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The Foramen of Magendie

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Introduction

Much controversy has arisen with respect to the presence of the foramen of Magendie, or posterior median aperture, in the roof of the fourth ventricle of the human brain. The doubt which existed for so long and exists even now in the minds of some investigators is accounted for not so much by minute proportions of the aperture as by the extreme delicacy of the tissues which must be inspected in order to perceive what the actual facts are.

The fragile tela chorioidea inferior is composed of a layer of ependyma within and a layer of pia mater of the finest web-like consistency without. It forms a part of the roof of the ventricle and is very easily damaged, whether it be in the process of fixation of the brain, or of dissection, or of dehydration and embedding preparatory to sectioning. When sections are to be made, to be accurate and to be assured of preventing injury, the brain must be left within the cranium; consequently, there are added the further difficulties of decalcification if the specimen is sufficiently advanced in age, and of arriving at the desired angle of section of the region involved. Scarcity of research material in general, and particularly at specifically designated ages, is an additional problem.

The difficulties are many. From the point of view of such obstacles, it will not be thought an exaggeration on the part of Rogers and West when, in their paper on the foramen in the Journal of Anatomy in 1931, they quoted from Titus Andronicus the line "What subtle hole is this?"

The purpose of our endeavor is to investigate not only the existence of the foramen of Magendie, but its embryology as well, i. e., its manner of and time of formation, in man. Research has been done to determine whether the foramen exists as a definite anatomical entity in fetal life, how it is formed, and when its appearance takes place. The possible size of the opening became also a part of the problem. In addition, the formation of the chorioid plexus will be briefly discussed from what has been to us an interesting angle.

At the outset, profound gratitude is due a number of gentlemen who, during the course of the research of which this thesis is an account, gave valued, frequent and indispensable assistance. They are Dr. Strong for his invaluable advice, direction and kind toleration; Dr. Essenberg for the material from Loyola's embryological collection; Mr. Warren for his guidance in technique; Dr. Job for the stimulation described by a member of the faculty as "contagious enthusiasm "; Dr. Tweedy and Mr. Dudek for the facilities of the Chemistry Department; and Mr. Mauer for the illustrations.

Review of Literature

Literature recording original investigation upon the subject of the foramen of Magendie is not abundant. Fairly considerable controversy has been heard and read on whether the foramen exists at all, but, at least in recent years, the preponderance of opinion, if not of proof, has been in favor of its existence.

Weed, in 1922, brought forth the opinion that "the greater weight of evidence today inclines to a consideration of the foramen of Magendie as a true anatomical opening in the velum --- a break in the ependyma and pia". Weed bases his conception upon the findings of Cannieu, Hess, Blake and Wilder. Hughson, in discussing the cerebrospinal fluid in 1925, stated that "in a consideration of the adult circulation of the fluid, we are obliged to accept the existence of the presence of the foramina of Luschka and Magendie". Dado's work under Strong in 1936 corroborated these opinions by showing the aperture to be present not only in the adult brain but in the fetal brain of the stages of 230 mm. (6 months) and 175 mm. (5 months).

The size of the foramen is a matter that has recently come into question. In contrast to what seems to have been the standard belief, as shown by the texts, i. e., that the opening is a relatively minute aperture in the otherwise intact roof of the ventricle, there have been observations of a radically different character. Rogers and West observed, in 1931, when operating in the posterior fossa of the skull, that the normal condition in the human adult is a complete defect in the lower part of the ventricular roof, from the inferior medullary velum above to the obex below and to the ligulae laterally. Dado and Strong demonstrated the same appearance in gross dissections and microscopic sections of adult brains and of fetal brains of the ages of 5 and 6 months.

The method of formation and development of the posterior median aperture has been a matter of dispute, but it has received less attention than has the question of the opening's mere existence. Weed in 1917 stated that he found the roof of the fourth ventricle unbroken up to the stage of 52 mm. of fetal life, which was the limit of his investigation in that direction. The conditions that prevailed and the early embryology can best be described in his own words:

"In a human embryo of 4 mm., the entire roof of the fourth ventricle is composed of cells with round or slightly oval nuclei and palely staining cytoplasm. The nuclei of the cells are poor in chromatin material as contrasted with the pyknotic character of the typical ependymal cells. The lining tissue is of the thickness of several cells. The ventricular cytoplasmic border is fairly smooth at this stage. -------- A similar accumulation of epithelial-like cells is found in a human embryo of 7 mm. --------- Similar accumulations of these epithelial-like cells are to be found in human embryos of 9 mm."

Weed goes on to describe how the "accumulation of epithelial-like cells" disappears gradually and is replaced by what he terms the "area membranacea superior". "In a human embryo of 14 mm., as is the pig of the same stage, the area membranacea superior has attained a great degree of differentiation. -------- In figure 57 the deeply staining typical ependyma is shown approaching from below. The cells end abruptly at the border of the area membranacea; the ventricle in this area is lined by cells possessing small elongated nuclei and long cytoplasmic processes, which unite to form a ventricular lining. -------- Thus, in human embryos of 18 mm. this differentiated area in the roof has reached its maximal differentiation. -------- In all specimens of human embryos of over 30 mm. examined, no evidence of the area membranacea superior could be found. ----------------

The final disappearance of the area membranacea superior in the human embryo is not accompanied by the same ingrowth of typical ependyma that characterizes the process in the pig. There is a great tendency, in the human, as indicated in figure 92, for a replacement of the area by the same type of epithelial-like cells which comprised the whole ventricular roof in the earlier stages and later formed lateral borders for the superior membranous area. Thus, in a human embryo of 24 mm., (No. 632 of the Carnegie collection) there is evidence of a very small membranous area surrounded by a border of epithelial-like cells. In a slightly larger specimen (No. 840, 24.8 mm.) the whole membranous area is occupied by the epithelial-like cells. The frequent association of these cells with the area indicates that in disappearing the area membranacea is probably replaced first by these cells, which in turn disappear, so that the whole roof is finally composed of the typical, densely staining ependyma. --------

"The ependymal lining of the caudal portion of the roof of the fourth ventricle undergoes a process of differentiation which results in the formation of the area membranacea inferior. This transformation has been observed in pig and human embryos; in both, the first definite evidence of the cellular change has been observed in specimens of 15 mm. The essential phases of the process are identical in the two embryos. The tendency of the deeply staining typical ependymal elements is to lose their highly pyknotic character; the nuclei become poorer in chromatin and the cytoplasm somewhat more abundant. In the first stages of the metamorphosis the lining cells come to assume epithelial-like appearances, but in the final change the nuclei become small oval bodies, poor in chromatin, resembling to some degree the nuclei of the adjoining undifferentiated mesenchyme.

"After the initial process of differentiation has begun, the area membranacea inferior increases rapidly in extent and the differentiated cells which characterize it come to occupy the greater portion of the caudal part of the chorioidal roof. -------------- In the largest human fetus at my disposal, in which the histological material was good enough to permit an accurate examination of the chorioidal roof (embryo No. 448, 52 mm., in the Carnegie collection) the area membranacea inferior appeared as an intact membrane supported by only a few pial cells."

Kollmann and Streeter advance the view that the rhombic roof is broken down during the third month of fetal life to form the foramen of Magendie and the two foramina of Luschka. Hess believes that in early embryological life the rhombic roof is bordered by a regular, meshed tissue; later, the small meshes in this tissue coalesce to form the larger foramen of Magendie. Blake, in a study of the chorioidal roof, found a caudal bulging of the inferior velum; this outpouching became more and more extensive in older embryos, and in man the pouch became sheared off at its neck, leaving the foramen of Magendie.

Methods and Material

Material for research consisted of celloidin sections, stained with hematoxylin-eosin, of fetal heads of five stages. The stages were of 57 mm. (in the third month), 69 mm. (3 months) and 84 mm. (in the fourth month), all of which were prepared by us, and those of five and six months, which were prepared by Dado and Strong.

The only outstanding difficulty experienced in the process of preparation lay in the removal of air from within the cavities of the specimens. This was accomplished in a very short time under a bell jar by means of suction produced by running water, after ordinary laboratory motor suction for a week had proved futile.

Results

The foramen of Magendie is present in the 84 and 69 mm. fetuses as a complete defect in the inferior portion of the rhombic roof. The condition is similar to the observations upon adult brains of Rogers and West and of Dado and Strong upon adult and older fetal brains.

The fourth ventricle of the 69 mm. specimen broadens out gradually as a direct continuation of the central canal. There is no roof separating the rhomboid cavity from the subarachnoid space in the interval between the obex caudally and the cerebellar beginnings in the alar plate rostrally. The posterior median aperture, or foramen of Magendie, is fully formed at this stage as a complete defect in the inferior portion of the ventricular roof. The foramen is bounded by the obex candally, the rhombic lips and chorioid plexus laterally, and the caudal portion of the developing cerebellum superiorly.

Figure 1 illustrates the open ventricle near its junction with the central canal. What seems to be a covering of the ventricle is a homogeneous, albuminous mass (v). It is probably cerebrospinal fluid that has undergone coagulation. The larger, dark mass (d) dorsal to the brain stem is of a similar character.

Figure 2 shows a more rostral section through the ventricular region, in the area where the cerebellum forms a roof for the fourth ventricle. The photograph illustrates that the ventricle is in this region separated superiorly by the cerebellum and laterally by the chorioid plexus from the subarachnoid space.

The 84 mm. specimen presents a similar but more mature picture of the region of the fourth ventricle. No membrane separates the ventricle in its inferior portion from the subarachnoid space. A serosanguinous exudate into the cerebrospinal spaces in the region under discussion rather confuses the picture at first, as shown by the illustrations (figures 3 and 4). However, examination with high power of the microscope reveals no evidence of even a remnant of a membranous separation between the ventricle and the subarachnoid space.

Figure 3 illustrates the central canal at its opening into the fourth ventricle. The caudal tip of the cerebellum is shown dorsally. The tip is not attached to the brain stem, nor does the cerebellum act as a complete barrier between the ventricle and the subarachnoid space. The foramen of Magendie at this stage exhibits the same boundaries as in the 69 mm. specimen. Figure 4 shows a section rostral to the foramen, where the ventricle is surrounded by the cerebellum, rhombic lips and chorioid plexus.

An interesting feature in the formation of the chorioid plexus was noted in sections of the 5 month fetal brain made by Dado (figures 5 and 6). The plexus seems to connect with the nervous tissue of the rhombic lips, as seen macroscopically. On high power microscopic examination, however, the plexus was seen to be formed at the point where the rhombic lip resolves itself into ependyma and pia mater. The mechanism of formation of the plexus is as usual; i. e., it is a vascularized, villous invagination of the ependyma and pia mater.

The plexus becomes progressively enlarged as the more rostral areas of the ventricle are reached. The plexus of one side approaches that of the other side in the more rostral regions, especially as the upper level of the cerebeller lobes is attained. An arch of chorioid plexus is thus formed, which replaces the central roof plexus of the more primitive stages.

Such a development of the chorioid plexus was observed upon further examination in the sagittal sections of the 6 month fetal brain made by Dado (figures 7 and 8). It was seen also in our cross sections of the stages of 84 and 69 mm. length (figures 2 and 4), and ultimately in our sagittal sections of the 57 mm. specimen, which is to be discussed immediately.

The 57 mm. fetus is just 5 mm. longer, and is slightly older, than the oldest fetus in which Weed found the rhombic roof intact. The roof of the fourth ventricle in the 57 mm. specimen is very immature in appearance. The area membranacea superior of Weed is replaced for the most part by ependyma. In a few regions, however, evidence of the more primitive epithelial-like cells which preceded the area membranacea superior is found. These patches of epithelium offer some support to Weed's opinion that the primitive epithelial condition of the roof reappears after the disappearance of the area membranacea superior and before the eppearance of the typical ependymal lining. Figure 9 shows a midsagittal section through the brain stem at this stage.* Figures 11-13 inclusive are those of regions lateral to the midplane.

*Owing to a slightly twisted condition of this fetal head in the gross condition, sections through a given portion of the brain stem will not always be through the correspon-ding portion of the remainder of the head. The central canal of the spinal cord and rhombencephalon is taken as a landmark for the midplane.

In the caudal portion of the roof the area membranacea inferior of Weed is still present. The roof is here made up of from three to four layers of cells which are somewhat flatter than typical ependyma and are more abundant in cytoplasm. Their round to oval nuclei are only moderately pyknotic and resemble the nuclei of the adjoining, undifferentiated mesenchyme. Figures 14-16 inclusive illustrate the histology of the area membranacea inferior and of the adjoining, undifferentiated mesenchyme. At the border of the roof and at the central chorioid plexus the area membranacea inferior merges with typical ependyma.

Chorioid plexus grows from the rhombic lips along the lateral aspects of the fourth ventricle. The plexus is formed by the usual mechanism. The appearance is similar to that which is seen in older fetal brains, as described heretofore in this paper. Figures 10 and 13.

The central portion of the area membranacea inferior is not intact; it is breaking down by a process of lysis of the component cells. Figures 9 and 14 illustrate the condition. The cellular constituents of the membrane have apparently gone into solution, leaving in their wake a trial of protoplasmic fragments. Even the latter are lacking in the lower part of the region, shown in the photographs.

External to the dissolving membrane is periaxial mesenchyme, arranged in trabeculae. It is seemingly the primitive arachnoid. External to the latter are primitive dura mater and bone.

Those investigators who deny the existence of a normal posterior median aperture in the roof of the fourth ventricle consider any opening in that location to be an artefact. To them such a defect in the roof is the result of an artificial breakdown of a normally intact structure. They believe that the aperture is the result of trauma and rupture, or the result of postmortem degeneration. The first of these alternatives, to be tenable, would presume a much greater and more abrupt region of destruction than the limited, gradual process evidenced in our material. The second alternative, that of postmortem degeneration, would also in all probability be more widespread and would involve the neighboring ependyma and meninges.

The gradual manner of dissolution of the area membranacea inferior, especially since the dissolution is beginning in the central part of the area, suggests that it is breaking down by design to form a normal median aperture. Such an aperture is the foramen of Magendie.

The age of the fetus upon which the observations were made is between the second and third month. The breakdown of the area membranacea inferior to form a median aperture, therefore, occurs in the third month of fetal life. This agrees with the observations of Kollmann and Streeter.

The median aperture at this stage is simply a break in the area membranacea inferior, due to beginning dissolution of its component cells. There are no well defined boundaries; the opening may be said to be bounded only by the remaining, undissolved, more peripheral portions of the membrane.

In summary of the formation of the aperture: The process is complete in the 69 mm. fetus, which is three months old. In Weed's 52 mm. fetus the rhombic roof is intact. In our 57 mm. specimen, which is in the third month, the process of breakdown of the rhombic roof is well begun. Consequently, the conclusion is drawn from such findings that the foramen of Magendie begins to be formed during the third month of fetal life and is completely formed by the end of the third month.

Conclusions

1. The foramen of Magendie exists as a complete defect in the caudal part of the rhombic roof;

2. The foramen is formed in the third month of fetal life by a breaking down of the area membranacea inferior of Weed through lysis of its component cells;

3. The chorioid plexus connects, at least in fetal life, with the rhombic lips at the point where the lip is thin and the ependyma is in contact with the pia matter.

Bibliography

1. Blake, J. A. 1900 The roof and lateral recesses of the fourth ventricle considered morphologically and embryologically. J. Comp. Neurol., vol.10, pp. 79-108, 7 pl.

2. Cannieu, A. 1897 Contribution à l'étude de la voûte du quatrieme ventricule chez les mammifères; le trou de Magendie. J. de Med. de Bordeaux, vol. 27, p. 547.

3. Dado, A. 1937 The posterior median aperture of the fourth ventricle of human adult and fetal brains. Dept. of Anat., Loyola, thesis, 5 pl.

4. Hess, Carl 1885 Das foramen Magendii und die oeffnungen an den recessus lateralis des vierten ventrikels. Morphol. Jahrb., Leipz., vol. 10, pp. 578-602, 12 figs.

5. Hughson, W. 1925 Embryogenesis of human cerebrospinal fluid; sources, circulatory pathways and destination, together with relation to blood and lymph vascular systems. Arch. Neurol. and Psychiat., vol. 14, pp. 240-250

6. Kollman, J. 1898 Lehrbuch der entwickelungsgeschichte des menschen, Fischer, Jena, pp. 511-512

7. Rogers, L., and C. M. West 1931 Foramen of Magendie, J. of Anat., vol. 65, pp. 457-467, 9 figs.

8. Weed, L. H. 1917 The development of the cerebrospinal spaces in the pig and in man. Contrib. to Embryol., vol. 5, No. 14, 17 pl.

1922 The cerebrospinal fluid. Physiol. Rev., vol. 2, pp. 171-203

9. Wilder, B. G. 1886 Notes on the foramina of Magendie in man and the cat. J. of Nerv. and Ment. Dis., vol. 13, p. 206

1893 The metapore (foramen of Magendie) in man and an orang. The Med. News, vol. 63, p 439

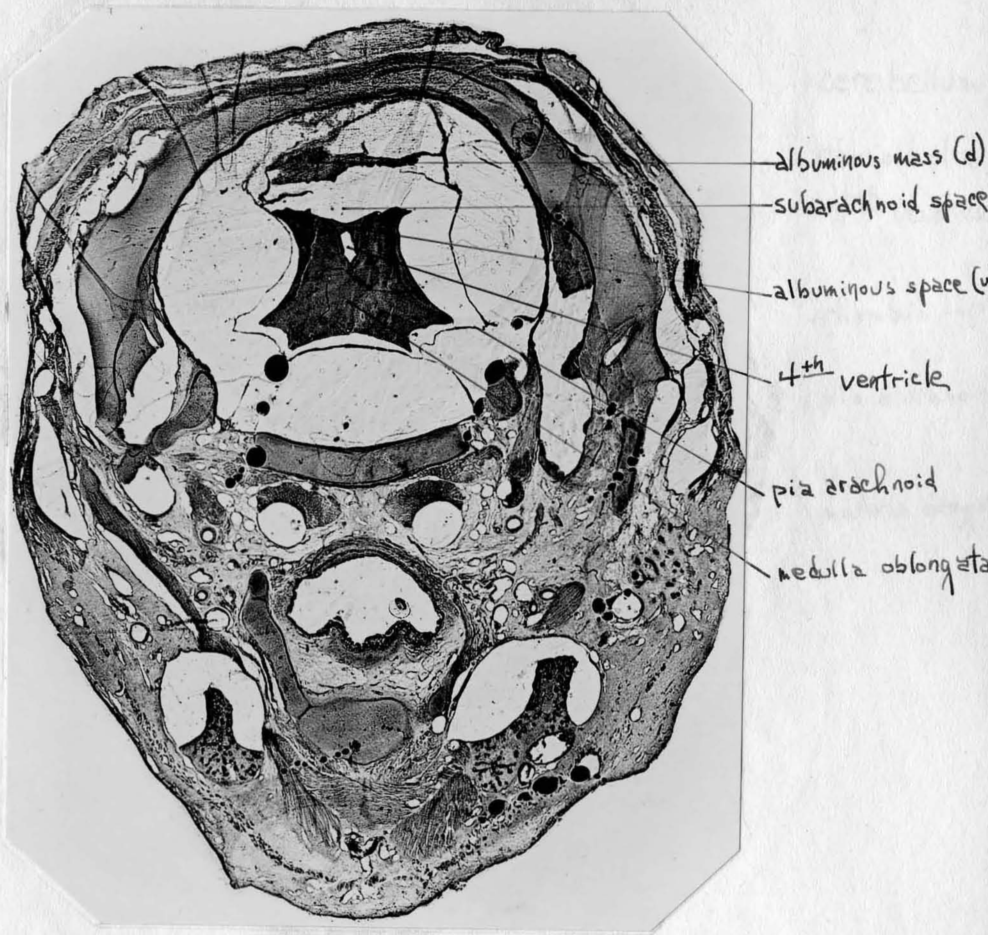

Figure 1: Transverse section through head of 69 mm. fetus, just rostral to junction of central canal with 4th ventricle

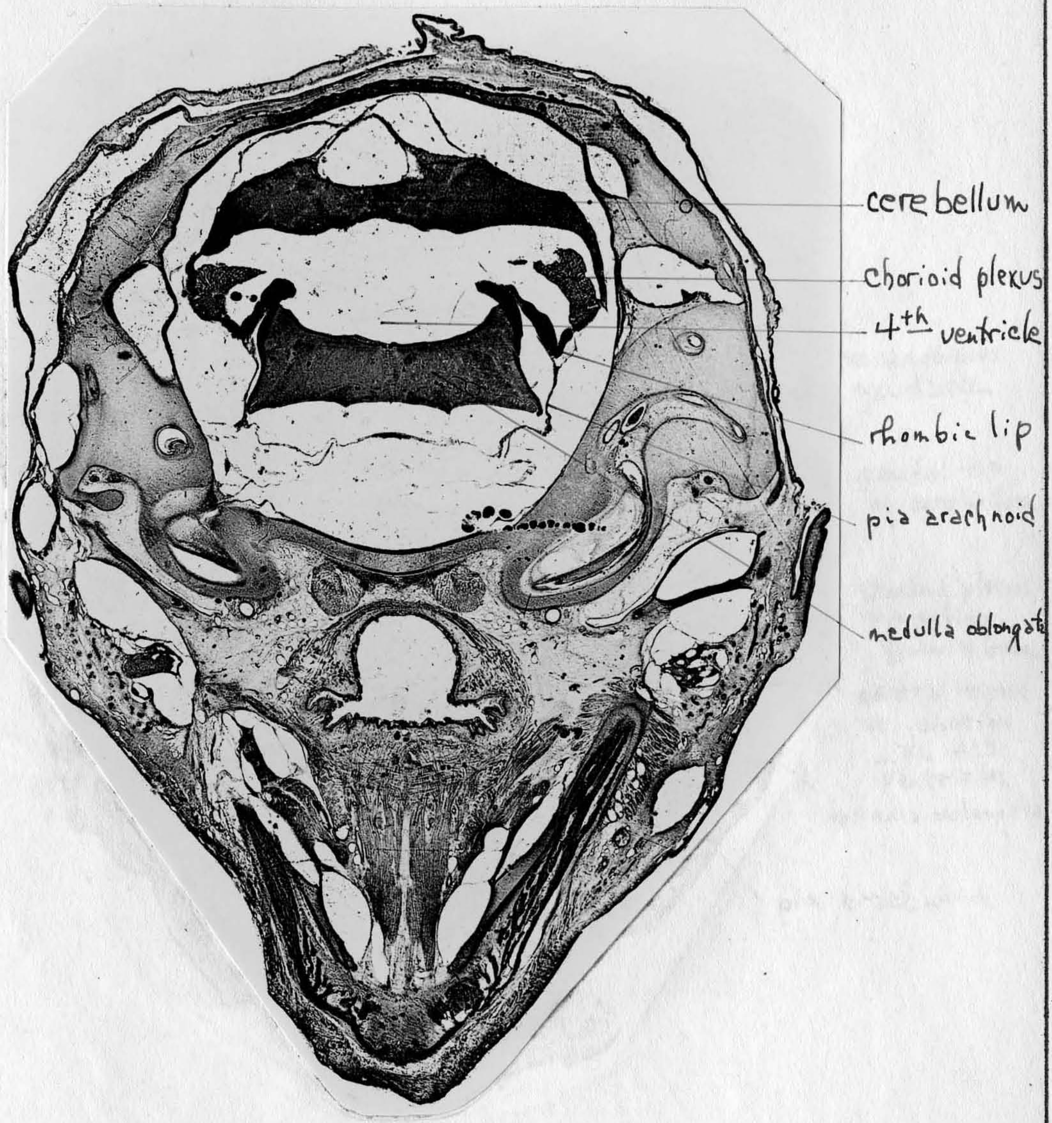

Figure 2: Transverse section through head of 69 mm. fetus and through the upper portion of the 4th ventricle, in the region where the cerebellum acts as a roof for the ventricle

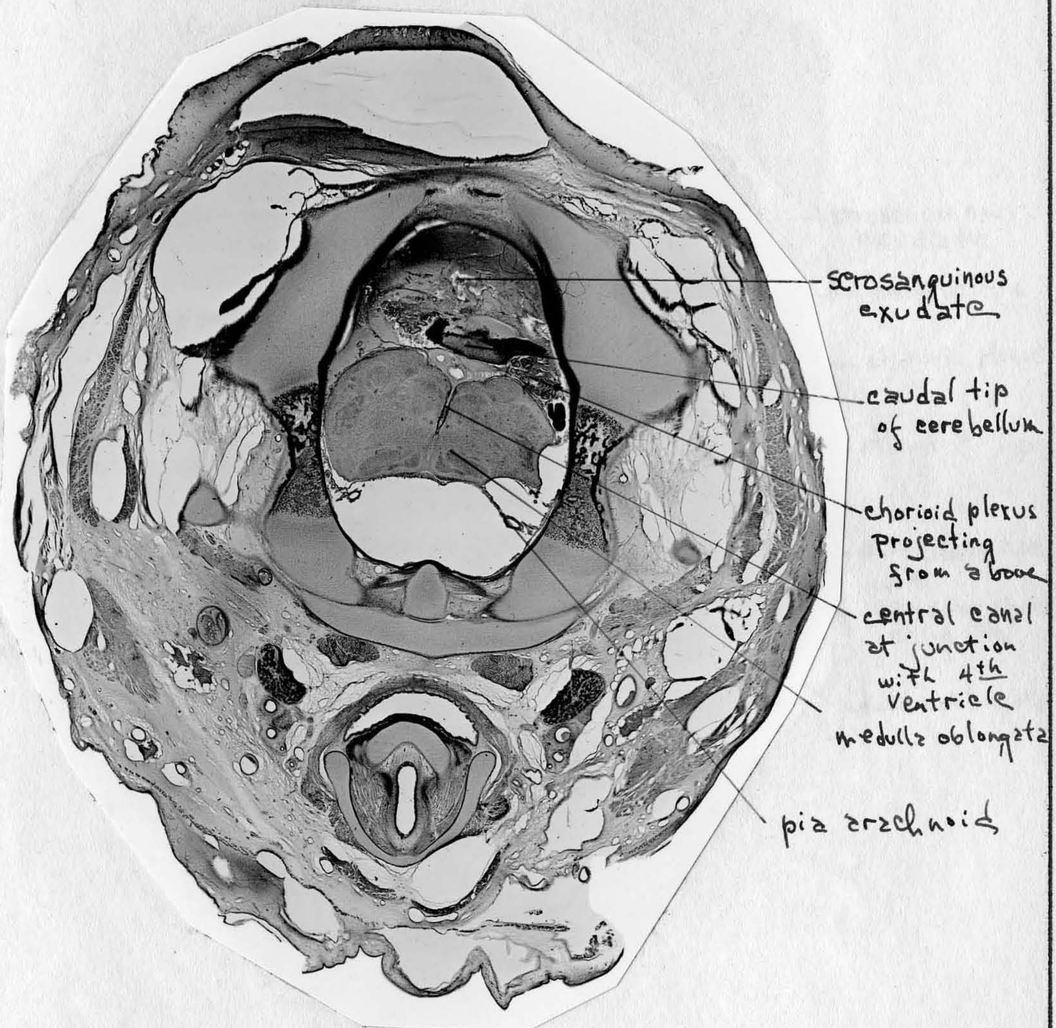

Figure 3: Transverse section through head of 84 mm. fetus at junction of central canal of rhombencephalon with 4th ventricle. X 5.7

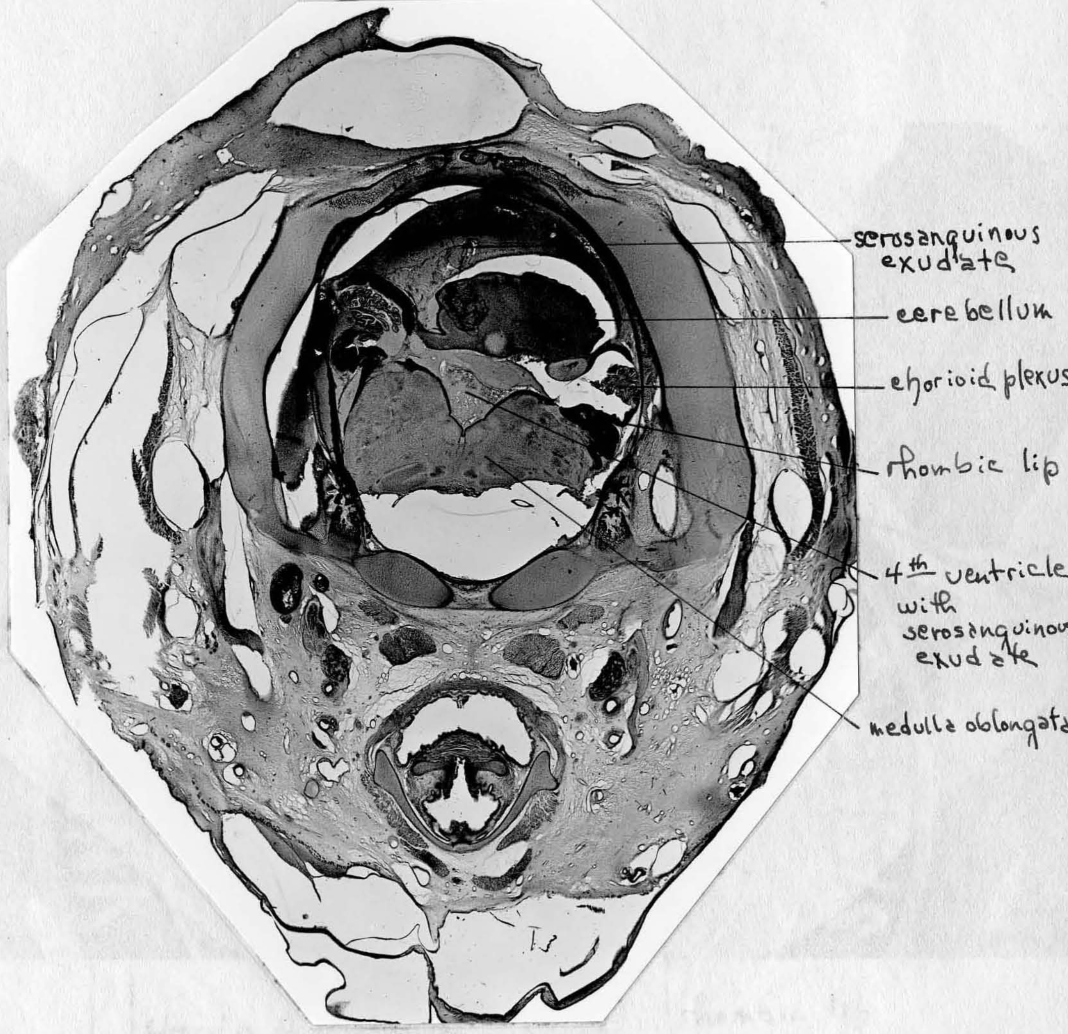

Figure 4: Transverse section through head of 84 mm. fetus in the region of the upper portion of the 4th ventricle, where the ventricle is surrounded by the cerebellum, rhombic lips and chorioid plexus X 5.7

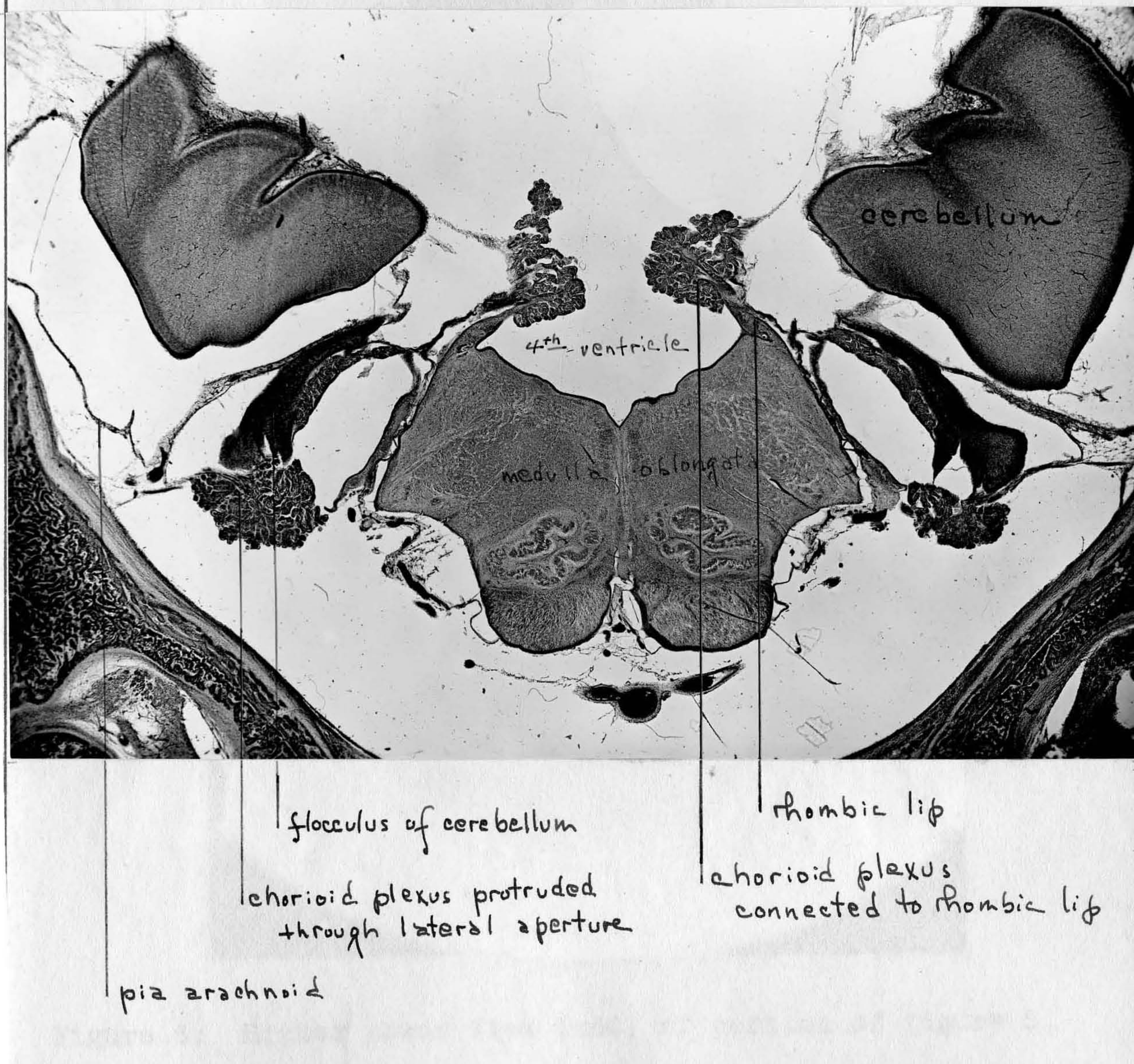

Figure 5: Section through upper portion of medulla of 5 month fetal brain. X8.6

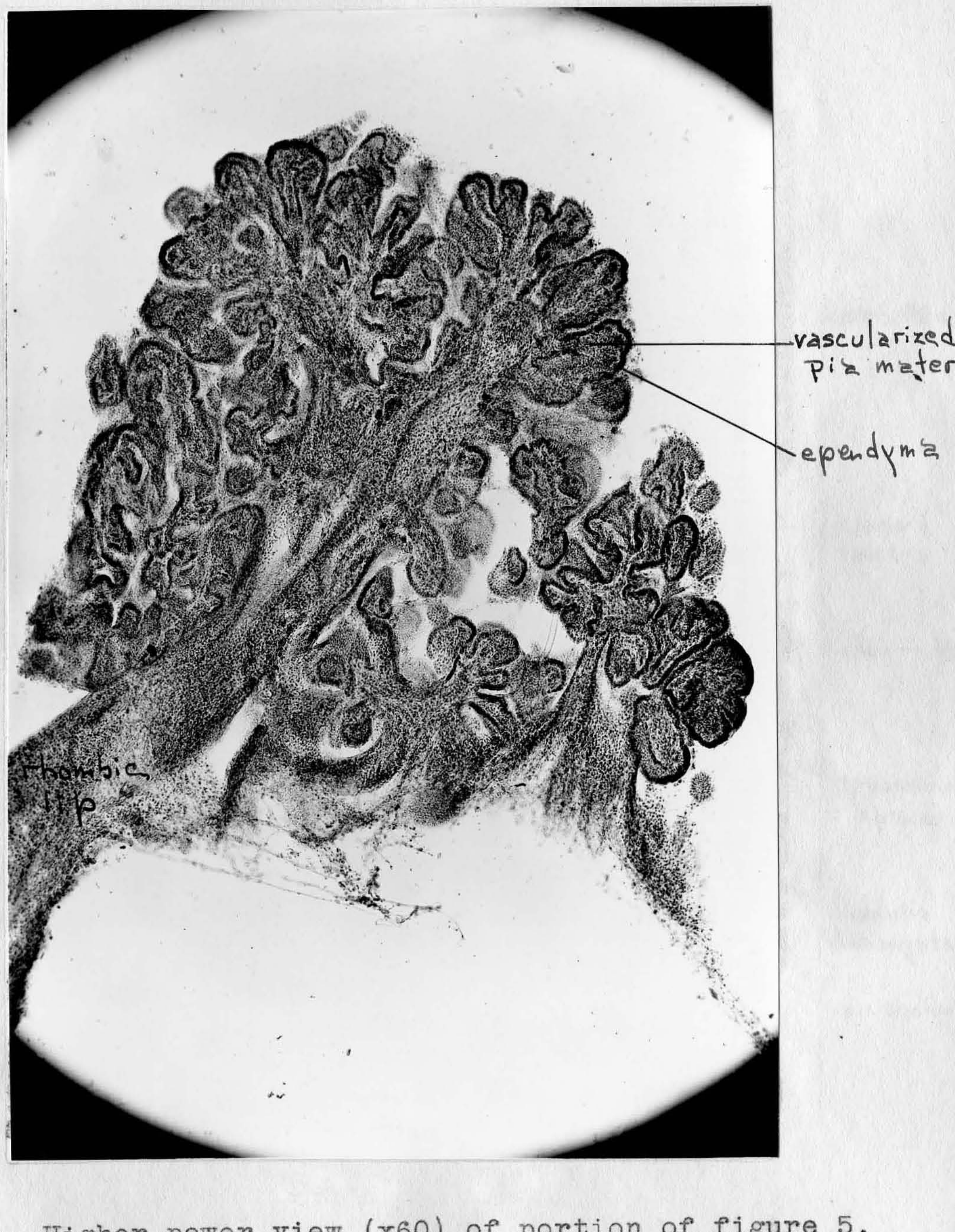

Figure 6: Higher power view (x60) of portion of figure 5, to show relation of chorioid plexus to rhombic lip

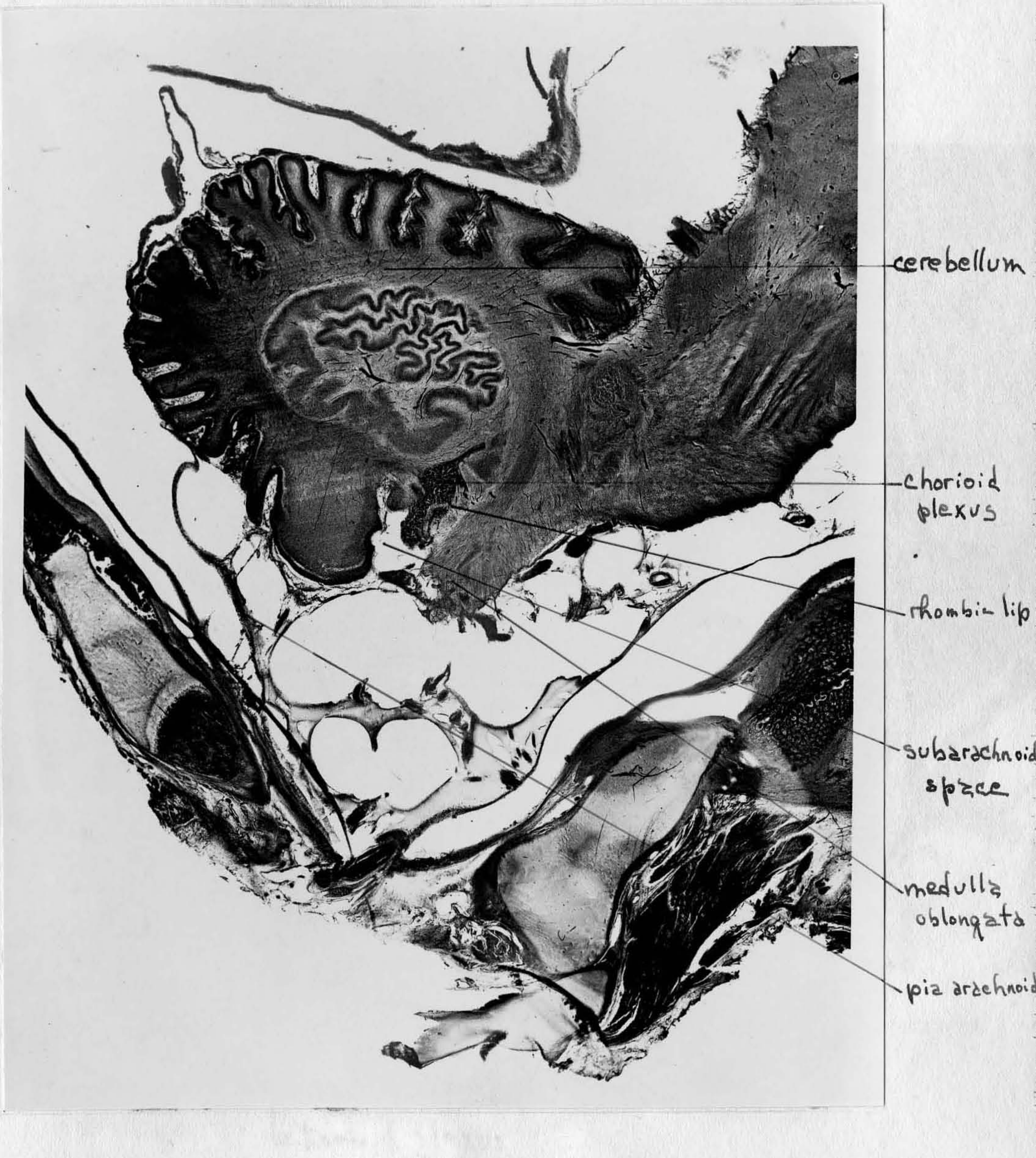

Figure 7: Sagittal section through head of 230 mm. fetus (6 months) in region of rhombic lip

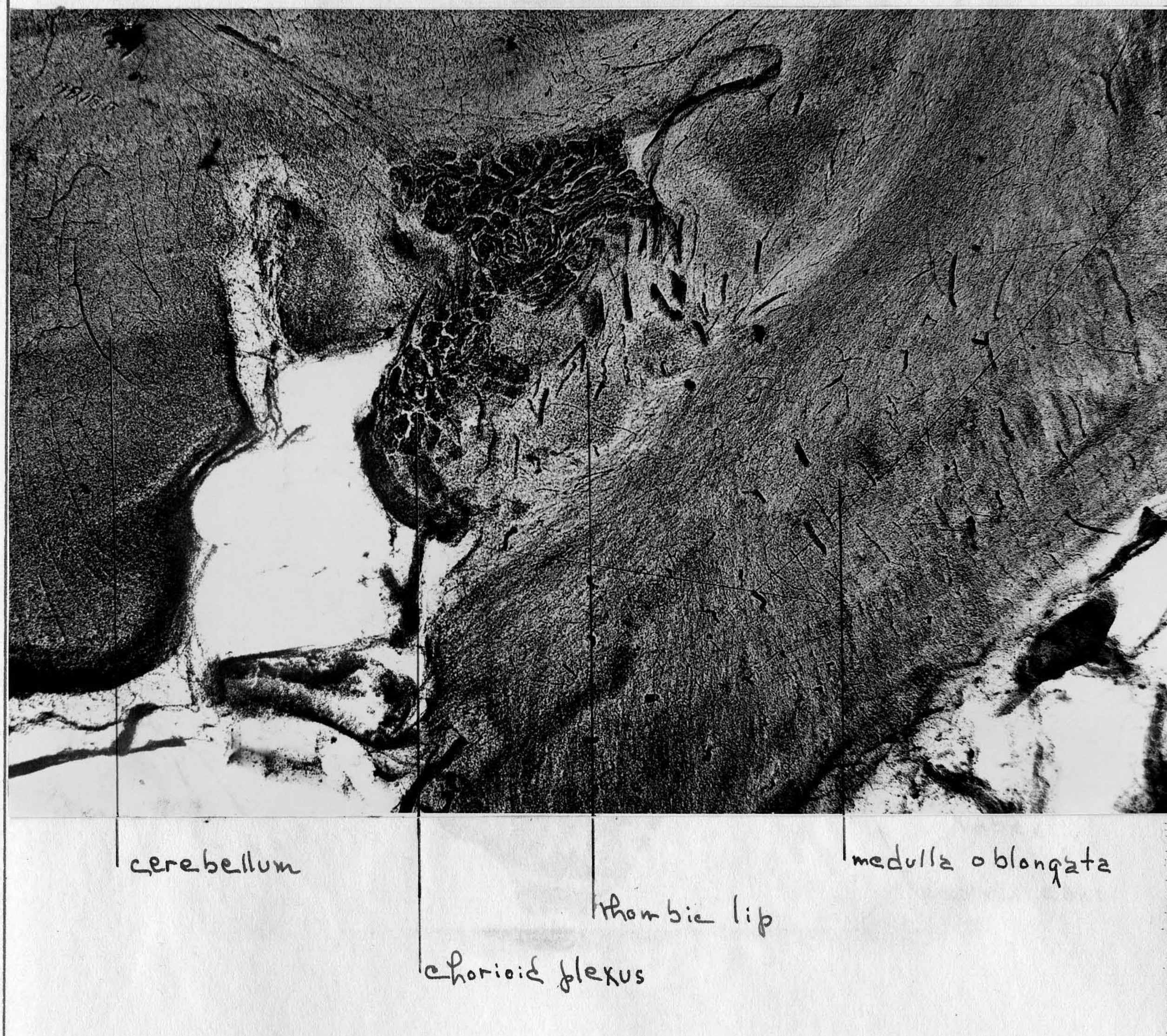

Figure 8: High power view of region depicted in figure 7

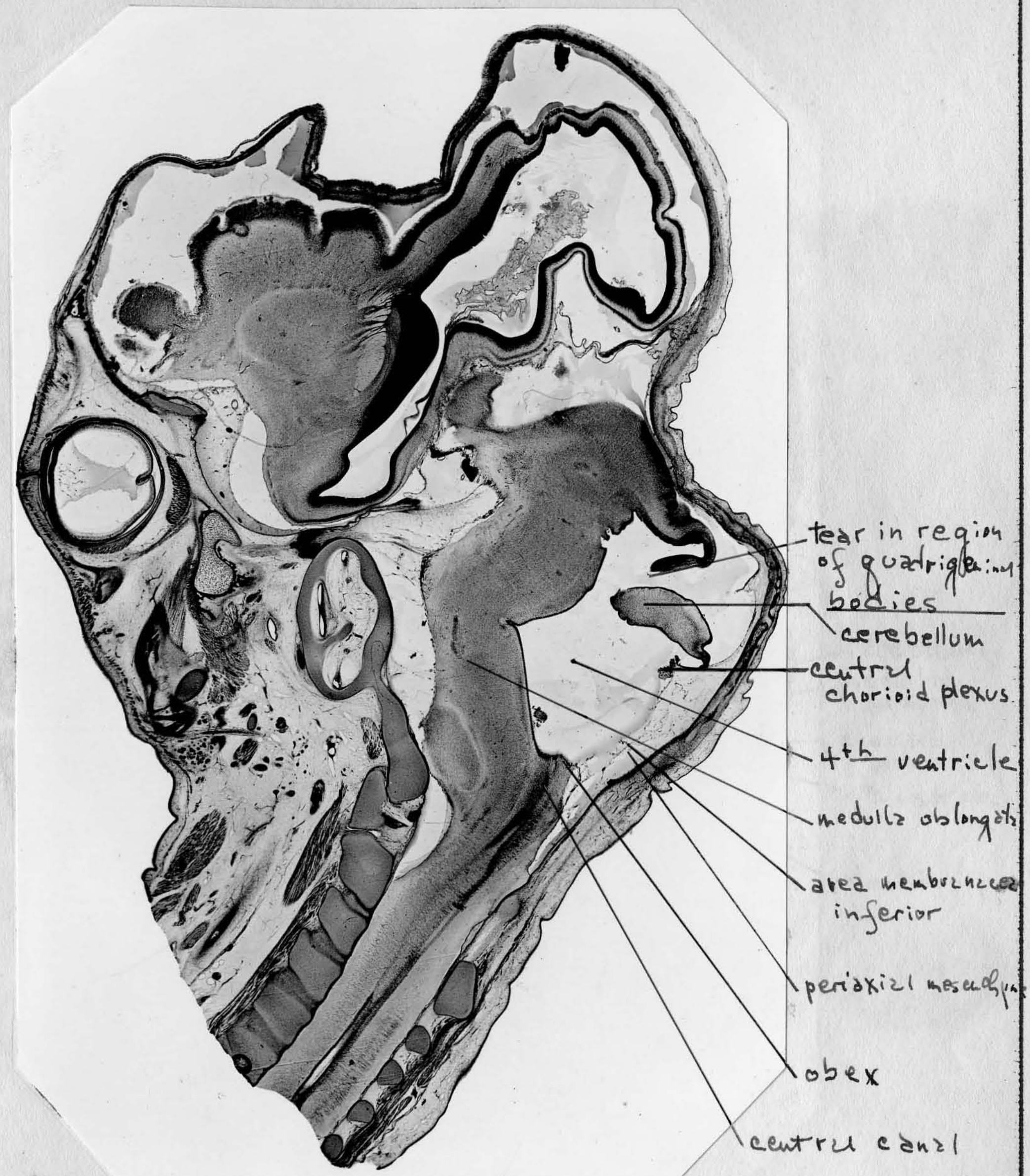

Figure 9: Sagittal section through midplane of 4th venticle region* in 57 mm. fetus X 6.7

*Cf. footnote on page 12

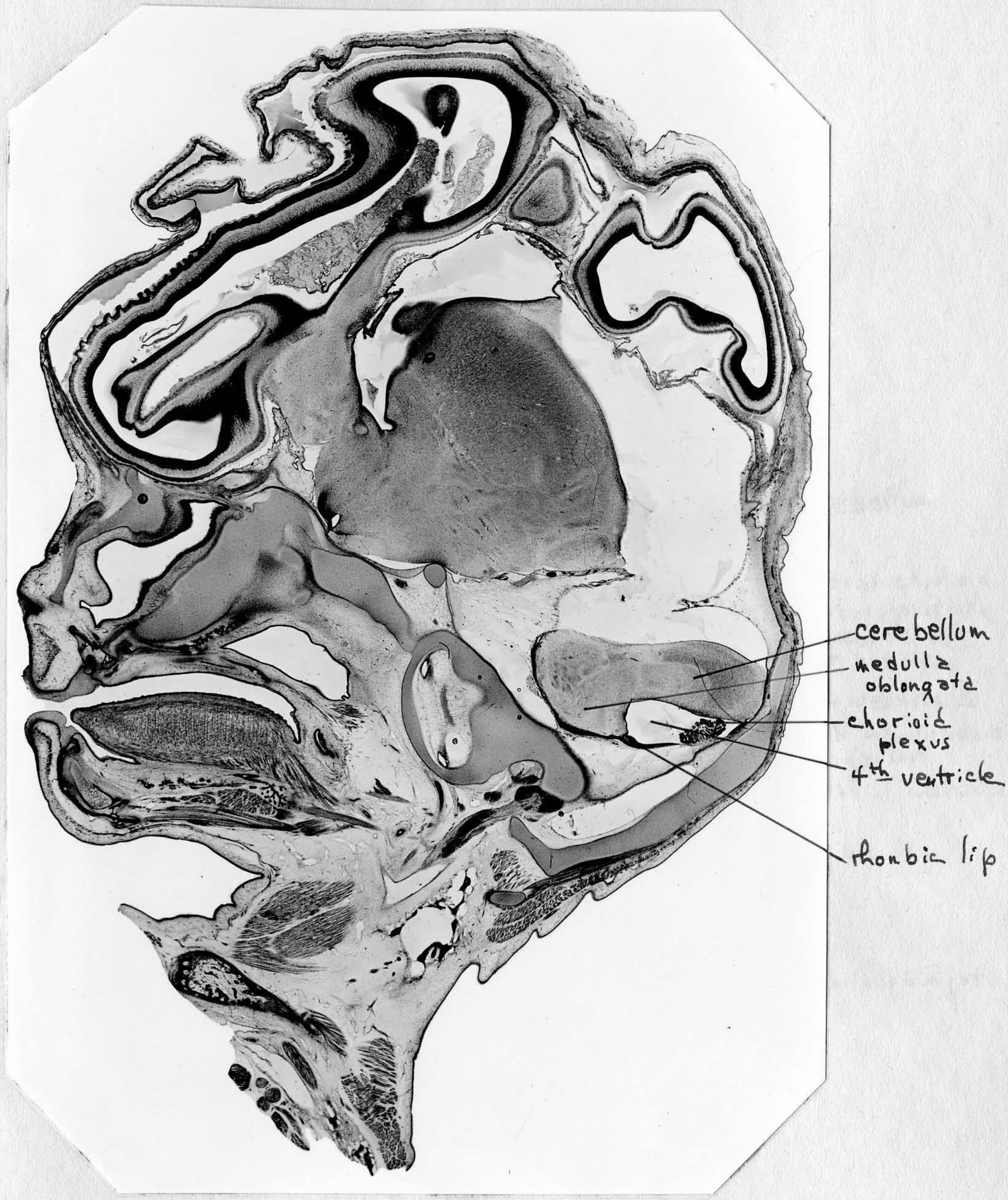

Figure 10: Sagittal section through region of rhombic lip*
in 57 mm. fetus X 5.7
*Cf. footnote on page 12

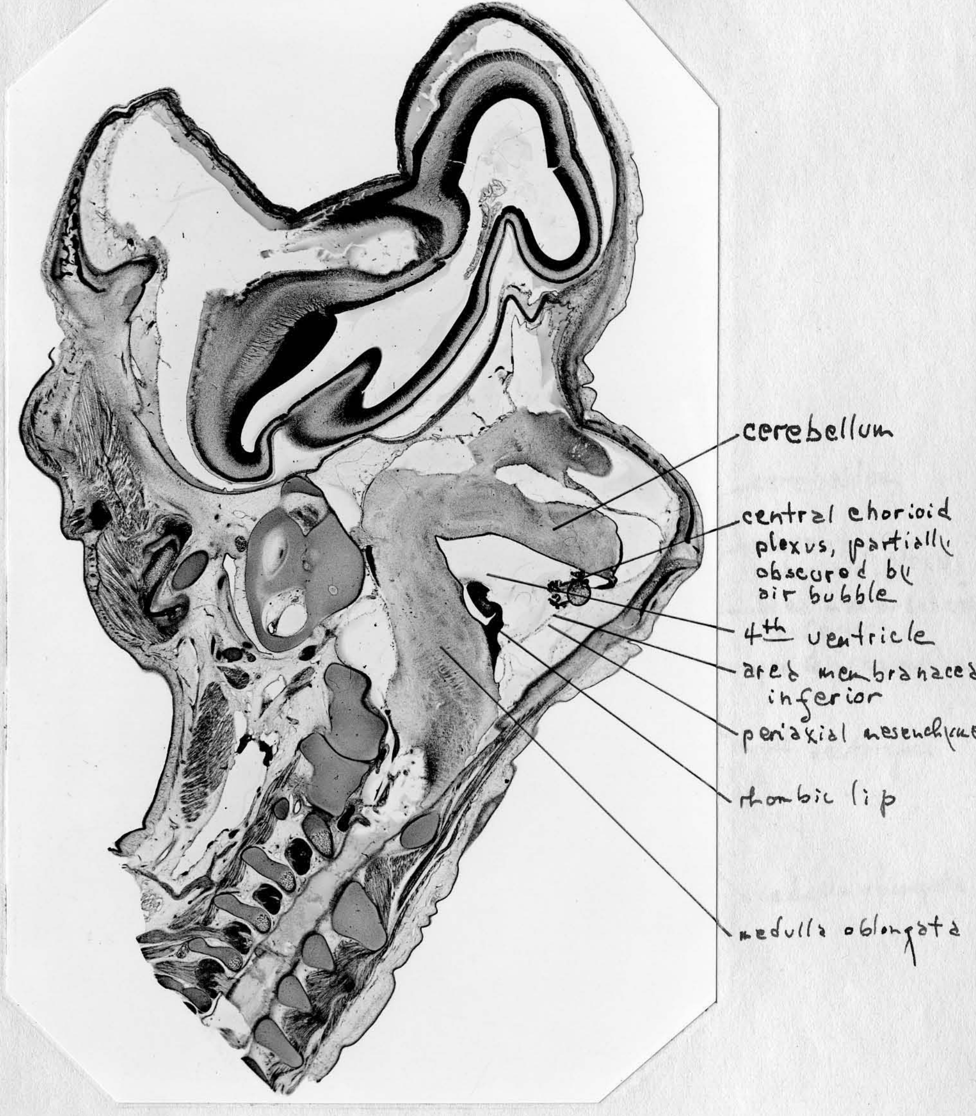

Figure 11: Sagittal section lateral to midplane of 4th ventricle region* in 57 mm. fetus X 5.7

*Cf. footnote on page 12

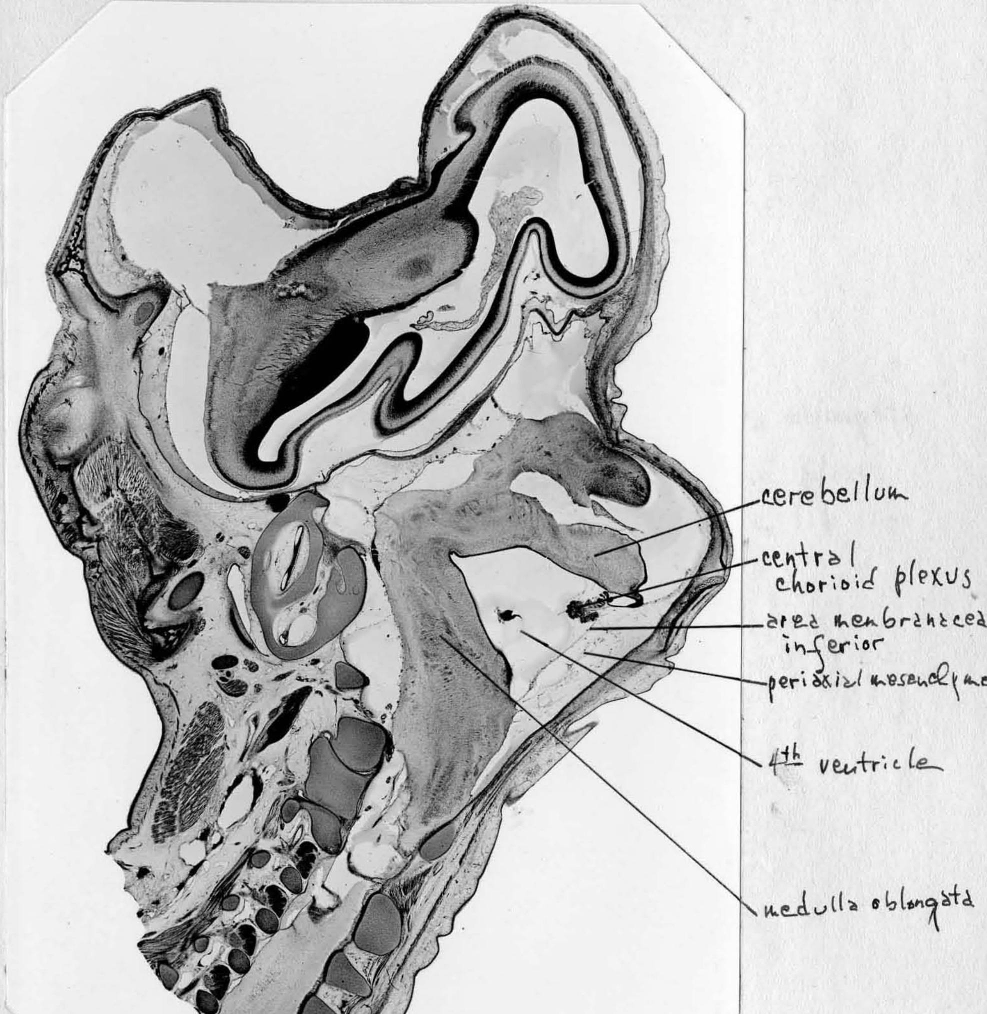

Figure 12: Sagittal section lateral to midplane of 4th ventricle region* in 57 mm. fetus X 5.7

*Cf. footnote on page 12

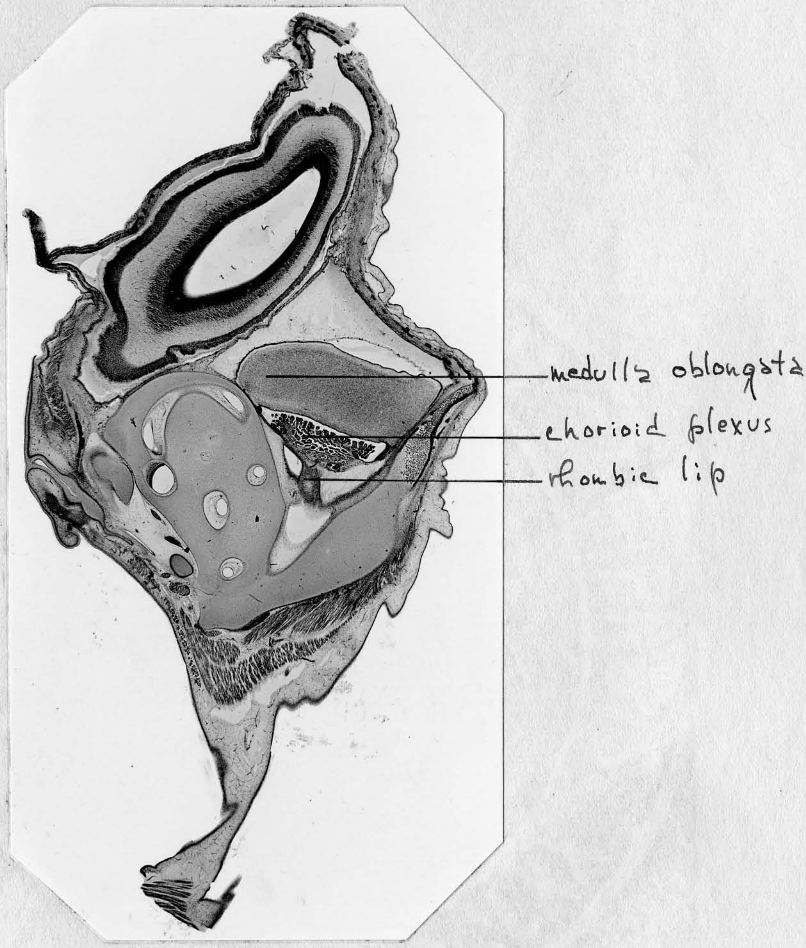

Figure 13: Sagittal section through rhombic lip* of 57 mm. fetus X5.7

*Cf. footnote on page 12

Figure 14: High power view (X100) of area membranacea inferior in its central portion

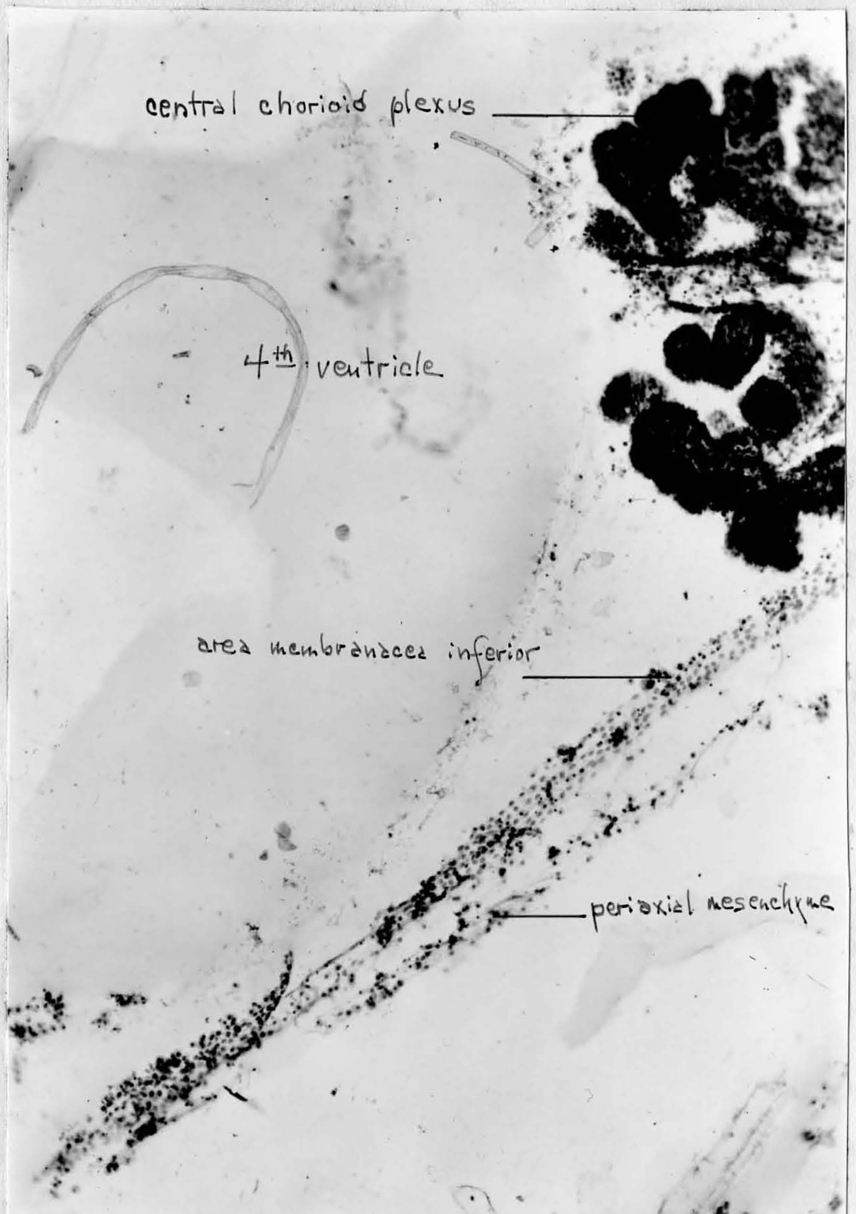

Figure 15: High power (X100) of area membranacea inferior in its lateral portion

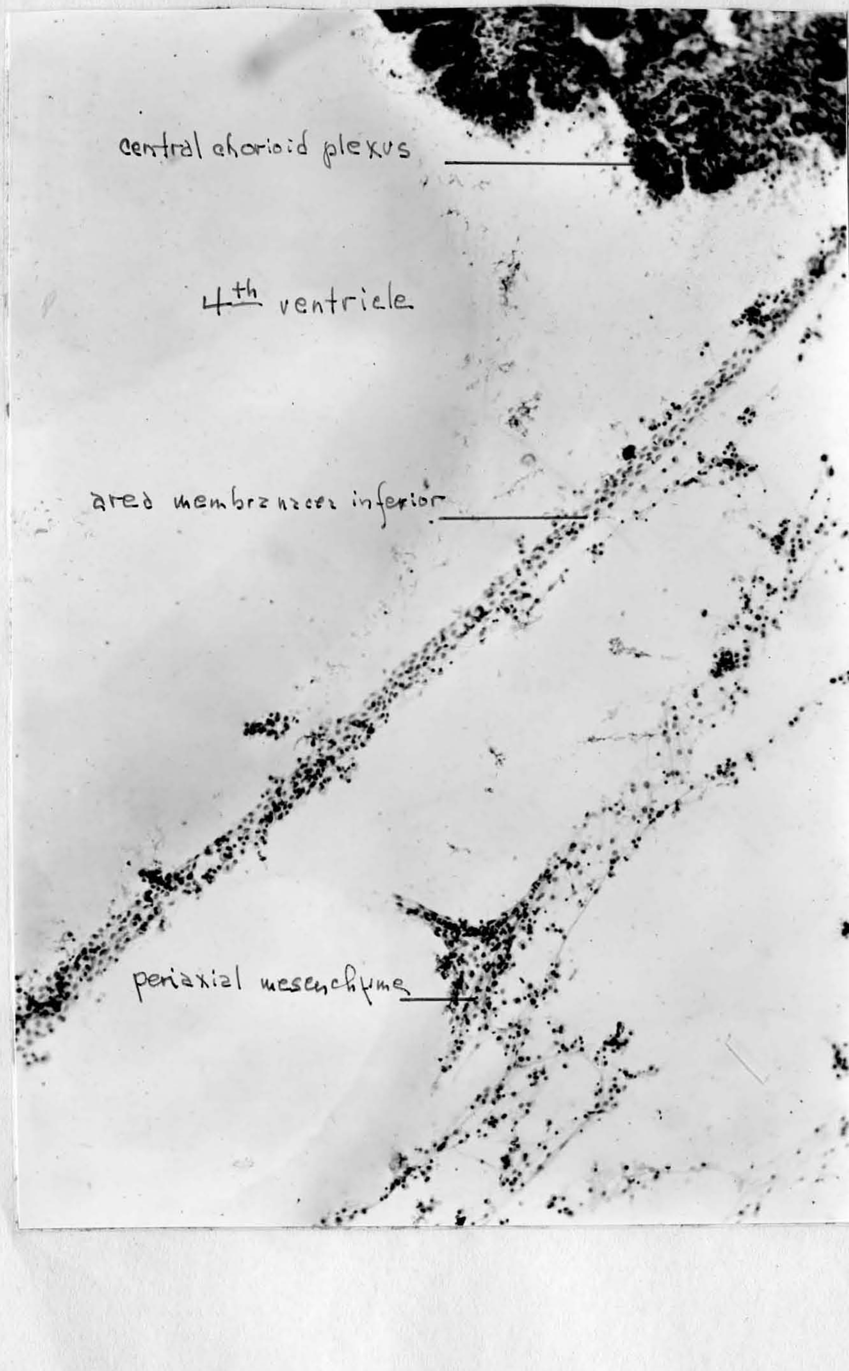

Figure 16: High power view (X100) of another region of the area membranacea inferior lateral to the midplane