J. Endocrin. (1962), **24**, 53–58
With 1 plate
Printed in Great Britain

THE PITUITARY GLAND OF NORMAL AND STALK-SECTIONED MONKEYS WITH PARTICULAR REFERENCE TO THE PARS INTERMEDIA

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(*Received* 23 *August* 1961)

SUMMARY

The pars distalis, pars intermedia and infundibular process make up, respectively, 61, 5 and 34 % of the volume of the pituitary gland of normal mature female rhesus monkeys. The pars distalis is relatively smaller in immature animals, and larger during pregnancy.

Section of the pituitary stalk is followed by a significant increase in the volume of the pars intermedia; the infundibular process always decreases in volume, while the pars distalis shrinks to a lesser and more variable extent.

Histological changes in the pars intermedia suggest that cellular hypertrophy, infiltration of atypical cells, and cyst formation all contribute to the increase in volume, and that the changes are at any rate partly degenerative in nature.

INTRODUCTION

Enlargement of the pars intermedia of the pituitary gland after division of the pituitary stalk has been reported in the rat (Uotila, 1939; Barrnett & Greep, 1951), rabbit (Brooks, 1938) and goat (Daniel & Prichard, 1958). None of these authors, however, attempted to compare the volume of the pars intermedia of stalk-sectioned animals with that of normal controls. Furthermore, since the infundibular process always shrinks considerably after division of the stalk, and since the pars distalis may also atrophy to some extent as a result of damage to the portal vessels, subjective estimations of any changes in the size of the pars intermedia could easily be misleading. Holmes (1960), for example, noted that the pars intermedia of the ferret's pituitary gland appeared hypertrophic after division of the stalk, but quantitative studies later showed that in fact no significant enlargement occurred (Holmes, 1961). Campbell & Harris (1957), who used a paper-weight method to estimate the relative and absolute volumes of various parts of the pituitary glands of rabbits, also concluded that division of the stalk was not followed by any significant hypertrophy of the pars intermedia, and thus disagreed with the earlier report of Brooks (1938).

In a paper published in 1959, Holmes, Hughes & Zuckerman noted that transection of the pituitary stalk in the macaque appeared to be followed by enlargement of the pars intermedia, although this impression was at the time unsupported by any quantitative data. Such data are now available for a total of thirteen pituitary glands from monkeys killed at varying intervals after division of the stalk.

MATERIAL AND METHODS

The pituitary stalk was divided in twelve mature female rhesus monkeys (including four reported on earlier) and one mature male. The hypothalamic region was approached by a trans-temporal route (see Holmes *et al.* 1959). In five of the animals a polythene barrier was placed between the cut ends of the stalk, but in the remaining eight no such barrier was used. Since the presence or absence of a barrier did not appear to affect the changes in the pituitary glands which followed the operation, the two groups have not been considered separately.

The animals were killed at intervals varying from 6 days to 12 months after operation, and the pituitary gland and hypothalamus prepared for histological examination as described in the previous paper. Serial sections of four specimens were cut at a thickness of 50 or 100 μ; the other nine were cut at a thickness of 6 and 14 μ.

The volumes of the pars distalis, pars intermedia and infundibular process were estimated by the paper-weight method described by Campbell & Harris (1957), using sections taken from each series at intervals of 300 μ and projected at a magnification of $\times 30$. For the purpose of this study, that part of the pituitary stalk (or infundibular stem) lying below the level of the superior surface of the gland, and surrounded by tissue of the pars distalis or pars intermedia, was considered to be a part of the infundibular process. The pars tuberalis was not studied.

Similar studies were made on pituitary glands from seven normal mature rhesus monkeys, and on glands from three immature and two pregnant animals. Details are given in Table 1.

OBSERVATIONS

Volume of pars distalis, pars intermedia and infundibular process

As shown in Table 1, the pars distalis of the normal mature female monkey forms about 61 % of the total volume of the pituitary gland, while the pars intermedia and infundibular process make up 5 % and 34 %, respectively. In the two pregnant animals, the absolute volume of the pars distalis was approx. 20 % greater than in non-pregnant monkeys, while there did not appear to have been any marked change in the volume of the rest of the gland. The pars distalis in immature animals however formed only 50 % of the total volume of the pituitary gland, the pars intermedia and infundibular process contributing 6 % and 44 %, respectively.

The volume of the pars intermedia of animals killed 10 days or more after division of the stalk was approx. 100 % greater than the mean volume in the normal mature control animals. This difference was statistically significant ($P < 0{\cdot}001$). The infundibular process was reduced to approx. 30 % of its normal volume 10 days or more after operation ($P < 0{\cdot}001$), while the pars distalis had decreased to about 70 % of the normal volume in animals killed 36 days or more after division of the stalk ($P < 0{\cdot}01$).

There was a significant negative correlation between the volume of the pars intermedia and that of the infundibular process ($r = 0{\cdot}77$; $P < 0{\cdot}01$), but not between the volume of the pars intermedia and that of the pars distalis.

Histology of the normal pars intermedia

The pars intermedia of the normal macaque's pituitary gland consists predominantly of cells of a single type. These are rounded or slightly elongated (Plate, fig. 1) and usually measure not more than $10 \times 13\ \mu$ in maximum dimensions, although a few cells may be larger; cell boundaries are often indistinct. Each cell contains a single round or oval nucleus with a prominent nucleolus and granules of chromatin. The cytoplasm is usually finely granular, but in some cells it may be grossly vacuolated.

Table 1. *Volume of constituent parts of pituitary glands of monkeys*

(Calculated in mm.³ from sections by a paper-weight method. Percentages of total gland volume are given in parentheses.)

	Pars distalis	Pars intermedia	Infundibular process
(*a*) Mean values for seven normal mature female monkeys			
	29·0 (61 %)	2·3 (5 %)	16·1 (34 %)
S.E.M.	1·39	0·23	0·58
Range	24·0–34·5	1·4–3·1	14·2–18·1
(*b*) Data for five other unoperated animals			
Females (3 months pregnant)	35·5, 33·6 (69 %)	1·2, 2·4 (4 %)	15·0, 11·7 (27 %)
Immature males (approx. 3 years)	12·2, 12·1	1·7, 1·4	11·3, 9·5
Immature female (2–3 years)	11·8	1·1	11·0
Immature animals combined	(50 %)	(6 %)	(44 %)
(*c*) Animals in which pituitary stalk had been divided (all mature)			
Female, 6 days after operation	31·8 (62 %)	2·9 (6 %)	16·2 (32 %)
Female, 10 days after operation	36·2 (78 %)	4·9 (10 %)	5·6 (12 %)
Female, 22 days after operation	40·9 (74 %)	6·1 (11 %)	8·4 (15 %)
Male, 36 days after operation	13·9 (66 %)	3·4 (16 %)	3·7 (18 %)
(*d*) Mean values for nine females killed 5–12 months after operation			
	20·4 (68 %)	4·5 (15 %)	5·1 (17 %)
S.E.M.	2·06	0·34	0·38
Range	9·0–31·7	3·4–5·9	3·6–6·4

The pars intermedia also contains a few smaller cells, but these are relatively uncommon in normal glands. Such cells are either elongated or polygonal in shape, with elongated or irregular nuclei and scanty cytoplasm.

Compared to the pars distalis and infundibular process, the pars intermedia is relatively avascular. The blood vessels lie in trabeculae of connective tissue, which in some areas enclose groups of parenchymal cells to produce a 'follicular' pattern. Small cysts filled with amorphous material were occasionally found in the glands studied.

Pars intermedia after division of stalk

The pars intermedia of four monkeys killed 6–36 days after division of the stalk varied only in degree. Six days after operation small elongated or polygonal cells with acidophilic cytoplasm and deeply staining nuclei lay amongst the parenchymal cells. These small cells were especially numerous in the glands of animals killed 10 and 22 days after operation (Plate, figs. 2 and 3) and fewer in the 36-day specimen, although this may have been simply due to individual variation. In each of these four glands many of the parenchymal cells were swollen and vacuolated, and contained enlarged nuclei (Plate, fig. 3). Small cysts filled with amorphous material, apparently formed from degenerated cells, were relatively common.

The pars intermedia of monkeys killed 5 months or more after operation was always thickened, and appeared folded (see illustrations in Holmes & Zuckerman, 1959). Normal parenchymal cells were always present, but in some parts of each gland many of the cells were swollen and vacuolated, and their nuclei enlarged (Plate, fig. 4). Other cells resembled the parenchymal elements, except that their nuclei were smaller than usual and stained more densely. Small polygonal or elongated cells with dense nuclei lay amongst the parenchymal cells in all specimens, but the numbers of these small cells varied in different glands and also in different parts of a single specimen. A few cysts were usually present, but these were small in relation to the bulk of parenchymal tissue.

No mitotic figures could be found in the pars intermedia of any of the glands examined.

DISCUSSION

The data presented show that the pars intermedia constitutes about 5 % of the volume of the whole pituitary gland of the normal mature female macaque. There is a striking variation in the degree of development of the pars intermedia in different species; thus in the human Rasmussen (1938) found that the parenchymal tissue of the pars intermedia made up less than 1 % of the total volume of the gland, and Plaut (1936) had previously observed that the pars intermedia was 'rudimentary' in the anthropoid apes compared with the monkeys. In some species outside the primate order, however, the pars intermedia may also be relatively small, and Oboussier (1948) states that it constitutes only 0·2 % of the whole gland in the elephant, and 2·4 % in the kangaroo. In the ferret, on the other hand, the pars intermedia occupies about 11 % of the total pituitary volume (Holmes, 1961), while the figures published by Campbell & Harris (1957) for the rabbit indicate a similar proportion in this species. It is impossible at present to draw any conclusions from these data as to the functional significance of the pars intermedia in mammals.

The limited amount of material examined in this study suggests that in immature rhesus monkeys the pars intermedia occupies approximately the same proportion of the total volume of the whole pituitary gland as in mature animals. The pars distalis however constitutes only 50 % of the volume of the immature gland, a feature which probably reflects the low level of gonadotrophic activity of the pars distalis before puberty. In pregnancy, on the other hand, the volume of the pars distalis is both relatively and absolutely greater than in non-pregnant monkeys, a feature which has been observed both in man and in lower animals (see Rasmussen, 1938). The data for male animals are insufficient to indicate whether or not there is a sex difference in the relative proportions of the different parts of the gland.

Transection of the pituitary stalk in the monkey was followed by an increase in the volume of the pars intermedia which was apparent by the 10th day after operation, and which persisted for at any rate 12 months. A number of factors might contribute to this change: parenchymal cells might increase in size or number; cells not normally present might infiltrate into the tissue, and perhaps proliferate there; while cystic changes could result in an overall increase in volume.

The histological changes suggest that most of these mechanisms may, in fact, play a part in increasing the volume of the pars intermedia. Thus, some of the parenchymal cells were swollen and vacuolated after division of the stalk, although others remained normal; many irregular cells with deeply staining nuclei appeared in the tissue, and small cysts were more conspicuous than in normal glands.

The role of cellular proliferation in the postoperative changes remains in doubt. In the goat, Daniel & Prichard (1958) found that mitotic activity occurred in the pars intermedia after the 3rd week following division of the pituitary stalk. In the monkey the volume of the pars intermedia had already increased by the 10th day, and it might therefore be expected that any proliferative activity would be most evident soon after operation. In fact no indications of such activity were found; but only four animals were killed within 36 days of transection of the stalk, and the evidence cannot be considered sufficiently conclusive to rule out mitotic activity from playing any part in the increase in volume.

It is not clear what initiates the various changes which occur, but the correlation between the decrease in volume of the infundibular process and the increase in that of the pars intermedia suggests that degeneration of the hypothalamo-hypophysial nerve fibres may be at any rate an indirect factor, and that shrinkage of the infundibular process might simply allow room for expansion of the pars intermedia. The histological changes which take place suggest, however, that the increase in volume is not due to a simple hypertrophy, but is to some extent a degenerative process.

There are not enough reliable studies to allow a comparison to be made between the changes which have been described in the pituitary gland of the monkey and those which occur in the glands of other animals after division of the pituitary stalk. The few quantitative data available (Campbell & Harris, 1957; Holmes, 1961) suggest that changes such as those described in the present paper do not necessarily occur in all species, but more evidence is needed before any general conclusions can be drawn.

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DESCRIPTION OF PLATE

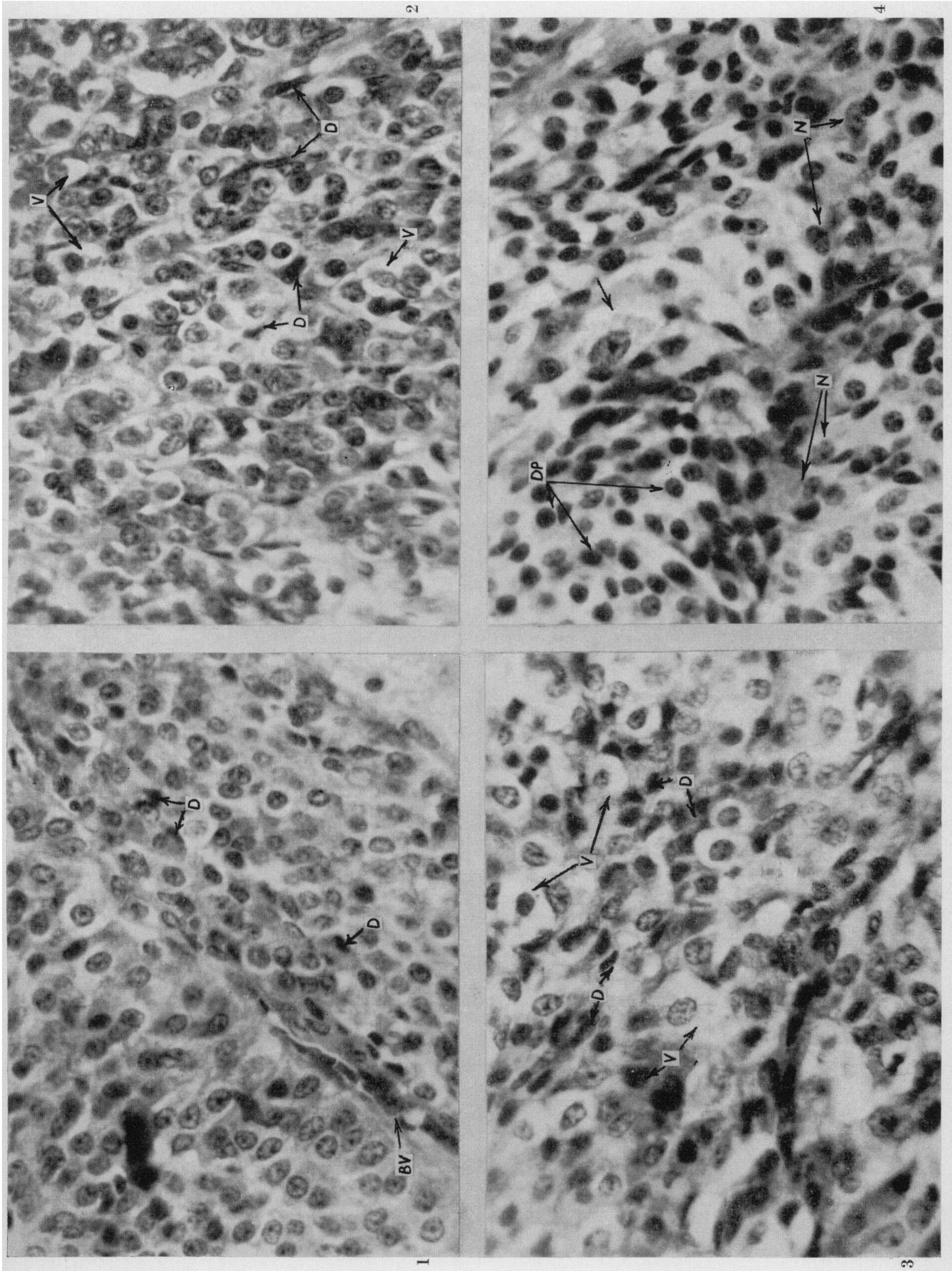
Tissue of the pars intermedia stained by Cleveland & Wolfe's method. ×700.

Fig. 1. Normal. Typical parenchymal cells; a few cells with smaller darkly stained nuclei (*D*) are present, and a blood vessel (*BV*) lies in the lower left-hand side.

Fig. 2. Ten days after division of pituitary stalk. Many normal parenchymal cells are shown; others are vacuolated (*V*). Cells with elongated or irregular nuclei (*D*) are more numerous than in normal tissue.

Fig. 3. Twenty-two days after division of stalk. Some parenchymal cells are grossly vacuolated (*V*), and many contain nuclei larger than normal. Cells with elongated or irregular darkly stained nuclei (*D*) are common.

Fig. 4. Twenty-six weeks after division of stalk. Normal parenchymal cells (*N*) are present, especially in lower half of the field. Some are enlarged and grossly vacuolated, and one (↓) contains a large nucleus. Many cells which appear to be parenchymal in type contain nuclei which stain more darkly than normal (*DP*). Cells with elongated or irregular nuclei are numerous.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