PITUITARY INCIDENTALOMA

"Pituitary incidentaloma is defined as a pituitary lesion discovered unexpectedly in an individual with no obvious symptoms to suggest pituitary disease."

Bevan JS, Clinical Medicine 2013

Presentation and surgical results of incidentally discovered nonfunctioning pituitary adenomas: evidence for a better outcome independently of other patients' characteristics

Marco Losa, Carmine A Donofrio, Raffaella Barzaghi and Pietro Mortini

Eur J Endocrinol 2013

Table 1 Main reason to perform the neuroimaging study that led to the incidental discovery of a nonfunctioning pituitary adenoma in 212 patients.

Cause	Asymptomatic incidentalomas (n=117)	Symptomatic incidentalomas (n=95)	All (n=212)
Headache	29 (24.8%)	13 (13.7%)	42 (19.8%)
Dizziness	17 (14.5%)	14 (14.7%)	31 (14.6%)
Stroke or transient ischemic attack	6 (5.1%)	13 (13.7%)	19 (9.0%)
Hearing impairment	9 (7.7%)	8 (8.4%)	17 (8.0%)
Head or cervical trauma	9 (7.7%)	8 (8.4%)	17 (8.0%)
Sinusitis	7 (6.0%)	5 (5.3%)	12 (5.7%)
Syncope	6 (5.1%)	5 (5.3%)	11 (5.2%)
Tumor staging	5 (4.3%)	5 (5.3%)	10 (4.7%)
Other causes	29 (24.8%)	24 (25.2%)	53 (25.0%)

Differential diagnosis of pituitary incidentaloma.

Diagnosis	Typical radiological and clinical features
Pituitary adenoma (most common)	• Microadenoma: hypodense lesion within the pituitary gland (<10 mm in diameter) • Macroadenoma: usually smooth contoured lesion, arising from within the sella, and often with suprasellar extension (≥10 mm in diameter)
Craniopharyngioma	• Calcification on CT scan • Cystic change • Diabetes insipidus • 'Hypothalamic' features (eg hyperphagia and weight gain)
Meningioma	• Homogeneous, increased signal (before and after MRI contrast) • Dural 'tail' and adjacent hyperostosis • Epicentre often suprasellar
Metastasis	• Unusual, irregular shape • Carotid artery compression • Diabetes insipidus • Other pointers to malignancy: weight loss, breast lump, smoker, abnormal chest X-ray
Hypophysitis	• Increased and homogeneous MRI contrast enhancement • Female gender • Recent pregnancy • Associated autoimmune diseases, eg type 1 diabetes mellitus
Carotid artery aneurysm (intrasellar)	• Markedly increased and homogeneous MRI contrast enhancement

CT = computed tomography; MRI = magnetic resonance imaging.

Bevan JS, Clinical Medicine 2013

EPIDEMIOLOGY OF PITUITARY INCIDENTALOMAS

- In combined **autopsy** data, average frequency of a pituitary adenoma was **10.6%**
- In adults who underwent **cranial imaging,** microincidentalomas were seen on **CT in 4-20%** and on **MRI in 10-38%** of patients
- **Macroincidentalomas** were found in **0.2%** of patients who underwent CT scans for central nervous system symptoms and by MRI in **0.16%** of a population study cohort
- In series including cystic lesions, **80% of incidentalomas were adenomas**

Diagnosis of pituitary incidentalomas

Diagnosis	*n* (%)
Adenoma	48 (70.6)
Microadenoma	18 (37.5)
Macroadenoma	30 (62.5)
Rathke's cleft cyst	9 (13.2)
Pituitary hyperplasia	5 (7.3)
Meningioma	2 (3.0)
Astrocytoma	1 (1.5)
Undetermined cystic lesion	3 (4.4)
Total	68 (100.0)

Histology and immunohistochemistry results

	n (%)
Adenoma—FSH and/or LH	9 (45.0)
Null cell adenoma	5 (25.0)
Adenoma—FSH, prolactin and TSH	1 (5.0)
Adenoma—prolactin	1 (5.0)
Adenoma—somatotroph	1 (5.0)
Papillary meningioma	1 (5.0)
Pilocytic astrocytoma	1 (5.0)
Normal pituitary gland	1 (5.0)
Total	20 (100.0)

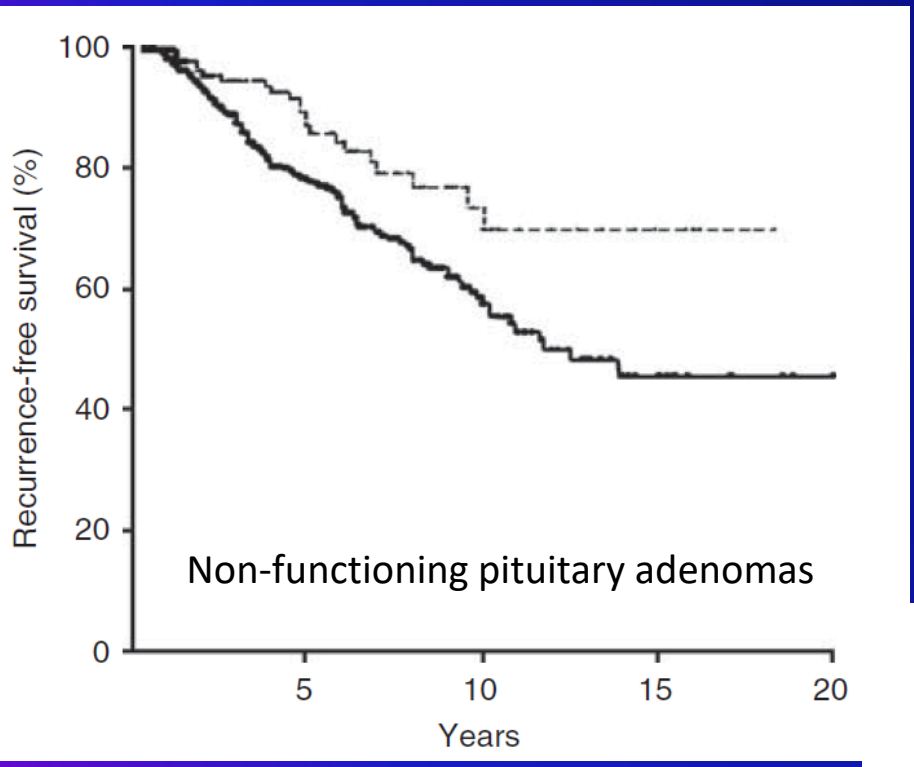
Esteves et al, Pituitary 2015

Histopathologic diagnoses of surgically treated pituitary incidentalomas

Diagnosis	Surgical group (n = 258)
Pituitary Adenoma	209 (81 %)
Rathke's cleft cyst	41 (15.9 %)
Arachnoid cyst	5 (1.9 %)
Craniopharyngioma	3 (1.2 %)

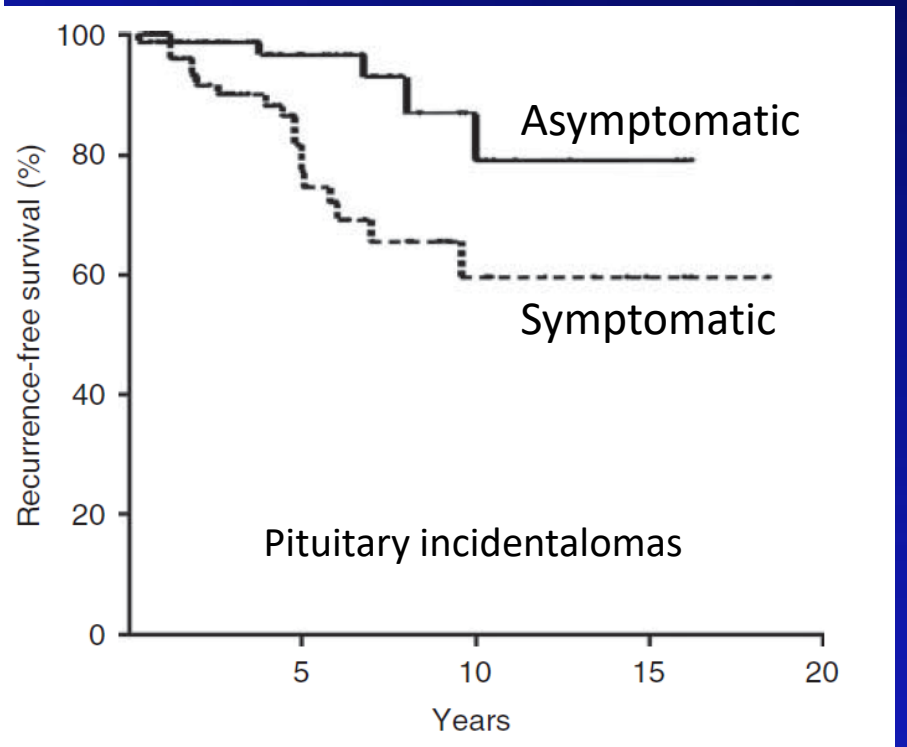
Bancos I, Best Pract Res Cl End Metab 2012

Recurrence free-survival in patients with non-functioning pituitary adenomas after surgery



Incidentalomas n=177

Control group n=512



Losa M et al, EJE 2013

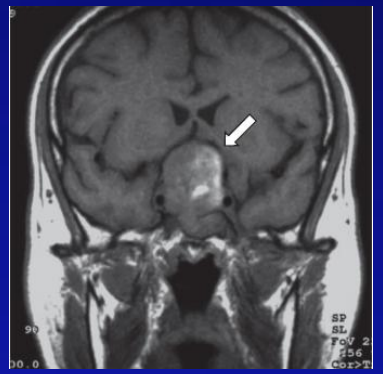
Pituitary Incidentaloma: An Endocrine Society Clinical Practice Guideline

JCEM 2011

Pamela U. Freda, Albert M. Beckers, Laurence Katznelson, Mark E. Molitch, Victor M. Montori, Kalmon D. Post, and Mary Lee Vance

3.1 We recommend that patients with a pituitary incidentaloma be referred for surgery if they have the following (1|⊕⊕⊕⊕):

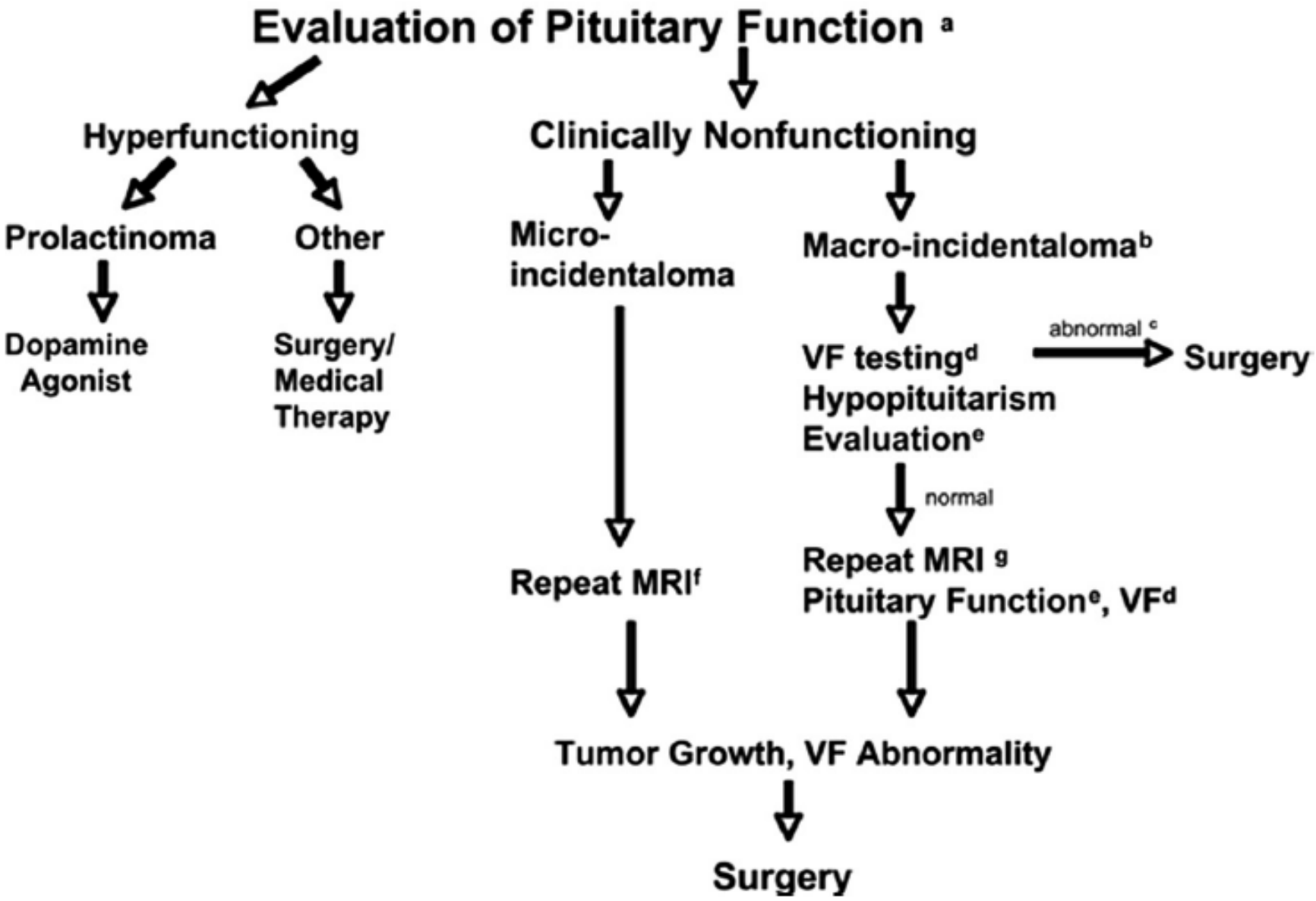
- A VF deficit due to the lesion
- Other visual abnormalities, such as ophthalmoplegia or neurological compromise due to compression by the lesion
- Lesion abutting or compressing the optic nerves or chiasm on MRI
- Pituitary apoplexy with visual disturbance
- Hypersecreting tumors other than prolactinomas



3.2 We suggest that surgery be considered for patients with a pituitary incidentaloma if they have the following (2|⊕⊕◯◯):

- Clinically significant growth of the pituitary incidentaloma
- Loss of endocrinological function
- A lesion close to the optic chiasm andf a plan to become pregnant
- Unremitting headache

Evaluation & Treatment of Pituitary Incidentalomas



FOLLOW-UP OF PITUITARY INCIDENTALOMAS

- MRI scan of the pituitary after **6 months** for **macroadenomas**
- MRI scan of the pituitary after **12 months** for **microadenomas**

- If the adenoma does not change in size MRI scan should be repeated **after 1 year for macroicidentalomas** and **every 1-2 years for microincidentalomas for 3 years**

- VF testing in patients with a pituitary incidentalomas that enlarges to abut or compress the optic nerves or chiasm on a follow-up imaging study
- VF is not needed in patients whose incidentalomas are not close to the chiasm and who have no new symptoms and are being followed closely by MRI

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1.1 We recommend that patients presenting with a pituitary incidentaloma undergo a complete history and physical examination that includes evaluations for evidence of hypopituitarism and a hormone hypersecretion syndrome. Patients with evidence of either of these conditions should undergo an appropriately directed biochemical evaluation.

1.1.1 We recommend that all patients with a pituitary incidentaloma, including those without symptoms, undergo clinical and laboratory evaluations for hormone hypersecretion (1|⊕⊕⊕◯).

Subclinical adenomas in postmortem pituitaries: classification and correlations to clinical data

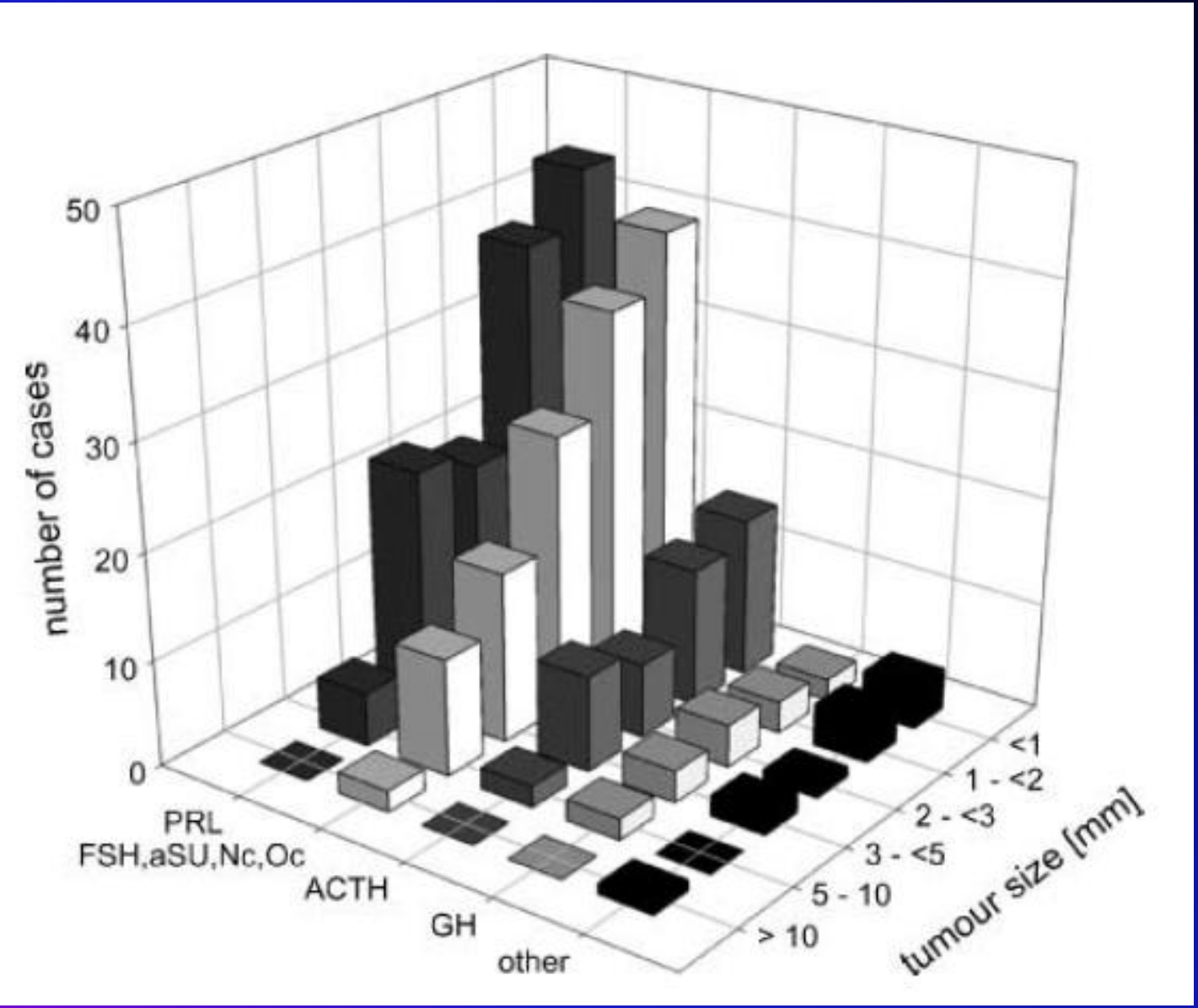
Hilke Buurman and Wolfgang Saeger

Adenoma type	Number of tumours	Included cases with multiple tumours	Percentage
GH cell adenoma, sparsely granulated	4	–	1.2
GH cell adenoma, densely granulated	3	–	0.9
PRL cell adenoma, sparsely granulated	132	12	39.5
Mixed GH cell–PRL cell adenoma	1	–	0.3
Plurihormonal adenoma type I	5	–	1.5
TSHoma	2	1	0.6
ACTH cell adenoma, densely granulated	27	3	8.1
ACTH cell adenoma, sparsely granulated	19	1	5.7
Crooke's cell adenoma	1	–	0.3
Gonadotroph cell adenoma	22	–	6.6
α-Subunit-only-adenoma	2	–	0.6
Plurihormonal adenoma type II	4	–	1.2
Null cell adenoma	75	15	22.5
Oncocytoma	31	3	9.3
Unclassified	6	–	1.8
Total	334	35*	100

*17 cases: 16 with 2 tumours and 1 with 3 tumours.

European Journal of Endocrinology (2006) **154** 753–758

Adenoma type and tumour size



Buurman and Saeger, EJE 2006

Recommendations for screening to exclude hypersecretion

There is general agreement that patients with pituitary incidentalomas should be tested for **PROLACTIN**

There is general agreement that patients with pituitary incidentalomas should be tested for **IGF-1**

There is **NO** general agreement that patients with pituitary incidentalomas should be tested for **ACTH HYPERSECRETION**

Some consider screening also for glucocorticoid excess in all patients, but others may limit screening to patients for whom there is a clinical suspicion.

Screening for hypercortisolism

- Urinary free cortisol (at least two measurements)
- Late-night salivary cortisol (at least two measurements)
- 1-mg overnight dexamethasone suppressiontest (DST)
- Longer low-dose DST (2 mg/d for 48 hrs)

Nieman LK et al JCEM 2008 “The Diagnosis of Cushing’s Syndrome: An Endocrine Society Clinical Practice Guideline”

Silent Corticotroph Adenomas

NIKI KARAVITAKI
OLAF ANSORGE
JOHN A.H. WASS

Arq Bras Endocrinol Metab 2007

Determination of ACTH (???)

Nonfunctioning pituitary tumours and pituitary incidentalomas

Molitch ME, Endocrinol Metab Clin N Am 37:151-171,2008

Subclinical Cushing's disease

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1.1.2 We recommend that patients with a pituitary incidentaloma with or without symptoms also undergo clinical and laboratory evaluations for hypopituitarism (1⊕⊕⊕◯).

In pituitary incidentaloma, deficits of **gonadotrophins** (not associated with hyper-PRL) have been found in up to **30%** of patients, of the **ACTH/cortisol axis** in up to **18%**, of **thyroid axis** in up to **28%** and of **GH axis** in up to **8%**.

Proposed screening

Total general agreement

- FT4
- Cortisol
- Testosterone (in males)

Less general, but still widely accepted

- TSH
- IGF-1
- LH and FSH

To reduce repeated blood sampling

Regarding size of the adenoma the recommendation for screening is strong for lesions of diameter equal or superior 6 mm.
Small microadenomas have a lower risk of hypopituitarism, but this is still possible

How do we interpret cortisol results

Basal cortisol < 6 mcg/dl → *adrenal insufficiency* → *start therapy*

Basal cortisol 7-17 mcg/dl → *stimulation test* → *diagnosis*

Basal cortisol > 17 mcg/dl → *normal* → *no further tests*

Basal cortisol 12- 17 mcg/dl → *test? Advice the patents of possible adrenal insufficiency in stressful conditions*

Reproducibility of the insulin tolerance test (ITT) for assessment of growth hormone and cortisol secretion in normal and hypopituitary adult men

Marija Pfeifer, Karin Kanc, Renata Verhovec and Andreja Kocijančič

Clinical Endocrinology (2001) **54**, 17–22

Table 3 Individual peak cortisol concentrations (nmol/l) during ITTs

	Cortisol concentration (nmol/l)		
	test 1	test 2	test 3
Normal men			
1	463	565	498
2	553	498	397
3	660	611	617
4	424	503	495
5	694	613	617
6	624	508	503
7	627	566	554
Median	624	565	503
Hypopituitary men			
1	3	7	
2	12	11	
3	13	17	
4	9	10	
5	21	16	
6	47	25	
7	335	143	
8	84	232	
9	412	270	
10	466	427	
11	101	55	
Median	47	25	

Test ACTH: 250 e 1 µg

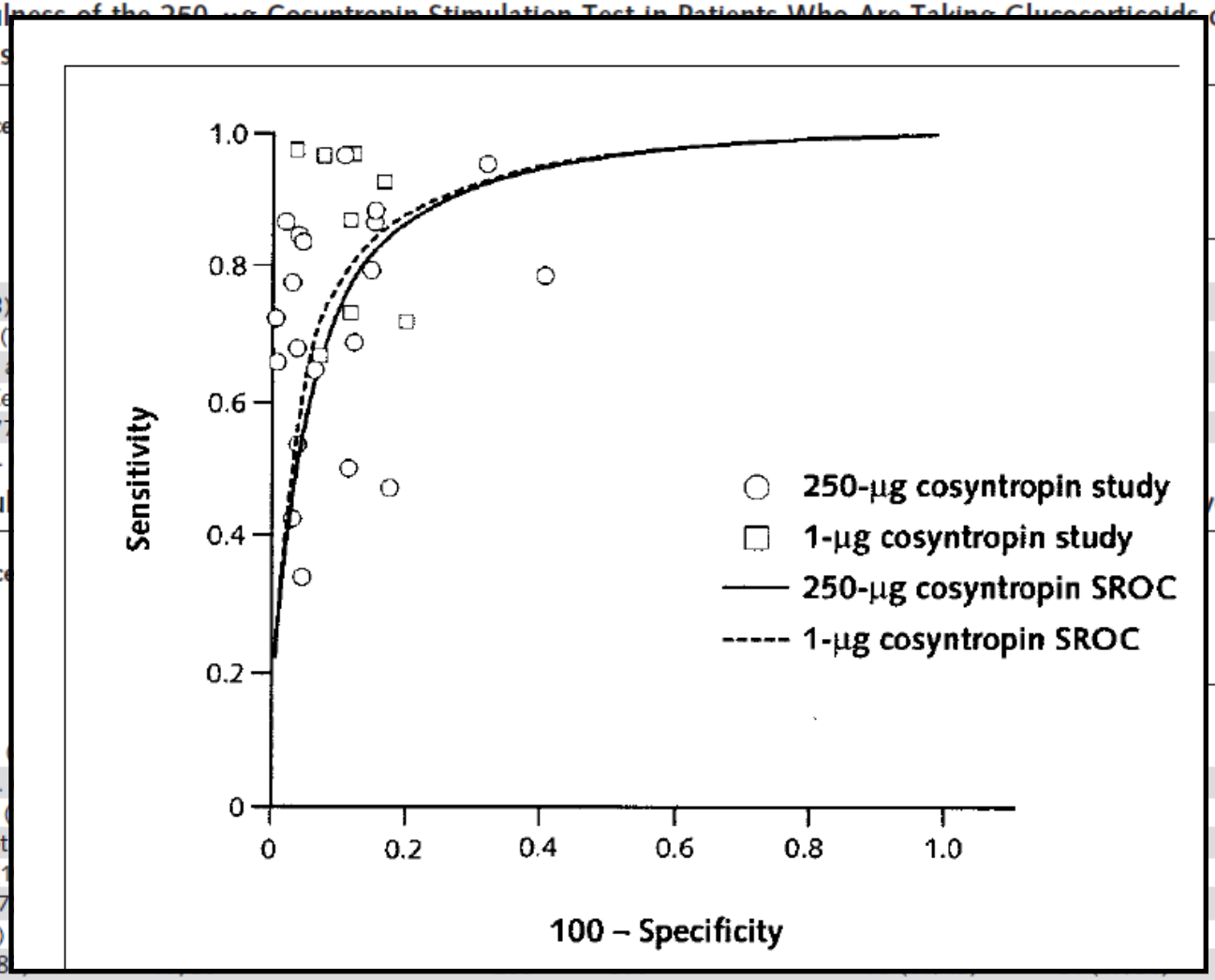
Dorin et al. Ann Intern Med 2003; 139: 194-204

Table 2. Usefulness of the 250-µg Cosyntropin Stimulation Test in Patients Who Are Taking Glucocorticoids or Have Pituitary Disease

Study (Reference							Positive Likelihood Ratio**	Negative Likelihood Ratio**
Kehlet et al. (73)							6.9	0.11
Lindholm et al. (							21.3	0.16
Cunningham et a							>100	0.58
Lindholm and Ke							73	0.27
Stewart et al. (7							6.0	0.12
Hartzband et al.							>100	0.20

Table 4. Useful ... ve Pituitary Disease*

Study (Reference							Positive Likelihood Ratio¶	Negative Likelihood Ratio¶
Tordjman et al. (							5.9	0.06
Rasmuson et al.							>100	0
Weintrob et al. (							9.0	0.11
Mayenknecht et							13.0	0.37
Ambrosi et al. (1							10.1	0.31
Talwar et al. (87							11.0	0
Abdu et al. (31)							14.3	0
Suliman et al. (8							3.8	0.33
Soule et al. (105)	IV, 30	–	200	500		75 (9/12)	88 (47/53)	6.3	0.28

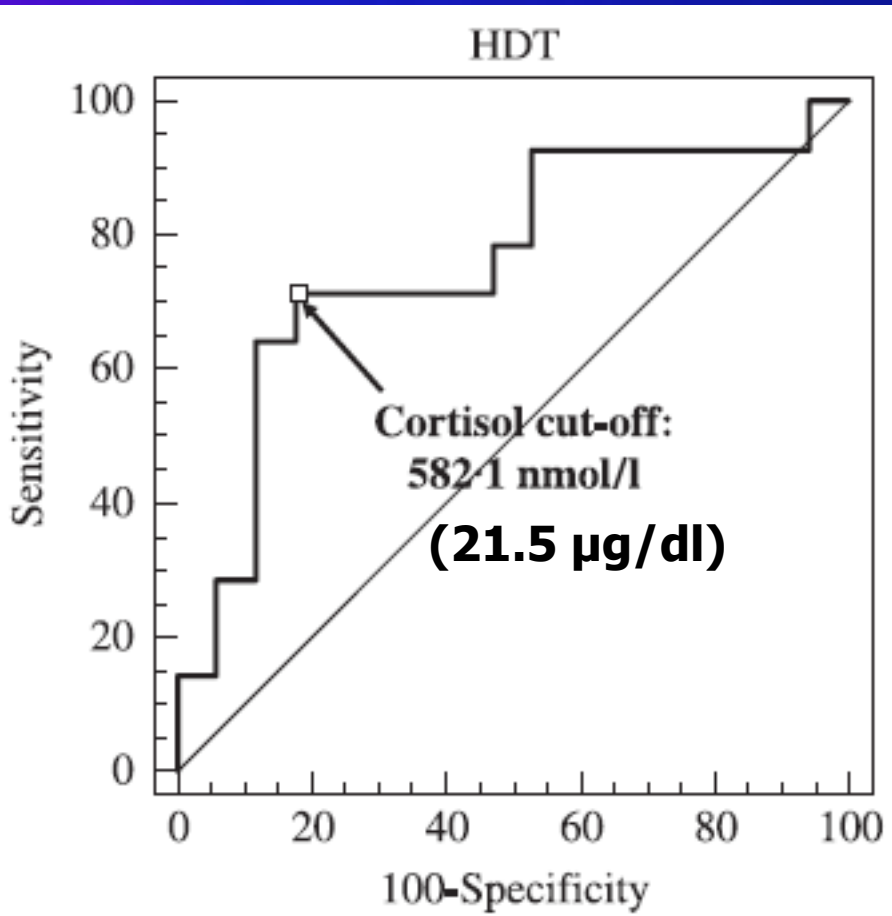


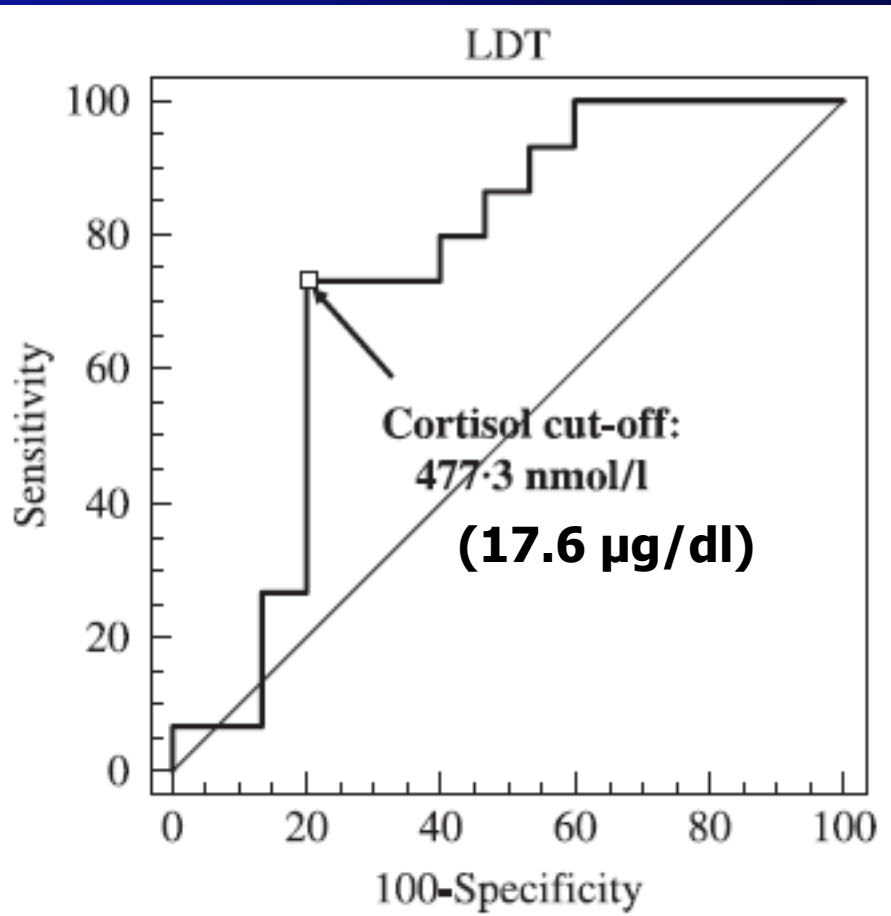
Hypothalamus–pituitary–adrenal axis evaluation in patients with hypothalamo–pituitary disorders: comparison of different provocative tests

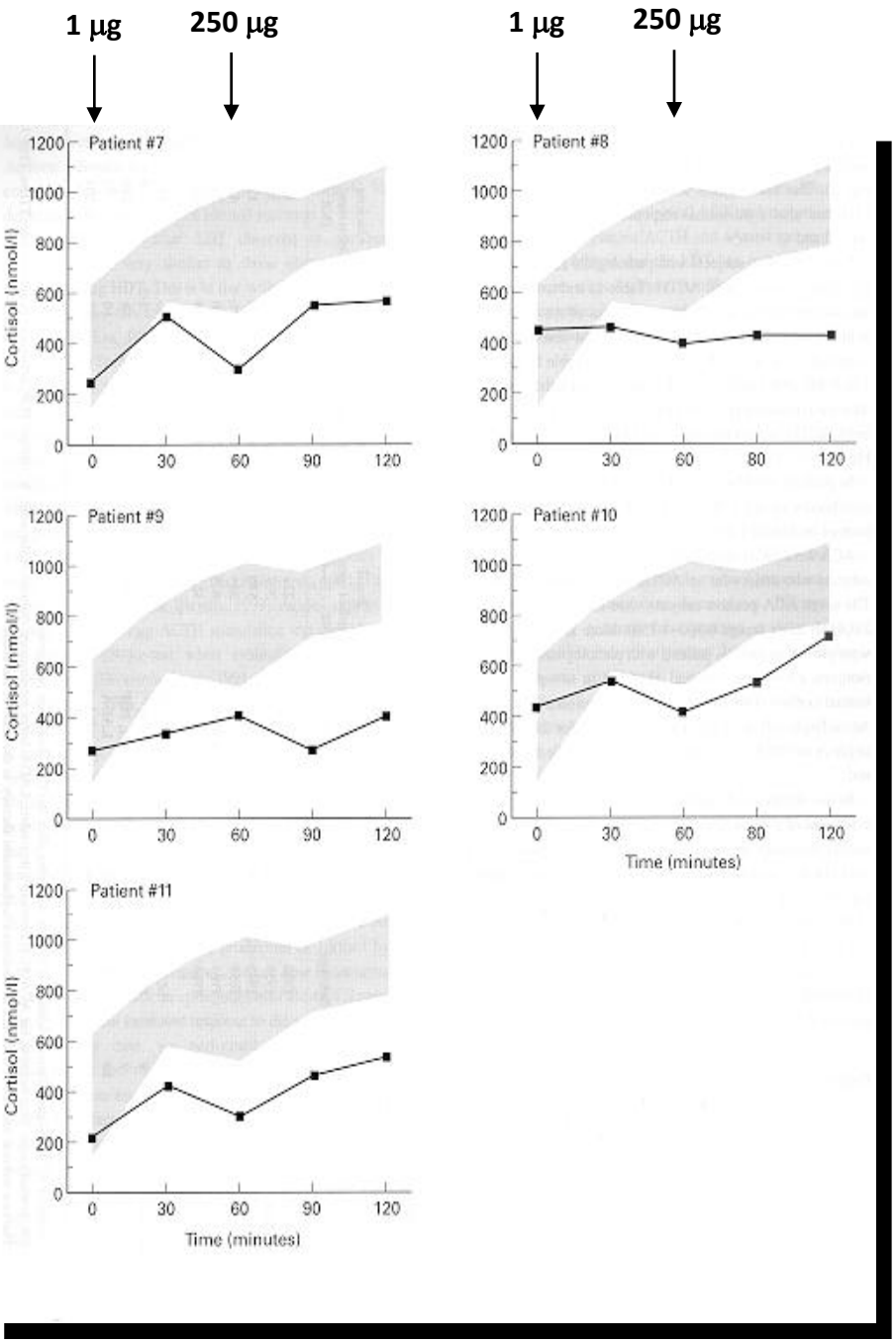
R. Giordano, A. Picu, L. Bonelli, M. Balbo, R. Berardelli, E. Marinazzo, G. Corneli, E. Ghigo and E. Arvat

Clinical Endocrinology (2008) 68, 935–941

31 pts







ACTH-LDT in subjects positive for 21OHAb

Subjects with impaired adrenal function

Laureti et al., Clin. Endocrinology 2001

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2.1.3 Clinical and biochemical evaluations for hypopituitarism 6 months after the initial testing and yearly thereafter in patients with a pituitary macroincidentaloma, although typically hypopituitarism develops with the finding of an increase in size of the incidentaloma (1|⊕⊕◯◯). We suggest that clinicians do not need to test for hypopituitarism in patients with pituitary microincidentalomas whose clinical picture, history, and MRI do not change over time (2|⊕⊕◯◯).