Figure 1. Description of the functional role exerted by the cerebral third ventricle, as reported by Mondino de' Liuzzi in Anathomia. (A) Original frontpage of Anathomia in a XIV century edition; (B) Original text (in brackets) in medieval Latin (from the 1316 A.D. manuscript kept at the Societŕ Medica Chirurgica in Bologna, Italy); (C) a portion of the Latin fragment shown in (B) containing the most important concepts; (D) English translation shown in (B). (From Toni R., Ancient views on the hypothalamic-pituitary-thyroid axis: an historical and epistemological perspective, Pituitary 3: 83-95, 2000).

Figure 2. Plates from the seventh book of the first edition (1543) of the Fabrica by Andreas Vesalius, showing what is believed to be the oldest anatomical images in Western literature of the hypothalamic-pituitary unit. (Courtesy of the Library of the Department of Human Anatomy of the University of Bologna, Italy, with permission.) 1) Enlarged view of the pituitary gland (A), hypothalamic infundibulum (B) and ducts comprising the foramen lacerum and superior orbital fissure (C, D, E, F) believed to drain the brain mucus or phlegm (in Latin pituita) from the pituitary gland to the nasopharynx; 2) anatomical relationships between the infundibulum (D), the dural diaphragma sellae (F), the internal carotid arteries (C, D) and oculomotor nerves (G); 3) composite image including a) an enlarged view of the rete mirabilis formed as a reticular plexus by the carotid arteries entering (A, B) and emerging (C, D) around the pituitary gland (E), b) detailed view of the reticular plexus arising from the carotids (B, C) on each side of the pituitary (A). (From Toni R., Ancient views on the hypothalamic-pituitary-thyroid axis: an historical and epistemological
Figure 3. Drawings by Leonardo da Vinci (1508-1509) taken from the Codici di Anatomia of the Windsor's Collection (Courtesy of the Library of the Department of Human Anatomy of the University of Parma, Italy). (A) Inferior surface of the brain, showing the rete mirabilis (arrow) that surrounds the pituitary gland; (B) three-dimensional representation of the cerebral ventricles. The third ventricle (3v) was believed to be the site of afference and elaboration of the "sensus communis" (Latin for peripheral physical sensations). (From Toni R., The Human Hypothalamus: clinical anatomy of endocrine, autonomic and behavioral responses, J. Endocrinol. Invest 2003, in press).
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>134</td>
<td>Galen describes in the &quot;De Usum Partium&quot; the hypothalamic infundibulum and pituitary gland as draining route and receptacle for brain mucous, and the existence of the &quot;rete mirabilis&quot;</td>
</tr>
<tr>
<td>1316</td>
<td>Mondino dei Liuzzi da Bologna in his &quot;Anothomia&quot; refers to the third cerebral ventricle as &quot;integrator&quot; of body functions</td>
</tr>
<tr>
<td>1522</td>
<td>Berangario da Carpi in his &quot;Isagoge Breves&quot; denies the existence of the Galenic &quot;rete mirabilis&quot; in the human brain</td>
</tr>
<tr>
<td>1543</td>
<td>Vesalius includes in the &quot;Fabrica&quot; the first anatomical drawings of the hypothalamic infundibulum and pituitary</td>
</tr>
<tr>
<td>1527</td>
<td>Fallopius in the &quot;Observationes Anatomicae&quot; and Casserio in the &quot;Tabulae Anatomicae&quot; mention the arterial polygon at the base of the brain then described by Willis</td>
</tr>
<tr>
<td>1664</td>
<td>Willis in his &quot;Cerebri Anatome&quot; argues that humors out of the third ventricle may be carried to the pituitary gland</td>
</tr>
<tr>
<td>1655</td>
<td>Schneider and Lower reject the Galenic idea that the pituitary gland filters brain secretions to the nose</td>
</tr>
<tr>
<td>1672</td>
<td>Lieutand discovers vessels in the pituitary stalk</td>
</tr>
<tr>
<td>1778</td>
<td>Sommering introduces the term &quot;hypophysis&quot;</td>
</tr>
<tr>
<td>1860</td>
<td>Von Luska describes the primary (or hypothalamic) capillary plexus of the portal vessels</td>
</tr>
<tr>
<td>1872</td>
<td>Meynert and Forel define the anatomical borders of what they call &quot;the neural portion extending forward the region of the subthalamus&quot; (i.e. the hypothalamus)</td>
</tr>
<tr>
<td>1893</td>
<td>His introduces the term &quot;hypothalamus&quot; and provides the first anatomical subdivision based on ontogenesis of the human brain</td>
</tr>
<tr>
<td>1894</td>
<td>Ramon Y Cajal discovers in rats the connection between the hypothalamus and posterior pituitary (supraoptico-hypophysial tract)</td>
</tr>
<tr>
<td>1928</td>
<td>E. Scharrer describes &quot;glandular cells&quot; in the fish hypothalamus (concept of &quot;neurosecretion&quot;)</td>
</tr>
<tr>
<td>1930</td>
<td>Popa and Fielding describe in the human pituitary stalk a portal vascular system interpreted as a route of the blood upward the hypothalamus</td>
</tr>
<tr>
<td>1940-1955</td>
<td>Harris and Green establish the basis for the neural control of the pituitary gland secretion and demonstrate its vascular link with the hypothalamus</td>
</tr>
<tr>
<td>1950-1958</td>
<td>Nauta and Kuypers describe the connections of the mammalian hypothalamus with the rest of the brain and propose that the limbic system influences pituitary function, introducing the concept of &quot;hypothalamic integration&quot;</td>
</tr>
<tr>
<td>1960</td>
<td>Martinez describes the structure of the median eminence</td>
</tr>
<tr>
<td>1962</td>
<td>Halasz put forth the concept of &quot;hypophysiotrophic area&quot; of the hypothalamus</td>
</tr>
<tr>
<td>1964</td>
<td>Szentagothai defines the tuberoinfundibular tract</td>
</tr>
<tr>
<td>1968</td>
<td>Guillemin and Schally isolate the first hypothalamic releasing factor</td>
</tr>
</tbody>
</table>
A HYPOTHALAMUS ANATÓMIAI HATÁRAI
Schematic representation of the major neural pathways connecting the periventricular, medial and lateral hypothalamic subdivisions with the rest of the brain. Groups with identical colors are functionally linked.
Figure 9-5 Hormonal secretion from the primate pituitary gland (hypophysis) is controlled by the hypothalamus. The anterior lobe of the pituitary gland (adenohypophysis) consists of the pars distalis, pars intermedia, and pars tuberalis. (The pars tuberalis, not shown, consists of a thin layer of cells surrounding the pituitary stalk.) The posterior lobe (neurohypophysis), an extension of the brain, consists of neural tissue, whereas the anterior lobe consists of non-neural glandular tissue. Releasing hormones secreted by hypothalamic neurosecretory cells include prolactin, growth hormone, thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and adrenocorticotropic hormone (ACTH). Antidiuretic hormone (ADH) and oxytocin (from the supraoptic nucleus) are secreted by the posterior lobe and act on the kidneys and uterus, respectively.
FUNCTIONAL DISTURBANCES

- Food and fluid disorders
- Growth and development
- Sexual and reproductive activity
- Behavioral syndromes
- Autonomic and vegetative disorders

2. Chiasma and optic N. lesions

3. ICP effect: Obstruction of CSF circulation

4. Death of the patient
GENERAL EFFECTS

- **HEADACHE**
  increased pressure-stretching of dural plate

- **BRAIN**
  frontal, temporal lobe, olfactory n.

- **OPTIC NERVES**

- **CAVERNOUS SINUS**

- **SPHENOID SINUS**
Metabolic sequelae of hypothalamic mass lesions I.

- **AUTONOMIC DYSFUNCTION**
  - cardiac arrhythmias, hypertension

- **BEHAVIORAL DYSFUNCTION**
  - rage, aggression, l. emotions

- **TEMPERATURE DYSREGULATION**
  - acute hyperthermia, poikilothermia, hypothermia
Symptoms of mass lesions II.

- **THIRST DISORDER**
  - diabetes insipidus, adipsia, compulsive drinking, hypernatraemia

- **SLEEPING DISORDERS**
  - reversal of sleep-awake cycle,
  - somnolence and coma

- **APPETITE DISORDERS**
  - obesity, hyperphagia, anorexia, aphagia
Summary of appetite control

Schwartz, Nature, 2002
INKURÁBILIS!

ENDOKRINOLÓGIAI CSAPDA
P.R. 19 éves beteg kórtörténete

• **ANAMNÉZIS:** 9 éves koráig normálisan fejlődött, csillapithatalan étvágya támadt, hizni kezdett, romlott a látása. CT vizsgálat hypothalamus daganatot mutatott, mütét történt amely gliómát verifikált. Irradiációs therápiában részesült.

• **Jelen panaszok:** Csillapithatatlan étvágy, hizás, nem menstruál, alvásvárlás, dühkitörések.

• **Status.** Broca- szabály, BMI stb.

• Babinski-Frőlich syndróma.
Sebészeti utak a suprasellaris és a III. kamra régióihoz
TUMORS OF THE HYPOTHALAMIC-PITUITARY REGION

1. EXTRAPARENCHIMAL:
   MENINGIOMA, METASTATIC CARCINOMA, CHORDOMA, NEURINOMAS, PAPILLOMA, CYSTS

2. INTRAPARENCHIMAL:
   HYPOTHALAMUS: HYPOTHALAMIC-OPTIC GLIOMAS, GERMINOMAS, TERATOMAS, HAMARTOMAS
   PITUITARY STALK: CRANIOPHARYNGIOMA, RATHKE’S CLEFT CYST, COLLOID CYST
   PITUITARY GLAND: ADENOMA, CARCINOMA
Hypothalamus hamartoma

Pediatric ages
Parahypothalamic localization
Intrahypothalamic localization
Symptoms

- Asymptomatic
- Pubertás praecox
- Gelastic epilepsy
- Compl.part., drop attack, Behavior changes (agression)
- Intellectual and memoria deficilt
Pubertás praecox
Pubertás praecox
Treatment

- Conservative therapy
- Direct surgery
- Stereotactic laesió
- Gamma knife, LINAC?
Transcallosal-interfornical aproach, total removal.
HYPOTHALAMIC GLIOMS 1.

- HYPOTHALAMUS
- N. OPTICUS, CHIASMA, TRACTUS TU.
- HISTOLOGY: BENIGN
- LONG ANAMNESIS ,
- TOTAL CURE OF THE PATIENT ???
- AIM OF THE TREATMENT: LONGER SURVIVAL IN POSSIBLE BEST QUALITY OF LIFE
HYPOTHALAMIC GLIOMS 2

- THERAPY:
- BIOPSIA - VERSUS - TUMOR REMOVAL
- RADIOTHERAPY ???
- LINAC, GAMMA KNIFE ???
10 ÉVES LÁNY,
FOKOZATOS
LÁTÁSROMLÁS
HIZÁS, RETARD.

CHIASMA SPONGIO-
BLASTOMA

PREOP

POSTOP
25 éves beteg:
Fokozatos, csaknem teljes vakságot okozó hypothalamus cystás astrocytoma
Radikális eltávolítás.
Radiotherápia nem indikált.
35 year old oligohidrosis, látászavar primer amenorrhea, mentális retard
Inoperábilis H-O-Hnyél tumor.
V.s. oligo-astrocytoma. Biopszia veszélyes, műtéttől eredmény nem várható. Radiotherápia?
Supraselláris ciszták

- Arachnoideális
- Colloid
- Rathke-tasak
- Craniopharingeoma
- Glioma
SUPRASELLARIS CISZTA
SUPRASELLARIS CISZTA, CONTROL CT A MŰTÉT NAPJÁN
SUPRASELLARIS CISZTA, CONTOL CT 9 NAPPAL A MŰTÉT ÚTÁN
COLLOID CISZTA (MR,T2,kontraszt.)
Colloid ciszta (MR, T1)
HYPOTHALAMUS GERMINOMA
HYPOTHALAMUS GERMINOMA
Suprasellaris germinoma, műtét után 3 nappal
HYPOTHALAMUS TU. FELNŐTT
KORBAN.(TERRATÓMA)
HYPOTALAMUS TU RADIKÁLIS ELTÁVOLITÁS

A SUPRASELLARIS CYSTERNÁS SZABAD
HYPOTHALAMUS-HYPOPHYSIS
SEBÉSZET extraparenchimális tumor
In 2007, because of nasal obstruction, she underwent an intranasal endoscopic operation in a provincial town.

Hystology: sinonasal carcinoma with neuroendocrine features.

She became pregnant but in consequence of the intrauterine death of the embryo, the cesarian section was indicated.

Epistaxis and total obstruction of airways developed and tracheostomy was performed.

She was declared incurable and sent home.
I got a letter from a Grandma who lives in a small village. She wrote that: You have successfully cured the neighbor's child. I ask You to try to treat my granddaughter, who was sent home to die.

Attached two photo
Sz. Piroska postop. CT felvétele, basis és orrekonstrukció
Pituitary adenoma

**TUMOR**: AUTONOM-IRREVERSIBLE-MONOClonal cell proliferation.

**FREQUENCY**: 10% of all intracranial tumors. (In 1999, 79 adenoma out of 810 intracranial tumors)

1-25% of general population

**ETIOLOGY**: ?

Hypothalamus - Pituitary - Periph. gland

Multifactorial
PITUITARY DENOMA

Pituitary adenomas are slow growing, benign tumors of the pituitary gland. They represent 10-15% of all brain tumors. Those that are small (less than 1 cm in largest diameter) are called microadenomas, while larger tumors (greater than 1 cm) are commonly called macroadenomas, and the multidirectional macroadenomas usually are called giant tumors. Pituitary tumors can also be divided into functioning and non-functioning tumors. As the classification implies, functioning tumors produce hormones, often in large, unregulated amounts. Correspondingly, non-functioning tumors do not produce significant amounts of hormones.
Pituitary microadenoma
Giant pituitary adenoma
Symptoms from pituitary adenomas can be classified as follows:

1) **Overproduction of hormones:** The specific symptoms experienced by a patient will depend on the type of hormone that is being overproduced. A tumor that produces large amounts of ACTH causes **Cushing Disease**, which leads to obesity, high blood pressure, and muscle weakness, among other symptoms. A **prolactinoma** is a pituitary adenoma that produces large amounts of prolactin. Symptoms of this include irregular menstruation, sexual dysfunction and breast discharge. A growth hormone producing tumor leads to **acromegaly**, a condition characterized by progressive enlargement of hand and foot size and an alteration of facial features. **TSH-adenoma**.

2) **Hypopituitarism:** A non-functioning adenoma can still lead to hormonal problems. It does so by compressing the pituitary gland and results in a decrease or cessation of normal hormone production by this organ.

3) **Visual deficit:** A large tumor can grow upwards, out of the sella turcica and compress the optic nerves (optic chiasm). Frequently, this leads to a specific form of “tunnel vision” called bitemporal hemianopsia.

4) **Non-specific symptoms:** Sometimes a sizable pituitary adenoma can lead to headaches or a sensation of pressure or fullness behind the eyes. Rarely, bleeding into a tumor can lead to severe headache, double and blurring vision (pituitary **apoplexy**).
Pathogenesis of pituitary adenomas(2)

- Normal pituicyte
- Apoptosis evasion
- Unlimited replicative potential
- Growth signal independence
- Anti-growth insensitivity
- Sustained survival

Oncogenic hits

Intra-pituitary environment

- Hormone hypersecretion
  - Acromegaly (GH)
  - Cushing disease (ACTH)
  - Hyperprolactinemia (PRL)
  - Hyperthyroxinemia (TSH)
  - Hypogonadism (FSH/LH)

Pathogenesis
- Compressive pituitary failure
- Central mass effects

Phenotype
- Hypogonadism
- Thyroid failure
- Adrenal failure
- Visual field disturbance
- Headache
- Cranial nerve palsy
- Parasellar invasion

Management
- Replace deficient hormone
- Shrink or abate mass
- Surgery
- Medical Rx
- Radiation

Pituitary autonomy

Chromosomal instability (PTTG)
Epigenetic events (methylation, de-acetylation)
FGFs, TGF-α, NGF
Estrogen
Hypothalamic hormones
Dopamine
GADD45γ
FGF2 CAMs

CNC
LOH 11, 13
Rib, MEN 1
Coronal T1 weighted MR image revealing a suprasellar extension on the right side of the pituitary complex. (B) Gadolinium enhanced coronal T1 weighted MR image indicating two hypointense lesions, clearly separated by a well enhanced normal pituitary.
Hematoxylin eosin staining showing relatively small cells in the adenoma left. A rosette like pattern with spindle shaped cells is evident (arrowheads). (B) The right sided tumour was composed of strongly acidophilic, more cellular, adenomatous cells with a diffuse pattern of cell growth. (C) Immunohistochemistry revealing immunoreactivity for thyroid stimulating hormone in the adenoma on the left. (D) Immunohistochemistry revealing immunoreactivity for growth hormone in the other on the right.
PITUITARY ADENOMAS
(CLASSIFICATION) I.

1. **BASED ON STAINING:** CHROMOPHOBES, ACIDOPHIL, BASOPHIL. (NO CORRELATION OF STRUCTURE WITH SECRETORY ACTIVITY)

2. **BASED ON ENDOCRINOLOGICAL INVEST.:** HORMONE SECRETING AND NON SECRETING

3. **BASED ON IMMUNOCYTOCHEMISTRY, ELECTRONMICROSCOPY, ENDOCRINOLOGICAL INVESTIGATION**
CLASSIFICATION II.

- SOMATOTROPH (GH CELL) 13-15%
- LACTOTROPH (PRL CELL) 25-28%
- CORTICOTROPH (ACTH) 8-10%
- THYROTROPH (TSH) 1%
- GONADOTROPH (FSH, LH) 7-9%
- MIXED SOM. AND LACT. 3-5%
- ACIDOPHIL STEM CELL 1-3%
- MAMMOSOMATOTROPH 1-2%
- NULL CELL, ONCOCYCTOMA 13-15%
- PLURIHORMONAL 1-3%
- SILENT ADENOMAS 5-7%
MANAGEMENT OF PITUITARY TUMORS

FIRST SYMPTOMS: PANEL DOCTOR, OPHTALMOLOGIST, GYNECOLOGIST, PEDIATRIST, DENTISTS

ENDOCRINOLOGY: LABORATORY TESTS BASAL AND DYNAMIC PITUITARY FUNCTION

NEURORADIOLOGY: CT (CONTRAST !), MRI (T1, T2, CONTRAST !)

NEUROSURGERY: INDICATION FOR SURGICAL TREATMENT, INDICATION FOR IRRAD.

ONCOLOGY: IRRADIATION
Magnetic resonance image (MRI) and (B) corresponding schematic illustration of the human hypothalamus (H) and pituitary gland seen in sagittal orientation. Note the high intensity or "bright spot" of the posterior pituitary by MRI in (A), sharply defining the boundary between the anterior pituitary gland. III = third ventricle (Modified from Lechan RM. Neuroendocrinology of Pituitary Hormone Regulation. Endocrinology and Metabolism Clinics 16:475-501, 1987.)

MRI and (B) schematic image of the pituitary fossa and its anatomic relationships seen in coronal orientation. The cavernous sinus contains the internal carotid artery and cranial nerves III, IV, V₁, V₂, and VI. The optic chiasm resides immediately above the pituitary gland and is separated from it by a cerebrospinal fluid-filled cistern. (Modified from Lechan RM. Neuroendocrinology of Pituitary Hormone Regulation. Endocrinology and Metabolism Clinics 16:475-501, 1987.)
Correlation of High Signal Intensity of the Pituitary Stalk in Macroadenoma and position of the optic chiasm
TREATMENT OF PITUITARY TUMORS

NO TREATMENT: MICRO INCIDENTALOMA, ENDOCRIN. AND IMAGING OBSERVATION

CONSERVATIVE: SECRETING ADENOMAS (PRL, GH, TSH) IN SELECTED CASES BROMOCRIPTIN, SMS, OCTREOTID

SURGICAL: NON SECRETING, NOT RES-PONDED TO MEDICAL TH., OPTIC LESION

RADIATION THERAPY: SUBTOTAL REMOVAL, INOPERABLE CONDITION, PRIMARY TH.
In 10-25% of the population a chromophobe pituitary adenoma (MT x16), a small tumour (diameter 2 mm) can be discovered at autopsy. Compared to the surrounding pituitary tissue, this tumour nodule is more cellular and has a much less apparent vascular network because its vessels have a thin, rudimentary wall poor in collagen.
TRANSCRANIAL APPROACH I.

INDICATIONS:

- EXTRA AXIAL LOCALISATION
- CONCOMITANT ANEURYSMS
- ABNORMALITIES OF CRANIAL BASE
- OPTIC NERVE DECOMPRESSION
- SUSPICION FOR MENINGIOMA
- LACK OF TECHNICAL BACKGROUND
- CONSTRUCTIVE DIAPHRAGMATIC SELLAE
TRANSCRANIAL APPROACH. II

TECHNIQUES:

- BIFRONTAL
- FRONTO-TEMPORAL
- TRANSVENTRICULAR
- KEYHOLE (FRONTOLATERAL)
FRONTO-TEMPORÁLIS  FELTÁRÁS
A DURA MEGNYITÁSA UTÁN
SZUPERCILIÁRIS FELTÁRÁS.
A BŐRMETSZÉS TERVEZÉSE
MINI CRANIOTOMIA
A DURA MEGNYITÁS UTÁN
A metszés helye 3 hónappal a műtét után
A F-T FELTÁRÁS LEHETSÉGES PROBLÉMÁI

HAJ LEVÁGÁS N. FACIALIS, TRIGEMINUS, AGYKÉREG SÉRÜLÉS, VÉRVESZTESÉG
Hypophysis macroadenoma
Hypophysis macroadenoma, controll CT

Radikális eltávolítás
A műteti behatolás hypophysis adenoma-eltávolítása után 7 nappal
TRANSSPHENOIDAL APPROACH I.

HISTORY:

(TRANSNASAL,SUBLABIAL,TRANSSINUS PARASEPTAL)

HARVEY CUSHING, 1909
OSCAR HIRSCH, 1910 (TRANSSINUS)

MICROSCOPE, ANTIBIOTICS, INTRAOP. X-RAY CONTROL
J. HARDY 1973

E. PÁSZTOR 1974, HUNGARY
TRANSSPHENOIDAL APPROACH III.

COMPLICATIONS

CAROTID ARTERY INJURY 1.1%
CENTRAL NS. INJURY 1.3
HEMORRHAGE 2.9
LOSS OF VISION 1.8
OPHTHALMOPLEGIA 1.4
CEREBROSPINAL FLUID LEAK 3.9
MENINGITIS 1.5
SEPTUM PERFORATION 6.5
SINUSITIS 8.5
ANTERIOR PITUITARY INSUFF. 19.8
DIABETES INSIPIDUS 17.8
DEATH 0.9

results of 958 surgeons
transseptal
Feltárás a jobb orrnyíláson keresztül
ostium

Septum-sphenoid
átkomna

Art. sphenoidalis
Nyálkahártya coag. és leválasztása lebenyszerűen
A SINUS SPHENOIDALIS MEGNYITÁSA

LEBENY
A SELLA TURCIKA FELTÁRÁSA

SPHENOID MUCOSA
A DURA M. FELTÁRÁSA
DURANYITÁS UTÁN, TUMOR ELTÁV.
A tumor mérsékelten vérzékeny
TUMOR ÜREG

DURA

VÉKONY TUMORSZÖVET
A VÉKONY RÉTEGŰ TU.
ELTÁVOLÍTÁS
TELJES ELTÁVOLÍTÁS
Ép mirigy
Vérzés csillapítás
A sinus fedése
Nyálkahártya vérzés csillapítás
A műtét befejezése.
MAKROADENOMA
ELTÁVOLÍTÁSA

INVASÍV, A CAROTIS INTERNÁT KÖRBEFOGJA
Saggitalis MR
Postop. control
Postop. control

Szabad sinus

hyp. nyél

hypophysis
ACTH-

**Szerkezet:** peptid 39 aminósav

**hatás:** mellékvesekéreg hormontermelés fokozása
  
  Főleg a glükokortikoidokra hat
  
  Koleszterin-pregnenolon átalakulásra

  CRH szintézis és release csökken

**szabályozás:**

  *serkentő:* CRH, ACTH, 5HT, AVP, GRF

  *gátló:* DA, NA, GABA, kortizol, progeszteron, Glükokortikoidok

**ACTH nő:** Cushing szindróma

  Hiperpigmentált (ACTH+alfa-MSH)

**ACTH esik:** Hányás, szőrzet kevés, pigment 0, vízretenció

  vérnyomás esik, libido esik
### Mellékvesekéreg hiperfunkció: Cushing szindróma

- Aldoszteron nő
- Androgén túlprodukció
- Glükokortikoid nő – fibroblaszt csökken

### III-14. táblázat. Cushing-kór tüneteinek gyakorisága

<table>
<thead>
<tr>
<th>tünet</th>
<th>gyakoriság (%)</th>
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</thead>
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<td>Elhízás (vagy testsúly növekedés)</td>
<td>97</td>
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<tr>
<td>Plethora</td>
<td>95</td>
</tr>
<tr>
<td>Libido csökkenés</td>
<td>95</td>
</tr>
<tr>
<td>Depressio vagy emocionális labilitás</td>
<td>85</td>
</tr>
<tr>
<td>Holdvilág arc</td>
<td>82</td>
</tr>
<tr>
<td>Oligomenorrhoea/amenorrhoea</td>
<td>80</td>
</tr>
<tr>
<td>Növekedés elmaradás (gyermekben)</td>
<td>80</td>
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<tr>
<td>Hypertonia</td>
<td>75</td>
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<tr>
<td>Hirsutismus</td>
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<tr>
<td>Elvékonyodott bőr</td>
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<tr>
<td>Bőr sérülékenysége</td>
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<tr>
<td>Csökkent glüköztolérancia</td>
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<tr>
<td>Izomgyengeség</td>
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<td>Osteoporosis vagy csonttörés</td>
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<td>Fajfájás</td>
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<td>Striák</td>
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<tr>
<td>Oedema</td>
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<tr>
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<td>Háti zsírpúp</td>
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<td>Hajhullás (nőkben)</td>
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<td>Lipideltérések</td>
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<tr>
<td>Csökkent sebgyógyulás</td>
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<tr>
<td>Infectiök</td>
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</tr>
<tr>
<td>Vesegöracs</td>
<td>20</td>
</tr>
<tr>
<td>Fokozott pigmentatio</td>
<td>10</td>
</tr>
<tr>
<td>Exophthalmus</td>
<td>5</td>
</tr>
</tbody>
</table>
Cushing

Vékony, eres bőr

Könnyen sérül

striák

izomgyengeség

Könnyen sérül

obesitas

beteg

Holdvilág arc

normál
MŰTÉT ELŐTT

MŰTÉT UTÁN 6 HÉTTEL
ELŐTT

UTÁN
<table>
<thead>
<tr>
<th>Authors</th>
<th>Center</th>
<th>Year</th>
<th>No. of patients</th>
<th>Correct adenoma identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchfelder et al. [3]</td>
<td>Erlangen, FRG</td>
<td>1993</td>
<td>41 (microadenomas)</td>
<td>21/41 (52%)</td>
</tr>
<tr>
<td>Magiakou et al. [35]</td>
<td>Bethesda, USA</td>
<td>1994</td>
<td>50 (children)</td>
<td>26/50 (52%)</td>
</tr>
<tr>
<td>Ram et al. [37]</td>
<td>Bethesda, USA</td>
<td>1995</td>
<td>18 (microadenomas)</td>
<td>8/18 (44%)</td>
</tr>
<tr>
<td>Knappe et al. [39]</td>
<td>Hamburg, FRG</td>
<td>1995</td>
<td>42 (children)</td>
<td>25/42 (59%)</td>
</tr>
<tr>
<td>Devoe et al. [40]</td>
<td>San Francisco, USA</td>
<td>1997</td>
<td>18 (children)</td>
<td>13/18 (72%)</td>
</tr>
<tr>
<td>Barrou et al. [41]</td>
<td>Paris, France</td>
<td>1997</td>
<td>54 (unselected)</td>
<td>42/54 (78%)</td>
</tr>
<tr>
<td>Watson et al. [42]</td>
<td>Bethesda, USA</td>
<td>1998</td>
<td>107 (microadenomas)</td>
<td>39/107 (36%)</td>
</tr>
<tr>
<td>Graham et al. [32]</td>
<td>Portland, USA</td>
<td>1999</td>
<td>58 (microadenomas)</td>
<td>29/58 (55%)</td>
</tr>
<tr>
<td>Kaltsas et al. [43]</td>
<td>London, GB</td>
<td>1999</td>
<td>69 (unselected)</td>
<td>50/69 (72%)</td>
</tr>
<tr>
<td>Semple et al. [44]</td>
<td>Charlottesville, USA</td>
<td>1999</td>
<td>105 (unselected)</td>
<td>87/105 (83%)</td>
</tr>
<tr>
<td>Kurosaki et al. [38]</td>
<td>Hamburg, FRG</td>
<td>2000</td>
<td>51 (microadenomas)</td>
<td>19/51 (37%)</td>
</tr>
</tbody>
</table>
Table 2. Cushing’s disease – Results of preoperative inferior petrosal sinus sampling (IPSS)/cavernous sinus sampling (CSS) in the literature (1985–2000)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Center</th>
<th>Year</th>
<th>Method</th>
<th>No. of patients</th>
<th>Correct adenoma localization (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oldfield et al. [51]</td>
<td>Bethesda, USA</td>
<td>1985</td>
<td>IPSS</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Lüdecke [33]</td>
<td>Hamburg, FRG</td>
<td>1991</td>
<td>IPSS</td>
<td>31</td>
<td>49</td>
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<tr>
<td>Oldfield et al. [45]</td>
<td>Bethesda, USA</td>
<td>1991</td>
<td>IPSS</td>
<td>105</td>
<td>71</td>
</tr>
<tr>
<td>Teramoto et al. [52]</td>
<td>Tokyo, Japan</td>
<td>1993</td>
<td>CSS</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>Magiakou et al. [35]</td>
<td>Bethesda, USA</td>
<td>1994</td>
<td>IPSS</td>
<td>50</td>
<td>76</td>
</tr>
<tr>
<td>Landolt et al. [53]</td>
<td>Zurich, Swiss</td>
<td>1994</td>
<td>IPSS</td>
<td>38</td>
<td>76</td>
</tr>
<tr>
<td>Doppman et al. [54]</td>
<td>Bethesda, USA</td>
<td>1995</td>
<td>IPSS</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CSS</td>
<td>15</td>
<td>40</td>
</tr>
<tr>
<td>Bachelot et al. [55]</td>
<td>Grenoble, France</td>
<td>1996</td>
<td>IPSS</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td>Mamelak et al. [56]</td>
<td>San Francisco, USA</td>
<td>1996</td>
<td>IPSS</td>
<td>23</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CSS</td>
<td>23</td>
<td>65</td>
</tr>
<tr>
<td>Teramoto et al. [34]</td>
<td>Tokyo, Japan</td>
<td>1998</td>
<td>CSS</td>
<td>35</td>
<td>91</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IPSS</td>
<td>35</td>
<td>63</td>
</tr>
<tr>
<td>Graham et al. [32]</td>
<td>Portland, USA</td>
<td>1999</td>
<td>CSS</td>
<td>59</td>
<td>83</td>
</tr>
<tr>
<td>Kaltsas et al. [43]</td>
<td>London, GB</td>
<td>1999</td>
<td>IPSS</td>
<td>69</td>
<td>83</td>
</tr>
<tr>
<td>Semple et al. [44]</td>
<td>Charlottesville, USA</td>
<td>2000</td>
<td>IPSS</td>
<td>16</td>
<td>75</td>
</tr>
<tr>
<td>Bonelli et al. [47]</td>
<td>Rochester, USA</td>
<td>2000</td>
<td>IPSS</td>
<td>92</td>
<td>70</td>
</tr>
<tr>
<td>Flitsch et al. [98]</td>
<td>Hamburg, FRG</td>
<td></td>
<td>CSS</td>
<td>15</td>
<td>80</td>
</tr>
</tbody>
</table>
SURGERY OF ACTH ADENOMAS

**RESECTION** is the treatment of choice.
Difficult to visualize by MRI, intraoperative localization with ACTH measurement.

Microadenomas 70% remission and 5% recurrence.
Macroadenomas 40% remission.

Repeated operation!

**NELSON’S SYNDROME:**
Cushing’s disease + bilateral adrenalectomies, without radiation therapy.
Surgery + radiation therapy.
MŰTÉT ELŐTT

MŰTÉT UTÁN
6 HÉTTEL
SURGICAL PROBLEMS OF ACTH ADENOMAS

1. NO ADENOMA DETECTED ON MR (17-64%) AND/OR OPERATION (5-20%)
   a. ACTH CELL HYPERPLASIA
   b. ECTOPIC ACTH SYNDROME
   c. ADENOMA IS HIDDEN WITHIN THE GLAND
   d. SMALL AND IS SUCCED AWAY

2. INTRAOPERATIVE DECISION
   a. INCISIONS IN TO THE GLAND
   b. HYPOPHYSECTOMY
3. MULTIPLE ADENOMAS, MACROADENOMAS (INVASIVE):
   DIFFICULT TO CONTROL THE COMPLETE SELECTIVE RESECTION

4. HIGH RATE OF SURGICAL FAILURES
   REMISSION RATE - 60-90%

5. HIGH RATE OF RECURRENCES
   10-35%
ACTH-adenoma  3134 ng ACTH/mg
Anterior lobe tissue  23 ng ACTH/mg

Direct intraoperative venous sampling (not performed in this case)

Preoperative cavernous sinus sampling (CSS)  53 ng ACTH/L
CHANGES OF PERIPITUIT. ACTH VALUES
GH SECRETION, REGULATION.
GH TERMELŐ ADENÓMA GYERMEKKORBAN GIGANTIZMUST OKOZ.

4 ÉVES ÁTLAGOS TEST ALAKAT ÉS ADENÓMÁS BETEG.
Pierre Marie, 1886 esetleírás; Főleg makroödéma, fejfájás, nyelv nagy, szív nagy tumor, gerincelváltozások, látótér kicsi, csontok nőnek kövérség, mell nagy, tej elv., fogak távol, áll nagy, bőr durva

Szív nő, de a koszorúér nem – szívelégtelenség 50-60 évre
Akromegália és gigantizmus

akromegália

Fogak elkülönülése

Nyelv nagy

Szív nagyobbodás

ásókéz

ujjpercek
Műteti kezelés két ülésben

SZ: 1968.10.1

A betegség kezdete 1997-2002
GH: 46ng/ml. Kezdődő látótérkiesés.

2002-ben paraseptális feltárás parciális eredménnyel

2003- akromegália csökkent de nem eléggé
2002-2005: GH 8-10 ng/ml, gyógyszeres kezelés 4-5 re csökkent, de az IGFI változatlanul magas maradt. A klinikai kép is progreszíált.
2006-ban jobb oldali superciliáris feltárásból a maradék adenómát eltávolítottuk

2007 aug.
GH: 0,3, IGFI norm.
GH termelő adenóma acromegáliát okoz
SURGERY OF GH-SECRETING ADENOMAS

- **SURGERY**: PRIMARY TREATMENT OF CHOICE
- LOWER GH LEVELS, SMALLER TUMORS, BEST SURGICAL RESULTS, 80% REMISSION RATE
- MACROADENOMAS: 50-60% BIOCHEMICAL REMISSION (RANDOM GH < 2.5 NG/ML, OGT < 1 NG/ML, NORM IGF-1)
- **COMBINED TREATMENT**: 87%
- CURED? TARGET OR SAFE GH LEVEL
GH secreting adenomas (literature)

- Tindall GT. et al., 93, J Neurosurgery, 103 cases, less than 5 microgram/L, 81%.
- Lüdecke DK., 99, Clin Endocr., intraop. hormone measurement, 78 cases, makroadenomas 88%, micro 92%, (invasive adenomas excluded).
- Lisett CA. 98, Clin Endocr. 73 cases, 5mU/l, micro: 39%, macro: 12%!
- Abash (Wilson CB) 254 cases, 5 microgr./L, within 30 days 76% remission, later 7% recurrence.
- Falbush R., 97 J Endocr., 531 cases, 5 microgr./L, 73% remission, after irradi. th and repeated op 41%,
## PROLACTIN-PROLACTINOMA

<table>
<thead>
<tr>
<th>Szerkezet:</th>
<th>peptid 198 aminosav</th>
</tr>
</thead>
<tbody>
<tr>
<td>hatás:</td>
<td>laktáció</td>
</tr>
<tr>
<td></td>
<td>(ösztrogén, gesztagének, inzulin, kortikoszteroid)</td>
</tr>
<tr>
<td></td>
<td>anyai ösztön, GH szerû hatás</td>
</tr>
<tr>
<td></td>
<td>csak emberben nő a szint terhességnél</td>
</tr>
<tr>
<td>Gátolja:</td>
<td>histamin, GABA, PIF, T4, T3, endothelin, glükokortikoidok</td>
</tr>
<tr>
<td>Serkenti:</td>
<td>DA, NA, Ach, ösztrogén, VIP, stressz, 5HT, TRH, GnRH</td>
</tr>
<tr>
<td></td>
<td>inzulin, alvás</td>
</tr>
<tr>
<td>Betegségek:</td>
<td></td>
</tr>
<tr>
<td><strong>PRL kevés:</strong></td>
<td>nem tud szoptatni</td>
</tr>
<tr>
<td><strong>sok:</strong></td>
<td>nő: meddőség,</td>
</tr>
<tr>
<td></td>
<td>ffi: impotencia</td>
</tr>
</tbody>
</table>
PRL-REGULATION
Diagnosis and treatment of pituitary apoplexy (1)

Pituitary apoplexy is defined as a clinical syndrome that may include headache, visual deficits, ophthalmoplegia, or altered mental status. It may result from either infarction or hemorrhage of the pituitary gland. Prognosis is significantly improved with early diagnosis and surgical treatment. Our case in which diffusion-weighted MR imaging assisted in the early detection of acute pituitary infarction and led, to surgical intervention early in the course of clinical apoplexy, with resulting complete recovery.
A 57-year-old man with a medical history of hypertension and hypercholesterolemia presented with sudden-onset blurred vision in the right eye that he described as being like "a curtain coming up" over the eye. This was initially associated with headache and nausea, but symptoms had partially resolved by the time the patient arrived at the emergency department. He denied paresthesias or weakness. A physical examination revealed an inferior temporal quadrantopsia but otherwise normal physical and neurologic results. The next morning, the patient’s vision was stable, and elective resection of the pituitary tumor was planned. That afternoon, the patient reported sudden complete vision loss in the left eye. He was immediately taken to surgery, where transphenoidal resection of a pituitary macroadenoma was performed. Histologic analysis revealed the presence of a necrotic pituitary adenoma with hemorrhage. Immediately after surgery, light perception returned to the left eye with 20/40 vision in the right eye. The patient developed mild adrenal and thyroid insufficiency, requiring hormonal replacement. He was eventually discharged home with a persistent but slowly improving left eye visual defect.
A, Nonenhanced CT scan shows a homogeneous, nonhemorrhagic, hypodense intrasellar mass.

B, Coronal spin-echo T1-weighted MR image (500/20 [TR/TE]) shows a large homogeneous intrasellar mass that compresses the optic chiasm, consistent with a nonhemorrhagic macroadenoma.

C, Coronal spin-echo T1-weighted MR image (500/20) shows no change after the administration of contrast medium (0.05 mmol/kg).

D, Tensor diffusion-weighted MR image (b = 1000 mm²/s) shows markedly increased signal intensity (arrow) within the pituitary mass, compared with that in normal gray and white matter.

E, ADC map shows markedly decreased signal intensity within the pituitary mass; mean ADC was 0.49 (10–3 mm²/s).

Diagnosis and treatment of pituitary apoplexy(3)