



Treatment of Pituitary Adenomas

First European Workshop on Treatment of Pituitary Adenomas at Rottach-Egern

Edited by Rudolf Fahlbusch and Klaus v. Werder
With a Foreword by Frank Marguth

With contributions by

H.-P. Althoff	E. Flückiger	U. Krause	G. C. Nicola	M. V. Sofroniew
A. Aulich	P. H. Forsham	H. L. Kruskemper	H. Nowakowski	H. G. Solbach
F. Bahner	T. R. Fraser	A. Kuwayama	T. Okada	N. Stahnke
F. Banks	U. Fricke	S. W. J. Lamberts	L. Oliver	H. Steinhoff
J. Bansemmer	T. Fukaya	R. Landgraf	G. Oppizzi	A. Stevenaert
D. Barwich	S. M. Gaini	A. M. Landolt	A. E. Panerai	K. Sugita
M. Basch	M. Giovanelli	S. Lange	A. Paracchi	L. Tagliabue
X. Baur	R. Göser	W. Lankisch	F. Peillon	M. Takanohashi
J. M. Bayer	A. Griner	J. H. Lawrence	E. F. Pfeiffer	G. Teasdale
P. Beck-Peccoz	K. W. M. Grossart	S. Levin	C. R. Pickardt	L. Tharandt
G. Benker	Th. Grumme	M. L'Hermite	H. J. Quabbe	C. A. Tobias
J. Beyer	C. Guiot	J. A. Linfoot	J. Racadot	G. Tomei
J. C. Birkenhäger	K. Hackenberg	A. Liuzzi	G. Ranft	G. P. Tonnamelli
W. J. Bock	W. Hadam	V. Locatelli	D. Reinwein	T. Torresani
B. Böttger	J. Happ	Ch. Lucke	J. Resetic	H. Traut
J. L. Born	D. Heesen	D. Lüdecke	H. J. Reulen	Y. Tsujita
H. J. Breustedt	J. Herrmann	J. Lyman	H. K. Rjosk	B. Tyrell
P. De Camilli	K. Hirakawa	M. Madler	C. Robyn	C. Uhlig
A. Caufriez	H. Huber	S. Manaka	R. Rothe	E. Vila-Porcile
D. F. Child	R. Illig	E. Manougian	V. Rothenbühler	E. Virasoro
P. G. Chiodini	A. Jadresic	F. Marguth	K. H. Rudorff	K. H. Voigt
C. Chong	A. Jefferson	W. Meese	H. Ruf	H. A. D. Walder
H. E. Clar	F. H. de Jong	E. Meijer	W. Saeger	A. Weindl
D. Cocchi	G. F. Joplin	A. Melo	M. Samii	S. Wende
G. Colussi	N. Kageyama	R. Mies	K. Sano	K. von Werder
G. Copinschi	A. Karduck	J. D. Miller	U. Scherer	W. Wiegelmann
U. Cordes	R. Kautzky	W. Mitschke	A. E. Schindler	O. Wilcke
L. Diamant	E. Kazner	H. R. Montz	K. Schöffling	K. von Wild
F. H. Doyle	E. Keller	E. D. F. Motti	D. Schrader	W. Winkelmann
W. Entzian	J. Kinnman	D. Moussy	W. Schuhmacher	T. Yoshida
G. U. Exner	G. S. Kistler	A. von zur Mühlen	K. Schürmann	W. Zäh
G. Faglia	H. Kley	E. E. Müller	G. Schwinn	
R. Fahlbusch	J. Köbberling	O. A. Müller	P. C. Scriba	
H. L. Fehm	D. Kondo	A. Nagamune	G. Sell	
C. Ferrari	M. H. Koocheck	M. Neubauer	R. J. Seymour	

336 Figures, 85 Tables



Georg Thieme Publishers Stuttgart 1978

680158935

CIP-Kurztitelaufnahme der Deutschen Bibliothek

Treatment of pituitary adenomas / 1. Europ. Workshop on Treatment of Pituitary adenomas at Rottach-Egern, October 1976. Ed. by Rudolf Fahlbusch and Klaus v. Werder. With contributions by H.-P. Althoff ... – 1. Aufl. – Stuttgart : Thieme; Massachusetts : PSG Publishing Company, 1978.

ISBN 3-13-553801-X (Thieme)

ISBN 0-88416-236-2 (PSG)

NE: Fahlbusch, Rudolf [Hrsg.]; Althoff, H.-P. [Mitarb.]; European Workshop on Treatment of Pituitary Adenomas <01, 1976, Rottach-Egern>

680158935

Some of the product names, patents and registered designs referred to are in fact registered trademarks or proprietary names even though specific reference to this fact is not always made in the text. Therefore, the appearance of a name without designation as proprietary is not to be construed as a representation by the publisher that it is in the public domain.

All rights, including the rights of publication, distribution and sales, as well as the right to translation, are reserved. No part of this work covered by the copyrights hereon may be reproduced or copied in any form or by any means – graphic, electronic or mechanical including photocopying, recording, taping, or information and retrieval systems – without written permission of the publisher.

© 1978 Georg Thieme Verlag, Herdweg 63, P.O.B. 732, D-7000 Stuttgart 1 – Printed in Germany by Karl Grammlich, Pliezhausen

Thieme: ISBN 3-13-553801-X

PSG: ISBN 0-88416-236-2

PSG: LCCCN 77-99148

Contents

Introductory remarks by the editors	III
List of contributors	IV
Introduction to the workshop: F. Marguth	
Foreword	1
ENDOCRINE AND MORPHOLOGICAL ASPECTS – PART I	
P.C. Scriba, C.R. Pickardt, K. v. Werder:	
Physiology of the hypothalamo-Pituitary unit	3
A. Weindl, M.V. Sofroniew:	
Morphology of the hypothalamo-Pituitary unit	10
H.G. Solbach, W. Wiegelmann, H. Kley, K.H. Rudorff, H.L. Krüskemper:	
Endocrine evaluation of pituitary insufficiency	38
H.J. Quabbe:	
Endocrinology of growth hormone producing tumors	47
M. L'Hermite, A. Caufriez, E. Virasoro, A. Stevenaert,	
G. Copinschi, C. Robyn:	
Endocrinology of prolactin-producing tumors	60
H.L. Fehm, K.H. Voigt, E.F. Pfeiffer:	
Endocrinology of ACTH producing pituitary tumors	77
Short contributions	
W. Winkelmann, U. Fricke, W. Hadam, D. Heesen, R. Mies:	
Evaluation of dopaminergic and serotonergic regulation of growth hormone and prolactin in acromegaly	87
G. Faglia, A. Paracchi, P. Beck-Peccoz, C. Ferrari:	
Assessment of the results of transsphenoidal hypophysectomy in acromegaly by means of TRH and L-Dopa tests	91
J. Beyer, J. Happ, U. Cordes, G. Sell, U. Krause, M. Samii, K. Schürmann:	
Pituitary function after surgical treatment of pituitary adenomas	94
K.H. Rudorff, W. Wiegelmann, J. Herrmann, H.K. Kley, H.G. Solbach,	
H.L. Krüskemper:	
Hypothalamo-pituitary dysfunction in eosinophilic granuloma	98
ENDOCRINE AND MORPHOLOGICAL ASPECTS – PART II	
E. Kazner, R. Fahlbusch, W. Lanksch, R. Rothe, U. Scherer, H. Steinhoff,	
Th. Grumme, S. Lange, W. Meese, A. Aulich, S. Wende:	
Computerized tomography in diagnosis and follow-up examination of pituitary adenomas	101
F. Peillon, J. Racadot, D. Moussy, E. Vila-Porcile, L. Oliver, O. Racadot:	
Prolactin-secreting adenomas.	
A correlative study of morphological and clinical data	114

VIII Contents

W. Saeger: Morphology of ACTH-producing pituitary tumors	122
J. Kinnman: Morphology of adenomas in acromegaly	130
A.M. Landolt, V. Rothenbühler, G.S. Kistler: Morphology of the chromophobe adenoma	154

Short contributions

P. De Camilli, L. Tagliabue, A. Paracchi, G. Faglia, P. Beck-Peccoz, M. Giovanelli: In vitro study on the release of GH by fragments of GH-producing human pituitary adenomas. Effect of TRH and DB cAMP	172
D. Kondo, S. Manaka, A. Nagamune, Y. Tsujita, K. Hirakawa, K. Sano: Electrophysiological study on pituitary adenoma cells in tissue culture	179
N. Kageyama, A. Kuwayama, T. Yoshida, T. Okada, T. Fukaya, M. Takanohashi, K. Sugita: Results of transsphenoidal operation and tissue culture studies in GH secreting pituitary adenomas	182
K. v. Wild, H. Ruf, M. Neubauer, H.-P. Althoff, K. Schöffling: Perioperative hormone measurements in patients with pituitary adenomas and hormone replacement therapy	186
R. Illig, T. Torresani, G.U. Exner: Plasma prolactin before and after TRH in 24 children with craniopharyngioma	193
G. Benker, K. Hackenberg, L. Tharandt, W. Zäh, H.E. Clar, W.J. Bock, D. Reinwein: Treatment of hypothalamic-pituitary tumors: Endocrine aspects with special regard to acromegaly	196

OPERATIVE TREATMENT

G. Guiot: Considerations on the surgical treatment of pituitary adenomas	202
R. Kautzky, D. Lüdecke, H. Nowakowski, D. Schrader, N. Stahnke, Ch. Lucke, H.G. Solbach, W. Wiegelmann: Transsphenoidal operation in acromegaly	219
R. Fahlbusch, H.K. Rjosk, K. v. Werder: Operative treatment of prolactin-producing adenomas	225
A. Jefferson: The treatment of chromophobe pituitary adenomas by means of transfrontal surgery, radiation therapy and supportive hormone therapy	237
R.J. Seymour, S. Levin, B. Tyrell, P.H. Forsham: Long-term results of cryohypophysectomy for the treatment of acromegaly	253
G.F. Joplin, L. Banks, D.F. Child, L. Diamant, F.H. Doyle, T.R. Fraser, A. Jadresic, M.H. Koochek: Treatment of acromegaly by pituitary implantation of 90y	261

J.H. Lawrence, C.A. Tobias, C. Chong, J. Lyman, J.L. Born,
 J.A. Linfoot, E. Manougian:
 The treatment of pituitary neoplasms with heavy particles 266

Short contributions

M. Giovanelli, S.M. Gaini, G. Tomei, E.D.F. Motti, P. Beck-Peccoz,
 A. Paracchi, P. de Camilli:
 Transsphenoidal microsurgery of hypersecreting pituitary tumors 272

G. Teasdale, K.W.M. Grossart, J.D. Miller:
 Comparison of cryosurgery and microsurgery in the management
 of acromegaly 280

O. Wilcke, D. Heesen, W. Winkelmann:
 Experiences in 78 ⁹⁰Yttrium implantations in acromegaly 284

G.C. Nicola, G.P. Tonnamelli, A. Greiner:
 Transsphenoidal surgery for secreting pituitary adenomas 287

W. Entzian, A. Melo:
 Transnasal-transsphenoidal approach to pituitary adenoma-extirpation:
 effects on visual functions 293

A. Karduck, W.J. Bock:
 Transmaxillar-transsphenoidal hypophysectomy: Approach and
 rhinological follow-up 299

H.E. Clar, K. Hackenberg, D. Reinwein, W. Schuhmacher, G. Ranft:
 Comparative results in cases of tumors of the sellar region after
 operation by transsphenoidal and transcranial approach 304

M. Samii, K. Schürmann:
 Operative treatment in relation to location and extension of pituitary
 adenomas: Results 310

K. Schürmann, H.J. Reulen, J. Beyer:
 A dramatic bleeding during transsphenoidal operation on an apparent
 pituitary adenoma caused by an intrasellar aneurysm 316

H.A.D. Walder, E. Meijer:
 Some considerations on the differential therapy of pituitary adenomas . . . 323

CUSHING'S SYNDROME

D. Barwich, F. Bahner:
 Pituitary tumors in adrenalectomized patients with Cushing's disease 326

H. Nowakowski, H.J. Breustedt, W. Mitschke, H.R. Montz:
 Anterior pituitary function in hypothalamic Cushing's syndrome
 with and without ACTH-producing adenomas 330

D.K. Lüdecke, R. Kautzky, J. Bansemmer, J. Resetic, H. Montz:
 ACTH secretion and neurosurgical management of Cushing's disease 333

S.W.J. Lamberts, F.H. de Jong, J.C. Birkenhäger:
 Treatment of Cushing's disease by unilateral adrenalectomy
 followed by external pituitary irradiation 339

O.A. Müller, X. Baur, R. Fahlbusch, M. Madler, F. Marguth, C. Uhlig,
 P.C. Scriba, J.M. Bayer:
 Diagnosis and treatment of ACTH-producing pituitary tumors 343

MEDICAL THERAPY

E. Flückiger:
Pharmacology of prolactin secretion 351

E.E. Müller, P.G. Chiodini, D. Cocchi, A.E. Panerai, G. Oppizzi,
G. Colussi, V. Locatelli, A. Liuzzi:
Neurotransmitter control of growth hormone secretion 360

K. v. Werder, R. Fahlbusch, R. Landgraf, C.R. Pickardt, H.K. Rjosk,
P.C. Scriba:
Medical treatment of hyperprolactinemia associated with
pituitary tumor 377

Short contributions

A.E. Schindler, R. Göser, H. Traut, E. Keller:
Ovulation induction with bromoergocryptine and pregnancy in
patients with pituitary tumors 390

H.K. Rjosk, R. Fahlbusch, H. Huber, K. v. Werder:
Growth of prolactin-producing pituitary adenomas during pregnancy 395

MEDICAL THERAPY OF ACROMEGALY

J. Köbberling, G. Schwinn:
Medical treatment of acromegaly 400

Short contributions

C. Lucke, A. von zur Mühlen:
Evaluation of bromocriptine (CB 154) in the treatment of active
acromegaly 411

P.H. Althoff, M. Neubauer, M. Basch, B. Böttger, K. v. Wild,
K. Schöffling:
Acromegaly and bromocriptine – results of long-term treatment 415

DISCUSSION (Except short contributions) 421

INDEX OF AUTHORS 438

SUBJECT INDEX 440

Physiology of the Hypothalamo-Pituitary Unit

P.C. Scriba, C.R. Pickardt and K. von Werder, Munich, FRG

Biogenic amines and hypophysiotropic hormones from the hypothalamus regulate the secretion of the anterior pituitary hormones. These, in turn, control the target glands (adrenals, thyroid, gonads) as far as the glandotropic hormones (ACTH, TSH and gonadotropins) are concerned. This system is subject to negative and, in some cases, positive feedback control through the free fractions of the circulating peripheral hormones (cortisol, thyroid hormones, sexual steroids). Some anterior pituitary hormones (growth hormone, prolactin) and the neurohormones from the posterior pituitary (antidiuretic hormone, oxytocin) exert their effect directly on the peripheral tissues and organs. A complete evaluation of this system would probably fill a textbook [21], this review will therefore be limited to some selected aspects.

The Traditional Interest of Neurosurgeons in Endocrinology

The clinical course of pituitary tumors may be beneficially influenced by a close observation of endocrine signs and symptoms, permitting an early diagnosis of hormonally active or inactive tumors. In the case of inactive tumors, earlier observations (19) revealed that half of the patients showed hypogonadism as a first symptom in their histories; on the other hand in 32 of 42 patients the neglecting of this sign resulted in delay of the diagnosis until deterioration of the visual fields set in. Today, in cases of prolactinoma [27], the female patients (N = 43) with a lower prolactin level tend to outnumber the males (N = 22). This is presumably due to an earlier diagnosis in the case of the females, because amenorrhea and galactorrhea are obviously more impressive endocrine signs than loss of libido and potency.

There is yet another case for endocrinology which should be brought up in this context. Table 1 shows the sites of action and the range of hormonal diagnostic procedures [20, 21]. With reference to the paper of Solbach et al. [22], we should like to emphasize briefly the principle of diagnostic floors — in German "Etagen-Diagnostik". In general, insulin hypoglycemia will stimulate at the hypothalamic level, whereas releasing hormones may indicate an insufficiency of the anterior pituitary and TSH-stimulation, for instance, will test the responsiveness of the target thyroid gland. The site of action is generally less clear if suppression tests have to be used for the differential diagnosis of hormone overproduction states (Table 1).

Laboratory Methods

Most of the diagnostic hormone determinations are nowadays performed by radioimmunoassay. Radioimmunoassay procedures have, in fact, contributed enormously to the knowledge we have today of the pathophysiology of the hypothalamo-pituitary unit.

And yet by far not all methodological questions have been solved satisfactorily in this field.

Studies by Leidenberger et al. [10] showed that the LH-values differed considerably in postmenopausal women when determined by radioimmunoassay or radioreceptor-assay. The ratio of the radioreceptorassay result over radioimmunoassay result was

Table 1 Site of Action and Range of Endocrinological Methods for the Investigation of Hypothalamic and Pituitary Disorders (from Scriba and von Werder [21])

	ACTH	TSH	LH, FSH	Growth hormone	Prolactin
1. Basal hormone levels					
Determination of (glandotropic) anterior pituitary hormones		Thyroxine	Testosterone, estrogens, progesterone	Somatomedins	—
Determination of peripheral hormones	Cortisol (circadian rhythm)	triiodothyronine			
2. Stimulation tests					
Stimulation of the axis hypothalamus-pituitary-peripheral gland	Insulin-hypoglycemia	—	Clomifene	Insulin-hypoglycemia, arginine,	Insulin-hypoglycemia, Phenothiazine
Withdrawal of peripheral hormones = stimulation of hypothalamus-pituitary	Metopirone	Antithyroid drugs	(Anti-androgen)	—	—
Stimulation of the anterior pituitary with hypophyseotropic hormones	Lysin-vasopressin (as CRF)	TRH	LH-RH	—	TRH
Stimulation of peripheral glands with glandotropic hormones	ACTH stimulation test	TSH stimulation test	HCG stimulation test	—	—
3. Suppression tests					
Hypothalamus-pituitary	Dexamethasone	T ₃ suppression test	—	Oral glucose tolerance test	Bromocriptin

higher than ten in some sera. Since the radioreceptor levels agreed with a sensitive in-vitro bioassay, it may be concluded that the radioimmunoassay of LH in serum retains unsolved problems of accuracy at least in terms of the biological significance of what is measured.

The interlaboratory comparison of radioimmunoassays for TSH performed by the German Thyroid Association may be regarded as another example for methodological problems [11]. The value for one sample varied widely around a mean of 22.9 μ U with an interlaboratory coefficient of variation of 64%. The results of the group were improved to a more accurate mean of 17.3 μ U (coefficient of variation = 22%), when standards in hormone-free serum were used as a reference for all participants. Figure 1 provides further information about the accuracy for the radioimmunoassay for TSH [1]. Regular-size TSH preparations and various big TSH preparations from human pituitaries show corresponding values when analyzed by radioimmunoassay and by cytochemical bioassay, i.e. no major discrepancies have been observed so far between radioimmunoassay and bioassay for the determination of TSH. However, certain aspects of

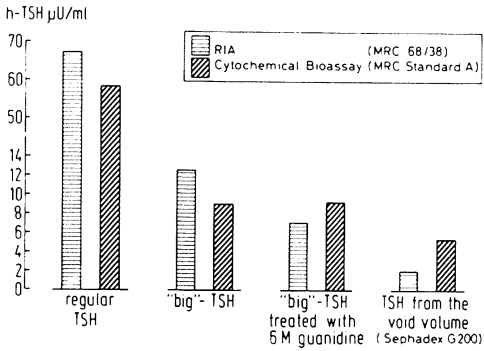


Fig. 1 Comparison of immunological and biological thyrotropin activity in preparations of regular TSH and "big"-TSH (from Erhardt and Doehler [1])

the methods for the quantitative determination of pituitary hormones obviously require continued attention.

The Radioimmunoassay for TRH

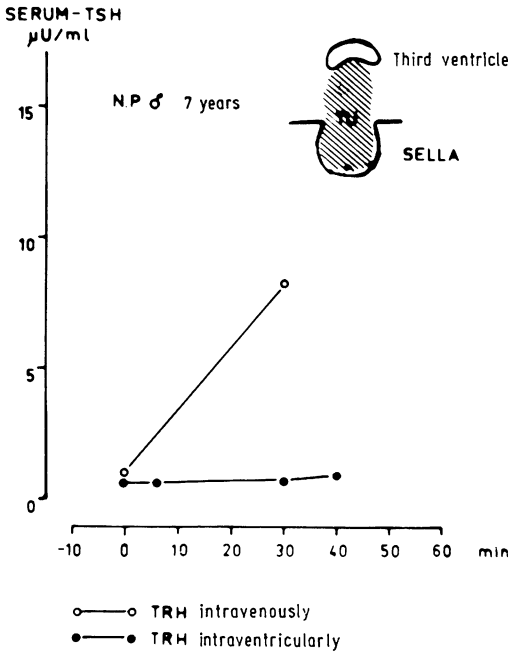
With regard to the determination of hypothalamic releasing hormones, I should like to refer to the recent work of Mitsuma et al. [12]. These authors have apparently developed a radioimmunoassay procedure which permits the analysis of TRH in peripheral serum. It is interesting to note that TRH levels appear to be low in hyperthyroidism. This would favor the early concept of a negative feedback regulation of TRH secretion by thyroid hormones, a concept challenged by the studies of Reichlin et al. [18] and Oliver et al. [15]. This TRH assay [12] might even be useful for the differentiation between hypothalamic and pituitary forms of secondary hypothyroidism.

TRH Stimulation Tests

In recent years releasing hormones have been applied widely for diagnostic stimulation tests. The normal specificity of TRH, for instance, in stimulating TSH and prolactin secretion has been repeatedly documented. This specificity may be altered in cases of pituitary adenomas which produce growth hormone or prolactin; TRH may now stimulate growth hormone secretion. On the other hand, the stimulatory effect of TRH on the lactotroph may be lost in cases of adenoma [26]. The concept of "receptor degeneration" in pituitary adenomas will be dealt with in greater detail later on.

The TRH-stimulation test may even provide insight into localization and extension of tumors in the hypothalamo-pituitary region. As reported previously [17], nine patients with secondary hypothyroidism and suprasellar disease showed a normal or exaggerated TSH response to TRH stimulation. However, a normal or exaggerated TSH response was also found in all patients but one with secondary hypothyroidism due to a hormonally inactive pituitary adenoma. It was concluded from this surprising observation, that the hypothyroidism in these cases was a result of suprasellar extension of the pituitary adenoma, leading to portal vessel occlusion or to direct interference with hypothalamic TRH-production [17]. A suprasellar extension may thus be anticipated in patients with a pituitary tumor, secondary hypothyroidism and TRH-responsive TSH secretion.

Fahlbusch and Pickardt [2] continued the work along these lines. Table 2 compares the TSH increase after intravenous and intraventricular TRH application, respectively, du-



ring a diagnostic puncture of the lateral ventricle. The far right column represents the control TSH response to intraventricular TRH. In contrast, the patient referred to in Fig. 2 did not respond to intraventricular TRH, but showed a perfectly normal TSH increment after intravenous TRH. These findings support the assumption that it may well be the interference with the TRH transport from the third ventricle [16, 17] or, respectively, from the hypothalamus to the anterior pituitary which causes secondary hypothyroidism in patients with suprasellar extension of pituitary adenomas.

Table 2 Increase in Serum TSH Concentration ($\mu\text{U/ml}$) after Intravenous and Intraventricular Administration of $50\mu\text{g}$ of TRH (from Fahbusch and Pickardt [2])

min	intravenous		intraventricular							i. venous ΔTSH at 30'	i. ventricular ΔTSH at 30'
	0'	30'	0'	5'	10'	20'	30'	40'	60'		
R.D.	2.4	12.5	4.1	3.1	3.2	5.0	6.1	6.1	6.0	10.1	2.0
M.M.	2.6	16.2	1.3	1.3	1.7	2.7	4.5	6.3		13.6	3.2
E.J.	1.1	6.4	1.8	2.0	2.6	3.8	6.8	9.3	11.1	5.3	5.0
R.F.	1.8	19.9	2.5		3.1	5.8	9.8	13.8	17.5	18.1	7.3
W.P.	4.3	20.8	3.2		4.5	10.0	13.2	12.8		16.5	10.0

On the Regulation of TSH Secretion

Fig. 3 gives the last example of TRH pathophysiology I should like to discuss. In this study of Horn et al. [8], the effect of repeated oral administration of 40mg TRH to a control group is shown. The first oral TRH administration resulted in the expected increase in TSH and prolactin. At the same time, the T_4 and T_3 levels were slightly raised towards the upper limit of normal, and T_4 remained on the borderline, in accord-

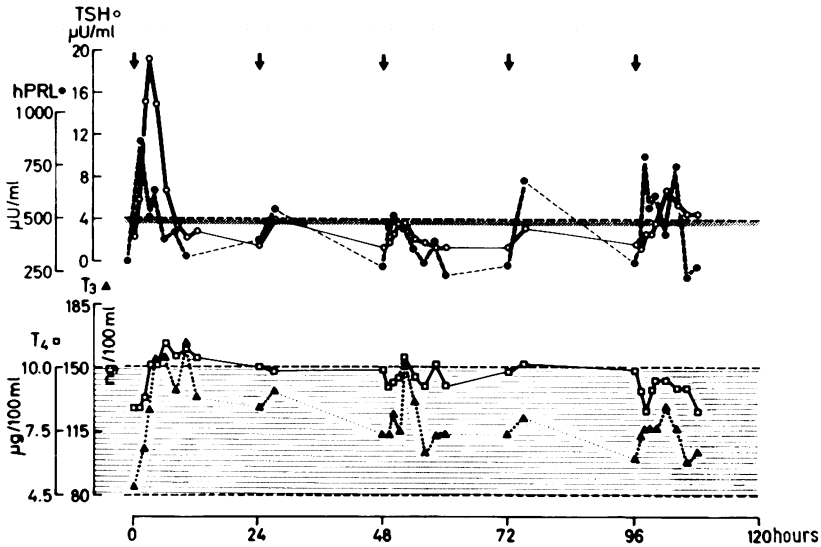


Fig. 3 Diminishing response of TSH and PRL secretion to repeated oral TRH administration (40mg, arrows, cf. text, from Horn et al. [7, 8])

ance with its long half-life. Subsequent oral TRH applications led to much less pronounced increments in TSH. After four weeks of such a regimen (Table 3), the T₄ and T₃ levels remained practically normal, whereas the TSH response was blunted [8]. Apart from the physiological information obtained regarding the regulation of TSH secretion by thyroid hormones and TRH, respectively, this result provides a strong argument against any form of hypothalamic hyperthyroidism and against the "Schreck-Basedow" [7, 8].

Table 3 Effect of Oral TRH Application in Healthy Subjects (N = 12, 40mg per day over a period of 4 weeks; from Horn et al. [8])

		before TRH	after TRH
Serum TSH (μU/ml)	basal	2.0 ± 0.8	1.0 ± 0.5*
	Δ TSH _{30min}	8.1 ± 3.0	3.0 ± 1.9*
Serum T ₃ (μg/100ml)		6.2 ± 1.9	6.5 ± 1.8
Serum T ₃ (ng/100ml)		112 ± 22	109 ± 32

* significance p < 0.005

Somatostatin

I am now turning briefly to the inhibitory hypothalamic hormones. Prolactin secretion appears to be the only example for a predominance of the inhibitory factor, PIF. Somatostatin, originally discovered as the inhibiting factor of growth hormone secretion, apparently plays a most interesting role as local inhibitory factor for many secretory processes and may have additional functions as a neurotransmitter [6]. Three selected

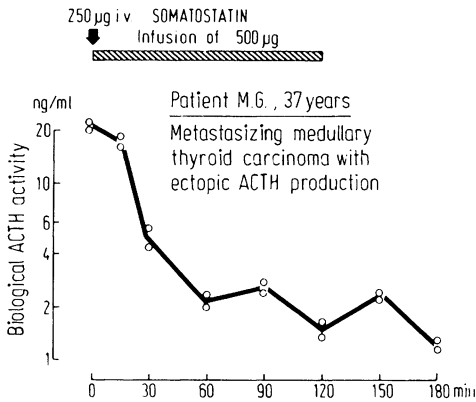


Fig. 4 Somatostatin inhibits ectopic ACTH secretion in a patient with calcitonin-producing medullary carcinoma of the thyroid and ectopic ACTH syndrome (from Müller et al. [13])

examples will be mentioned: first, the inhibition of ACTH secretion in Nelson's syndrome [24]; second, the same inhibition in 3 patients with Addison's disease [3]; and third, a patient, studied by Müller et al. [13], with a calcitonin-producing medullary carcinoma of the thyroid and an ectopic ACTH syndrome, where the ACTH levels could also be lowered by somatostatin (Fig. 4).

Unidentified pituitary Hormones?

Are there still unknown anterior pituitary hormones? This question arose during electronmicroscopic studies of Hachmeister [5] on pituitary adenomas operated on by Dr. Marguth and colleagues. In a number of hormonally inactive adenomas, i.e. from patients showing no hormonal excess according to the currently available radioimmunoassays, secretory granules were observed which did suggest some unidentified hormonal activity. Lipotropins might be a possibility; unfortunately this question is far from being solved, since Dr. Schwandt's peptide B turned out to contain neurophysin, which itself is not lipolytic [14].

An interesting observation came from Boston recently. In a thorough study carried out on 60 patients with pituitary adenomas, Kourides et al. [9] observed 5 patients who showed an excess production of alpha-subunits, not explained by an excess of thyrotropin or gonadotropin. The field of unidentified secretory products of pituitary adenomas is obviously still open for new insights; these would be highly welcome in order to facilitate the handling of pituitary adenomas by monitoring through hormone determinations.

Antidiuretic Hormone

It is obvious that the discussion of neurohormones, of diabetes insipidus and of disorders of ADH secretion and thirst [20, 23] had to be excluded by the conveners. Just in order to remind the audience of the existence of these factors, I should like to mention the experiments of Gottsmann et al. [4, 25]. Here ADH secretion was a sensitive indicator of stress, as shown for 15 min kinesis [25]. The increase and the peak in serum ADH were already observed at moderate severity of kinesis [4] (Fig. 5). With respect to the impending Bavarian evening, it may be noteworthy that kinesis is a more potent stimulus for ADH secretion than thirst.

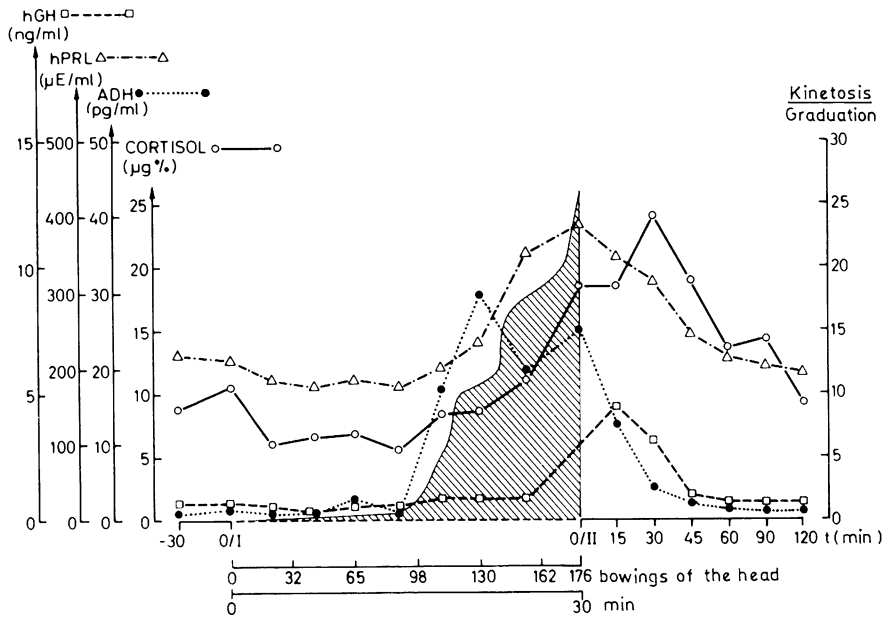


Fig. 5 Increase of serum ADH concentration as well as of other "stress hormones" during Coriolis stimulation. The hatched area represents the severity of kinetosis, up to vomiting (from Gottsmann et al. [4])

Acknowledgments

This investigation was supported by the Deutsche Forschungsgemeinschaft (SFB 51)

References

- 1 Erhardt, F.W., K. Doehler: Biological and immunological activities of high molecular TSH from human pituitaries. *Acta endocr. (Kbh.) Suppl.* 208:1, 1977
- 2 Fahlbusch, R., C.R. Pickardt: The effect of intraventricular TRH in patients with diseases of the hypothalamic and pituitary region. *Acta endocr. (Kbh.) Suppl.* 193:90, 1975
- 3 Fehm, H.L., K.H. Voigt, R. Lang, K.E. Beinert, S. Raptis, E.F. Pfeiffer: Somatostatin: A potent inhibitor of ACTH-hypersecretion in adrenal insufficiency. *Klin. Wschr.* 54:173, 1976
- 4 Gottsmann, M., Th. Eversmann, E. Uhlich, K.v. Werder, G. Ulbrecht: Stress hormone secretion during coriolis stimulation. *Pflügers Arch.Europ.J.Physiol. (Suppl.)* 365, 1976, Abstr. 98
- 5 Hachmeister, U.: Ultrastructural aspects of anterior pituitary tumors. In: *Modern Aspects of Neurosurgery*. Vol. 4, ed. by H. Kuhlendahl, M. Brock, D. Le Vay, T.J. Weston. *Excerpta med. (Amst.)*, ICS 306:108, 1973
- 6 Hökfelt, T., S. Efendic, C. Hellerström, O. Johansson, R. Luft, A. Arimura: Cellular localization of somatostatin in endocrine-like cells and neurons of the rat with special reference to the A_1 -cells of the pancreatic islets and to the hypothalamus. *Acta endocr. (Kbh.) Suppl.* 200, 1975
- 7 Horn, K.: Trijodthyronin (T_3). Zur Bestimmung und pathophysiologischen Bedeutung (Habilitationsschrift). Urban und Schwarzenberg, München-Berlin-Wien, 1976
- 8 Horn, K., R. Fahlbusch, U. Hachmeister, C.R. Pickardt, K.v. Werder, P.C. Scriba: Recurrent goiter and amenorrhea-galactorrhea syndrome in a patient with a thyrotropin (TSH) and prolactin (PRL) producing pituitary adenoma. *Excerpta med. (Amst.)*, ICS 378:517, 1976

- 9 Kourides, I.A., B.D. Weintraub, S.W. Rosen, E.C. Ridgway, B. Kliman, F. Maloof: Secretion of alpha subunit of glycoprotein hormones by pituitary adenomas. *J. Clin. Endocr.* 43:97, 1976
- 10 Leidenberger, F., R. Willaschek, V. Pahnke: Application of a radioligand receptor assay for the determination of luteinizing hormone in human serum. *Acta endocr. (Kbh.) Suppl.* 193:127, 1975
- 11 Marschner, I., F.W. Erhardt, P.C. Scriba: Ringversuch zur radioimmunologischen Thyrotropinbestimmung (hTSH) im Serum. *J. Clin. Chem.* 14:345, 1976
- 12 Mitsuma, T., Y. Hirooka, N. Nihei: Radioimmunoassay of thyrotropin releasing hormone in human serum and its clinical application. *Acta endocr. (Kbh.)* 83:225, 1976
- 13 Müller, O.A., R. Landgraf, R. Ziegler, P.C. Scriba: Ektopisches ACTH-Syndrom bei medullärem Schilddrüsenkarzinom: Hemmbarkeit der ACTH-Spiegel durch Somatostatin. *Acta endocr. (Kbh.) Suppl.* 208:49, 1977
- 14 Neureuther, G., P. Schwandt, J. Otto: Radioimmunoassay for porcine lipotrophic peptide B. *Acta endocr. (Kbh.)*, 85:291, 1977
- 15 Oliver, C., R.L. Eskay, R.S. Mical, J.C. Porter: Radioimmunoassay for TRH and its determination in hypophysial portal and peripheral plasma of rats. Abstr. T.4 49th Meeting Amer. Thy. Ass., Seattle, 1973
- 16 Oliver, C., N. Ben-Jonathan, R.S. Mical, J.C. Porter: Transport of thyrotropin-releasing hormone from cerebrospinal fluid to hypophysial portal blood and the release of thyrotropin. *Endocrinology* 97:1138, 1975
- 17 Pickardt, C.R., F. Erhardt, R. Fahlbusch, B. Grüner, P.C. Scriba: The diagnostic significance of the stimulation of TSH secretion by administration of thyrotropin releasing hormone (TRH) in diseases of the hypothalamus and pituitary. *Excerpta med. (Amst.)*, ICS 306:105, 1973
- 18 Reichlin, S., J.B. Martin, M. Mitnick, R.L. Boshans, Y. Grimm, J. Bollinger, J. Gordon, J. Malacara: The hypothalamus in pituitary-thyroid regulation. *Rec. Progr. Horm. Res.* 28:229, 1972
- 19 Schwarz, K.: Pathophysiologie und Klinik der Hypophysentumoren (Referat). *Symp. Dtsch. Ges. Endokr.* 15:223, 1969
- 20 Scriba, P.C.: Endocrinology of the hypothalamus and the pituitary gland. *Excerpta med. (Amst.)* ICS 306:83, 1973
- 21 Scriba, P.C., K. von Werder: Hypothalamus und Hypophyse. In: *Klinische Pathophysiologie*, 3. Aufl., Hsg. W. Siegenthaler, Thieme, Stuttgart, 1976, p. 278
- 22 Solbach, H.G., W. Wiegelmann, H.L. Krüskenper: Endocrine evaluation of pituitary insufficiency. This volume, 1977, p ...
- 23 Sridhar, C.B., G.D. Calvert, H.K. Ibbertson: Syndrome of hypernatremia, hypodipsia and partial diabetes insipidus: A new interpretation. *J. Clin. Endocrinol. Metab.* 38:890, 1974
- 24 Tyrrell, J.B., M. Lorenzi, J.E. Gerich, P. P.H. Forsham: Inhibition by somatostatin of ACTH secretion in Nelson's syndrome. *J. Clin. Endocrinol. Metab.* 40:1125, 1975
- 25 Uhlich, E.: Vasopressin. Thieme Copythek, Stuttgart, 1976
- 26 von Werder, K.: Wachstumshormone und Prolactinsekretion des Menschen. (Habilitationsschrift). Urban und Schwarzenberg, München-Berlin-Wien, 1975
- 27 von Werder, K., R. Fahlbusch, R. Landgraf, C.R. Pickardt, H.K. Rjosk, P.C. Scriba: Medical treatment of prolactin producing adenomas. This volume, p. 377