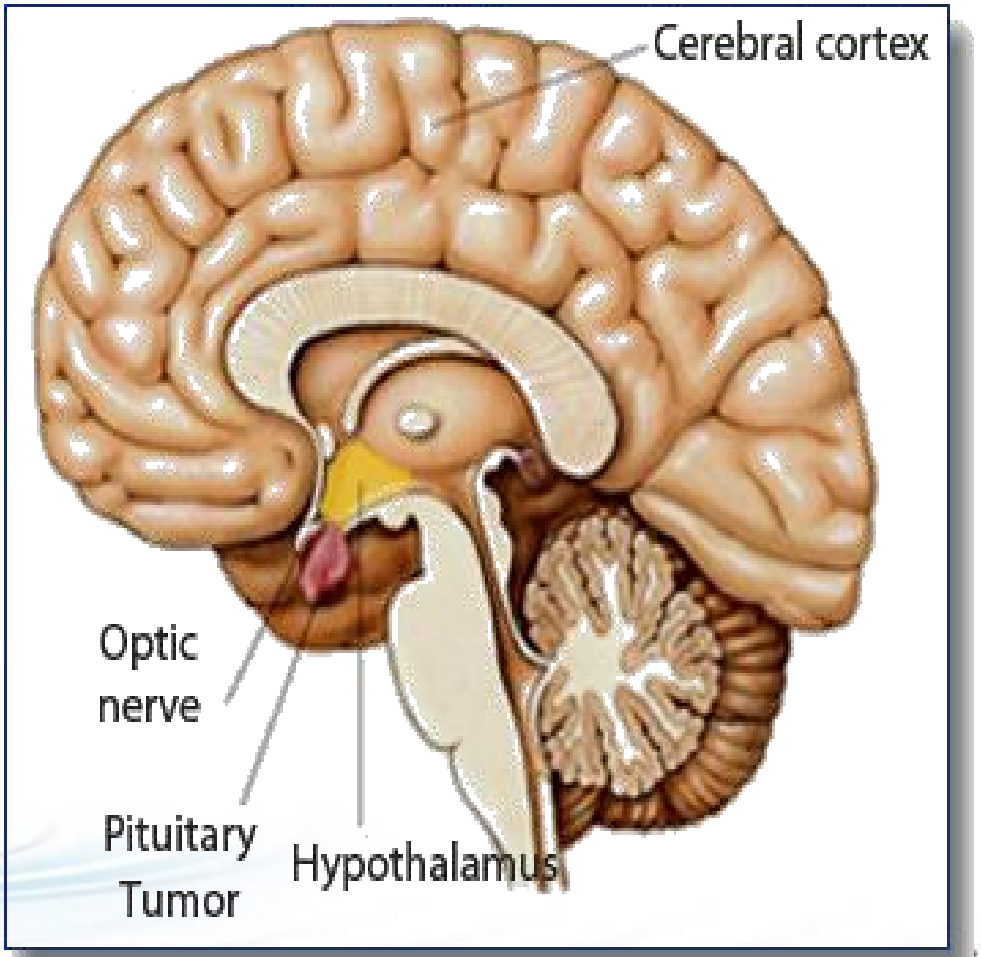
Pituitary Tumour
垂体瘤

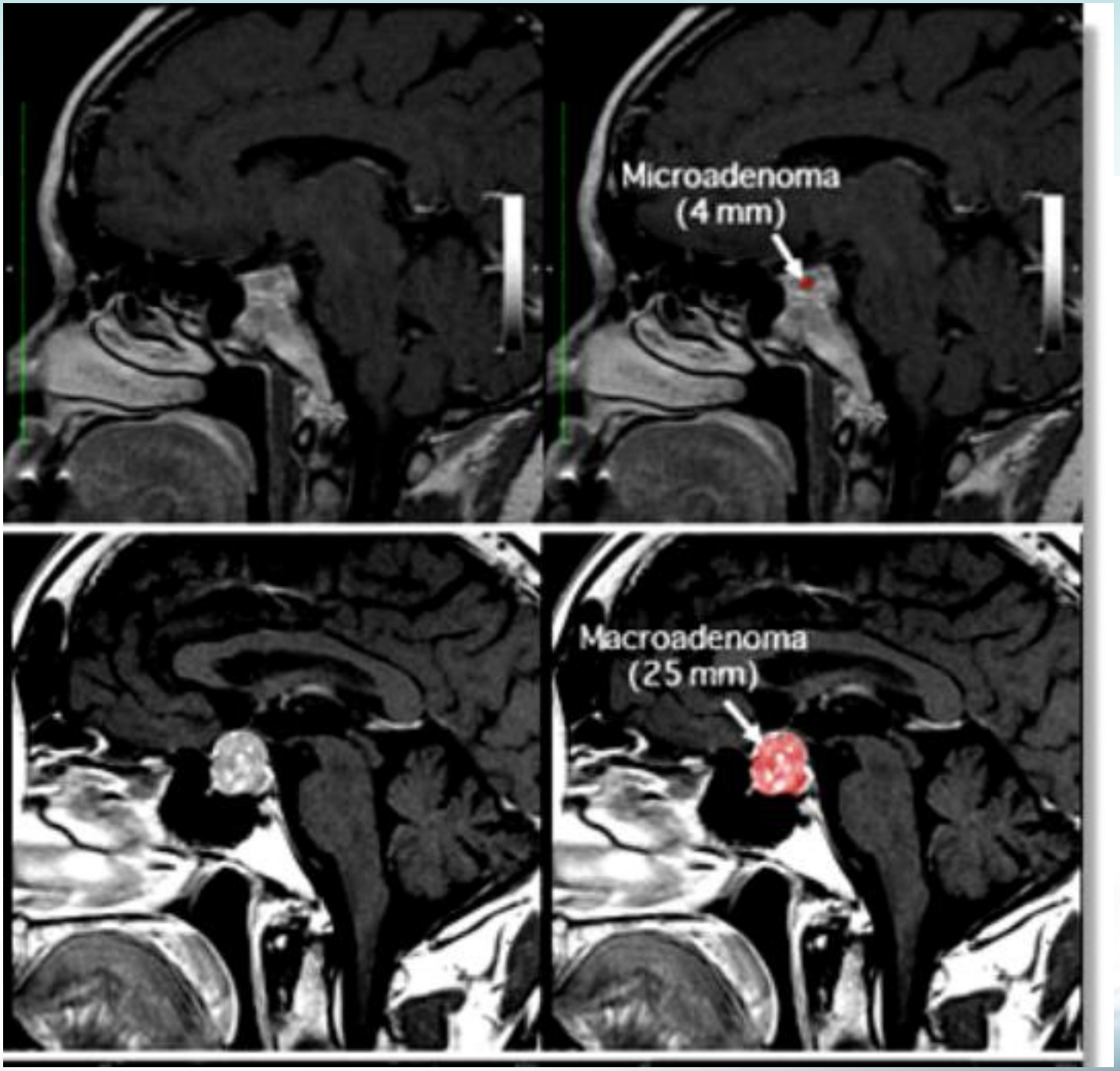
General Information概述

- Pituitary adenomas are typically benign, slow-growing tumors
- Pituitary adenomas are approximately 15% of primary brain tumors.
- Pituitary adenomas can invade adjacent structures (**cavernous sinus海绵窦**)
- Pituitary adenomas have separate names based on their size：

A microadenoma 微腺瘤< 1 cm

A macroadenoma大腺瘤 > 1 cm





side-view MRI

***Microadenoma*:**
cushing disease
Patient 1

***Macropituitary adenoma*:**
patient 2

side-view MRI

Macropituitary adenoma：patient 3

- Most pituitary adenomas occur spontaneously, not inherited.
- Cases of familial pituitary tumorsare rare.
- **Multiple Endocrine Neoplasia type 1** (MEN 1) is a rare condition characterized by simultaneous tumors of the pituitary, pancreas and parathyroid glands. **多发性内分泌腺病1型**

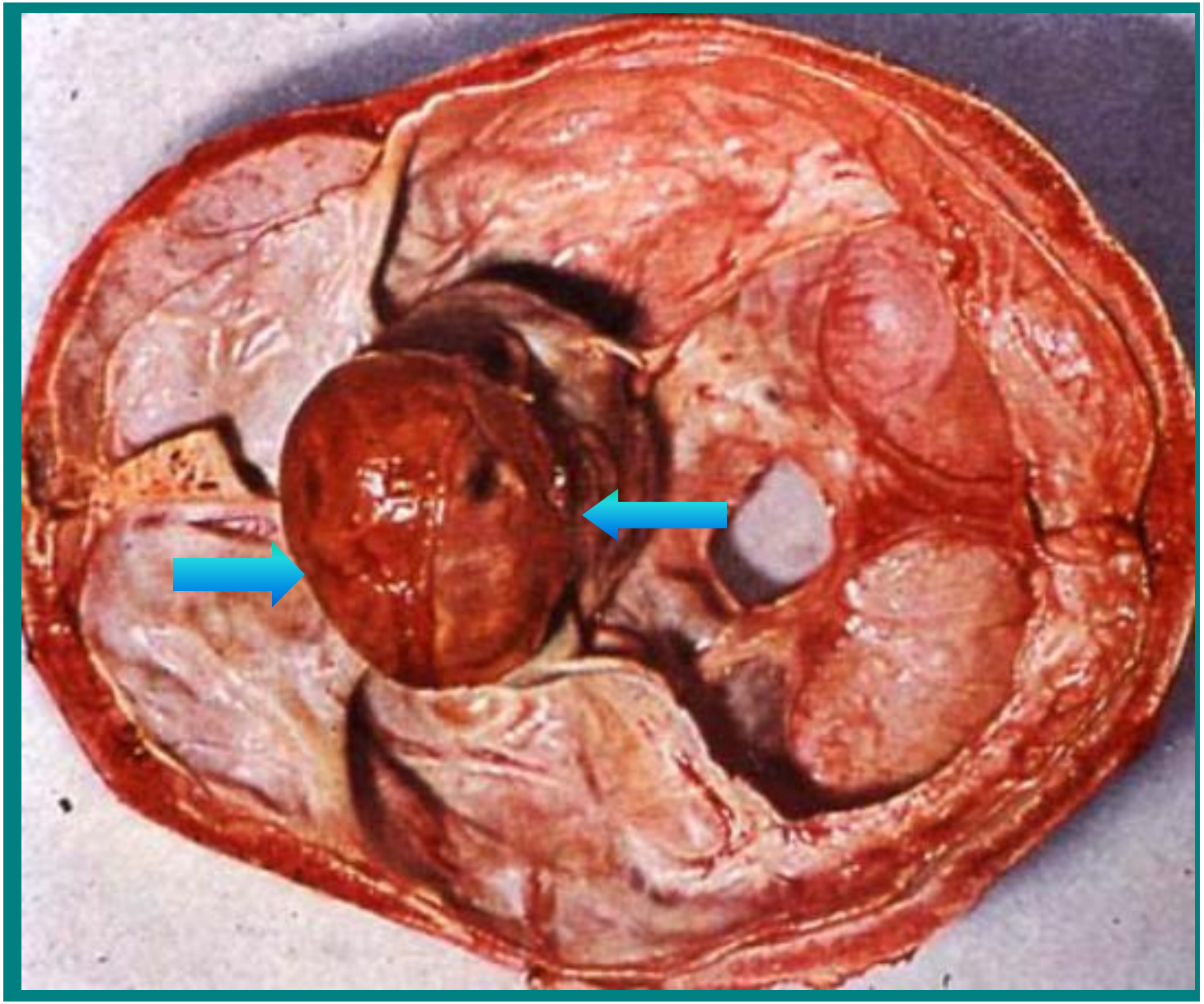


Fig:

Large pituitary tumour

图：

巨大的垂体瘤

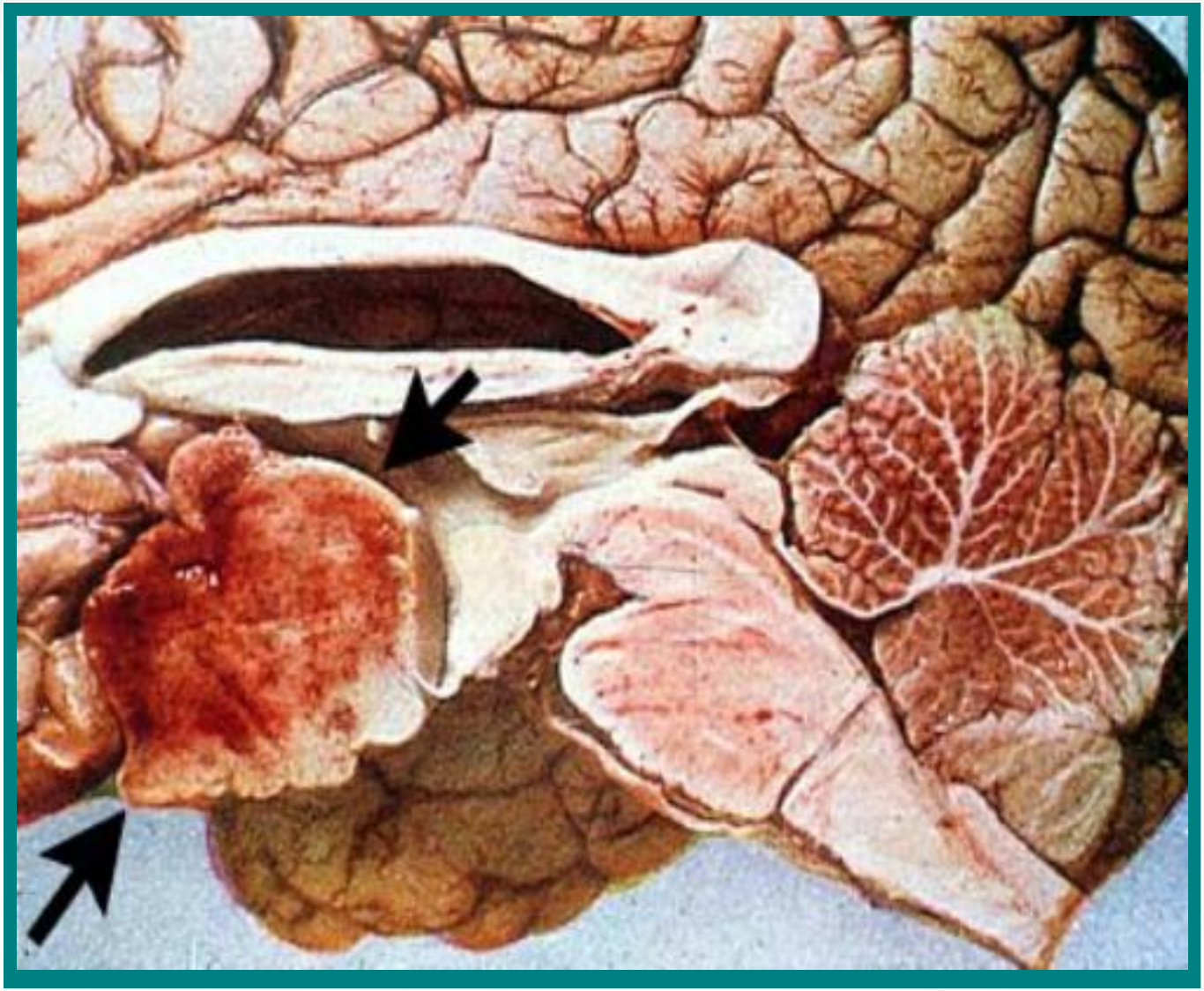


Fig:

Large pituitary craniopharyngioma duct tumor

图：

巨大的垂体颅咽管瘤

Symptoms Caused by Pituitary Adenomas

◆Pituitary adenomas are generally thought of as either hormone-producing or hormone-inactive tumors

1.Hormone-producing pituitary adenomas produce an active hormone in excessive amounts.

2.Hormone-inactive (non-functional) pituitary adenomas typically cause problems related to the size of the tumor

Symptoms Caused by Pituitary Adenomas

◆**Hormone-producing pituitary adenomas 激素分泌型垂体腺瘤**

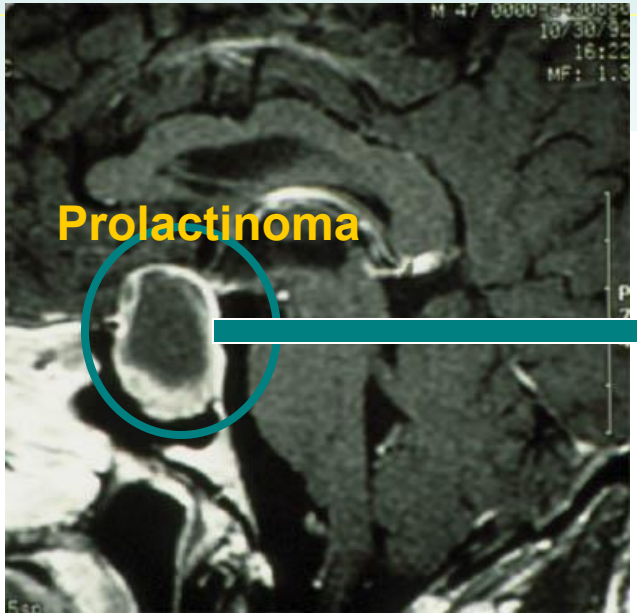
The three most common hormone-producing adenomas are:

***1.* Prolactinoma泌乳素瘤:** causes loss of menstrual periods and breast milk production in women.

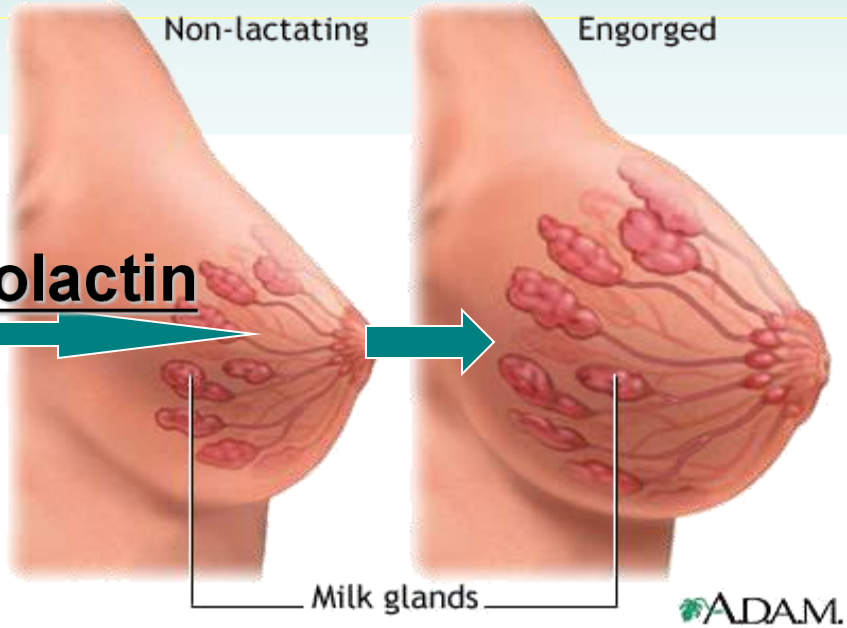
2. Growth hormone-secreting pituitary adenoma生长激素瘤: excessive **growth hormone** (GH) production causes acromegaly in adults or gigantism in children.

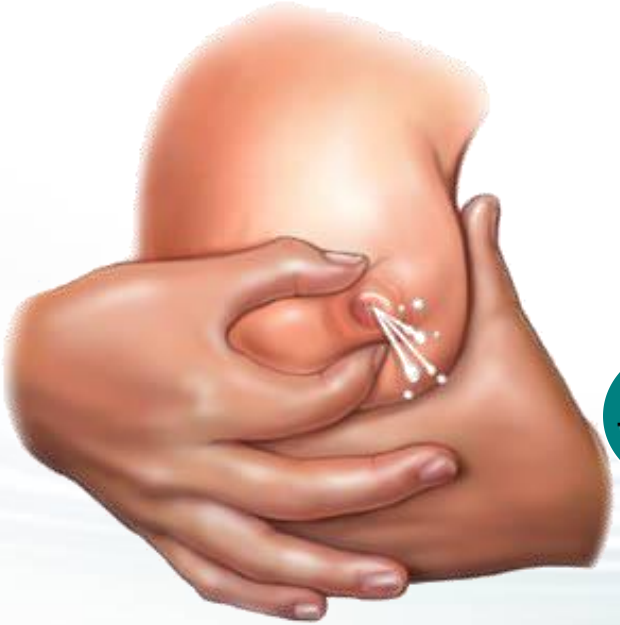
3. ACTH-secreting pituitary adenoma: excessive **ACTH** hormone produced by the pituitary gland causes **Cushing's disease库欣氏病**.

4.Other tumors are very rare： TSH producing Adenoma



prolactin





溢乳

Galactorrhea

milk

Fig: the height of giantism kid and adult巨人症患者

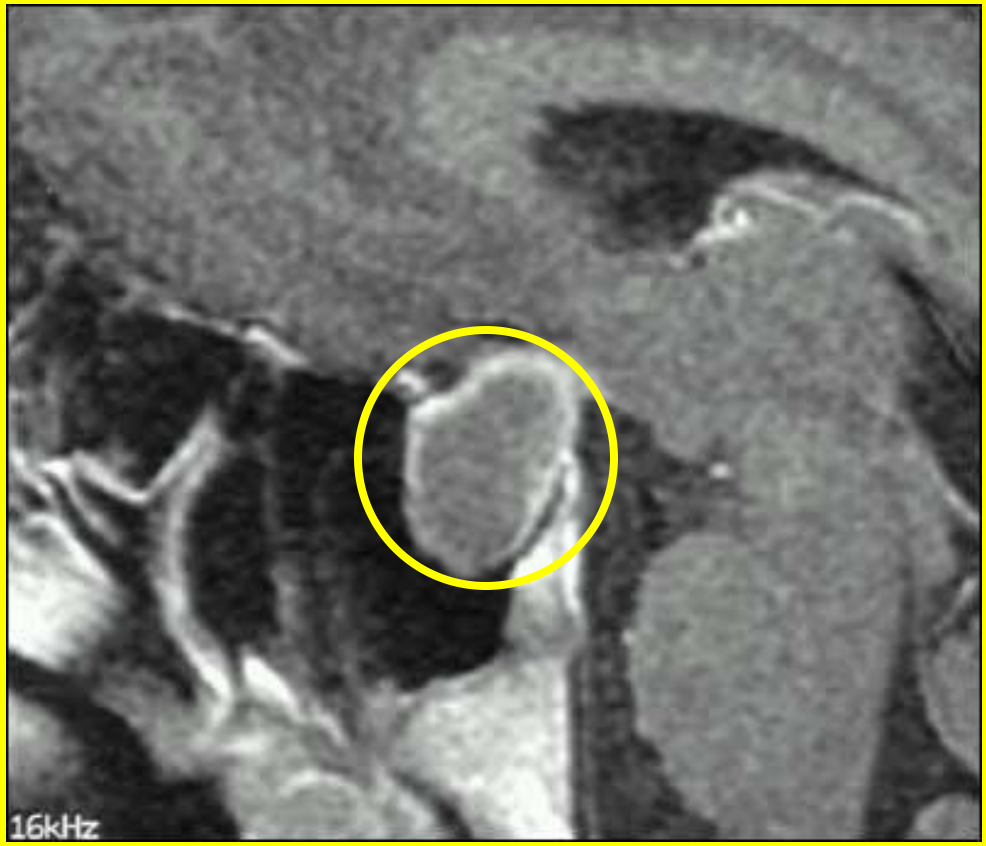


Fig: MRI of gangtic GH pituitary tumour

图：巨大的生长激素瘤MRI

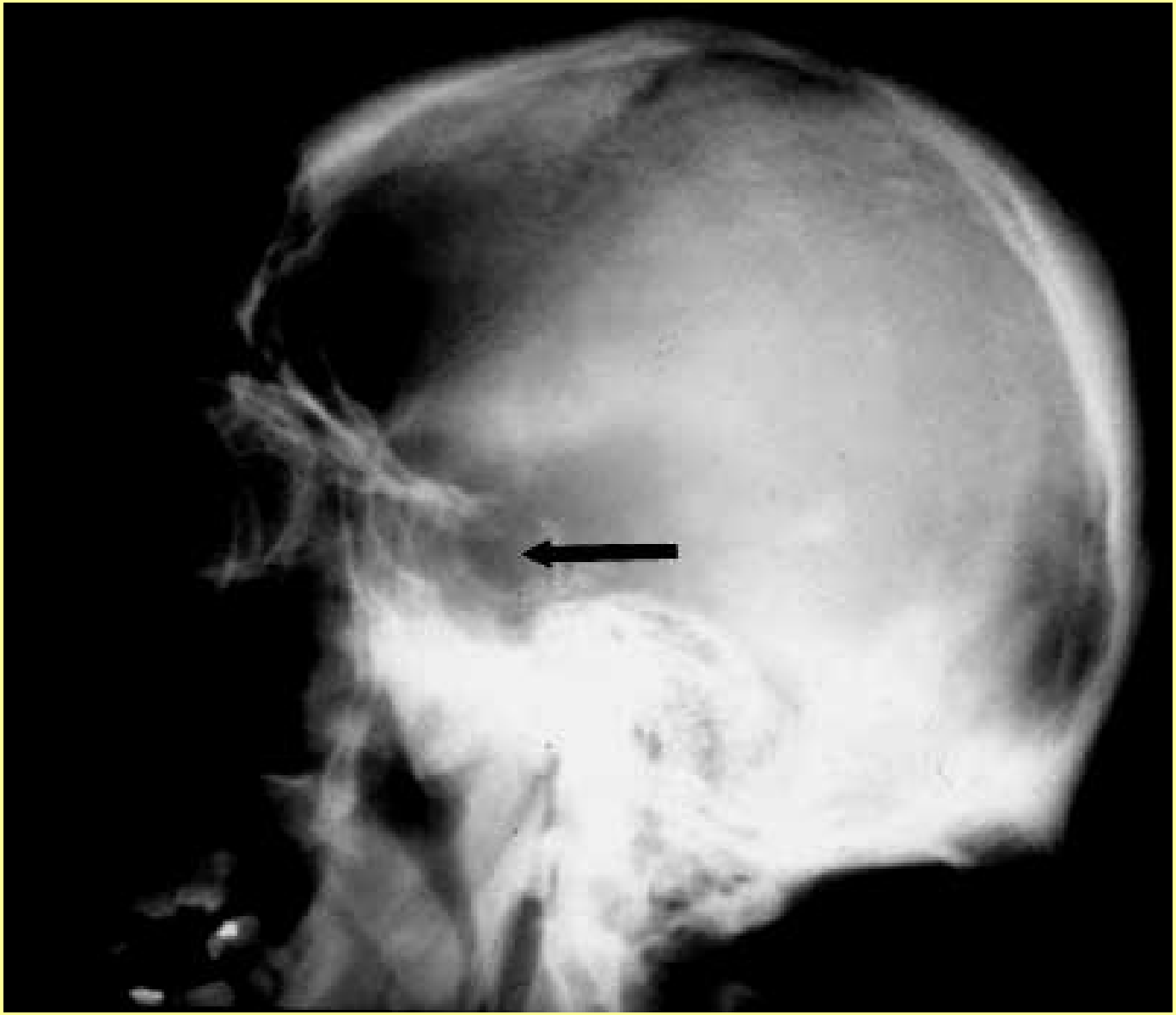
Fig: contrast of two hands

图：手掌对比（和正常人比较）

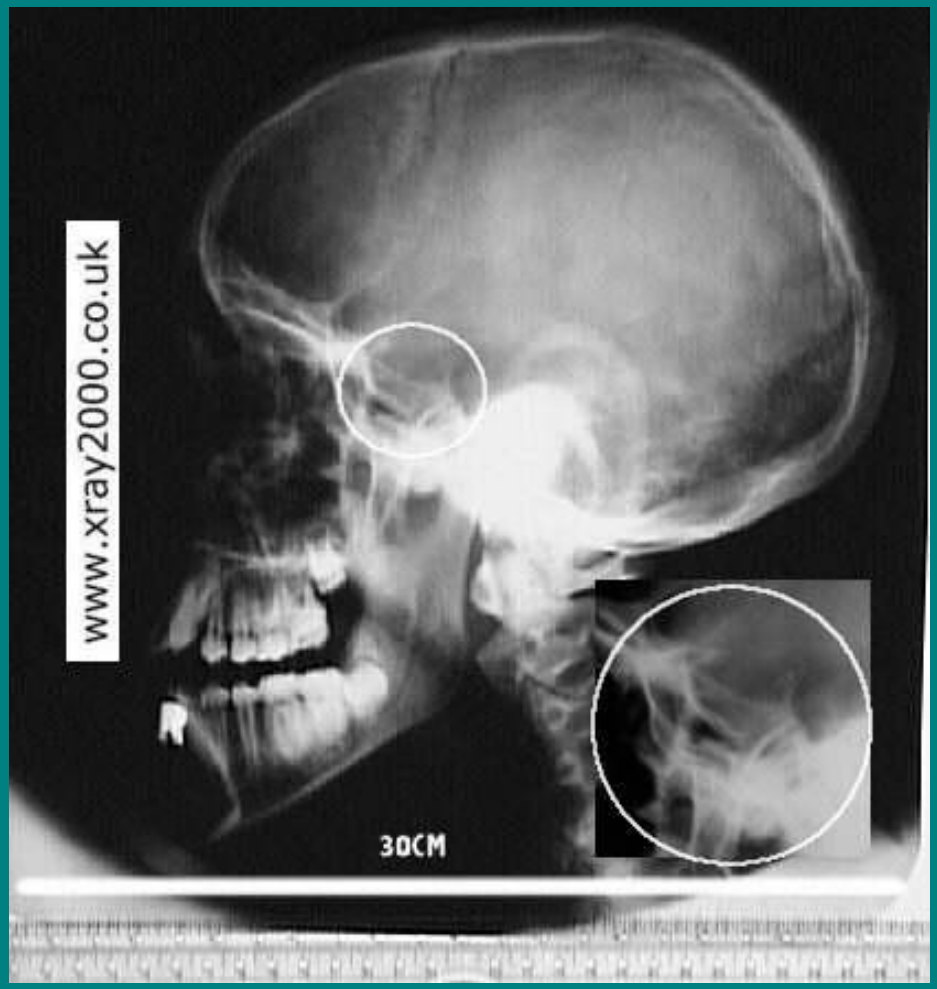
Fig:

Hands of a patient with acromegaly

图：肢端肥大症患者手掌



图：垂体瘤患者头颅X光片



fig：x-ray of skull and fingers of a patient with acromegaly

肢端肥大症患者头颅及手指x线摄片

肢端肥大症 Acromegaly
16 yrs
25 yrs
44 yrs

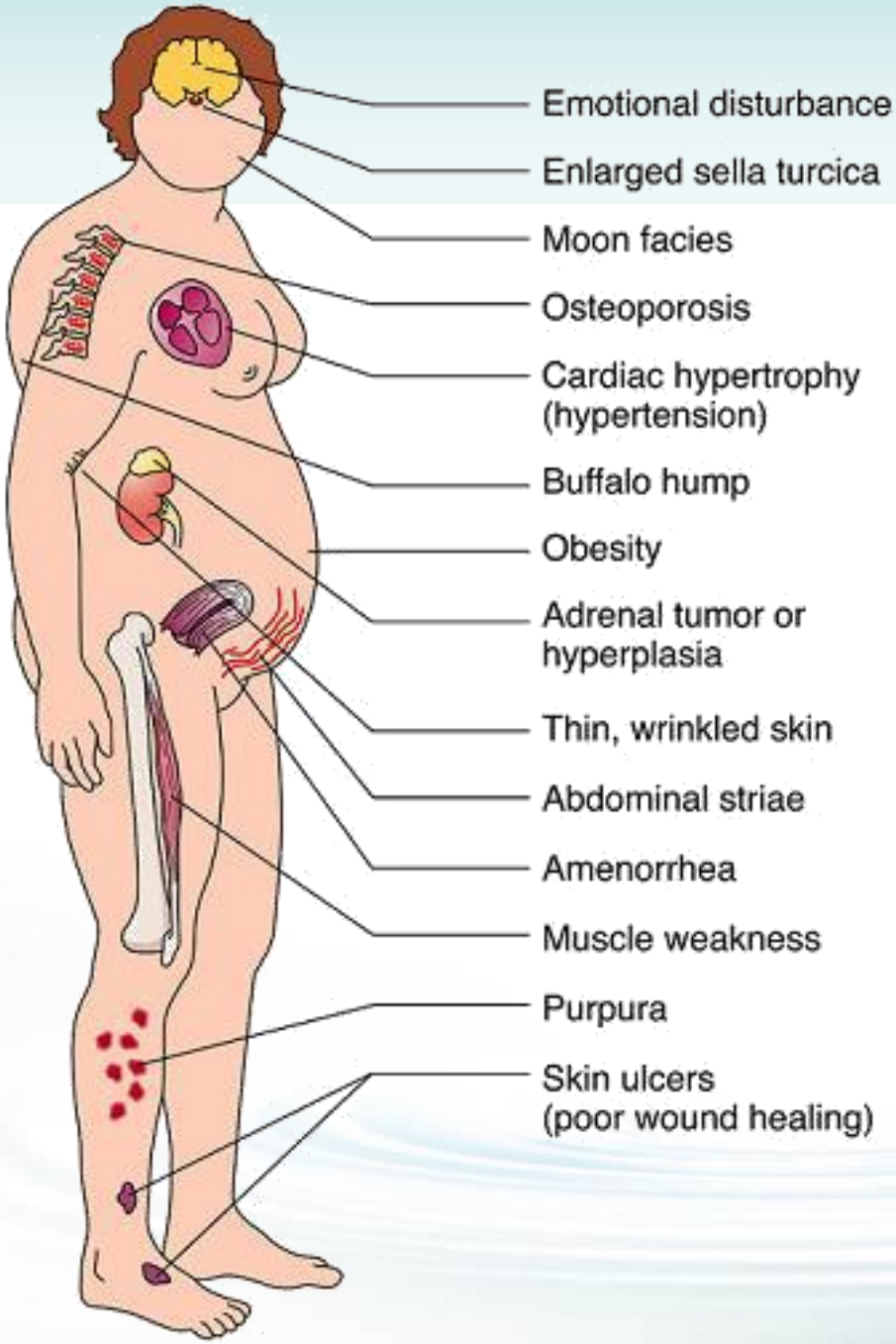

Emotional disturbance
Enlarged sella turcica
Moon facies
Osteoporosis
Cardiac hypertrophy
(hypertension)
Buffalo hump
Obesity
Adrenal tumor or
hyperplasia
Thin, wrinkled skin
Abdominal striae
Amenorrhea
Muscle weakness
Purpura
Skin ulcers
(poor wound healing)

Fig:Central Obesity

向心性肥胖

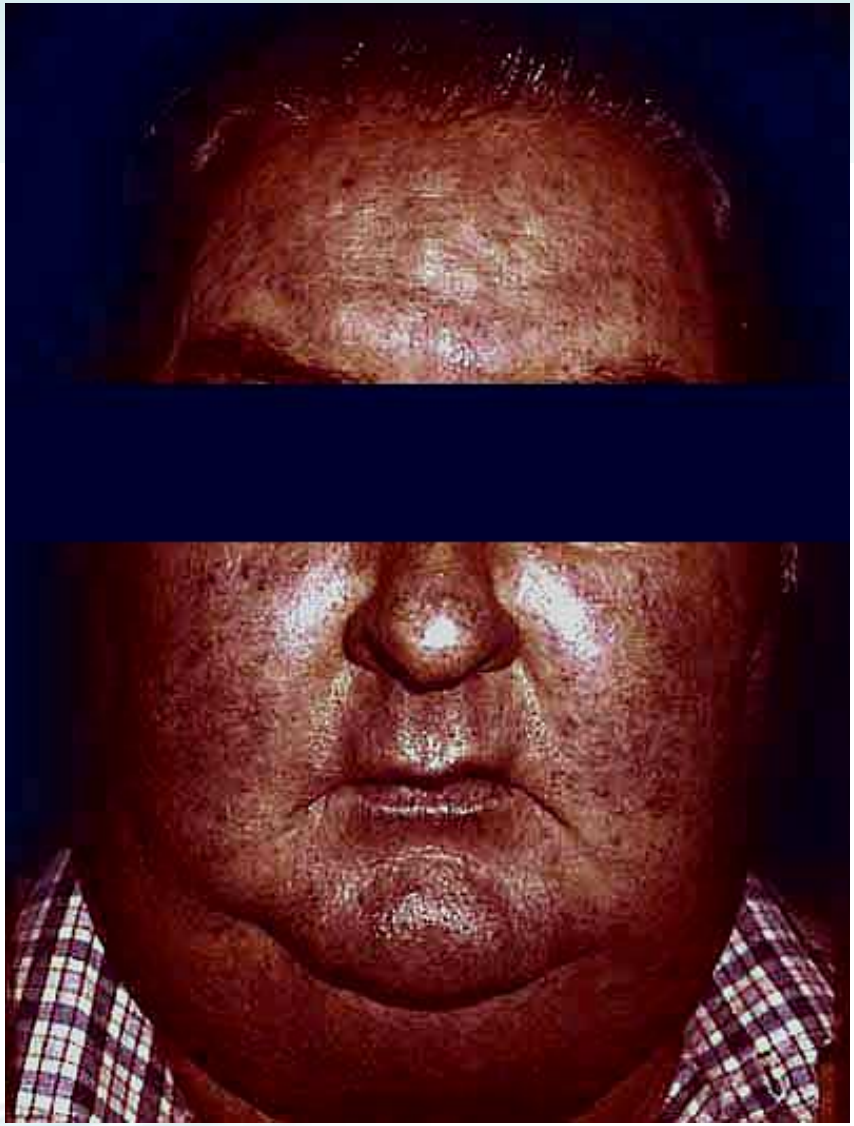


Fig: Moon Face 满月脸

Symptoms Caused by Pituitary Adenomas

◆**Symptoms related to the mass effect from Macroadenomas**
大腺瘤的压迫症状

1.Visual Loss :compress the **optic chiasm视交叉.**

A progressive loss of the outer peripheral vision occurs (called a "**bitemporal hemianopsia**"颞侧偏盲)

Loss of visual acuity (blurry vision), Changes in color perception

2.Pituitary Failure （垂体功能减退）

Compression of the normal pituitary gland can lead to **hypopituitarism :** Symptoms can include:

- **Sexual dysfunction**
- **Inadequate cortisol** causing low blood pressure, fatigue, and inability to handle stressful situations
- **hypothyroidism**：Low thyroid functioning

Symptoms Caused by Pituitary Adenomas

◆**Symptoms related to the mass effect from Macroadenomas**

3.The "Stalk Effect"

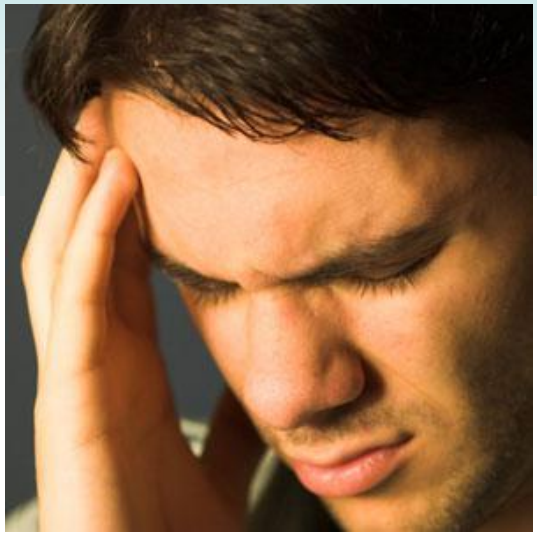
cause a mild elevation in the hormone prolactin. ---- irregular menstrual periods.

4.Headache

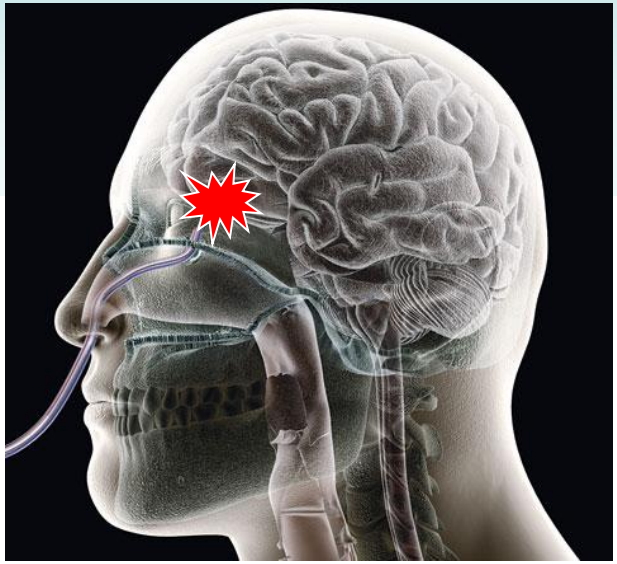
5.Pituitary Apoplexy

generally presents with sudden onset headache and visual loss, and is a surgical emergency

Visual loss 视野缺损



Headache



pituitary apoplexy
垂体卒中

Symptoms

Gynecomastia
男子女性型乳房

low libido性欲低下

Diagnosis诊断

The diagnosis of a pituitary adenoma is made based as follows：

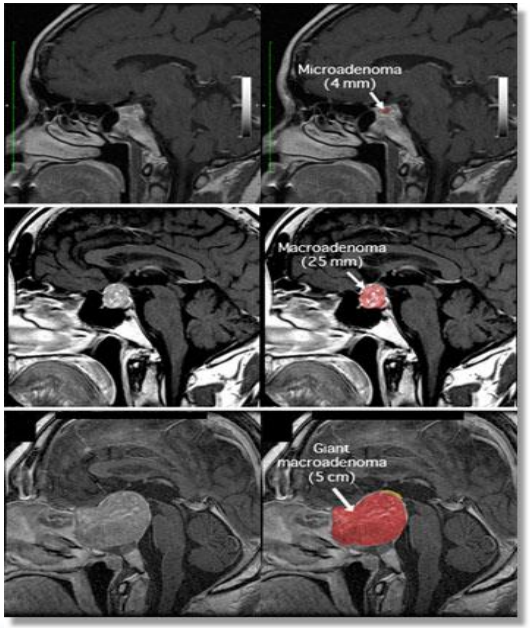
1.Pituitary Function Testing： 内分泌激素测定

2.Imaging： 首选MRI

- Adenomas larger than 4 mm can be reliably detected by MRI scans
- MRI scan is preferred to computed tomography

Pituitary Hormone test

MRI



Treatment 治疗

The optimal treatment depends on multiple factors:

- Hormone production by the tumor (if present)
- Size of the tumor
- How invasive the tumor is into surrounding structures
- The age and health of the patient

Typically, more than one specialist is involved in the management of pituitary adenomas.

Treatment 治疗

1.Medical therapy 内科治疗：Endocrinologist needed！！！

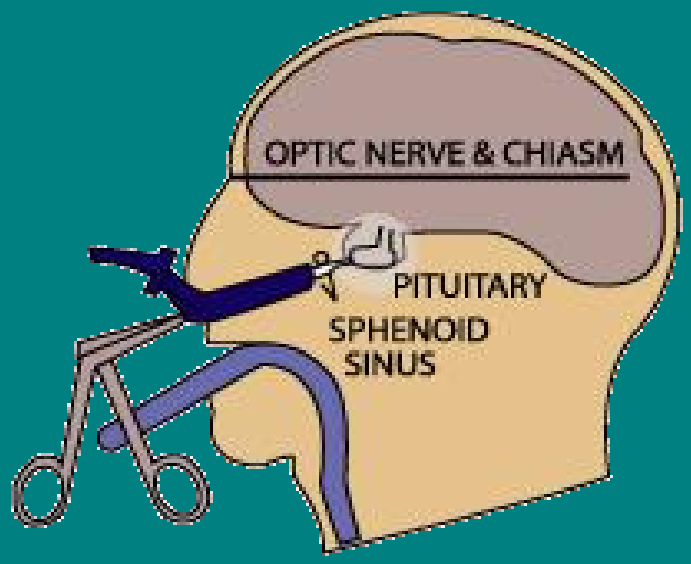
●**For example：a.Cabergoline 卡麦角林**(Dostinex) and **Bromocriptine溴隐亭** (Parlodel) is the first line**一线治疗** of treatment for patients with a **prolactinoma泌乳素瘤**；**b.**Medical therapy can play an important role in the management of **Cushing's disease** and **acromegaly肢端肥大症**. C. **hypopituitarism 垂体功能低下**

Treatment 治疗

2.Surgery 手术治疗

●The vast majority of pituitary adenomas that require surgery are best removed through the nose.

●Urgent **transphenoidal经蝶骨surgery** is advised for pituitary apoplexy.

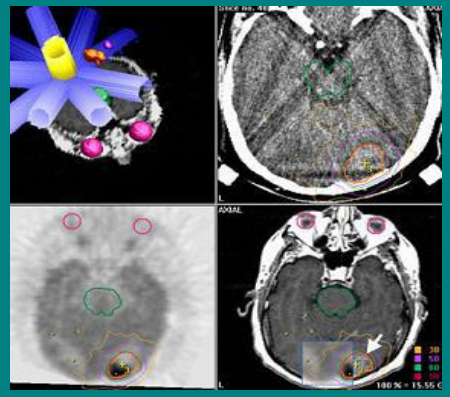


Treatment 治疗

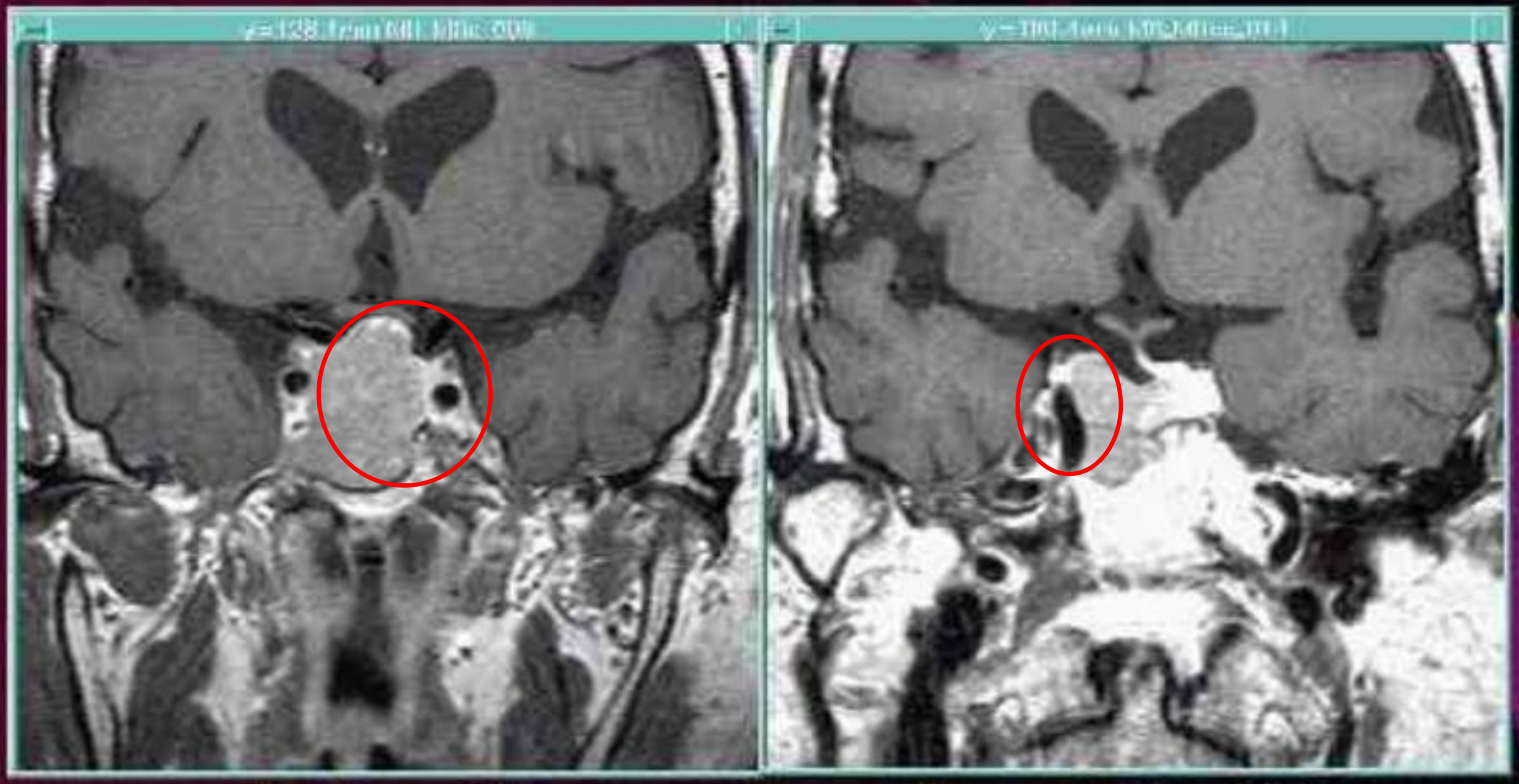
3.Radiotherapy 放射治疗

●**Stereotactic radiotherapy** is a technique in which a high dose of radiation can be delivered to the tumor target.

●Radiation therapy is typically reserved for pituitary tumors that cannot be cured surgically and are not controlled with medical drug therapy



Large Pituitary NF Adenoma



Before GK

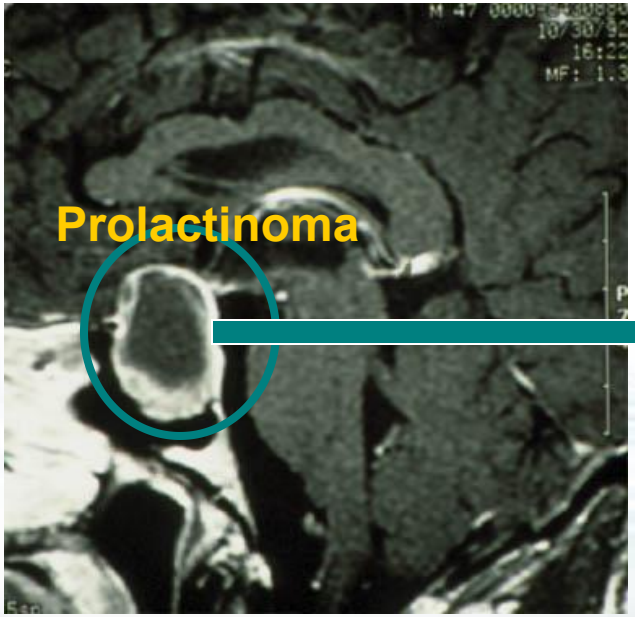
1 year after GK

Prolactinoma

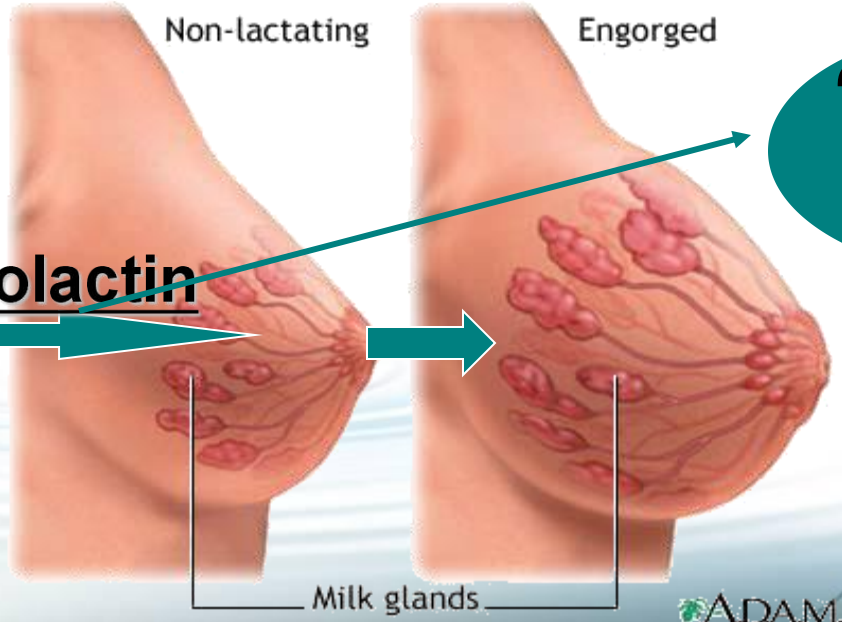
泌乳素瘤

General Information概述

- This type of pituitary tumor (adenoma) produces an excessive amount of the hormone prolactin.
- Prolactinomas are the most common type of hormonally-active pituitary tumor.

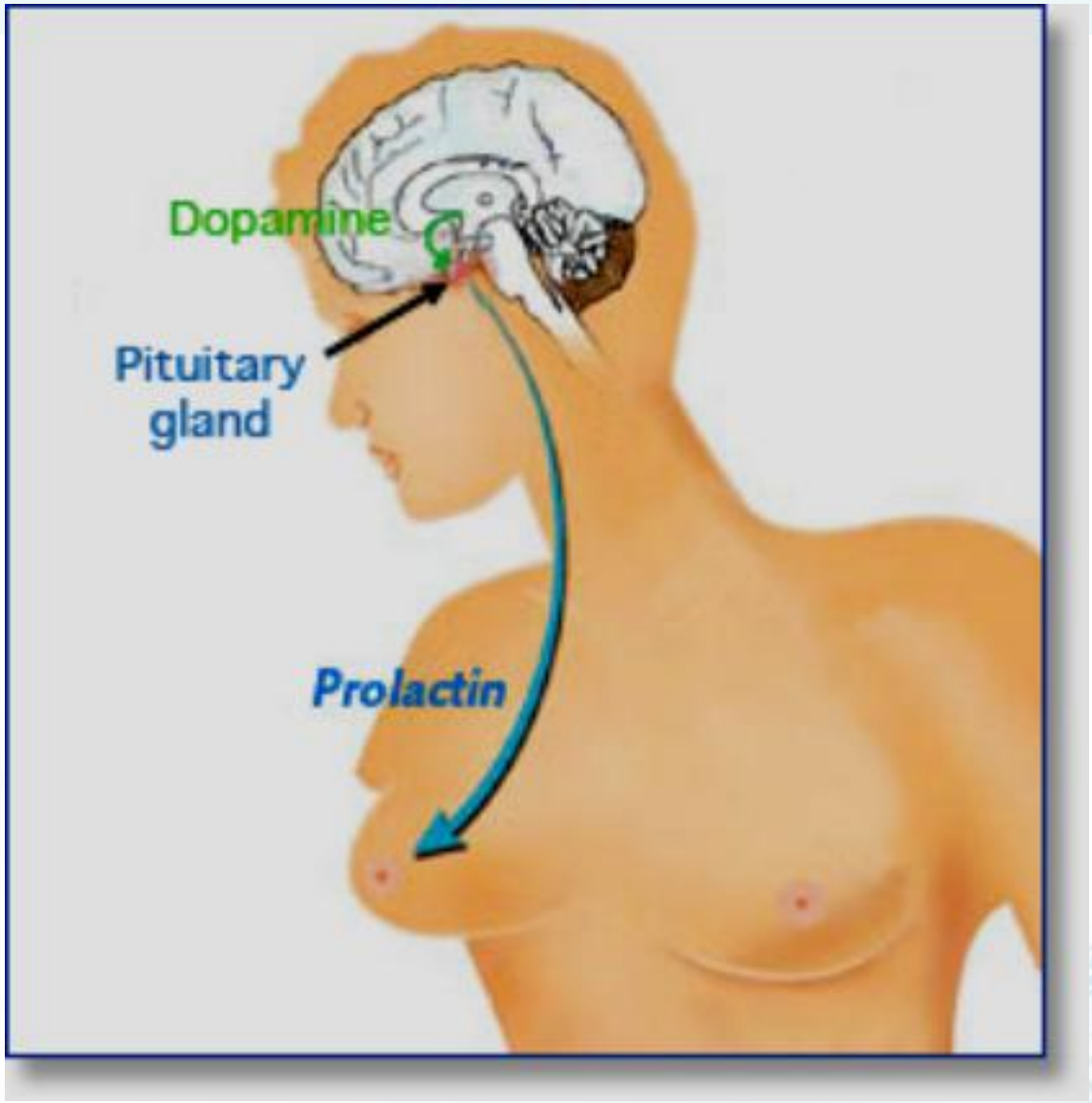


prolactin



? other

milk



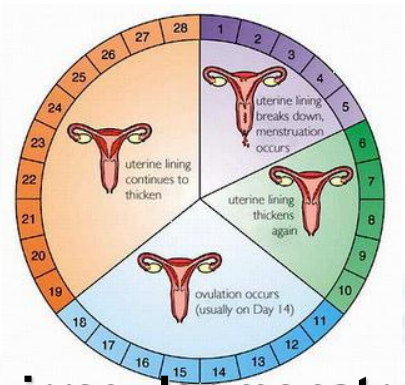
◆Prolactin is a hormone essential for milk production by the breast. The release of prolactin is controlled by the amount of dopamine produced by the brain

What is Prolactin?
什么是泌乳素？

1.Prolactin is a hormone produced by the pituitary gland
2.At the end of pregnancy, the pituitary producing more prolactin.
3.This important hormone causes several body changes:
■Breast milk is produced (“**galactorrhea**”溢乳)
■Menstrual periods are stopped (“amenorrhea”闭经)
■Sexual interest (libido性欲) is decreased
4.The brain controls the amount of prolactin production with dopamine多巴胺 .(the more dopamine, the less prolactin that is made.)

Symptoms症状:In women

- ◆small increases in prolactin cause **irregular menstrual** periods or complete loss of menses. ----So, discovered early.
- ◆higher prolactin levels----- there is **milk** production by the breasts
- ◆complain of a reduced sex drive
- ◆Large prolactinomas may cause hypopituitarism, visual loss, and headache (see also in men)



irregular menstrual
月经失调

Galactorrhea
溢乳

headache

Libido Decreased
性欲

Symptoms:In men

■Symptoms are usually caused as a result of the **size** of the tumor

■In some cases, men experience enlargement of the breast tissue (**gynecomastia男子女性型乳房**)

■Large pituitary tumors (**macroadenomas大腺瘤**) may cause:

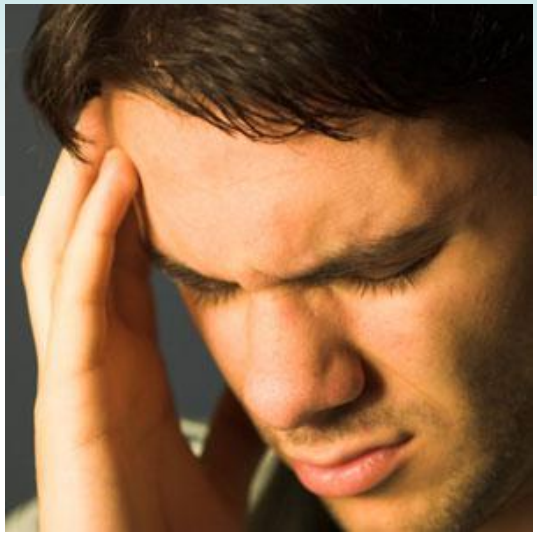
1.**Hypopituitarism**（most cases: **low libido性欲低下**).

2.**Visual loss 视野缺损** from compression of the optic nerves.

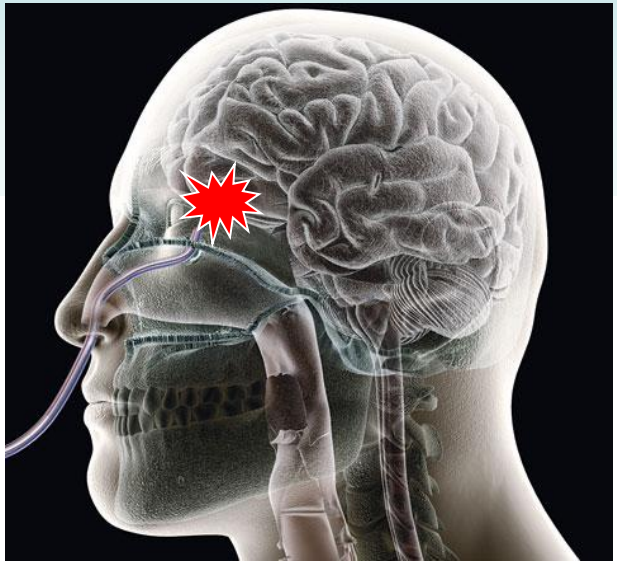
3.**Headache**

4.**pituitary apoplexy（垂体卒中）**

Visual loss 视野缺损



Headache



pituitary apoplexy
垂体卒中

Symptoms:In men

Gynecomastia
男子女性型乳房

low libido性欲低下

Diagnosis诊断

1.Hormonal test 激素检测 and symptom症状：

measuring the level of prolactin （usually more than 300ug/L）

2.Other possible causes include:

- Pregnancy 妊娠
- Stress 应激
- Low thyroid function 甲减
- Kidney failure 肾衰
- Liver failure 肝衰
- A large other tumor occuring in the same area (prolactin levels are usually less than 200ug/L)

3.prolactin level is usually proportional to the size of the tumor.

- Large tumors may have prolactin levels in the thousands
- In some cases, very high prolactin levels can be test again with a diluted sample

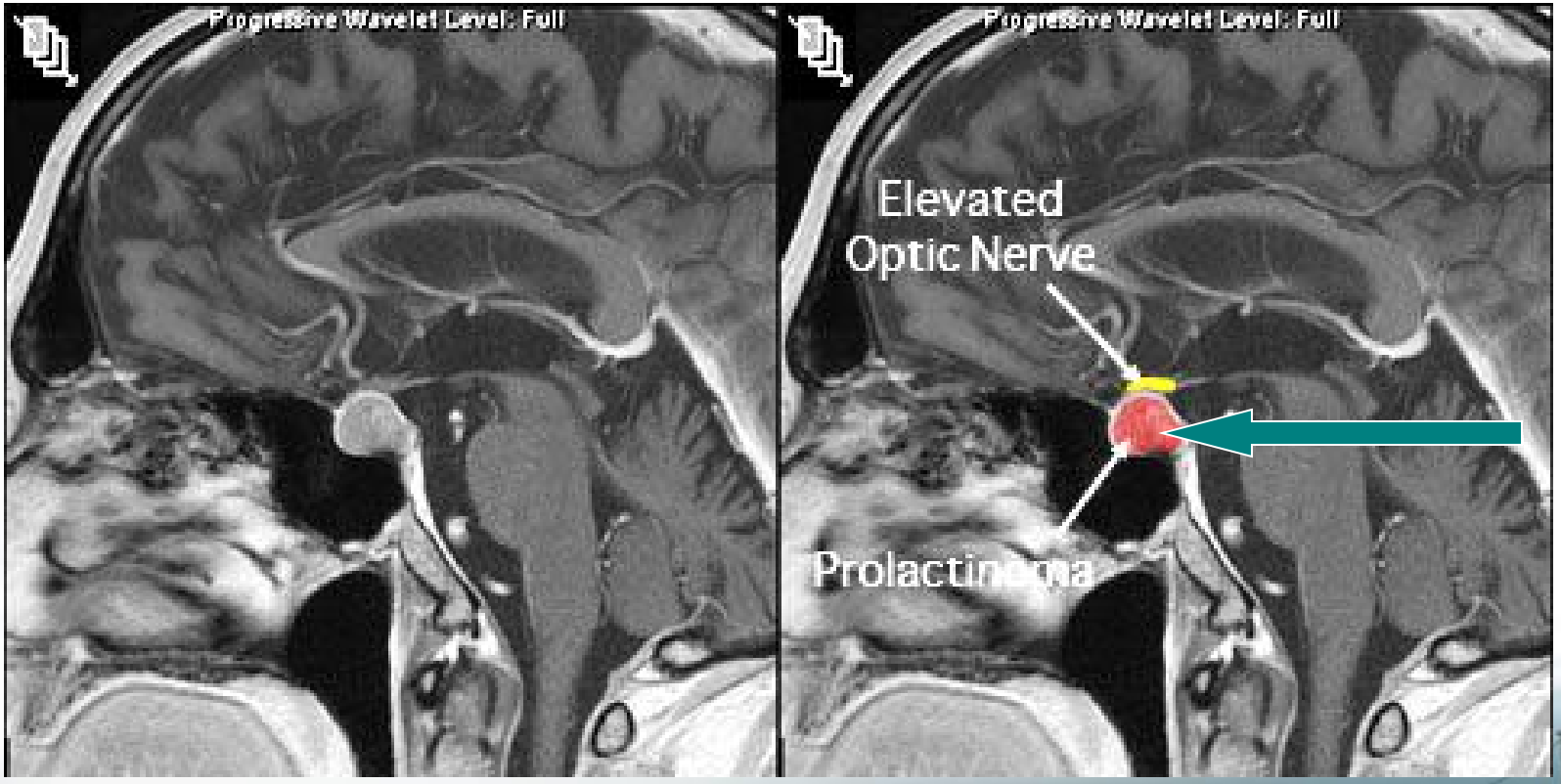
Diagnosis诊断

4.MRI Imaging 磁共振影像

◆Most prolactinomas can be detected using MRI

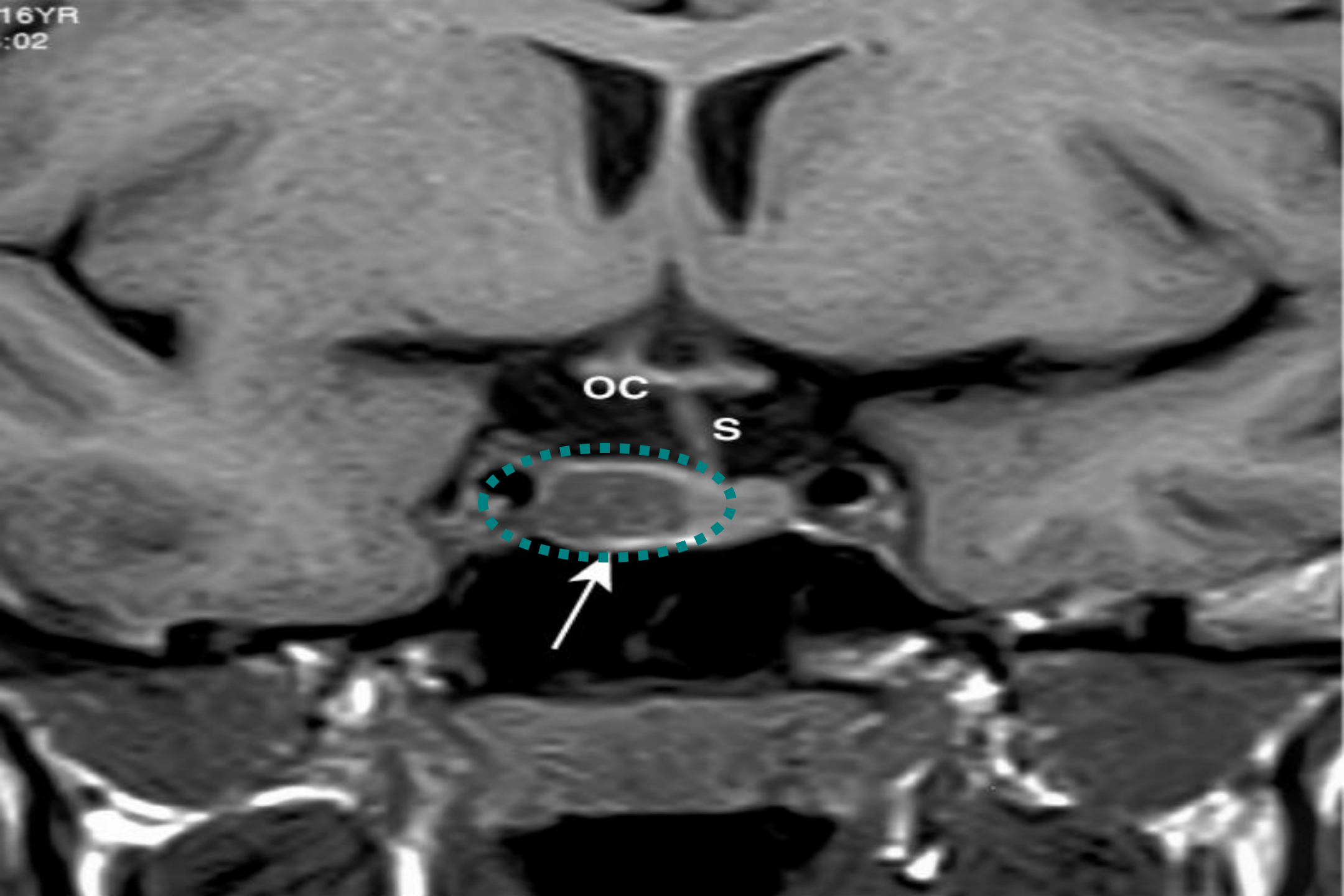
◆It is best to obtain a special MRI "Pituitary Protocol" in order to best visualize the tumor

◆ Smaller tumors may not be visible using computed tomography (CT) scans



Prolactinoma

泌乳素瘤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Treatment 治疗

1.Medical therapy 内科治疗

●In general, the first line一线治疗 of treatment for patients with a prolactinoma is medical rather than surgical.

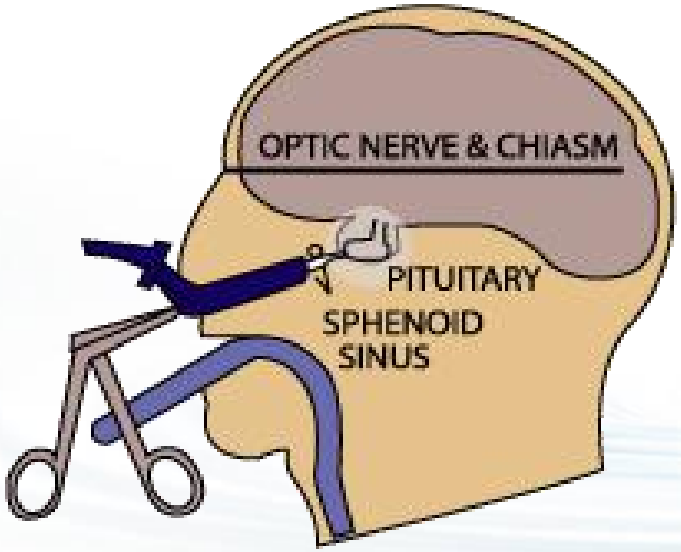
●**Cabergoline 卡麦角林**(Dostinex) is usually the preferred medication **Bromocriptine溴隐亭** (Parlodel) is sometimes used,

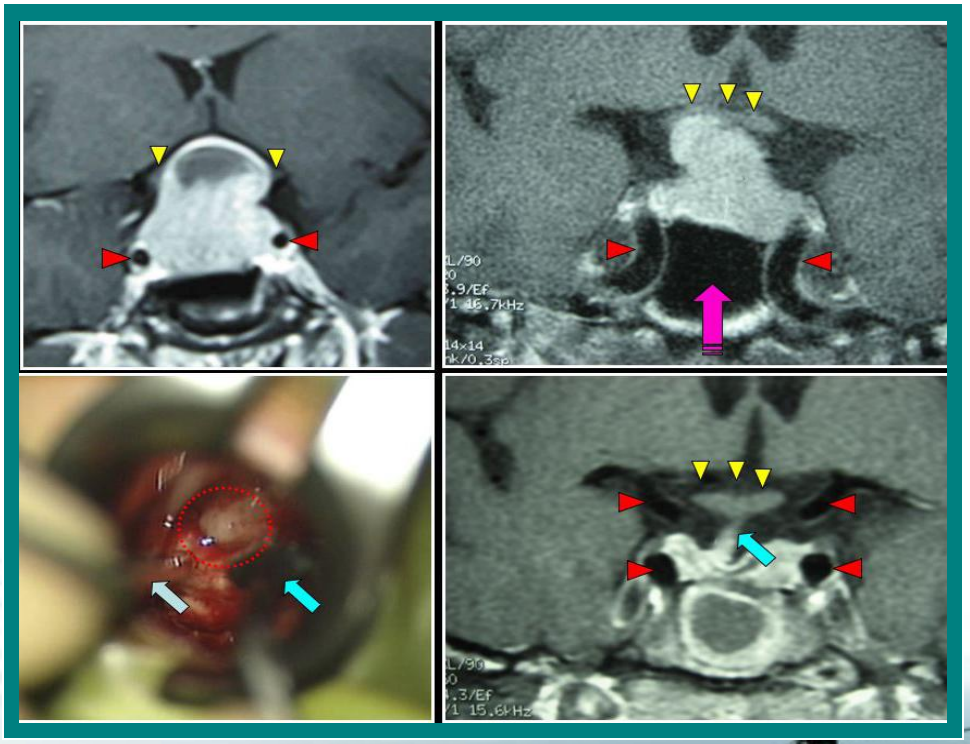
Treatment 治疗

2.Surgery 手术治疗

●For patients that do not respond to medical treatment with cabergoline or bromocriptine

●Urgent **transphenoidal经蝶骨surgery** is advised for pituitary apoplexy.





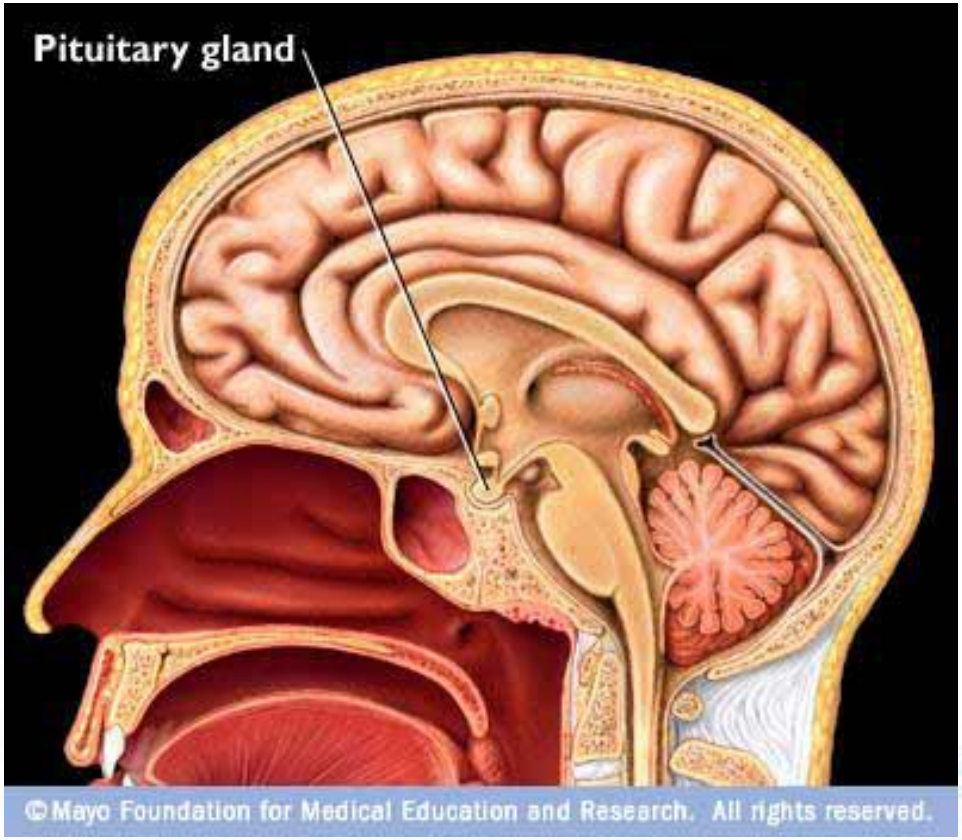
Treatment 治疗

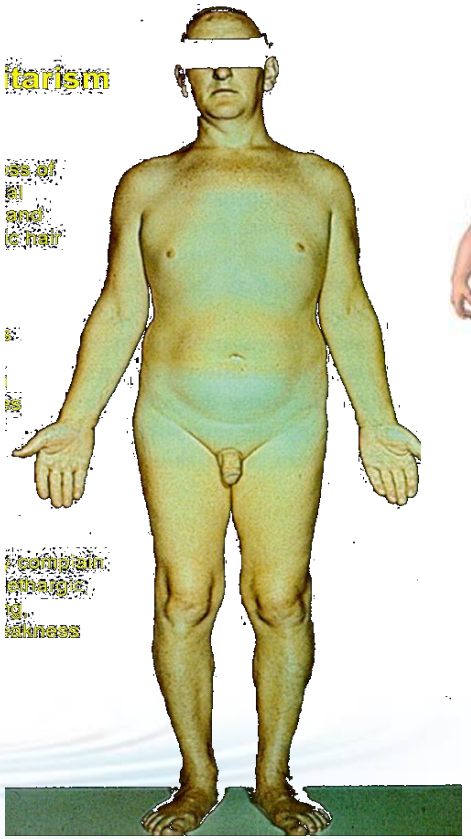
3.Radiotherapy 放射治疗

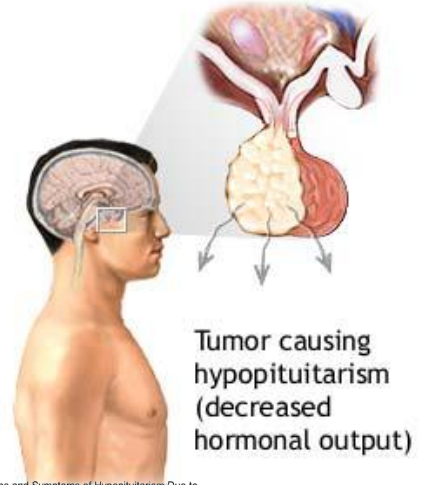
- radiation is used in few patients.
- Stereotactic radiation is generally preferred over external radiation therapy

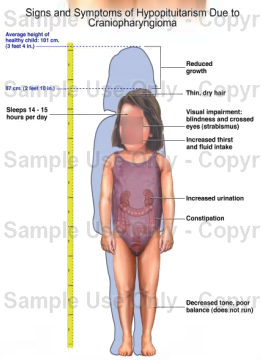
伽玛刀治疗垂体瘤

Hypopituitarism
腺垂体功能减退症

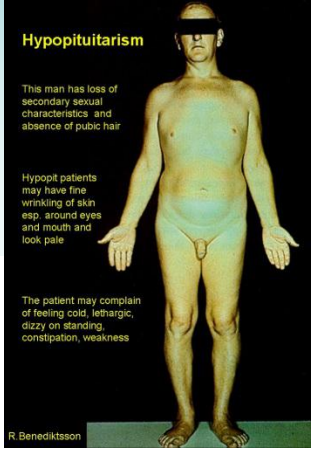






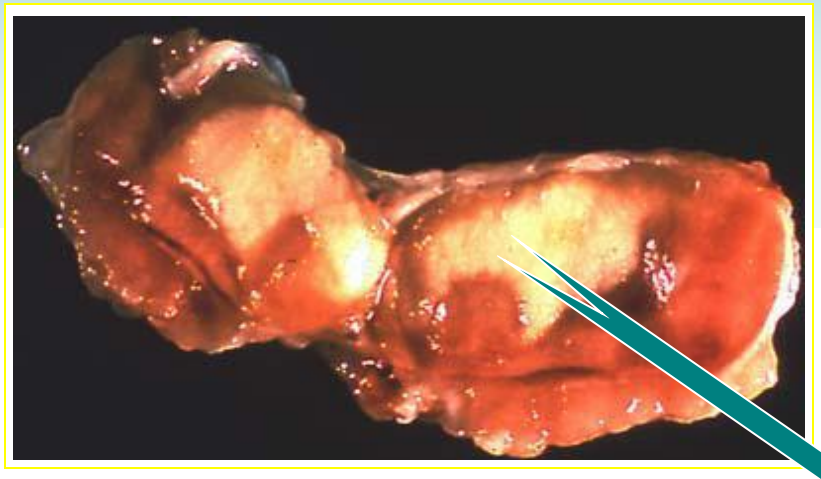


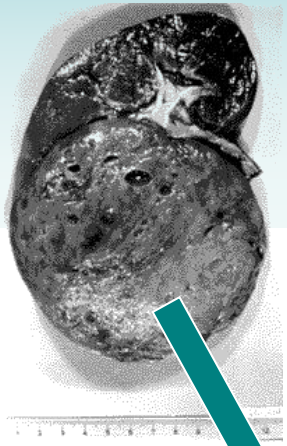
Hypopituitarism
腺垂体功能减退症



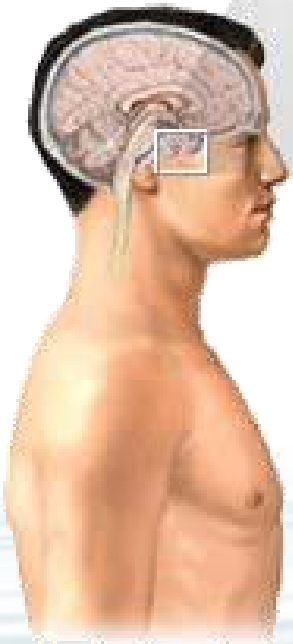
General Information概述

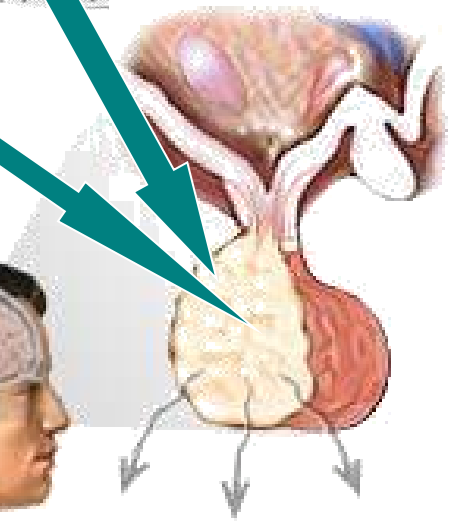
- Hypopituitarism is any under function of the pituitary gland
- Causes include damage to either the pituitary or the hypothalamus;
- Injury to the pituitary itself can occur from an enlarging **pituitary tumor, 垂体肿瘤 radiation treatment放射治疗** to the pituitar y, **pituitary apoplexy垂体卒中 / trauma外伤/ hemochromatosis血色病**.
- As pituitary damage increases /hormonal function decreases.
- Hormone function loss due to increasing damage is predictable. The most vulnerable functions to least vulnerable are **growth hormone (GH), gonadotrophins (LH and FSH), TSH and ACTH**





Dwarfism





Tumor causing hypopituitarism (decreased hormonal output)

ADAM.

Hypopituitarism
腺垂体功能减退症

General Information概述

•Pituitary malfunction can cause deficiencies in specific hormones with a wide range of symptoms and treatment options.

•All patients who require long-standing cortisol, thyroid and/or DDAVP replacement should wear a "med-alert" bracelet at all times to notify medical personnel in case of illness or trauma.

Hormone Deficiencies: Symptoms and treatment:症状与治疗

◆**Deficiency of adrenocorticotropic hormone (ACTH) and cortisol:** The most dangerous and life-threatening deficiency.

1.**Symptoms:** include **weakness**, **nausea**, **abdominal and joint aches**, **electrolyte abnormalities**, **low blood pressure** and **shock**.

2.Treatment: Replacement therapy consists of administering cortisol. Prednisone and hydrocortisone are the most common oral preparations of cortisol. The dosage may need to be temporarily increased during periods when the body is stressed because of illness, infection, surgery or trauma.

Hormone Deficiencies: Symptoms and treatment:症状与治疗

Deficiency of TSH and thyroid hormone

1.Symptoms: Symptoms of thyroid hormone deficiency include cold intolerance, dry skin, constipation, muscle aches, menstrual irregularities and weight gain. The combination of symptoms is very uncomfortable and often drives patients with pituitary disease to seek medical attention.

2.Treatment: Replacement therapy consists of giving thyroxine (marketed as Synthroid™, Levoxyl™, or Levothroid™). Blood levels are closely monitored as over-replacement may cause complications such as osteoporosis or heart disease.

Hormone Deficiencies: Symptoms and treatment:症状与治疗

Deficiency of luteinizing hormone (LH) or follicle stimulating hormone (FSH): Results in low estrogen levels in women and low testosterone in men.

1.Symptoms: Symptoms range from "hot flashes" to low sex drive. These hormones also have protective effects on bone.

2.Treatment: Estrogen can be given orally as premarin or estrace, or can be given as a twice weekly patch. Women taking estrogen also need to take progesterone, unless they have had a hysterectomy. In men, testosterone is administered either via bi-weekly injection into the muscle at home or daily skin patch.

Hormone Deficiencies: Symptoms and treatment:症状与治疗

Growth hormone (GH) deficiency: Generally, all children with GH deficiency should receive replacement therapy. However, GH therapy in adults is more controversial.

1.**Symptoms:** There is some evidence that GH deficiency in adults may increase risk of death from vascular disease. GH deficiency also results in decreased lean body mass and may also have negative psychological effects.

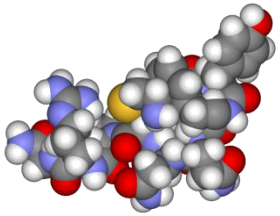
2.Treatment: GH is administered via daily injection. The long-term effects of GH treatment in adults are currently being studied.

Hormone Deficiencies: Symptoms and treatment:症状与治疗

Vasopressin (ADH) deficiency

1.Symptoms: Lack of ADH causes diabetes insipidus, with excessive thirst and urination. Patients may become severely dehydrated if they do not drink enough liquid.

2.Treatment: ADH is currently replaced by administration of DDAVP, a synthetic version of the hormone, by pill, nasal spray or injection.

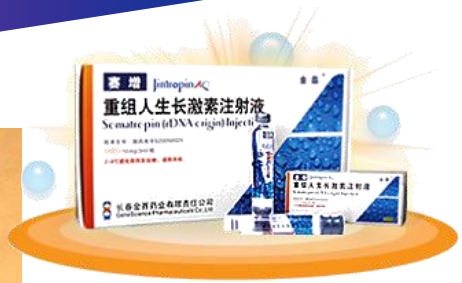


The sequence of Hormone Replacement

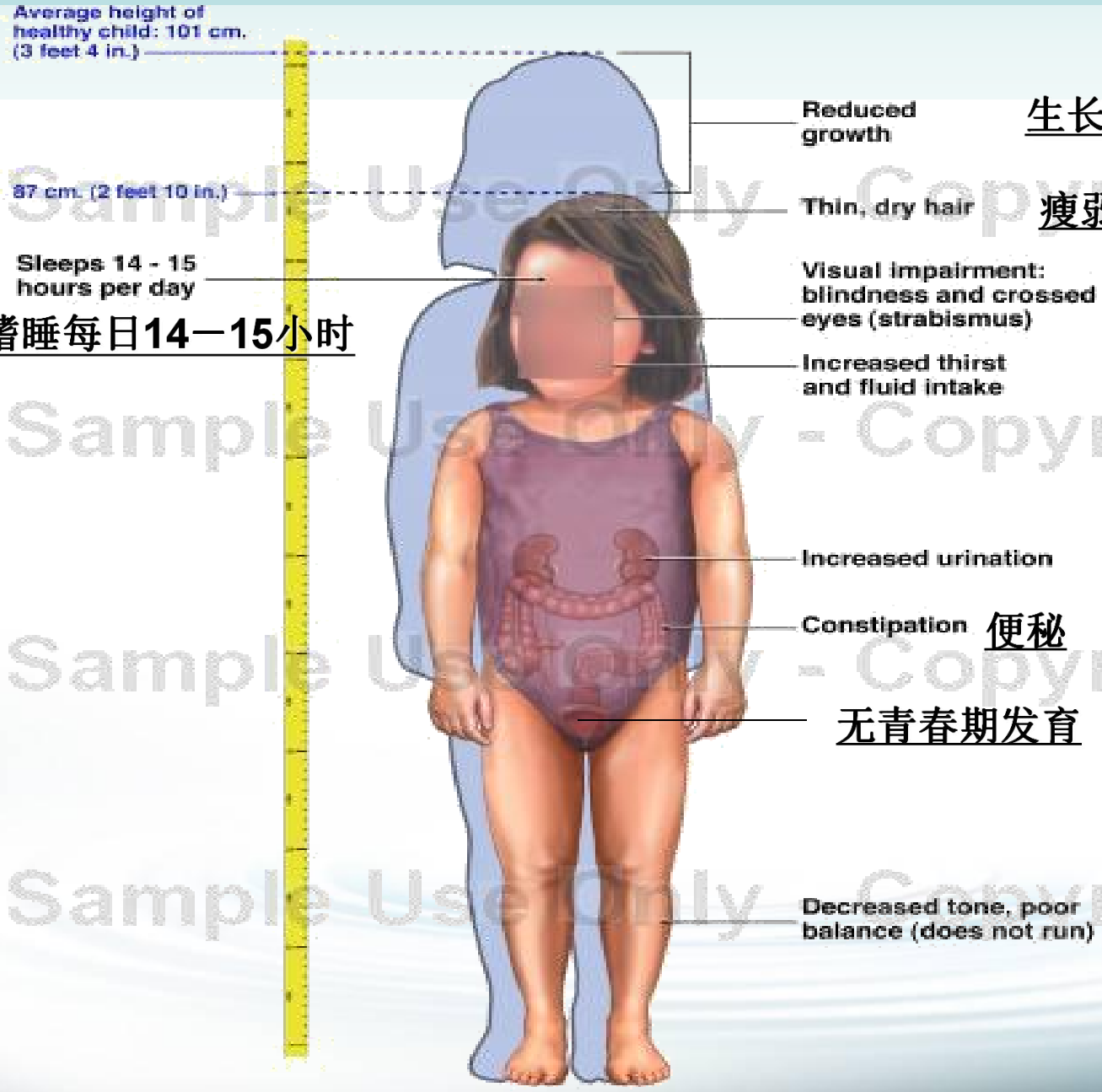
激素替代治疗的顺序

The Replacement Sequence

Hydrocortisone>Thyroxine>Vassopressin>GH>Gonads



Signs and Symptoms of Hypopituitarism



生长减速

瘦弱头发干枯

嗜睡每日14—15小时

视力损害：眼盲及斜眼

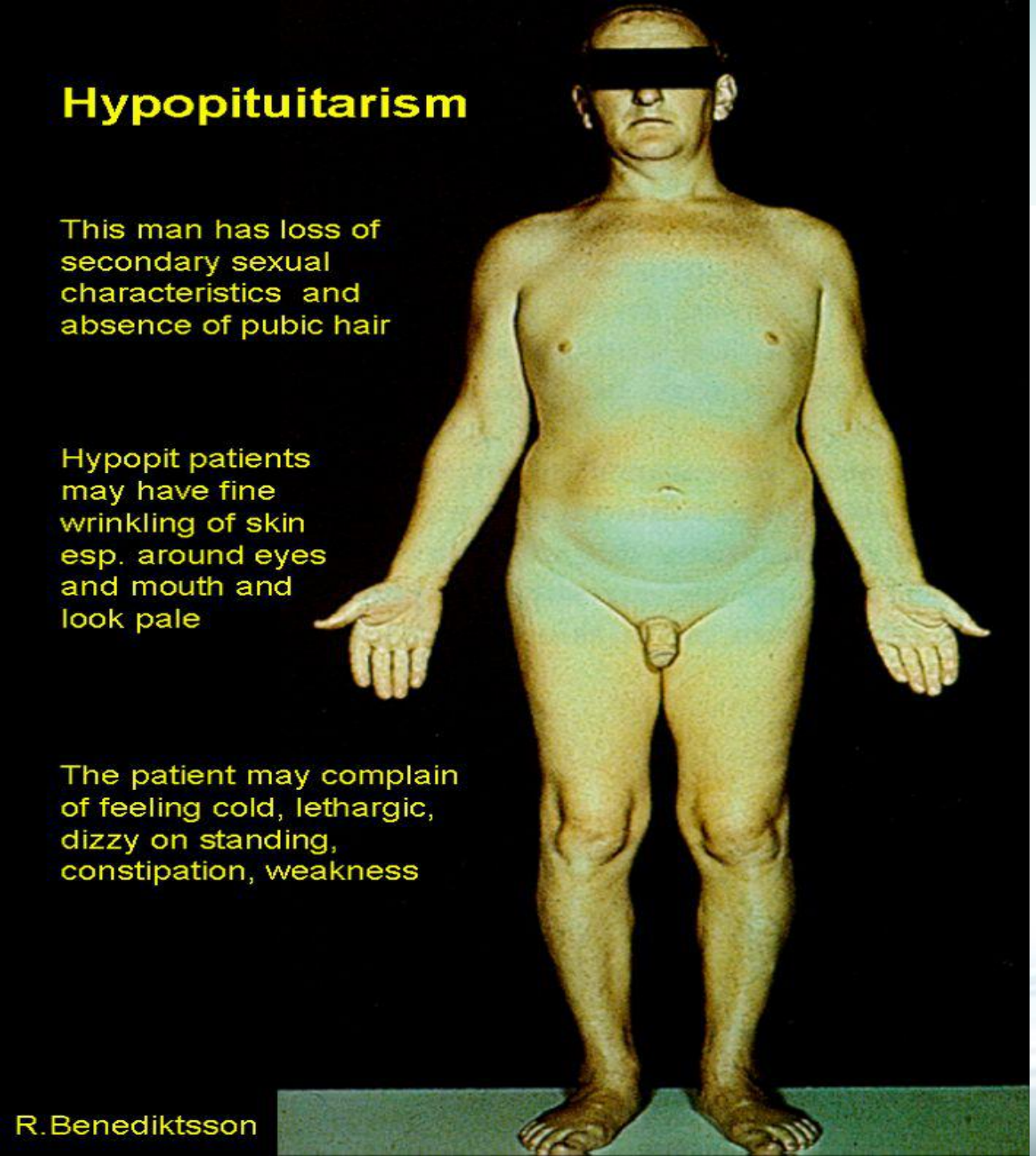
尿崩

便秘

无青春期发育

平衡力差，张力低下

Sample Use Only - Copyr



1.第二性症缺乏，性毛缺少

2.眼眶口唇周围皱纹增多苍白

3.主诉怕冷、嗜睡、头晕、便秘、软弱

Hormone Deficiencies: Symptoms :症状

甲减后与甲减前的对比

Diabetes Insipidus:尿崩症

定义和分类

- 下丘脑-神经垂体分泌AVP不足:中枢性
- 肾脏对AVP反应缺陷:肾性
- 一 **临床综合征**
- 主要表现:多尿、烦渴、多饮、低比重尿、低渗透压尿

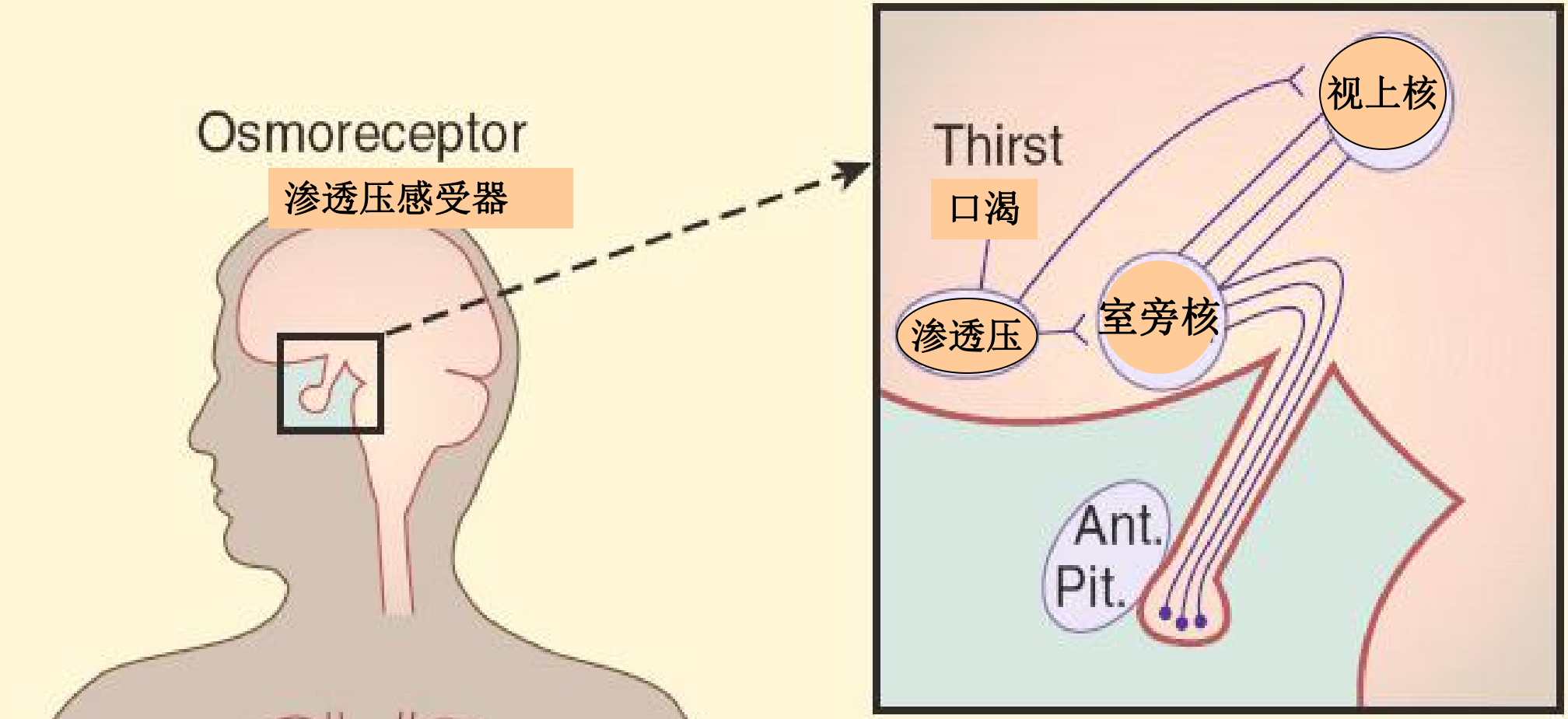
Symptoms

1. 可见于任何年龄，青少年多，男>女(2:1)

- 多尿、烦渴、多饮，急起，起病日期明确
- 尿量 > 3-4L/d (可达18L/d)，偶有40L/d者
- 饮水和排水大致相等，体力下降
- 智力接近正常

2. 伴随病症状(原发病症状)

- 肿瘤压迫症状
- 外伤后症状
- 垂体前叶功能减退症状



ADH分泌示意图

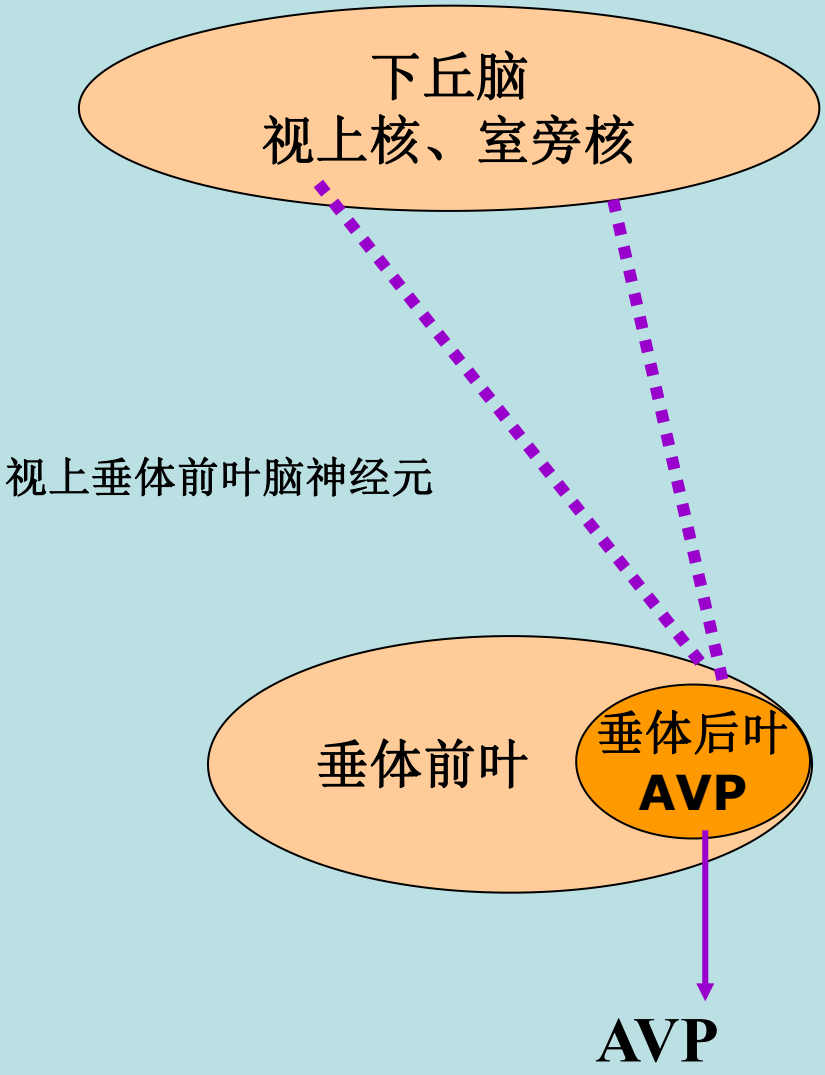
ADH分泌示意图

ADH的分泌与作用：

▪合成部位：下丘脑视上核(AVP)、室旁核(OXT)

▪属下丘脑神经内分泌细胞，神经元轴突末梢止于垂体后叶。下丘脑(视上核)垂体神经束，传导神经冲动

▪ADH的作用与机制：AVP属蛋白质激素，通过cAMP系统起作用



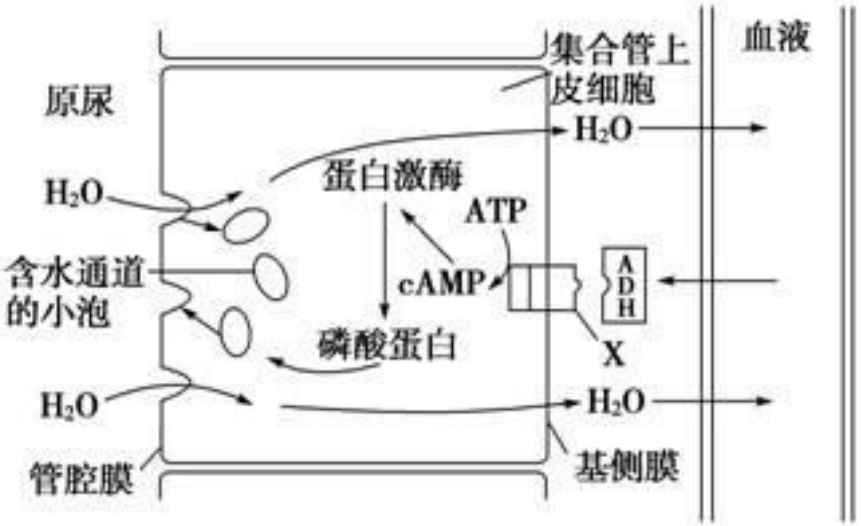
AVP的作用

■调节体内水代谢，维持水平衡

AVP→远曲小管和集合管→AVPR结合

→激活蛋白激酶，膜蛋白磷酸化→

水孔蛋白2表达→水份重吸收



ADH释放的控制调节

1)渗透压调节：

下丘脑视上核细胞及附近有渗透压感受器

血浆渗透压正常：280～310mOsm/(kg·H_2O)，

血渗压在280～284mOsm/kg·H_2O时，AVP分泌

2)血容量及血压调节：

左、右心房及腔静脉、肺静脉有血容量感受器

颈动脉和主动脉处有压力感受器

ADH释放的控制调节

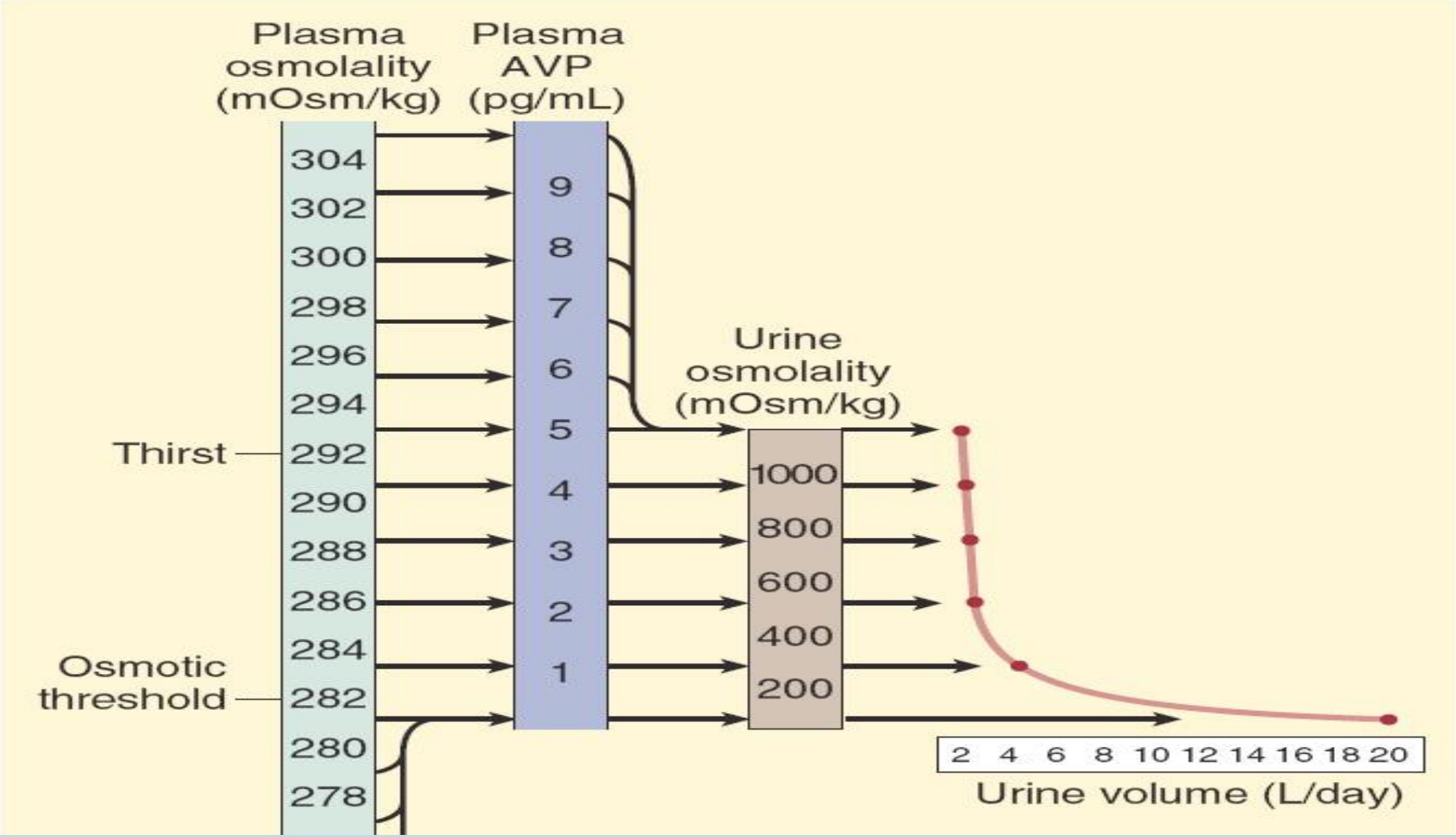
3)神经调节：

组织胺、激肽酶、乙酰胆碱刺激AVP释放

从卧位变为立位，AVP水平上升2倍

4)口渴

5)糖皮质激素：提高AVP释放的渗透阈值



血浆渗透压与血浆加压素以及尿渗透压、尿容量的生理关系

病因与发病机制

一、继发性尿崩症

任何病变破坏下丘脑正中隆起(漏斗部)以上部位，常引起永久性尿崩症；病变在下丘脑正中隆起以下者为暂时性尿崩症

- 下丘脑-神经垂体肿瘤约50%(颅咽管瘤、松果体瘤)
- 转移瘤(肺癌、乳腺癌)
- 其他：脑炎、脑膜炎、肉芽肿性疾病、淋巴细胞性垂体炎
- 创伤性尿崩症约10%

二、 特发性尿崩症

约占30%；找不到任何原因。下丘脑视上核和室旁核神经细胞明显减少。该病患者血中存在有下丘脑室旁核神经核团抗体

三、 遗传性尿崩症

家族史，常染色体显性遗传，由AVP-NPII基因突变引起，NPII(神经垂体素)蛋白质二级结构破坏

四、 按照发病机制分类:

1 **中枢性尿崩症** 由于下丘脑视上核、室旁核神经细胞破坏导致AVP严重缺乏或部分缺乏

2 **肾性尿崩症** 家族性、间质性肾炎、电解质紊乱等引起肾脏对AVP不敏感，致肾小管吸收水障碍

3 **妊娠期尿崩症** 具中枢性和肾性尿崩症特点,常见妊娠后三个月发生，分娩后自然缓解。循环AVP酶增高, 与AVP降解增加有关

正常人血、尿渗透压及尿量的变化

- 血渗压:280～310mOsm/kg·H_2O(平均300)
- 24h尿渗压：40～400mOsm/kg·H_2O
- 禁饮后达600～1000mOsm/kg·H_2O(平均800)
- 24h尿量 1000～2000ml
- 昼尿：夜尿 = 3～4:1
- 12h夜尿≤750ml
- SG:1.020以上或SG最高－最低≥0.009
- 血浆AVP: 2.3～7.4pmol/L
- 禁水后明显上升

实验室检查

1. 禁水试验

正常人禁水一定时间后,因血渗压升高,AVP分泌增多,尿量减少,尿液浓缩,维持血渗压无明显变化,尿渗>800mOsm/kg·H_2O;尿崩症的表现相反

禁水方法

- 禁水时间8～12h不等，视每日尿量多少而定
- 试验前测体重, BP, 尿比重或尿渗压
- 禁水后每2h排尿一次, 测尿比重或尿渗压
- 禁水后每1h测体重, BP
- 有条件时, 试验前及结束时可测血渗压

结束禁水试验的提示

1）体重减少>3%～5%

2）BP下降>20mmHg以上

3）体位性低血压

4）连续2次尿渗压上升 < 30mOsm/kg·H_2O

5）连续2次尿量和尿比重变化不大

2.禁水-加压素试验

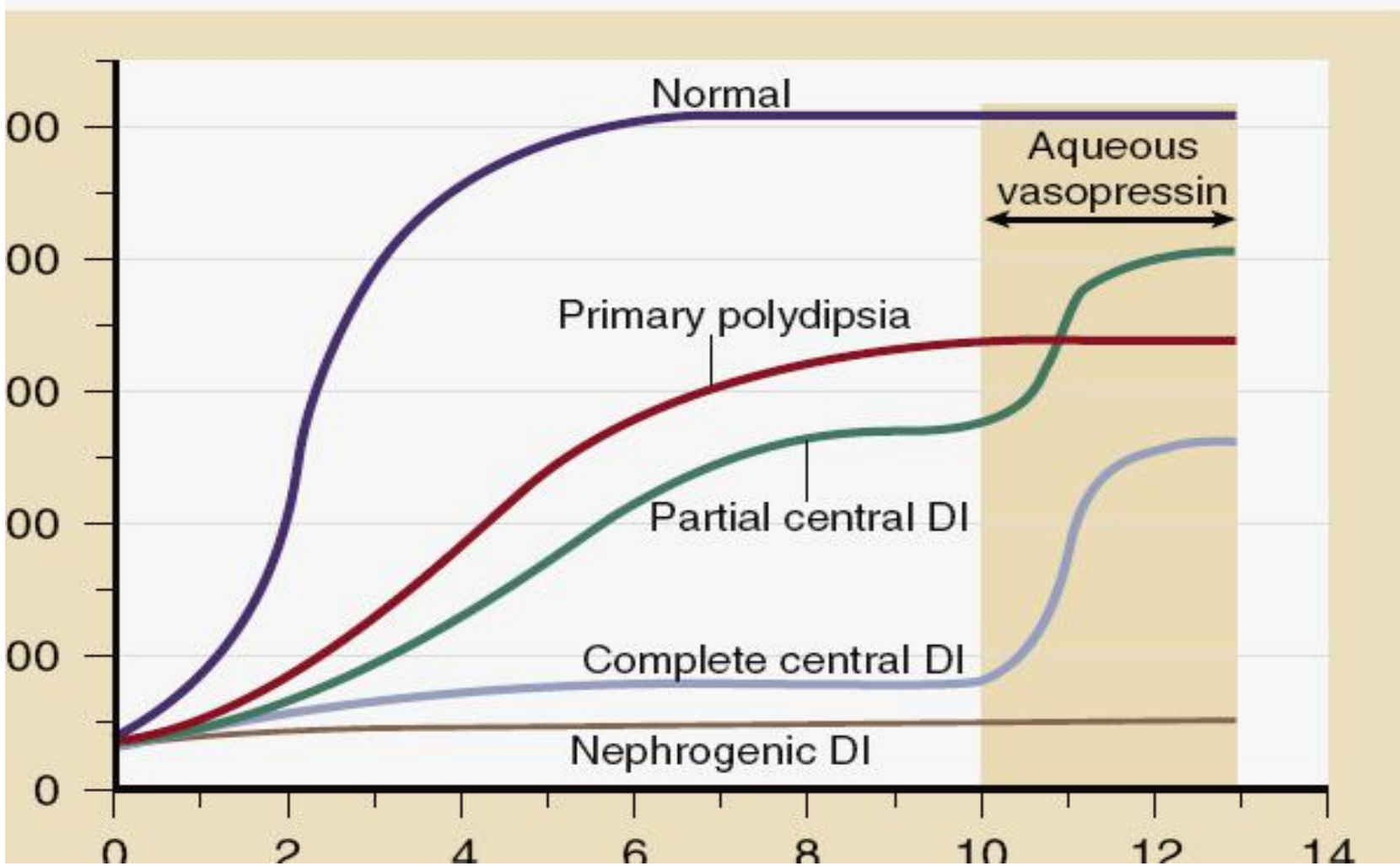
方法：在禁水试验的基础上，出现“结束禁水试验的提示”后,测定血渗压;皮下注射水剂加压素5U,1h和2h后分别测尿渗压和血渗压以作为对照

结果：

- 正常人尿渗压变化不大
- 精神性多饮者与正常相似
- 尿崩症尿渗压上升>9%以上

尿崩症的实验室特点

	血渗压 mOsm/kg	尿渗压 mOsm/kg	尿渗/血渗	加压素后尿渗上升	尿量	尿比重
正常	290±10	>800 (为血渗2.5倍)	尿>血	<5%	减少	>1.020
精神	正常	小幅上升	尿>血	<5%	减少	<1.020
尿崩症 (完全性)	>295	不变	尿<血	>50%	不变	<1.010
尿崩症 (不完全性)		<600	尿>血	>10%	减少	<1.020 >1.015



图示:禁水试验和禁水试验鉴别不同原因的尿崩症

DI = diabetes insipidus(尿崩症)

诊断标准

1）尿量 > 4～10L/d

2）SG: 1.005～1.003

3）尿渗透压<血渗透压

（尿渗压:< 50～200mOsm/kg·H_2O）

4）补水不充分时血钠升高(血钠>150mmol/L)

5）血浆AVP下降

6）禁水试验尿渗压、尿比重不能增加

7）ADH(抗利尿激素)可明显改善症状

鉴别诊断

1. 精神烦渴：AVP正常，禁水及禁水加压试验后上述检查正常

2. 肾性尿崩症: 家族性X连锁遗传性疾病；出生后出现症状，男孩多见，伴有生长发育迟缓；AVP正常，禁水加压后尿量不减少，尿比重不升高

3. 慢性肾脏疾病：有肾小管疾病表现，高钙血症、低钾血症等，多尿程度轻

创伤性尿崩症的临床特点

病因: 脑部创伤、手术损伤垂体和下丘脑

1 . **暂时性尿崩症：**术后第一天发生，数天内恢复

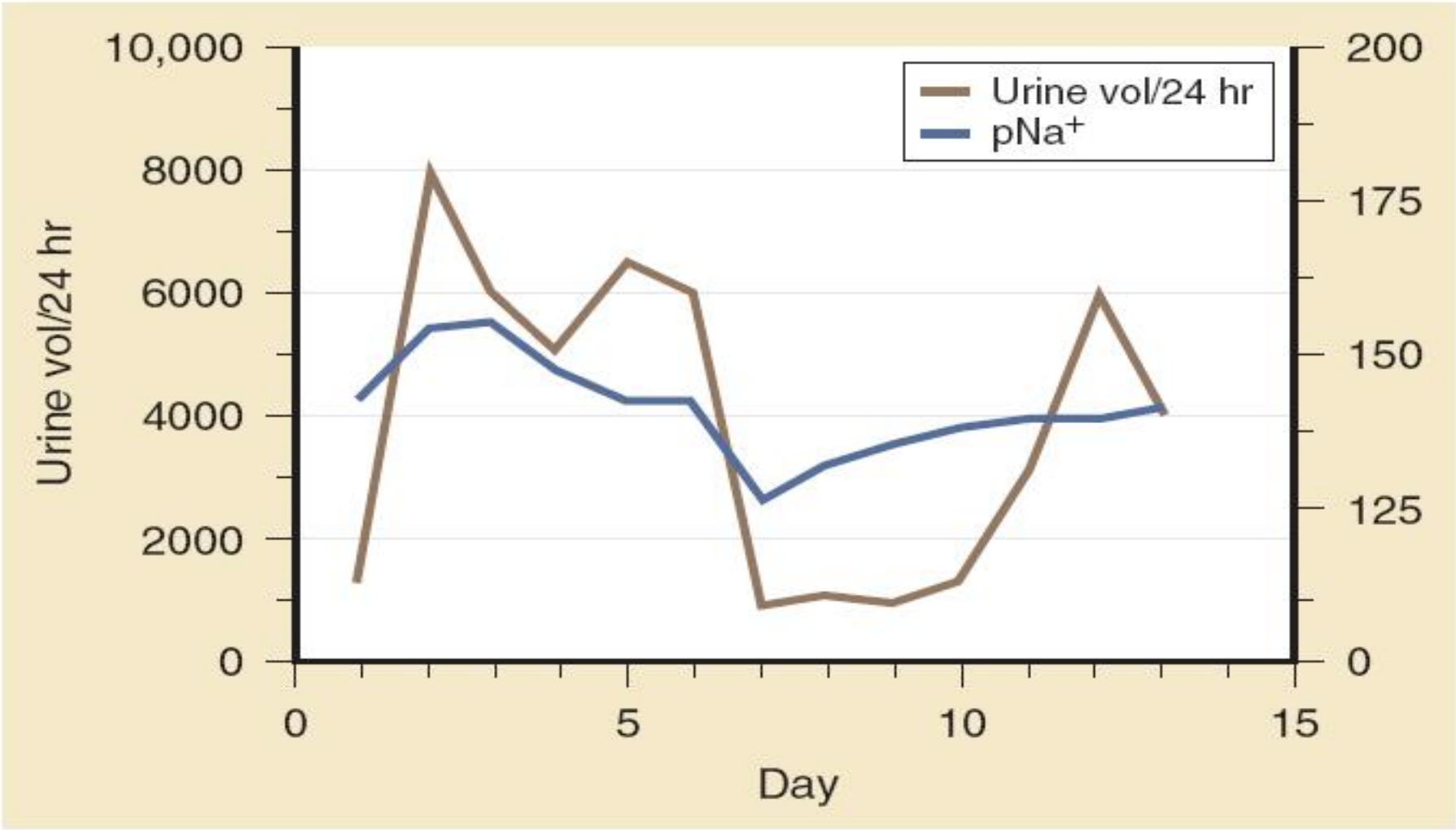
2 . **持续性尿崩症：**持续数周者可形成永久性尿崩症

3. **三相性尿崩症(垂体损伤)：**

①急性期：尿量增加，尿渗压下降，持续4~5天。原因为神经原性休克(AVP不释放)

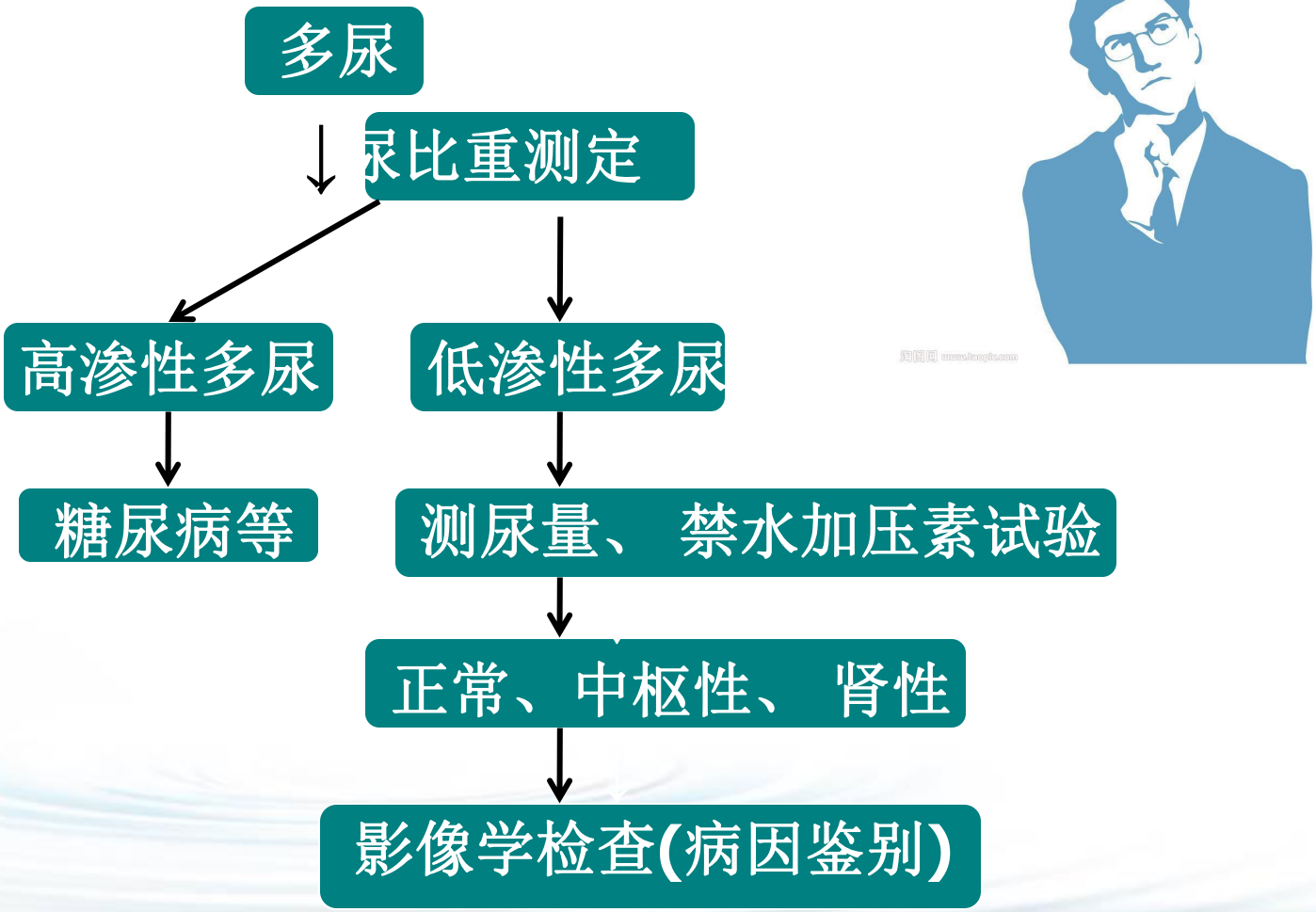
②中间期：尿量减少，尿渗压上升，约5~7天。此时AVP溢出损伤神经元

③持续期(永久性尿崩症)：神经元损伤



图示：垂体柄损伤时三相性变化
外伤后立即出现尿崩症持续7～10天，
显著多尿，加压素不适当增加，
低钠以及需要禁水。10天后，尿崩症消失

诊 断 思 路



治 疗

一、激素替代治疗：完全中枢性尿崩和妊娠尿崩首选

1. 水剂加压素: 5 ~ 10U静滴，作用时间3 ~6h;手术时或临时使用

2 .长效尿崩停: 鞣酸加压素油剂 5U/ml 深部肌肉注射 0.1~0.2ml开始,

使用量以尿量 < 2500ml为宜（AD：过量水中毒 感染等）

3. DDAVP(1-脱氨-8右旋精氨酸加压素)人工合成AVP类似物, 鼻喷

吸入或皮下或肌肉或静脉或口服(商品名 **弥凝**) 给药

治 疗

二、非激素类抗利尿剂:部份性中枢性尿崩症

1. 氯磺丙脲：0.2～0.5g qd，刺激垂体释放AVP加强AVP对肾小管的作用

2. DHCT/吲达帕胺：机制不明，通过排钠大于排水，使肾小球滤过率降低，增加近曲小管水分吸收，进入远曲小管原尿减少

3. 安妥明：能刺激AVP的释放

4. 酰氨脒嗪(卡马西平) 0.2 tid，能刺激AVP的释放

治 疗

三、非激素类抗利尿剂:肾性尿崩症

1. 去除原因:停药，纠正电解质紊乱

2. 药物:

- **噻嗪类:**同前
- **消炎痛:**减少肾血流量和近端小管对水和电解质的重吸收， 抑制PG合成酶25～50mg， tid
- **阿米托利**:肾浓缩功能增强， 减少尿量10～20mg/d，分次服；
- **吲哚帕胺:**类似HCT 2.5～5mg， qd～bid 监测血钾
- 锂盐所致肾性尿崩症:阿米托利+HCT 消炎痛+DDAVP

四、继发性尿崩症:病因治疗

- 精神性烦渴:睡前少量DDAVP
- 行为疗法：对下丘脑受损后尿崩症并渴感受损病人

谢 谢！