glucosuria/polyuria
Sexual dysfunction
Spade-shaped
hands and feet
Peripheral
neuropathy
Arthrosis

Typical facies of acromegaly

It be showed largeness
in the size of nose, ears , lips

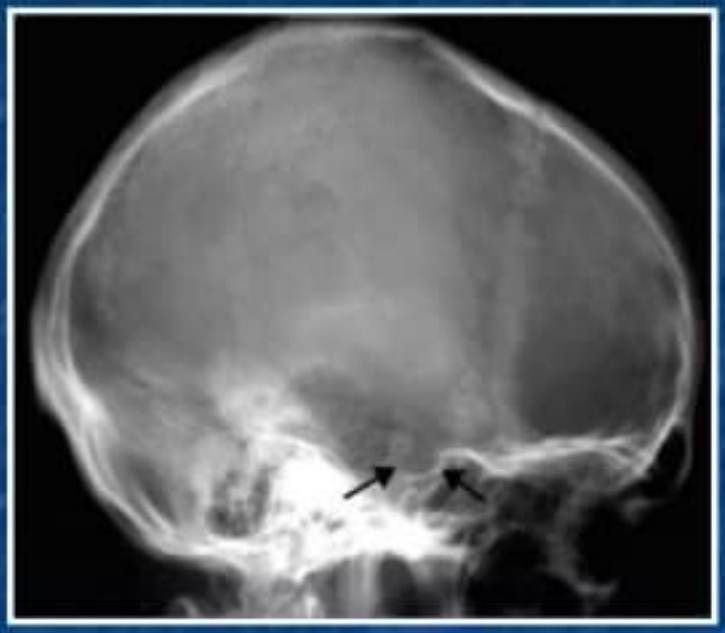
It be showed
growth in hands



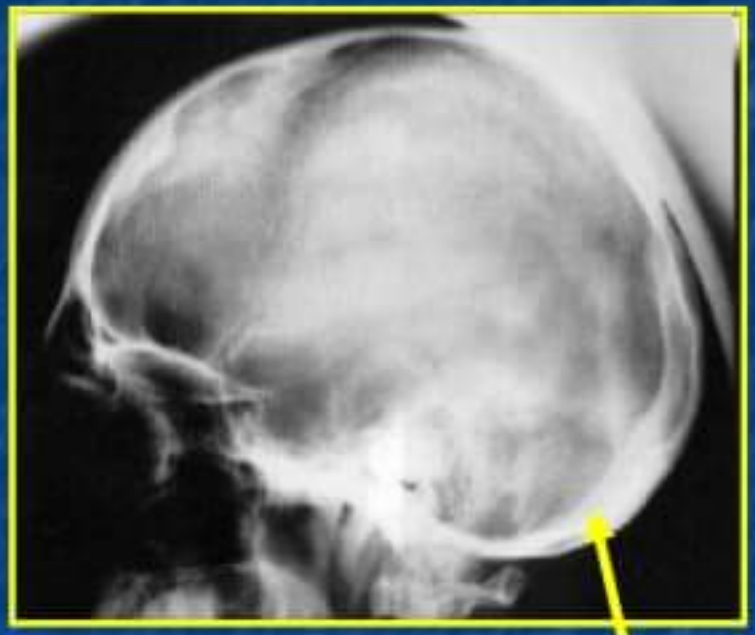
It be showed largeness
in the size of tongue

Typical facies of acromegaly

Frontal bossing
Thickening of the nose
Macroglossia
Prognathism



Lateral skull X-ray
The bones of the skull are normal.
Sella turcica (arrow)



Typical Skull X-Ray
(Thickening of the Calvarium)
of an Acromegalic patient

Pituitary Gland

Somatothroph adenoma

- Second most common
- GH stimulates the hepatic secretion of IGF-1 (somatomedin C)
- Gigantism or acromegaly
- Failure to suppress GH production in response to a glucose challenge is one of the most sensitive tests for acromegaly

Pituitary Gland

Corticotroph adenoma
- Cushing disease
- Nelson syndrome

Gonotroph adenoma

Thyrotroph adenoma

Nonfunctioning pituitary adenoma

Pituitary carcinoma (<1% of all pituitary tumors)

Complications of acromegaly

Cardiovascular:

- Ischemic heart disease
- Cardiomyopathy
- Congestive heart failure
- Arrhythmias
- Hypertension

Respiratory:

- Kyphosis
- Obstructive sleep apnea

Metabolic:

- Diabetes mellitus/IGT
- Hyperlipidemia

Neurologic:

- Carpal Tunnel syndrome
- Stroke

Neoplastic:

- Coorectal
- Breast and prostate - uncertain

Musculoskeletal:

- Degenerative arthropathy
- Calcific discopathy, pyrophosphate arthropathy

Treatment of acromegaly

Somatostatin analogues (SSAs):

Octreotide (*Sandostatin*) **and lanreotide** (*Somatuline Depot*) 50 mcg s/c tid; can increase to 500 mcg tid; doses of 300-600 mcg/day or higher seldom result in additional benefit. **Lanreotide** is given as a long-acting subcutaneous injection once a month.

Dopamine agonists:

Bromocriptine (*Parlodel*) ***20-30 mg PO qd (10-60 mg/day)*** in divided doses. Safety not demonstrated at >100 mg/d.

Cabergoline (*Dostinex*)

Growth hormone antagonists:

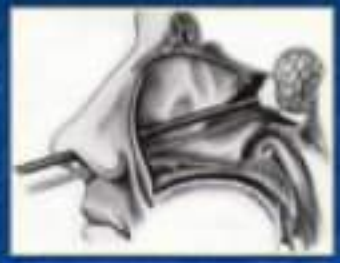
blocks the effect of growth hormone on body tissues.

Pegvisomant (*Somavert*) ***40 mg s/c***

10 mg s/c qd initially; may increase or decrease q 4 – 6 week by 5-mg increments as determined by IGF-I levels; not to exceed 30 mg/d.

Surgery

- Acromegaly is traditionally treated with ***transsphenoidal pituitary surgery and adenoma removal***
- ***Endonasal Transphenoidal surgery***
- ***Septal Pushover/Direct Sphenoidotomy***
- ***Endoscopic approach***



Radio-therapy

- ***Conventional radiation therapy*** this type of radiation is usually given every weekday over four to six weeks. It may take five to 10 years or more for your growth hormone levels to return to normal
- ***Stereotactic radiosurgery*** Radiation can also be given stereotactically, with precisely focused, intense beams aimed at a tumor from multiple directions. This strategy can deliver a high dose of radiation to tumor cells while limiting the amount of radiation to nearby normal tissues
- Current stereotactic technologies deliver radiation with a ***gamma knife***, a linear accelerator or a proton beam

Icsenko-Cushing's disease

CORTICOTROPH ADENOMAS

(small basophilic microadenomas that secret ACTH)

is a disease, which is manifested by the bilateral hyperplasia of adrenal glands, increased secretion of ACTH and hormones of adrenal cortex.

First, the disease was described by the Russian ***neuropatolologist N.M. Icsenko in 1924. In 1932*** the same symptom was described by the American ***neurosurgeon Harvey Cushing.***

Icsenko-Cushing's disease and Icsenko-Cushing's syndrome

Icsenko-Cushing's syndrome

is a syndrome due to excess cortisol from pituitary, adrenal or other sources (exogenous glucocorticoids, ectopic ACTH, etc.)

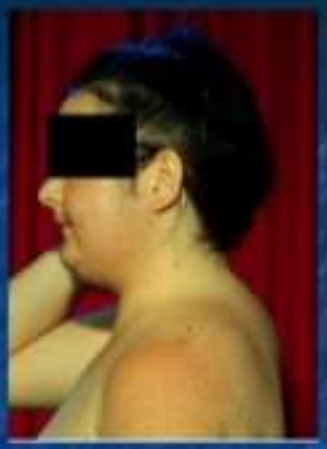
Icsenko-Cushing's disease

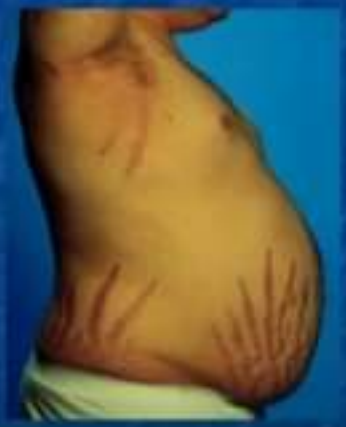
is hypercortisolism due to excess pituitary secretion of ACTH (about 70% of cases of endogenous Icsenko-Cushing's syndrome)

Icsenko-Cushing's disease

Centripetal obesity
Moon face
Buffalo hump
Skin atrophy
Easily bruised
Striae
Cutaneous fungal infections
Hyperpigmentation
Oligo- or amenorrhea
Hirsutism and Virilization with adrenal tumors

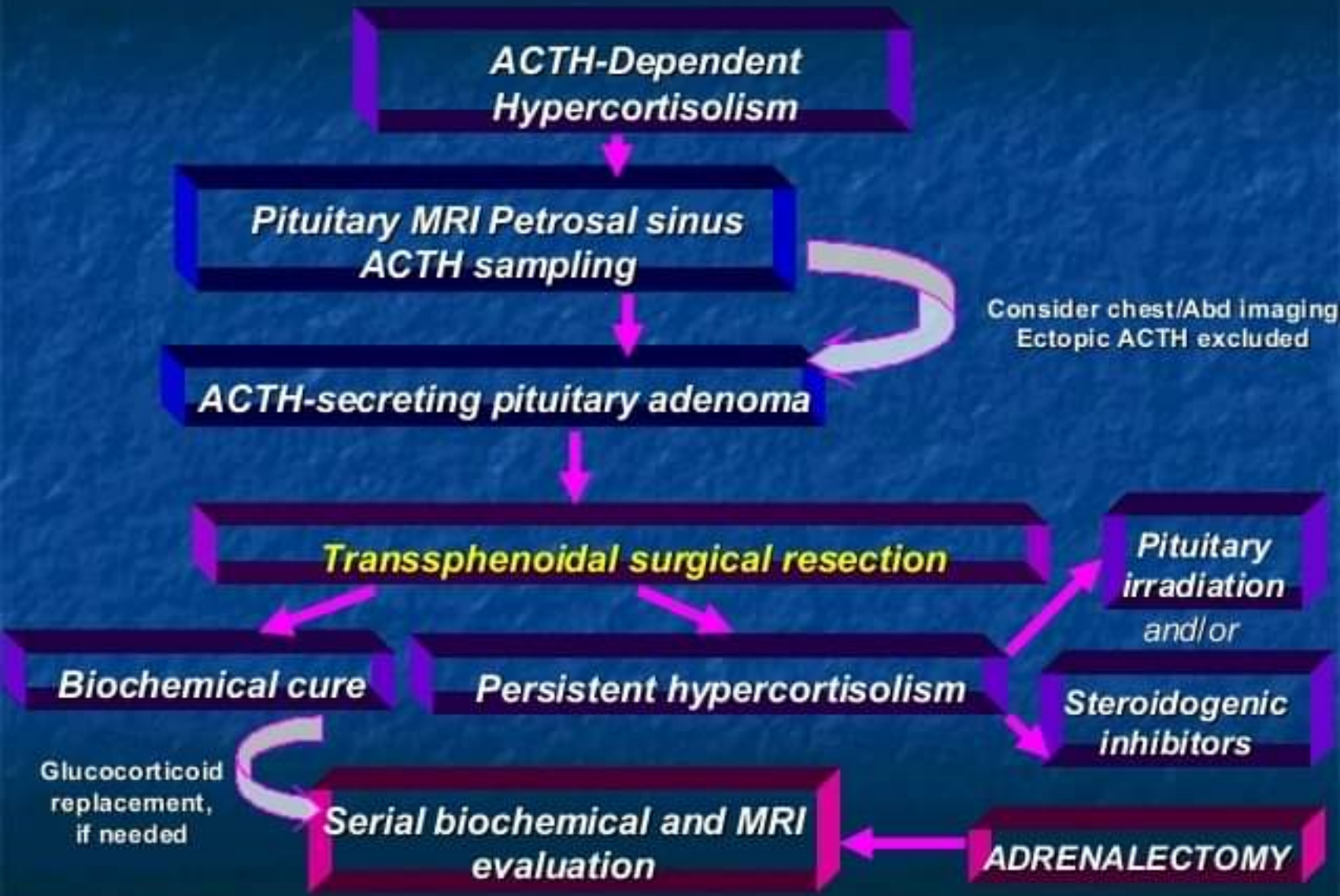
Icsenko-Cushing's disease





Proximal muscle wasting & weakness
Osteoporosis
Glucose intolerance or steroid diabetes
Hypokalemia
Thromboembolism
Depression
Infection
Glaucoma

TREATMENT OF ICSENKO-CUSHING DISEASE



GONADOTROPH ADENOMAS

- Majority produce FSH, some FSH and LH, rarely only LH
- Occur in middle-aged men and women usually are macroadenomas
- May cause amenorrhea or galactorrhea, ↓ libido in men

THYROTHROPH ADENOMAS

- produce TSH ► hyperthyroidism

NON-SECRETORY ADENOMAS

- in 4th decade of life
- may grow to large size- macroadenomas 1 cm
- local mass effect: headache, visual disturbances and *panhypopituitarism:* hypogonadism, hypothyroidism, hypoadrenalism
- most consist of chromophobic cells or intensely eosinophilic cells

Gigantism

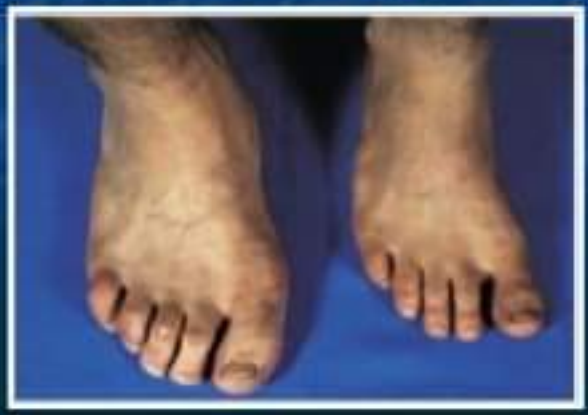
or **giantism**, (from Greek *gigas*, *gigantas* " giant") is a condition characterized by excessive height growth and bigness significantly above average height.

Height is 2.25 - 2.40 metres.

Features of acromegaly/gigantism.

A 22-year-old man with gigantism due to excess growth hormone is shown to the left of his identical twin.
The increased height and prognathism.

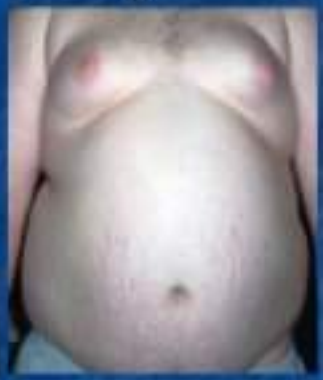
Enlarged hand and foot of the affected twin are apparent.
Their clinical features began to diverge at the age of approximately 13 years.

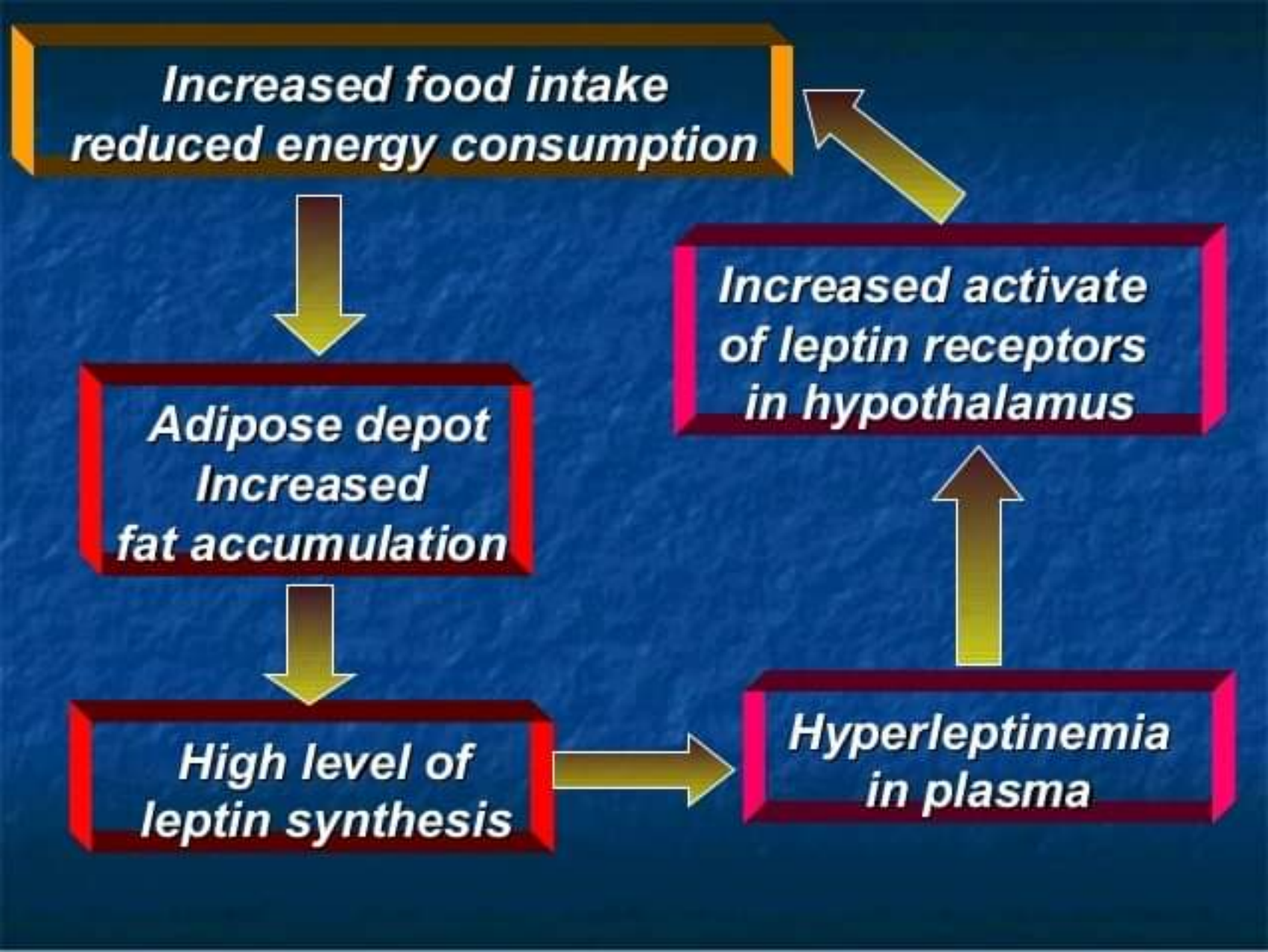


HYPOTHALAMIC SYNDROME

- Obesity is not cushingoid (not central)
  - Striae (pink and not very large)
- Hypertension (constant or permanent)
  - Glucose intolerance





Increased food intake
reduced energy consumption
Adipose depot
Increased
fat accumulation
High level of
leptin synthesis
Hyperleptinemia
in plasma
Increased activate
of leptin receptors
in hypothalamus

HYPOTHALAMIC SYNDROME

Autonomic-vascular form

Sympatho-adrenaline crisis:

Increasing pressure
Tachycardia
Cardiac respiration
Pallor
Fear
Trembling
Agitation

Vago-insular crisis:

Hypotention
Bradycardia
Sweating
Heat sensation
Redness of the face

Neuroendocrine form

Violations of water-salt metabolism
Disturbance of thermoregulation
Oligo- or amenorrhea
Obesity
Hypertension

Neurotrophic form

Change the color of the skin
Narrow
Bright device
Dryness and rash
on the skin
Early graying and hair loss

Sleep Disorders and Vitality

The attack sleepiness in other moment
Cataplexy
Acoustic and color nightmarish dreams

Treatment of hypothalamic syndrome

Sympatho-adrenaline crisis:

Piroksan 1% - 1,0 g i/m

Piroksan 0.015 1 tablet 3 times/day 3 weeks

Dopehit 0.25 1 tablet 3 times/day 3 weeks

Vago-insular crisis:

Atropine sulfate 1% - 1,0 s/c

Extract of belladonna 0.015 1 tablet 3 times/day 3 weeks

Nootropics:

Lutsetam 800 mg 2 times/day 3 weeks

Symptomatic therapy:

ATP 1.0 g i/m (10 days)

Glutamic acid 0.25 3 times/ day 3 weeks

Dehydration therapy:

Hypothiasid 50 – 100 mg/day

$MgSO_4$ 25 % solution i/m 10 – 15 times

Physiotherapy:

Galvanizing hypothalamic nucles 10 days to 15 minutes

Hypocaloric diet: 1000-1500 kcal/day

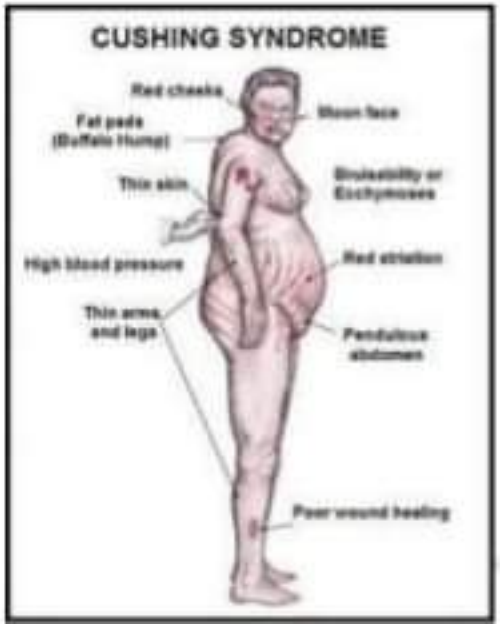
Hyperpituitarism

Hyperprolactinaemia

- Excess production of prolactin
- In females it produces amenorrhea-galactorrhea syndrome
  - Infertility
  - Milk secretion not related to pregnancy or puerperium
  - In males it may cause impotence

Cushing's syndrome

- Excess secretion of ACTH
- Central or trunkal obesity with thin arms and legs, moon face
- Wasting & thinning of skeletal muscle, atrophy of skin and subcutaneous tissue
- Osteoporosis
- Hypertension . Diabetes mellitus
- Amenorrhoea, hirsuitism and infertility
- Insomnia, depression, confusion and psychosis



Pituitary Gland

Prolactinomas

- Most frequent hyperfunctioning adenoma
- Amenorrhea, galactorrhea, loss of libido, infertility
- Tend to undergo dystrophic calcification
- Any mass in the suprasellar department may disturb the normal inhibitory influence of the hypothalamus (via dopamine secretion) on prolactin secretion resulting in hyperprolactinemia

Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Definition

The syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) is defined by the hyponatremia and hypo-osmolality resulting from inappropriate, continued secretion or action of the hormone despite normal or increased plasma volume, which results in impaired water excretion.

* What does ADH do?
  * Causes kidneys to reabsorb water →
  * ↓ urine output →
  * ↑ fluid volume

SIADH – Sign & Symptoms

- Water retention
  - Edema
    - Weight gain
- Urine
  - Concentrated
  - increase Sp. gravity

Diabetes – Type 1

Inability of the body to produce or excrete insulin

When are Children most likely to be diagnosed with Diabetes?

- Peak incidence is:
  - 5-7 years of age
  - Puberty

It can occur at any age.

Emerging Trends of Diabetes

- Incidence of Type 1 diabetes increasing, the etiology is unknown. This trend is most apparent in very young children
- Obesity is causing increased incidence of Type 2 diabetes in children and teens
- As children with chronic illness survive longer(i.e. cystic fibrosis)with more extreme measures and (i.e. transplants), diabetes becomes another side effect of their illness

Etiology

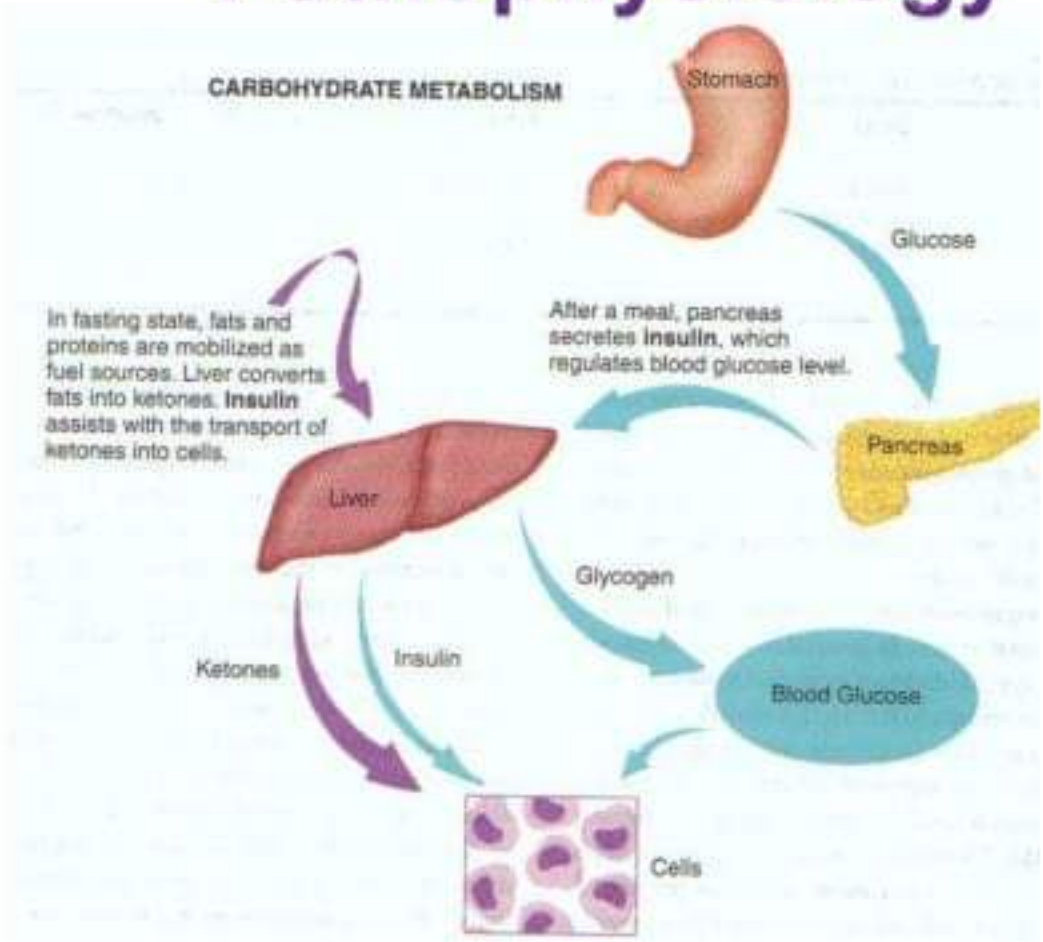
- Autoimmune process

- Inflammatory process in the insulin secreting islet cells of the pancreas

- Destruction of the islet cells

- Failure to produce or excrete insulin

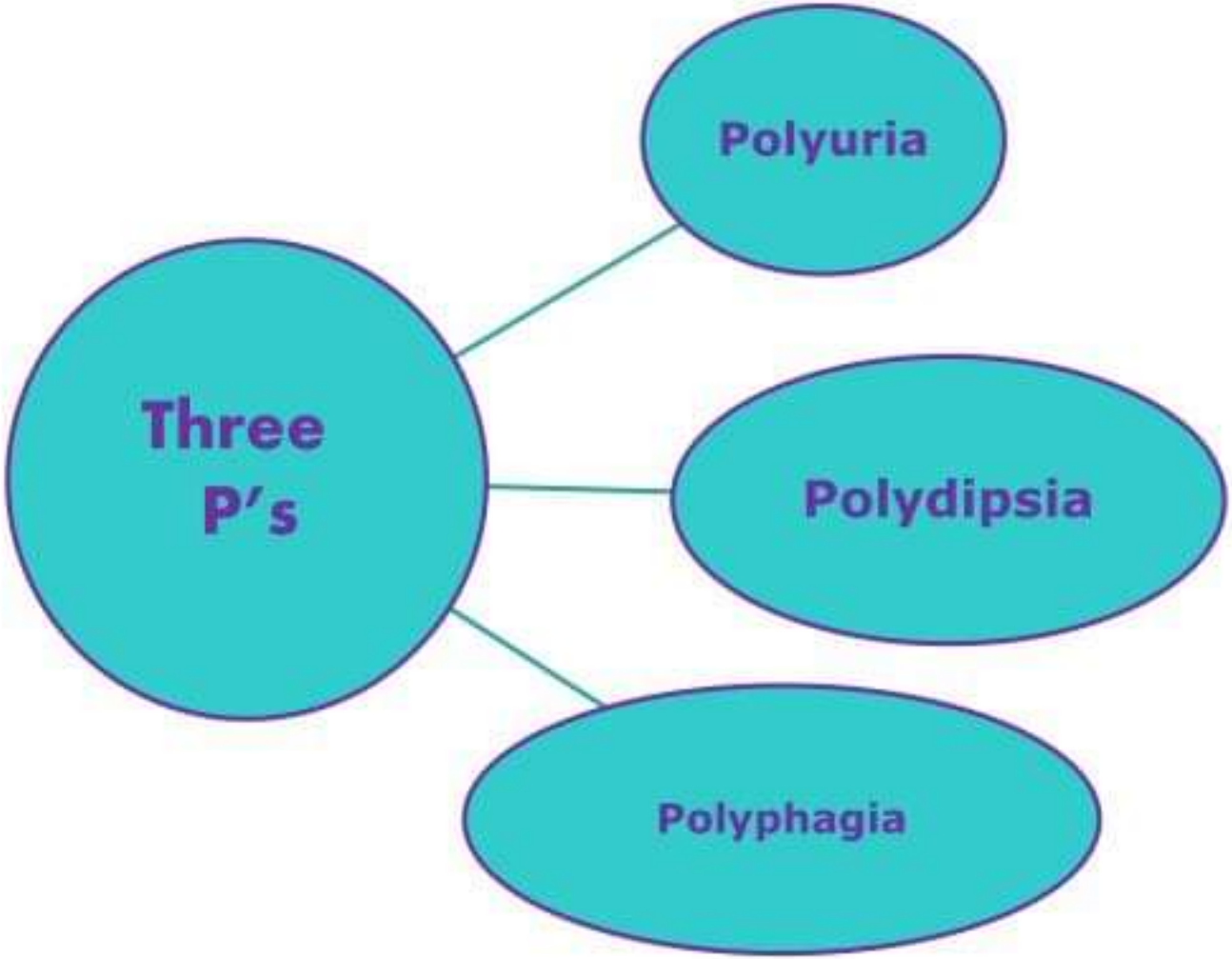
Pathophysiology



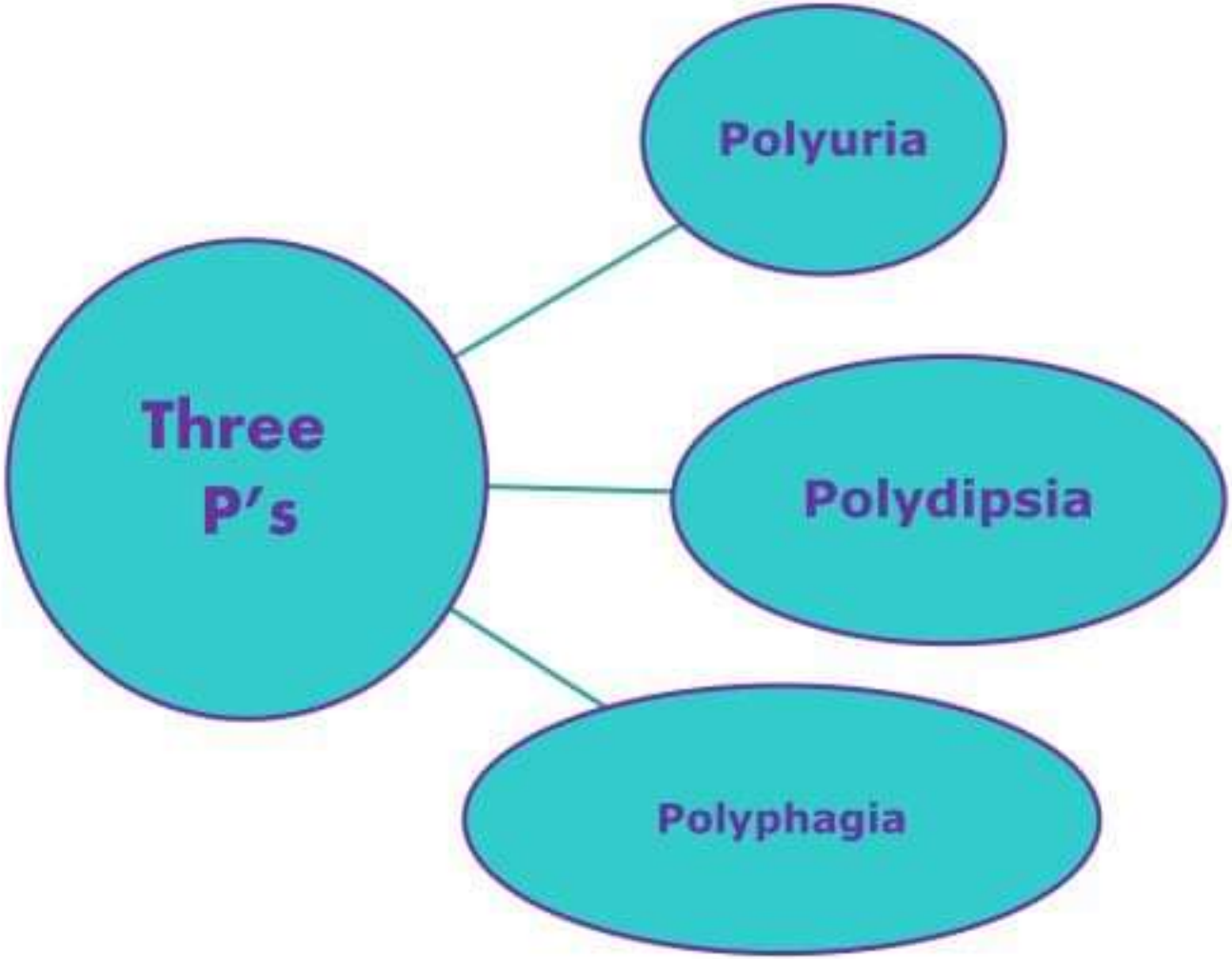
Failure to produce **insulin** leads to elevated blood glucose

HYPERGLYCEMIA

Clinical Manifestations



Clinical Manifestations



How would you tell *polyuria* in a toddler?

Answer: Enuresis in a toilet-trained child

Other manifestations of hyperglycemia

- Fatigue – unexplained
  - Weight Loss (gradual, over several weeks)
  - Blurred vision
  - Headache
  - Hunger

Diagnosis

Symptoms of diabetes plus Plasma Glucose Levels of:

- Fasting plasma glucose ≥ 126 mg/dl

  or

- Two-hour plasma glucose ≥200 mg/dl

  or

- Random serum glucose concentration ≥200 mg/dl

Ketonuria is a frequent finding

Goals of Insulin Therapy

Maintain serum glucose levels from:

- Toddlers and preschoolers
  - 100 – 180 before meals
  - 110-200 at bedtime
- School-age
  - 90- 180 before meals
  - 100 – 180 at bedtime
- Adolescents
  - 90 – 130 before meals
  - 90 – 150 at bedtime

Basal-bolus Therapy

- ADA recommendations for children

Administration

- Basal insulin administered once a day Glargine (Lantus) or twice daily (Humulin or Ultralente)

- Bolus of rapid-acting insulin (Lispro or Aspart) given with each meal and snack or consumes carbohydrates