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G Wortzman and N B Rewcastle

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# Tomographic Abnormalities Simulating Pituitary Microadenomas

George Wortzman[1]
N. B. Rewcastle[2]

**False-positive and false-negative interpretations of sellar tomography were found in about one-fifth of cases in a recent autopsy study correlating the presence of pituitary microadenomas with abnormal sellar tomograms. An analysis of minor variations in the bony configuration of the sella disclosed variations due to posterior lobe asymmetry, intercavernous venous channels, bony asymmetry, and an empty sella in 27 of the 120 sellas examined. In some instances, the asymmetry resulted from a combination of these causes. A further study of 50 pituitary glands in situ showed posterior lobe asymmetry to be a common anomaly (76%) that can produce an obvious disparity between the two halves of the sella. Thus, the minor radiologic criteria of local thinning of the anterior wall or floor, slant of the floor, or asymmetry of the two halves of the sella must be interpreted with caution as being indicative of the presence of pituitary microadenoma. In the absence of clinical or biochemical dysfunction, the changes more likely result from explainable anatomic causes.**

A recent autopsy study correlating the presence of pituitary microadenomas and abnormal sellar tomograms urged caution in diagnosing a microadenoma by sellar tomography [1]. False-positive and false-negative interpretation of tomographic findings were found in about one-fifth of 120 cases. The 27 cases of false-positive findings were reexamined as to origin of the minor variations in the bony configuration of the sella. The results of this analysis plus a further study of 50 pituitary glands in situ are the subject of this report.

## Materials and Methods

The earlier report [1] contains a detailed description of methods. Briefly, this consisted of an en bloc removal of the pituitary and the sella in an unselected autopsy population only excluding cases with a clinically apparent pituitary tumor. Hypocycloidal tomograms were done on the specimens in anteroposterior (AP) and lateral projections at 2 mm intervals. Interpretation was by three neuroradiologists independently and also together. Criteria for sellar abnormality were the findings of a slanted sellar floor, local cortical thinning of the lamina dura and erosion, or bulging of the anterior wall or floor of the sella. These criteria were based on earlier work by Vezina and Sutton [2] and McLachlan et al. [3]. Care was taken that the normal variations of sphenoid sinus development and septal attachments were not interpreted as abnormal. Cognizance was also taken of the normal variations of the dorsum, which frequently has a concavity centrally with its lateral margins more anteriorly situated.

Following subsequent decalcification of the block of tissue, the specimens were imbedded in paraffin, cut in a midsagittal plane, and then sectioned at 1 mm intervals. At each level, slides were stained with: (1) hematoxylin and eosin, (2) the Mann stain for acidophils and basophils, (3) periodic acid-Schiff stain for carbohydrate residues, (4) Gordon stain for reticulum, and (5) immunoperoxidase for prolactin.

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[1]Department of Radiology, University of Toronto, Mt. Sinai Hospital, 600 University Ave., Toronto, Ontario M5G 1X5. Address reprint requests to G. Wortzman.

[2]Department of Neuropathology, University of Toronto, Toronto, Ontario. Present address: Department of Pathology, Foothills Hospital, Calgary, Alberta.

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Pathologic study identified 43 adenomas in 32 of the 120 pituitaries so examined. These adenomas were mostly under 2 mm in size and distributed chiefly in the periphery of the gland. High false-positive and false-negative interpretation rates of tomographic findings were found in the correlative study then done. Of the 27 cases considered abnormal on tomography, six had a coexisting adenoma, but in no case was the adenoma of such size or position so as to consider it to be the cause of the tomographic abnormality.

The group of 27 cases was reexamined. The microscopic structure of the pituitary gland and the bony sella were correlated with the AP and lateral tomographic studies. The results of this analysis are discussed below.

A further postmortem study of 50 pituitary glands in situ was carried out. This study consisted of careful dissection of the pituitary gland both before and after removal of the dorsum sella to determine the relative positions of the anterior and posterior lobes of the pituitary in relation to the midline of the sella.

## Results

Explanations for sellar variations in the 27 false-positive cases are summarized in table 1. In most cases, one cause for the misinterpretation was found; in four of the cases, more than one factor was instrumental in causing the changes considered compatible with a microadenoma.

Posterior lobe asymmetry was the most common cause of the interpretation of sellar abnormalities and was seen in 15 cases; in 13 of these, it was the only alteration present (figs. 1 and 2). This asymmetry, which consisted of a posterolateral rather than a midline relationship of the posterior lobe to the anterior lobe, instigated the second part of this study, verifying this to be a true finding rather than a technical artifact. Intercavernous venous channels were always present, but, in eight of the cases, the size and position of the channel was considered to be responsible for the abnormal configuration of bony cortex (figs. 3 and 4). In one of these cases, there was a coexisting adenoma; in another, there was bone asymmetry. An asymmetry of the bony walls of the sphenoid sinus that could not be readily attributed to a variation in sinus development or of sinus septal attachment was found in four cases; in three of these, it was the only variation seen. The sellar configuration was considered due to a partially empty sella in two cases (fig. 5); in one, it was the sole explanation. Instances of minor degrees of empty sella in the original study did not cause any significant deformity. Rathke pouch cysts were frequent findings, being seen in 29 of the original 120 subjects. They were present in four of 27 false-positives. In only one case was the presence of the cyst considered to be of significance, but, in that case, there was also a coexisting posterior lobe asymmetry (fig. 6).

The results of the in situ examination of the pituitary gland are summarized in figure 7 with an example of an eccentric posterior pituitary lobe shown in figure 8. The posterior lobe is frequently eccentric in its relation to the anterior lobe and was midline in only 24% of cases. In 14% of cases, the posterior lobe was situated well laterally. The results of this second study verify that the findings described above in 15 of the 27 cases studied were real rather than due to an artifact or an asymmetry developing in the preparation of the pathology sections.

TABLE 1: **Explanations for False-Positive Sellar Abnormalities in Autopsy Specimens**

| Explanation | No. Specimens |
|---|---|
| Posterior lobe asymmetry | 13 |
| Bony wall asymmetry | 3 |
| Venous channel erosion | 6 |
| Empty sella | 1 |
| Venous channel and adenoma | 1 |
| Venous channel and bone asymmetry | 1 |
| Rathke cyst and posterior lobe asymmetry | 1 |
| Empty sella and posterior lobe asymmetry | 1 |
| Total | 27 |

## Discussion

In 1936, Costello [4] found clinically silent pituitary adenomas in 225 of 1,000 autopsies. Sections were done in the longest axis of the gland, either sagittally or transversely, cut by hand with thicknesses of 1–1.5 mm. Most adenomas found were 1.5 mm or greater. McCormick and Halmi [5] reported 9.1% adenomas in 1,600 consecutive autopsies. In our previous report [1], microadenomas were found in 32 (27%) of 120 cases. The adenomas were usually under 2 mm in size. This higher incidence of adenomas is attributed to the greater number of sections taken. Criteria for identification of an adenoma were uniformity of cells, a stromal pattern different from the rest of the gland, and evidence of compression of adjacent pituitary parenchyma. More than one adenoma was found in eight of the 32 cases. Immunoperoxidase staining identified 16 of 39 microadenomas to be prolactinomas. As in the series of Costello [4], the adenomas were usually peripheral in location with some projecting from the surface of the gland under the capsule.

Since the early 1970s, an extensive body of literature pertaining to the sella and pituitary has appeared reflecting advances in the fields of neurosurgery, endocrinology, pathology, gynecology, and radiology.

These diagnostic advances include the development of sensitive and specific radioimmunoassays for blood prolactin, new staining techniques to identify pituitary cell secretory products, refinement of transphenoidal microsurgery, and the medical treatment of the prolactinoma with bromocriptine [6–16].

McLachlan [3] in 1970 and Vezina and Sutton [2] in 1974 showed that careful tomographic investigation of the sella turcica allowed recognition of bony erosion due to acromegaly and also due to prolactin-secreting pituitary microadenomas. The thinning of the cortex and the erosion or bulging of the wall or floor may be quite subtle and not

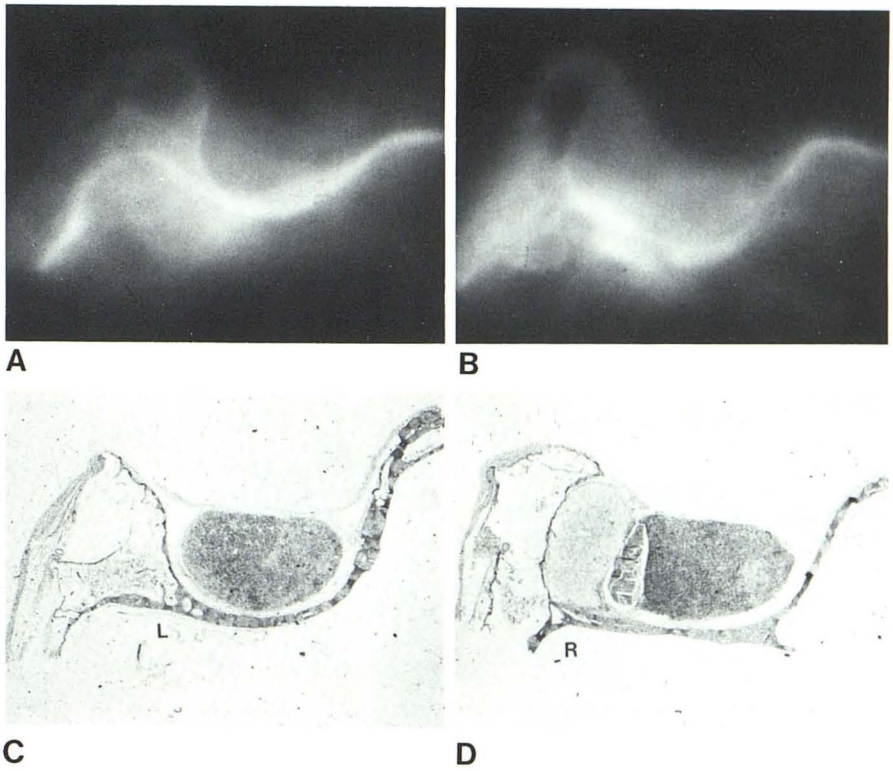



Fig. 1.—Eccentric posterior pituitary lobe. **A**, Lateral tomographic cut 4 mm to left of midline. Sloped anterior wall. **B**, Right-sided cut 4 mm from midline. Steeper anterior wall slope, increased AP diameter, and thinned dorsum. **C**, Histopathology corresponding to **A**. **D**, Histopathology corresponding to **B**. Eccentrically placed posterior lobe of pituitary accounts for marked difference in sellar configuration.

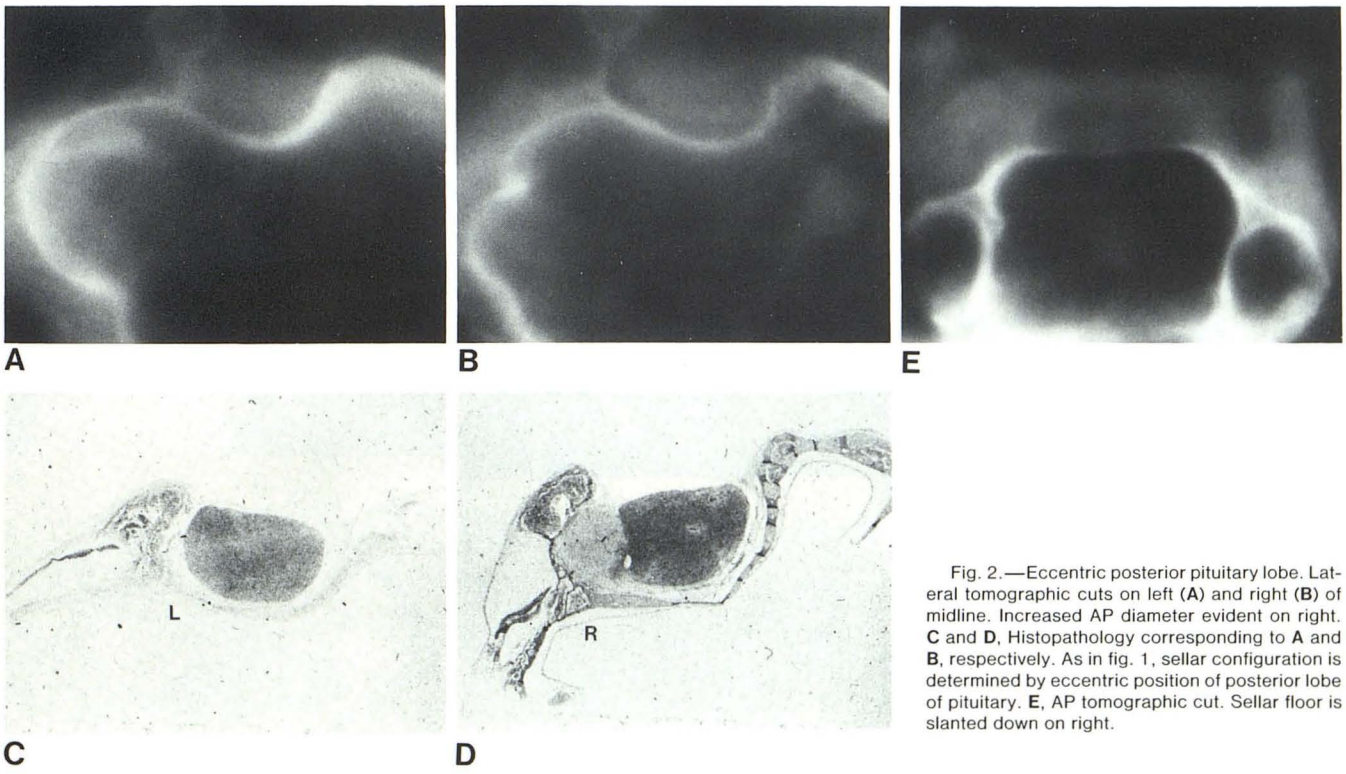



Fig. 2.—Eccentric posterior pituitary lobe. Lateral tomographic cuts on left (**A**) and right (**B**) of midline. Increased AP diameter evident on right. **C** and **D**, Histopathology corresponding to **A** and **B**, respectively. As in fig. 1, sellar configuration is determined by eccentric position of posterior lobe of pituitary. **E**, AP tomographic cut. Sellar floor is slanted down on right.

appreciated without the aid of pluridirectional tomography. The validity of these criteria has been verified both in radiologic and surgical literature [14, 17–21].

It has long been appreciated that there are, however, many asymmetries in the development of the sphenoid sinus, both as to the pattern of septation and the degree of pneumatization [22–25]. With the recent popularity of transsphenoidal neurosurgery, there has been again an interest

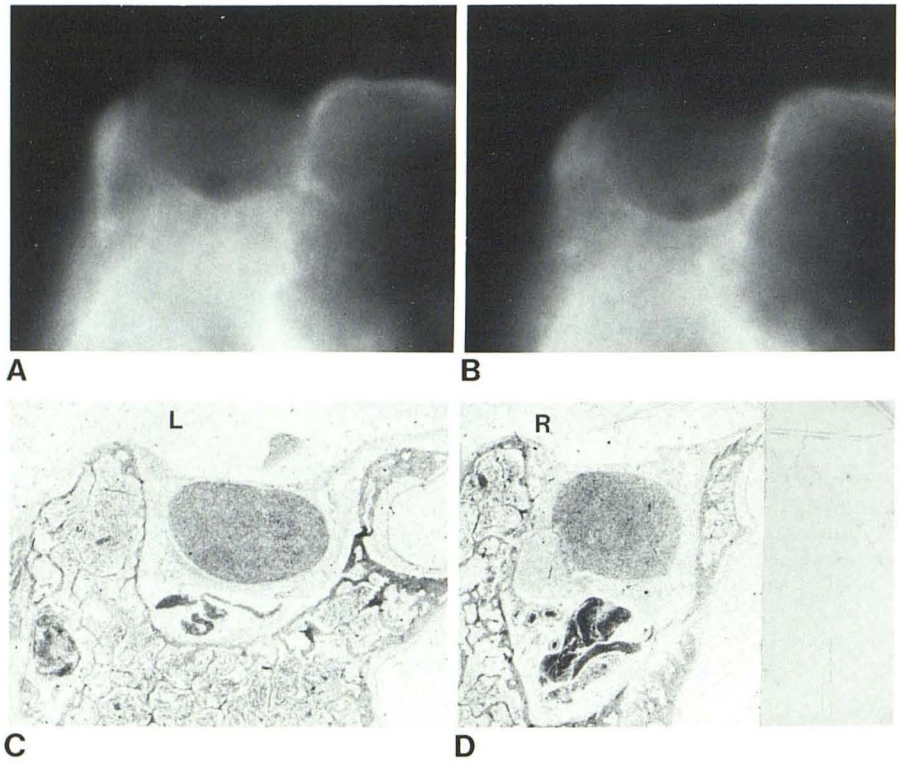



Fig. 3.—Venous channels. Left (**A**) and right (**B**) tomographic cuts. Deepened floor on **B** interpreted as compatible with microadenoma. **C** and **D**, Corresponding histopathology sections (to **A** and **B**, respectively). Large crossing venous sinus beneath pituitary gland causes irregularity of sellar floor. Low, small posterior lobe on **D** causes minor erosion of dorsum.

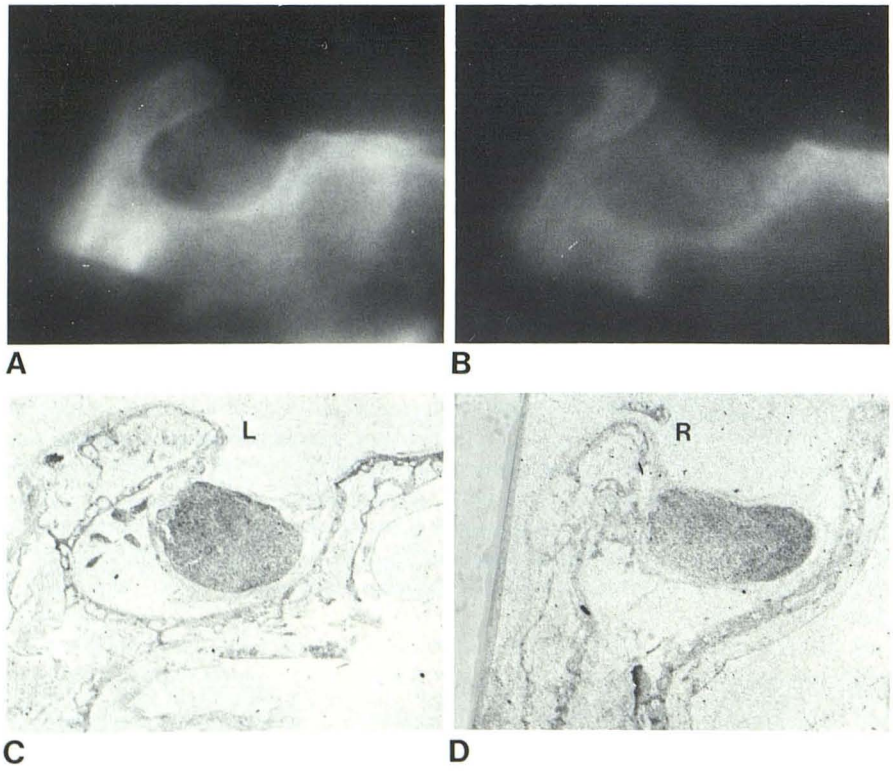



Fig. 4.—Venous channels. Left (**A**) and right (**B**) tomographic cuts. Erosion of dorsum and posterior sellar floor on right. **C** and **D**, Histopathology sections corresponding to **A** and **B**, respectively. Large venous sinus posteroinferior to pituitary gland causes asymmetry of two sides of sella.

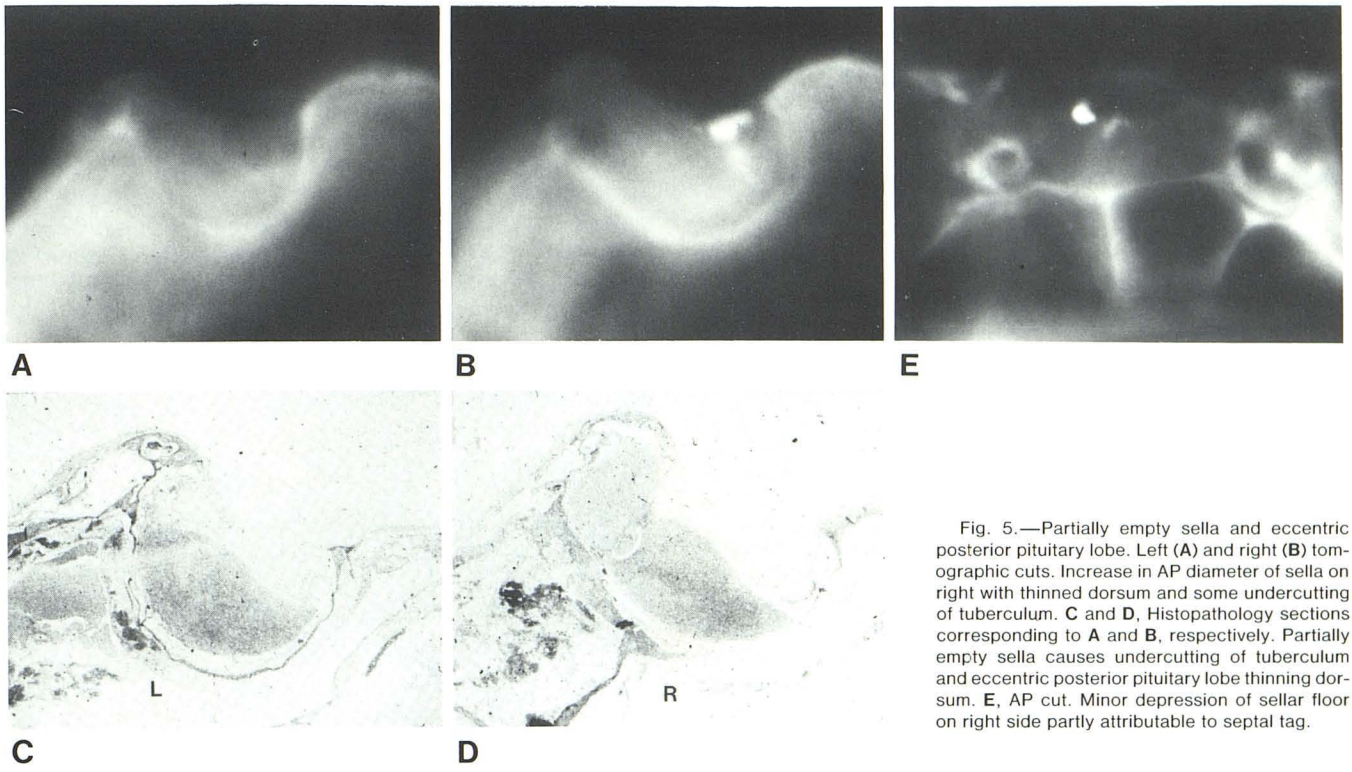



Fig. 5.—Partially empty sella and eccentric posterior pituitary lobe. Left (**A**) and right (**B**) tomographic cuts. Increase in AP diameter of sella on right with thinned dorsum and some undercutting of tuberculum. **C** and **D**, Histopathology sections corresponding to **A** and **B**, respectively. Partially empty sella causes undercutting of tuberculum and eccentric posterior pituitary lobe thinning dorsum. **E**, AP cut. Minor depression of sellar floor on right side partly attributable to septal tag.

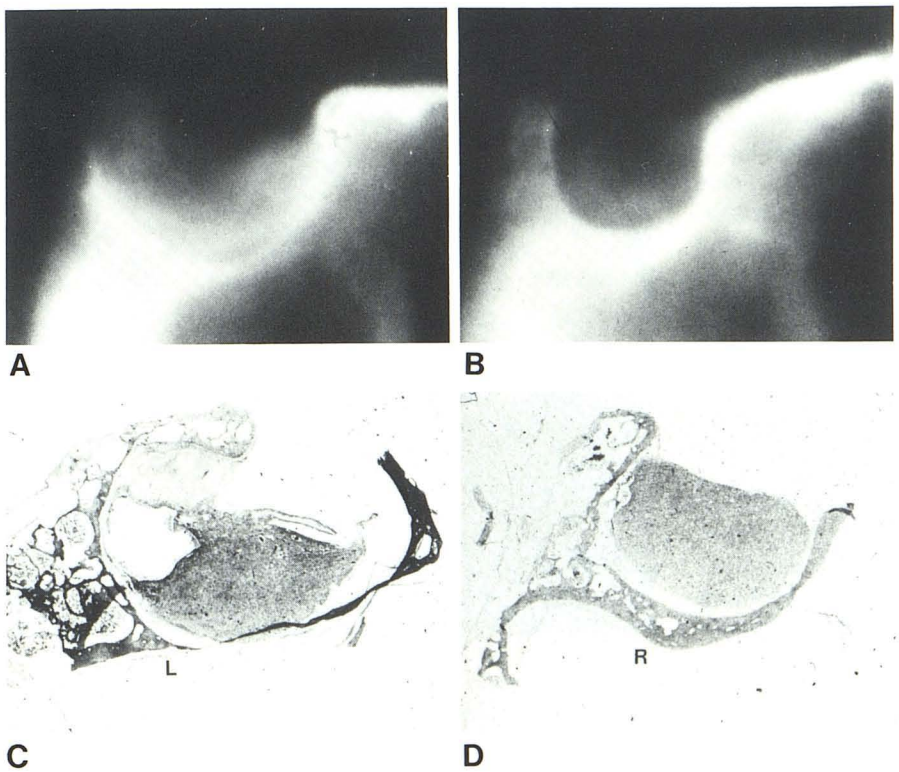



Fig. 6.—Rathke pouch cyst and eccentric posterior lobe of pituitary. Left (**A**) and right (**B**) tomographic cuts. Ballooned configuration on left when compared with right. **C** and **D**, Histopathology sections corresponding to **A** and **B**, respectively. Large Rathke pouch cyst and eccentric posterior pituitary lobe correlate with tomographic changes.

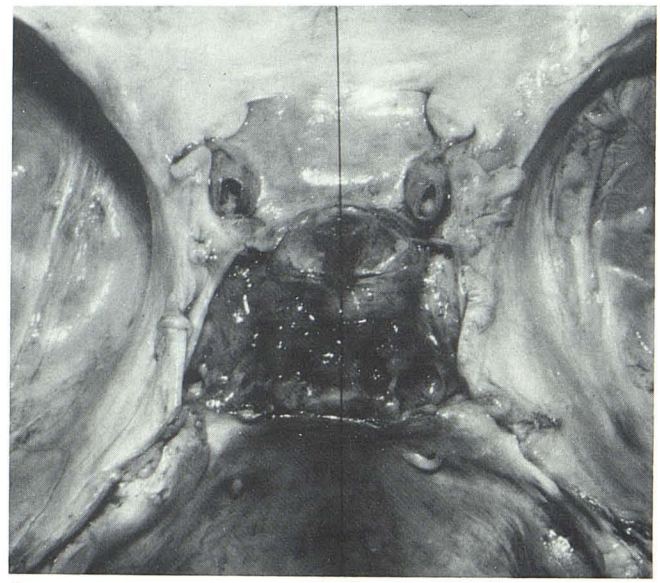

Fig. 7.—Posterior pituitary lobe asymmetry. Findings in 50 consecutive examinations of pituitary glands in situ. Posterior lobe was central in 24%, but eccentric as depicted in the rest. In 14%, the lateral margin of the posterior lobe was flush with the lateral margin of the anterior lobe; the other 62% of less eccentric placed glands had their lateral margins as depicted by the broken line.

in variations in anatomy of the sphenoid sinus and sellar region with anomalies of the bony walls of the sella being identified [26–28]. Swanson and duBoulay [29] examined 85 cases with no clinical evidence of a pituitary lesion, yet the plain films in 31.7% demonstrated changes that were identical with those described for a small intrasellar lesion. The unanswered question, however, was whether these changes were due to a coexisting but asymptomatic adenoma. Other authors have pointed out normal variants in sellar configurations secondary to a sloped sellar floor, thinning of the sellar cortex, the pattern of aeration and/or septation of the sphenoid sinus, or thickening of the mucosal membrane of the sinus [30–32].

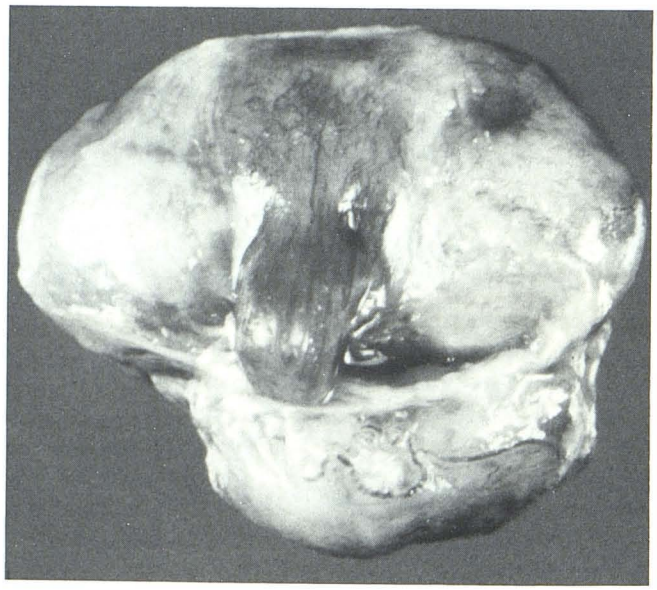
Earlier autopsy studies stressed either the incidence of microadenomas or the variations of adjacent structures such as carotid vessels, arachnoid cisterns, cavernous sinuses, and the optic chiasm and nerves [33, 34]. More recent autopsy studies have dealt more with the histopathology of the pituitary gland and its relation to sellar tomographic abnormalities [1, 35–37] and have pointed out the nonspecificity of the sellar changes previously considered due to a pituitary microadenoma.

The present study carries this a step further and reveals several reasons for apparent abnormalities. The most significant is an asymmetric position of the posterior lobe of the pituitary gland with its secondary effect on the dorsum sella. This led to the greatest number of errors of interpretation despite care being taken during the original study to avoid errors due to an asymmetry of the dorsum. In a comprehensive study, DiChiro and Nelson [38] pointed out the many irregularities in the appearance of the dorsum and described the depression of bone that accommodates the posterior lobe of the pituitary gland. This depression was called "fossula hypophyseos" by Karlas, "impressio hypophysios" by Wegard, and "fossetta pituitaria" by Cardillo and Bossi (all cited in [38]). The resultant thinness of bone in the area of depression varies and the central part may be absent resulting in a corticated "window" [39]. This depression of the anterior aspect of the dorsum may involve the adjacent sellar floor. The asymmetry creates difficulties when comparing sequential lateral tomographic sections of the sella, as the asymmetry, when due to the eccentric nature of the posterior lobe of the pituitary, is recognized as a unilateral increase in the AP diameter of the sella.

A defect and irregularity of the sellar floor were seen in other cases of this series secondary to crossing venous sinuses. Cysts of the pouch of Rathke proved almost as common as microadenomas in the initial autopsy series, but were not shown to be responsible for any evident bony change. In the case where the partially empty sella was the



A



B

Fig. 8.—**A**, Pituitary gland in situ before removal (from the back and above). The dorsum has been amputated. The black thread runs in midline. **B**, Pituitary gland and stalk after removal, viewed from above, shows eccentric position of posterior lobe.

sole abnormality, the changes of the sella were considered to be due to an asymmetric invagination of subarachnoid space.

In addition to the anomalies and changes of the sella described above, there have been reports of other factors causing changes compatible with an intrasellar lesion. There is a report of an apparently eroded dorsum that at autopsy proved due to a congenital lack of ossification [40]. Erosion of the floor of the sella simulating the changes of a pituitary microadenoma has also been reported in two cases of an anomalous arterial communication between the intracavernous segments of internal carotid arteries in association with agenesis of one internal carotid [41].

Pluridirectional tomography is still of aid before transsphenoidal removal of a pituitary microadenoma and usually reflects the side of the microadenoma and will show the anatomy of sphenoid pneumatization and septation. However, there are many patients with hormonal dysfunction where an adenoma has been found despite negative tomographic studies [12, 18]. In a recent radiologic-surgical correlative study, good correlation existed between the tomographic localization and the location of the tumor at surgery in most cases [42]. In nearly 20% of 89 cases reported, however, the sellar changes suggestive of adenoma on tomography had no relation to the location of the tumor as seen at surgery. This further indicates the need for caution in the interpretation of tomographic findings. Protocols for the study of pituitary adenomas have changed radically over the past 2–3 years as advances in equipment and techniques continue, and they are the subject of recent review articles [43, 44].

Interpretation of plain films and tomographic studies of the sella turcica must be undertaken with caution. In addition to variations of sphenoid pneumatization and septation, one can be misled by a change in the AP diameter of the sella secondary to eccentric position of the posterior lobe of the pituitary. An anatomic review shows the posterior lobe to be more frequently eccentric in its relation to the anterior lobe than to being a truly midline attachment. In addition, bone defects simulating erosion of the sellar floor may be secondary to intercavernous venous channels, bony wall asymmetry, or to anomalies of sphenoid sinus development and other explainable anatomic variations.

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