

Cellular Composition of the Human Pituitary Pars tuberalis as Revealed by Immunocytochemistry *

Burton L. Baker**

Department of Anatomy and the Reproductive Endocrinology Program,
The University of Michigan Medical School, Ann Arbor, Michigan, USA

Summary. An attempt was made to determine if any of the specialized secretory cell types common to the pars distalis also occur in the pars tuberalis of the human hypophysis. Available for study were 18 specimens of the inferior pars tuberalis, which partially surrounds the infundibular stem, and 3 specimens of the superior pars tuberalis that is attached to the median eminence. Antisera to human somatotropin, mammotropin, chorionic gonadotropin, follicle-stimulating hormone, FSH β , luteinizing hormone, LH β , thyrotropin, TSH β , as well as to β^{1-24} -corticotropin, porcine β^{17-39} -corticotropin, and ovine LH were used with the Sternberger peroxidase-antiperoxidase immunocytochemical procedure to identify the probable cells of origin for these hormones.

The evidence indicated that gonadotropic cells constitute the major portion of the parenchymal cell population in the pars tuberalis. They occurred throughout all of the pars tuberalis and were usually arranged in clusters. Somatotropic, mammotropic, corticotropic, and thyrotropic cells were rare and not found in all specimens. When present, they often formed a common group suggesting that their occurrence in the pars tuberalis resulted from displacement of primordial tissue of the pars distalis during embryogenesis.

Key words: Pituitary gland (Human) – Pars tuberalis – Cytology – Gonadotropic cell.

Introduction

The parenchymal cell types composing the pituitary pars tuberalis of man and the functional role played by this lobe have not been identified. According to

Send offprint requests to: Dr. Burton L. Baker, Department of Anatomy, Medical Science Building II, The University of Michigan, Ann Arbor, Michigan 48109, USA

* Supported in part by research grants HD-03159 and HD-08333 from the National Institute for Child Health and Human Development

** We thank Dr. L.A. Sternberger for providing the PAP complex and others for antisera (Table 2) and hormones (Footnote 2) as listed

Romeis (1940) the pars tuberalis has sometimes been regarded as being histologically similar to the pars distalis, but less differentiated, since most of its cells appear chromophobic in sections prepared with differential staining techniques. With respect to occurrence in the human pars tuberalis of specific secretory cell types of the pars distalis, Romeis noted the consistent absence of α -cells (somatotropes), although others had reported their occasional presence. In the inferior one-half of almost every pars tuberalis examined, Romeis observed sparsely scattered clusters of β -cells (basophils) that resembled those in the pars distalis. Midgley (1966b), incidental to an investigation of gonadotropes in the human pars distalis, demonstrated with immunofluorescence the presence of cells containing luteinizing hormone in the inferior portion of the pars tuberalis.

Reported here is an attempt to determine if any of the hormones secreted by the pars distalis might be produced in the pars tuberalis also. Immunocytochemistry was used, this technical approach being feasible because hormones of the pars distalis have become available in synthetic or sufficiently pure form so that reasonably specific antisera to them can be prepared. The information obtained might suggest some of the functions performed by the pars tuberalis, since accumulation of a hormone within the cytoplasm of a parenchymal cell probably indicates that the hormone is also secreted by the cell.

Materials and Methods

For this study the pars tuberalis will be considered in two parts: superior and inferior. The superior pars tuberalis is the portion that adheres to the median eminence of the hypothalamus. The inferior pars tuberalis is attached to and partially surrounds the infundibular stem of the hypophysis, the infundibular stem and pars tuberalis together constituting the pituitary stalk. To secure the superior pars tuberalis a block of tissue, including the hypothalamus, was excised from the brain by frontal cuts along the posterior side of the optic chiasma and the posterior borders of the mammillary bodies; by sagittal cuts medial to the optic tracts; and by a transverse cut through the anterior and posterior commissures. To prepare the inferior pars tuberalis for study, the hypophysis was divided transversely into superior and inferior halves and the superior half with attached pituitary stalk was used.

The specimens were obtained from autopsies performed in the University of Michigan Hospital; eighteen of the inferior pars tuberalis (Table 1) and three of the superior portion were suitable for immunocytochemistry. The postmortem interval before autopsy averaged 6 h with a range of 3 to 16 h. All individuals except four were males; they ranged in age from 6 weeks to 72 years. None exhibited primary pathology of the endocrine system. Since a large proportion of these individuals died from violent causes, pathological change in other parts of the body was often minimal.

The tissues were fixed in Bouin's fluid for 48 h, dehydrated in ethanol, cleared in carbon disulfide, and embedded in Paraplast. The mediobasal portion of the brain, including the superior pars tuberalis, was sectioned serially at a thickness of 3 to 5 μ m on a frontal plane. The superior half of each hypophysis, with stalk (including the inferior pars tuberalis) attached, was sectioned serially on either a transverse or sagittal plane. Every fortieth section from each tissue block was stained with either the Masson trichrome procedure (hypophysis) or cresyl violet (hypothalamus) in order to facilitate selection of desirable sections for immunocytochemical analysis of the pars tuberalis.

The peroxidase-antiperoxidase (PAP) procedure of Sternberger, essentially as described by Petrali et al. (1974), was used for localization of hormones. The antisera to pituitary hormones, and the heterologous antiserum to rabbit IgG (1:10), were applied to the tissue section for 30 min each. The period of incubation in the substrate containing 3,3'-diaminobenzidine (DAB) varied from 5 to 25 min, the duration being determined by the time required to elicit intense immunostaining of cells. A variable number of sections from the different cases were immunostained. If tissue preservation was exceptionally good, as many as 25 slides were prepared. For observation of the distribution of gonadotropic cells as many as six sections from different regions of the pars tuberalis were studied.

Table 1. Localization of cell types in the pars tuberalis of the human hypophysis

Case No.	Sex	Age (Yr)	Somatotropic cell	Mammotropic cell	Corticotropic cell	Gonadotropic cell	Thyrotropic cell
<i>Inferior portion</i>							
1	F	26	0	0	0	++	0
2	F	36	0	0	0	++	+
3	F	48	0	0	0	+	0
4	F	76	+	0	0	++	0
5	M	6 wk	+	+	0	++	+
6	M	17	0	0	0	++	+
7	M	26	0	0	0	+	0
8	M	36	0	0	0	++	+
9	M	39	0	+	0	++	+
10	M	40	0	+	+	++	+
11	M	44	+	+	0	++	+
12	M	48	0	0	+	++	+
13	M	55	0	+	0	++	+
14	M	59	0	0	0	++	+
15	M	65	0	0	0	++	0
16	M	70	0	0	0	++	+
17	M	71	+	0	0	++	+
18	M	72	0	0	0	++	0
<i>Superior portion</i>							
19	M	36	0	0	0	++	0
20	M	41	0	0	0	++	0
21	M	57	0	0	+	+	0

F female; *M* male; ++ Many cells; widely distributed; + Rare cells; usually near pars distalis

The antisera to hormones of the pars distalis that were employed in this study are summarized (Table 2) together with their origins and the dilutions used for immunostaining. Along with antisera to intact hormones, antisera to the β -subunits of FSH, LH and TSH were used because the β -subunit accounts for the biological properties of the complete hormone and imparts immunological specificity to the hormone (Vaitukaitis and Ross, 1972). For immunostaining of thyrotropic and FSH-gonadotropic cells, major reliance was placed on anti-hTSH β ¹ and anti-hFSH β , respectively. These antisera were preabsorbed by addition of hCG at a concentration of 1.5 to 2.5 I.U./ μ l, the solution then being incubated at 4°C overnight. For LH-gonadotropic cells, anti-hCG was used routinely.

Since determination that hormones were absent from the pars tuberalis was as important as observing their presence, regular verification of the capacity of these antisera to permit immunostaining of specific cell types in the pars distalis was necessary. For the inferior pars tuberalis this was accomplished by concurrent immunostaining of the portion of the pars distalis attached to the pituitary stalk in each sagittal section. Also, each time a section of a transversely cut pituitary stalk, or of the superior pars tuberalis was immunostained, effectiveness of the antiserum was demonstrated concurrently in a section of the pars distalis similarly treated.

Several other controls for the procedure and for assessment of antiserum specificity were included. Immunostaining was absent when normal rabbit serum was substituted for a hormonal antiserum, when DAB was omitted from the incubating solution, and when the antiserum was preabsorbed

¹ Abbreviations used in this report are as follows: "anti-", an antiserum to the hormone given in the suffix; h, human; p, porcine; o, ovine; r, rat; CG, chorionic gonadotropin; Prl, prolactin (mammotropin); LH, luteinizing hormone; FSH, follicle-stimulating hormone; TSH, thyroid-stimulating hormone

Table 2. Antisera used for demonstration of cell types in the pituitary pars tuberalis

Cell type	Antiserum	Dilution	Source	References on specificity for pars distalis
Somatotropic	Anti-hGH, B85	1/200	B.L. Baker	Baker et al. (1969); Baker (1974)
Mammotropic	Anti-hPrI	1/25	Calbiochem, Inc.	Baker, Yu (1977)
Corticotropic	Anti- β^{1-24} -corticotropin, B44	1/100	B.L. Baker	Baker, Drummond (1972); Baker (1974)
	Anti- $p\beta^{17-39}$ -corticotropin, B37	1/25	B.L. Baker	
Gonadotropic	Anti-hCG, 391-3	1/1000	A.R. Midgley, Jr.	Phifer et al. (1973); Baker (1974)
	Anti-hLH, Batch 1	1/500	NIAMDD, Natl. Pit. Agency	
	Anti-hLH β	1/1000	A.F. Parlow ^c	
	Anti-hFSH, Batch 3 ^a	1/200	NIAMDD, Natl. Pit. Agency	
	Anti-hFSH β ^b	1/1000	A.F. Parlow ^c	
Thyrotropic	Anti-oLH, 573	1/1000	A.R. Midgley, Jr.	
	Anti-hTSH β ^b	1/1000	J.G. Pierce	Baker et al. (1972); Baker (1974)
	Anti-hTSH ^b	1/1000	W.D. Odell	

^a Preabsorbed with hCG by the National Pituitary Agency

^b Preabsorbed in this laboratory by addition of 1.5 to 2.5 I.U. hCG/ μ l of antiserum at a dilution of 1/150 to 1/300

^c Rat Pituitary Hormone Distribution Program, NIAMDD

with its hormonal antigen². Specificity would be indicated also by absence of immunological cross-reactivity of the antisera with related hormones. Special attention was given to the glycoprotein hormones (LH, FSH and TSH) since the gonadotropic cell seemed to be the dominant type in the pars tuberalis. At sufficiently high concentrations of the absorbing hormone, variable cross-reactivity between the glycoprotein hormones was observed (Table 3). Absorptions of antisera with hormones other than with the original antigen, were carried out in the following manner. First the influence of increasing dilutions of the primary antiserum on the intensity of immunostaining was observed. Selected for routine use in immunostaining, and for studies on cross-reactivity with other hormones, was a dilution somewhat less than the highest dilution that would still give maximal staining intensity. Ten μ l of hormonal absorbant dissolved in physiological buffered saline was added to 10 μ l of the antiserum giving final concentrations of 0.5, 2.5, 5, and 50 ng/ μ l for the absorbant. The mixture was incubated at 4°C overnight. Then the utility of the absorbed antiserum for immunostaining was compared with that of nonabsorbed antiserum; cross-reactivity and nonspecificity were indicated by absence of immunostaining.

Specificity of an antiserum was indicated also if a cell stained with it was not stained with any of the other antisera. Two procedures were followed to observe this possibility. On consecutive sections,

² The hormones used as absorbants and their providers were as follows: hGH (NIH-GH-HS 1395) and hPrI (NIH-HPr-VLS-3), the National Pituitary Agency of the National Institute for Arthritis, Metabolism and Digestive Diseases; hCG (Lot No. 102C-0360, Sigma); hTSH (Lot 420018, Calbiochem, Inc.); hFSH (Lot 389549, Calbiochem, Inc.); hLH (Lot 389557, Calbiochem, Inc.); hTSH β (N-870-B), hFSH β (N-596-C) and hLH β (BS-S39-B), Dr. A.F. Parlow, NIAMDD; and β^{1-24} -corticotropin, $p\beta^{17-39}$ -corticotropin, Ciba-Geigy, Ltd

Table 3. The influence of cross-absorption on the effectiveness for immunostaining of antisera to glycoprotein hormones or their β -subunits

Antiserum/absorbant	Final concentration of absorbant (ng/ μ l)			
	0.5	2.5	5	50
<i>Anti-hCG</i>				
hCG	+	0	0	0
hTSH β	+	+	+	\pm
hTSH	+	+	\pm	\pm
hFSH β			+	\pm
hFSH			+	\pm
<i>Anti-hFSHβ^a</i>				
hFSH β	+	\pm	0	
hFSH	+	+	0	0
hTSH β			+	\pm
hTSH			+	\pm
<i>Anti-hTSHβ^a</i>				
hTSH β	+	0	0	0
hTSH	+	0	0	0
hFSH β			+	0
hFSH			+	0

+ = intense staining (i.e., no neutralization of the antiserum); \pm = weak staining (i.e., partial neutralization); 0 = no staining (i.e., complete neutralization of the antiserum)

Anti-hCG and anti-hFSH β were evaluated on the basis of staining of gonadotropic cells, and anti-hTSH β by its staining of thyrotropic cells

^a Preabsorbed with hCG

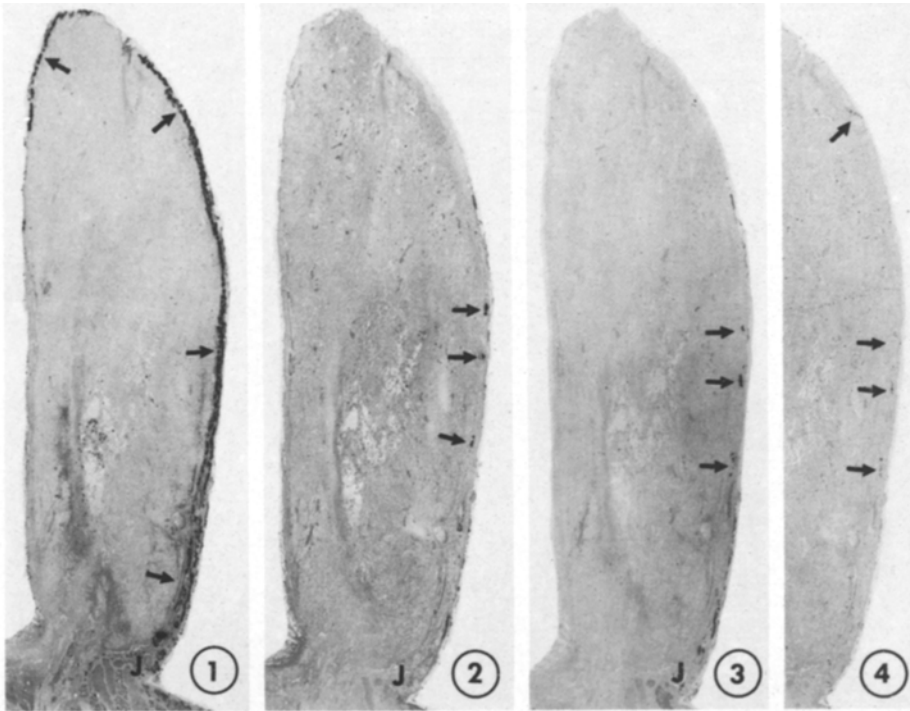
attempts were made to examine a single cell, or group of cells, when immunostained for two to three different hormones. Also double immunocytochemical staining was employed with DAB and 4-chloro-1-naphthol serving as labels for detection of different hormones, thus permitting differentiation of cell types on the basis of their contrasting colors.

In order to compare immunostained cells with those described previously on the basis of standard cytological staining techniques, some sections containing the pars tuberalis were prepared with the Brookes' (1968) combination of carmoisine L-wool green S-orange G for differentiation of somatotropes from mammatropes, and the Adams and Swettenham (1958) performic acid-PAS-Alcian blue-orange G procedure for differentiation of gonadotropes from thyrotropes.

Results

As demonstrated routinely with anti-hCG, it appeared that the gonadotropic cell³ (Figs. 1, 7, 11) was the dominant cell type of the human pars tuberalis in all specimens studied (Table 1). Gonadotropic cells were distributed throughout the

³ The terminology for cell types in the pars distalis, as recommended by the Nomina Histologica (1975) is not applied here to cells of the pars tuberalis in order to avoid the implication that the function of the latter cells is conclusively revealed. Thus, instead of "gonadotrope" (or "gonadotroph"), "gonadotropic cell" will be used



Figs. 1–4. Sagittal sections of pituitary stalk from 40 yr-old male showing inferior pars tuberalis. *J*, junction between pars tuberalis above and pars distalis below. $\times 13$

Fig. 1. Immunostained with anti-hCG. Pars tuberalis (arrows) forms narrow border on anterior (right) side of stem. It appears dark because of high density of gonadotrophic cells

Fig. 2. Immunostained with anti- β^{1-24} -corticotropin. Arrows point to the only clusters of corticotrophic cells in this expanse of pars tuberalis

Fig. 3. Immunostained with anti-hTSH β . Arrows point to the only thyrotrophic cells present in this section

Fig. 4. Immunostained with anti-hPrL. Only a few faint mammatropes (arrows) appear in this section. Note that in Figures 2–4, three different cell types appear as components of single clusters

full extent of the pars tuberalis from the inferior region of continuity with the pars distalis, superiorly alongside the infundibular stem and median eminence to termination of the pars tuberalis in the sulcus (Fig. 11) that separates the median eminence from the tuber cinereum. In the inferior pars tuberalis clusters of gonadotrophic cells and single gonadotrophic cells were scattered between long, longitudinally oriented, portal blood vessels (Fig. 7) that extend throughout this pituitary lobe. In the superior pars tuberalis, gonadotrophic cells were commonly located close to the external lamina of the median eminence (Fig. 11). The gonadotrophic cell was usually ovoid, but occasionally polygonal (Figs. 9, 12, 14). Rarely such cells occurred singly but more commonly they were aggregated in clusters.

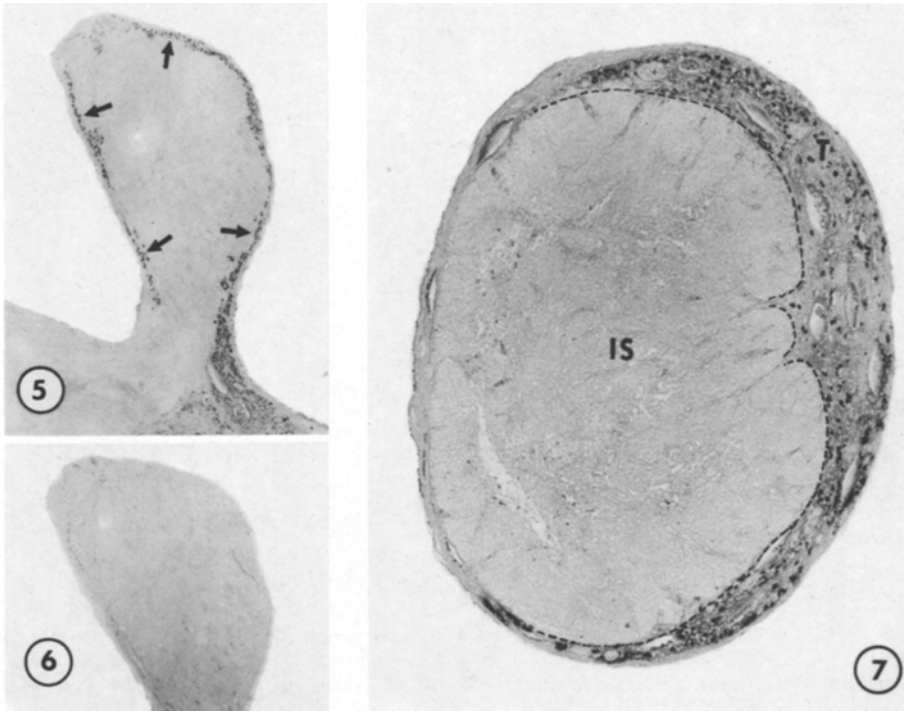


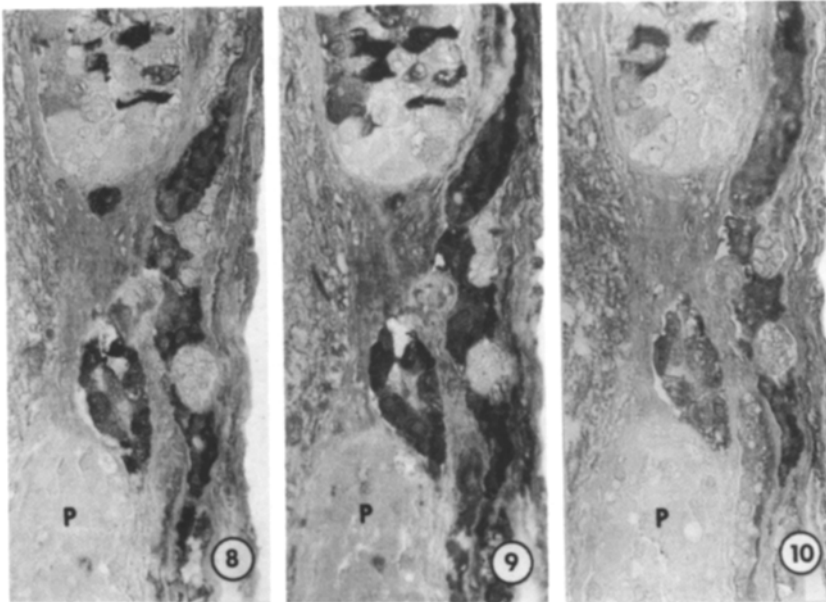
Fig. 5. Sagittal section of inferior pituitary stalk from 26 yr-old pregnant woman. Immunostained with anti-hCG. Many dark gonadotrophic cells (arrows) mark extent of pars tuberalis on anterior (right) and dorsolateral sides (left) of infundibular stem. $\times 13$

Fig. 6. Section of pituitary stalk, adjacent to that illustrated in Figure 5, immunostained with anti-hCG after antiserum had been preabsorbed with hCG. No staining of gonadotrophic cells. $\times 13$

Fig. 7. Transverse section of the pituitary stalk from 44 yr-old male, immunostained with anti-hCG. Pars tuberalis (*T*) (external to interrupted line) covers anterior (right) and lateral sides of infundibular stem (*IS*). Several portal vessels in pars tuberalis. Gonadotrophic cells (black dots) scattered throughout pars tuberalis. $\times 37$

On the basis of the following considerations the presence of LH appears to have been demonstrated in gonadotrophic cells. Insofar as individual cells and cell groups could be identified in consecutive sections, cells immunostained with anti-hCG (Fig. 9) were also revealed with anti-hLH (Fig. 8), anti-hLH β (Fig. 10) and anti-oLH. Also, prior absorption of anti-hCG with hCG eliminated its usefulness for immunostaining (Figs. 5, 6).

Gonadotrophic cells also seemed to contain FSH. Both anti-hFSH and anti-hFSH β were preabsorbed with hCG to remove contaminating antibodies to LH and thus increase the specificity of the antisera. When consecutive sections were immunostained with anti-hCG preabsorbed with hFSH (5 ng/ μ l) (Fig. 12)



Figs. 8–10. Consecutive sections of pars tuberalis from 40 yr-old male, a specimen illustrated in Figures 1–4. **Figs. 8, 9, and 10** immunostained, respectively, with anti-hLH, anti-hCG, and anti-hLH β . With few exceptions the same cells, or clusters of cells, are stained in each section. Below a group of unstained parenchymal cells (*P*). $\times 375$

and with anti-hFSH β preabsorbed with hCG (Fig. 13), at least some cells were found to contain both LH and FSH although one cannot conclude that all LH-gonadotropic cells contained FSH.

Cells containing other hormones of the pars distalis were observed rarely in the inferior pars tuberalis (Table 1) and, if present, only a few appeared in restricted foci. Among these occasional cells were somatotropic, corticotropic (Figs. 2, 15), thyrotropic (Figs. 3, 16), and mammatropic cells (Figs. 4, 17). Corticotropic cells were immunostained with both anti- β^{1-24} -corticotropin and anti- β^{17-39} -corticotropin. Similarly, identical thyrotropic cells were revealed with anti-hTSH and anti-hTSH β , both antisera having been preabsorbed with hCG. That the gonadotropic cell differed from the somatotropic, mammatropic and corticotropic cells was indicated by double immunocytochemical staining, with which procedure the gonadotropic cell appeared gold (DAB) and the other types steel-blue (4-C1-1-naphthol). Also they were shown to be different by comparing consecutive sections, one of which was immunostained for gonadotropic cells, and the other for a different cell type. The latter procedure was not completely satisfactory because so few of the non-gonadotropic cells were present for observation.

The various cell types were usually grouped in a cluster (Figs. 2–4, 15–17) and they appeared most commonly in the zone of the inferior pars tuberalis that continues into the pars distalis. In the superior pars tuberalis cell types other than gonadotropic cells were not found in two of the three specimens, but in the third

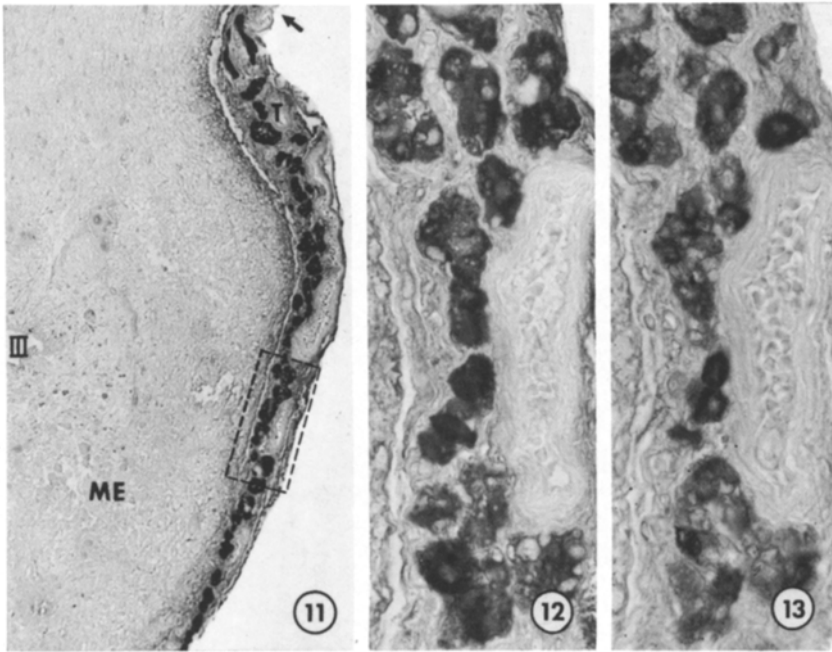
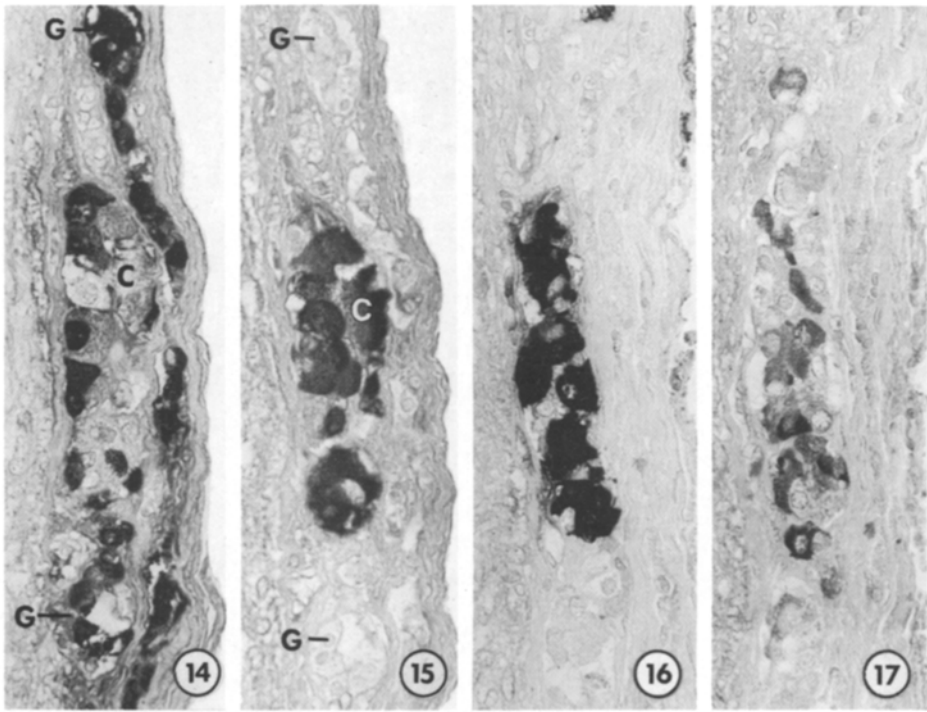


Fig. 11. Section through lateral zone of median eminence (*ME*) with pars tuberalis (*T*) alongside and reaching superiorly to junction with tuber cinereum (arrow). Forty-one yr-old male immunostained with anti-hCG. Clusters of gonadotrophic cells (black) extending throughout pars tuberalis. *III*, Third ventricle. $\times 100$

Figs. 12 and 13. Adjacent sections close to area outlined in Figure 11. Figure 12 immunostained with anti-hCG, Figure 13 with anti-hFSH β preabsorbed with hCG. The same cells stained in both sections; few, if any, parenchymal cells remaining unstained. $\times 480$

several corticotrophic cells appeared in the region of continuity between the median eminence and infundibular stem. In accord with the scarcity of mammotrophic and somatotrophic cells, cells stained with carmoisine L and orange G, respectively, of the Brookes procedure could not be found. With the Adams-Swettenham procedure, light PAS staining, that is characteristic of gonadotropes, occurred in many cells, while Alcian blue staining was observed rarely. Due to the type of fixation, postmortem cellular changes, and probably the nature of the cells themselves, the results of such histochemical staining were unsatisfactory.

Accurate differential counting of the proportion of the parenchymal cell population made up by gonadotrophic cells was not possible because of variable cytolysis that occurred during the postmortem interval preceding fixation. However, on the best preserved specimens (Cases 10 and 20, Table 1) of the inferior and superior pars tuberalis such counts were attempted. From these data it is estimated that at least 80% of the parenchymal cells are gonadotrophic. Thus, only a small portion of the total cell population could have included other secretory types. Observation of the pars tuberalis from all cases immunostained for gonadotrophic cells revealed exceedingly few unstained parenchymal cells. The areas



Figs. 14–17. Enlargements of areas in Figures 1–4. **Figs. 14 and 15** adjacent sections. **Figs. 16 and 17** neighboring sections. $\times 375$

Fig. 14. Immunostained with anti-hCG

Fig. 15. Immunostained with anti- β^{1-24} -corticotropin. Although all cells cannot be matched accurately in Figures 14 and 15, some corticotropic cells are clearly different from gonadotropic cells. Many gonadotropic cells (*G*) different from corticotropic cells (*C*)

Fig. 16. Immunostained with anti-hTSH β preabsorbed with hCG

Fig. 17. Immunostained with anti-hPrI. Mammotropic cells much smaller than presumptive thyrotropic cells (Fig. 16)

illustrated in Figures 14–17 were selected from the inferior portion of the pars tuberalis to show cell groups that contained multiple cell types. Such groups containing cell types other than gonadotropic cells were rare (Table 1). In Figs. 12 and 13 of the superior pars tuberalis almost all parenchymal cells contained gonadotropin.

Discussion

Since it appears that the gonadotropic cell is the dominant glandular component in the human pars tuberalis, special consideration must be given to the specificity

of our antisera for the glycoprotein hormones. The production of specific antisera against human LH, FSH and TSH has been difficult because these hormones contain a common α -subunit that could account for the frequently observed immunological cross-reactivity between them (Vaitukaitis and Ross, 1972); also preparations of these hormones are commonly contaminated with the other two hormones. Data derived from competitive binding studies are helpful in assessing the specificity of such antisera but they cannot be applied unreservedly to immunocytochemical usage because the influence of technical procedures on the status of tissue antigens is unknown.

With respect to anti-hCG, complete cross-reaction between it and hLH has been demonstrated by numerous investigators including Midgley (1966 a). Hence, anti-hCG has been useful in radioimmunoassays for hLH and its utility for immunostaining of LH in the human hypophysis has been demonstrated (Midgley, 1966 b). In this study anti-hCG was neutralized completely with hCG at a concentration of 2.5 ng/ μ l but this did not occur with a 20-fold concentration (50 ng/ μ l, Table 3) of hTSH, hFSH or their β -subunits. Hence, anti-hCG seemed to be specific for localization of LH.

Competitive binding studies have shown that specific antisera can be prepared to the β -subunits of hTSH and hFSH (Vaitukaitis et al., 1973). With respect to anti-hFSH β , complete neutralization resulted from preabsorption with hFSH β and hFSH at a concentration of 5 ng/ μ l (Table 3) while this effect was not obtained with a 10-fold higher concentration (50 ng/ μ l) of hTSH β or hTSH. Thus, when anti-FSH β was preabsorbed with hTSH within the concentration range of 5 to 50 ng/ μ l to remove antibodies to TSH, and since it was preabsorbed with hCG routinely to neutralize antibodies to LH, it should have been specific for demonstration of FSH.

The difficulty experienced in completely eliminating LH from TSH preparations is well recognized. In this study anti-hTSH β was preabsorbed with hCG to remove antibodies to LH. Further, immunostaining of presumptive thyrotropic cells with anti-hTSH β was prevented by preabsorption with hTSH β and hTSH at a concentration of 2.5 ng/ μ l but a 20-fold higher concentration (50 ng/ μ l) of hFSH β and hFSH was required to obtain this effect.

For the following reasons it is concluded that most of the cells revealed in the pars tuberalis with anti-hCG are LH-gonadotropic cells. (1) Anti-hCG cross-reacts with hLH and prior absorption of the antiserum with hCG prevents immunostaining of these cells. (2) The same cells were stained with anti-LH, anti-hLH β , and anti-oLH. (3) The presumptive LH-gonadotropic cells of the pars tuberalis far surpass in number all other cell types immunostained with antisera to pars distalis hormones, and few parenchymal cells remain that could contain other hormones. Thus, it seems certain that the LH-gonadotropic cells are different from the somatotropic, mammatropic and corticotropic cells. Further, most of the gonadotropic cells cannot be thyrotropic cells because so few of the latter could be detected with anti-hTSH and anti-hTSH β . On the other hand, we could not prove that rare LH-gonadotropes did not contain TSH because of the paucity of thyrotropic cells and variable postmortem cytolysis. Finally, these observations indicate that most gonadotropic cells contain both FSH and LH, as appears to be true of gonadotropes in the human pars distalis (Phifer et al., 1973; Robyn et al., 1973).

The presence of gonadotropic cells in the pars tuberalis may be characteristic of mammals in general. As in man, FSH/LH-gonadotropic cells are prominent in the superior portion of the pars tuberalis of the rhesus monkey (unpublished data). In the rat, Baker and Yu (1975) demonstrated with immunocytochemistry that gonadotropic cells are characteristic components of the caudal pars tuberalis associated with the infundibular stem. However, cephalically in the pars tuberalis attached to the median eminence gonadotropic cells are rare, in marked contrast to their considerable frequency in man and the monkey (Baker, unpublished). Other evidence supporting the concept that gonadotropic cells occur in the pars tuberalis of mammals is available. Thus Legait et al. (1970) and Stoeckel et al. (1973) described PAS-positive cells in the pars tuberalis of the rat which they regarded as being gonadotropic. Dellmann et al. (1974) supported this conclusion with electron microscopy.

The demonstration that gonadotropic cells are plentiful in the superior pars tuberalis means that some cells of origin for LH and FSH lie close to nerve terminals in the external lamina of the median eminence that contain, and presumably secrete, gonadotropin-releasing hormone. The functional significance of such a close positional relationship between effector and receptor structures warrants investigation.

Finally, these observations may have clinical significance. When hypophysectomy is performed in man the superior pars tuberalis, and possibly some of the inferior pars tuberalis, remains in situ. Because of the many gonadotropic cells in this tissue the potential for continued LH and FSH secretion is high. Hence, it is possible that persistent secretion of gonadotropin might influence the clinical result when hypophysectomy is performed for therapeutic purposes. In contrast, functionally significant secretion of gonadotropins after hypophysectomy of rats might not be expected because the comparable portion of the pars tuberalis contains few gonadotropic cells.

References

- Adams, C.W.M., Swettenham, R.V.: The histochemical identification of two types of basophil cells in the normal human adenohypophysis. *J. Path. Bact.* **75**, 95–103 (1958)
- Baker, B.L.: Functional cytology of the hypophysial pars distalis and pars intermedia. In: *Handbook of physiology. Sect. 7. Endocrinology, Vol. IV, Part 1*, pp. 45–80 (R.O. Greep and E.B. Astwood, eds.). Washington, D.C.: American Physiological Society 1974
- Baker, B.L., Drummond, T.: The cellular origins of corticotropin and melanotropin as revealed by immunohistochemical staining. *Amer. J. Anat.* **134**, 395–410 (1972)
- Baker, B.L., Midgley, A.R., Jr., Gersten, B.E., Yu, Y.-Y.: Differentiation of growth hormone- and prolactin-containing acidophils with peroxidase-labeled antibody. *Anat. Rec.* **164**, 163–172 (1969)
- Baker, B.L., Pierce, J.G., Cornell, J.S.: The utility of antisera to subunits of TSH and LH for immunohistochemical staining of the rat hypophysis. *Amer. J. Anat.* **135**, 251–268 (1972)
- Baker, B.L., Yu, Y.-Y.: Immunocytochemical analysis of cells in the pars tuberalis of the rat hypophysis with antisera to hormones of the pars distalis. *Cell Tiss. Res.* **156**, 443–449 (1975)
- Baker, B.L., Yu, Y.-Y.: An immunocytochemical study of human pituitary mammotropes from fetal life to old age. *Amer. J. Anat.* **148**, 217–239 (1977)
- Brookes, L.D.: A stain for differentiating two types of acidophil cells in the rat pituitary. *Stain Technol.* **43**, 41–42 (1968)

- Dellmann, H.-D., Stoeckel, M.E., Hindelang-Gertner, C., Porte, A., Stutinsky, F.: A comparative ultrastructural study of the pars tuberalis of various mammals, the chicken and the newt. *Cell Tiss. Res.* **148**, 313–329 (1974)
- Legait, H., Legait, E., Roux, M.: Étude morphologique et expérimentale sur la pars tuberalis de l'hypophyse de quelques mammifères. *C.R. Ass. Anat.* **54**, 261–265 (1970)
- Midgley, A.R., Jr.: Radioimmunoassay: a method for human chorionic gonadotropin and human luteinizing hormone. *Endocrinology* **79**, 10–18 (1966a)
- Midgley, A.R., Jr.: Human pituitary luteinizing hormone: an immunohistochemical study. *J. Histochem. Cytochem.* **14**, 159–166 (1966b)
- Petralli, J.P., Hinton, D.M., Moriarty, G.C., Sternberger, L.A.: The unlabeled antibody enzyme method of immunocytochemistry. Quantitative comparison of sensitivities with and without peroxidase-antiperoxidase complex. *J. Histochem. Cytochem.* **22**, 782–801 (1974)
- Phifer, R.F., Midgley, A.R., Spicer, S.S.: Immunohistologic and histologic evidence that follicle-stimulating hormone and luteinizing hormone are present in the same cell type in the human pars distalis. *J. clin. Endocr. Metab.* **36**, 125–141 (1973)
- Robyn, C., Leleux, P., Vanhaelst, L., Golstein, J., Herlant, M., Pasteels, J.L.: Immunohistochemical study of the human pituitary with anti-luteinizing hormone, anti-follicle-stimulating hormone and antithyrotrophin sera. *Acta endocr. (Kbh.)* **72**, 625–642 (1973)
- Romeis, B.: Innersekretorische Drüsen. II. Hypophyse. In: *Handbuch der mikroskopischen Anatomie des Menschen*, Vol. VI, Part 3 (W. von Möllendorff, ed.). Berlin: Springer 1940
- Stoeckel, M.E., Hindelang-Gertner, C., Porte, A., Dellmann, H.-D., Stutinsky, F.: Sur les caractères cytologiques spécifiques de la pars tuberalis de l'hypophyse et sa différenciation précoce chez le foetus de rat. *C.R. Acad. Sci. (Paris)* **277**, 97–100 (1973)
- Vaitukaitis, J.L., Ross, G.T.: Antigenic similarities among the human glycoprotein hormones and their subunits. In: *Gonadotropins* (B.B. Saxena, C.G. Beling, and H.M. Gandy, eds.), pp. 435–447. New York: Wiley Interscience 1972
- Vaitukaitis, J.L., Ross, G.T., Pierce, J.G., Cornell, J.S., Reichert, L.E., Jr.: Generation of specific antisera with the hormone-specific β -subunit of hTSH or hFSH. *J. clin. Endocr. Metab.* **37**, 653–659 (1973)

Accepted March 21, 1977