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JUAN A. DEL REGATO, M. D., *Editor*

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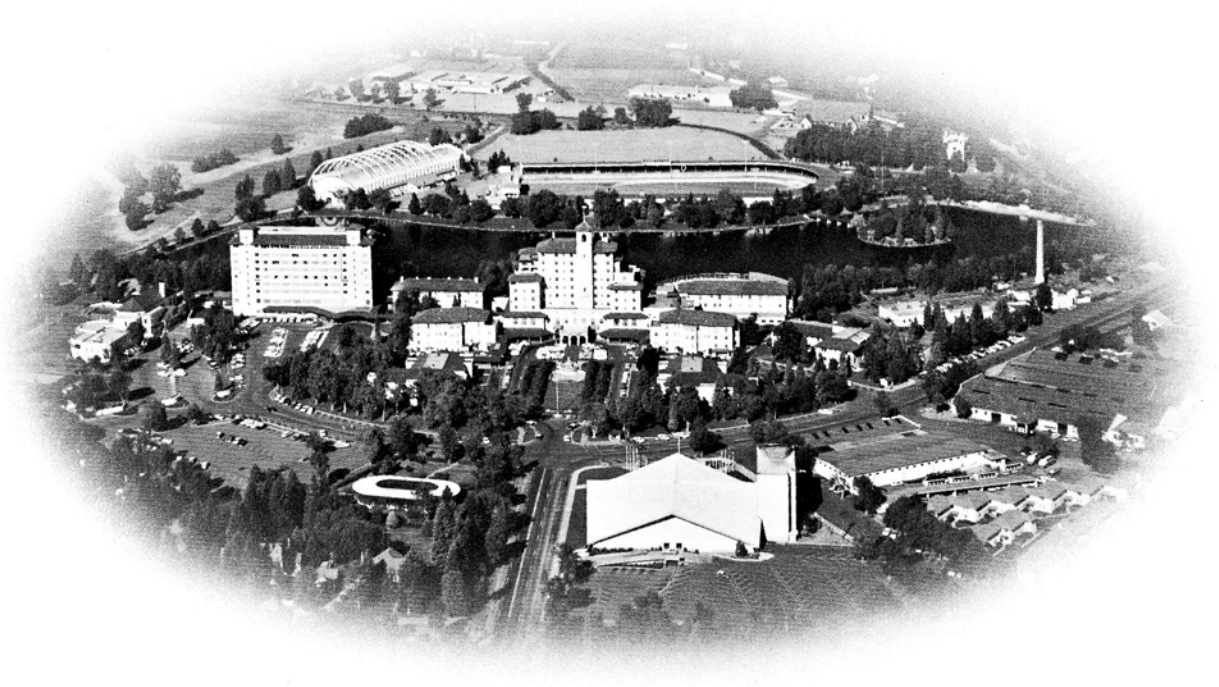


INTRACRANIAL TUMORS

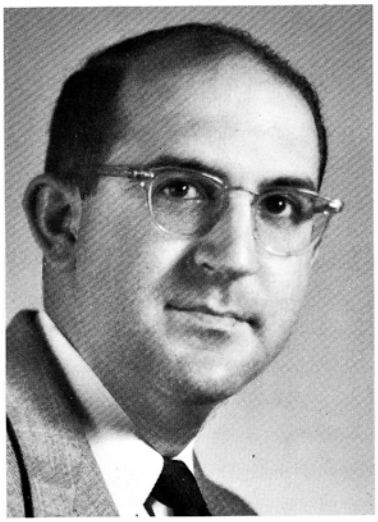
THIS CANCER SEMINAR on intracranial tumors took place in Colorado Springs on November 3rd, 1962. The audience of neurosurgeons, radiologists and pathologists was rewarded by an unusual display of diagnostic acumen from Dr. Juan Taveras; it would be difficult to ascertain which section of the participating audience was most impressed by the didatic clinico-radiologic rationalizations and masterful interpretations of Dr. Taveras. Dr. Harry M. Zimmerman contributed the wealth of his authoritative views in this forbidding field of tumor morphology and shed light on the general discussions. Dr. Paul C. Bucy added his experience in the clinical interpretation, his insight in the pathology and his concepts of the adequate surgical handling of these exclusive tumors.

The discussions in Colorado Springs were enriched by the opinions and comments submitted in advance by our national and foreign correspondents, to whom we remain most grateful.

We owe a special word of thanks to the administrative and technical personnel of the BROADMOOR HOTEL, of Colorado Springs, whose efficient cooperation has contributed so much to the success of these Cancer Seminars at their International Center.

J. A. del REGATO, M.D.
Colorado Springs, October, 1963.

OUR GUEST SPEAKERS

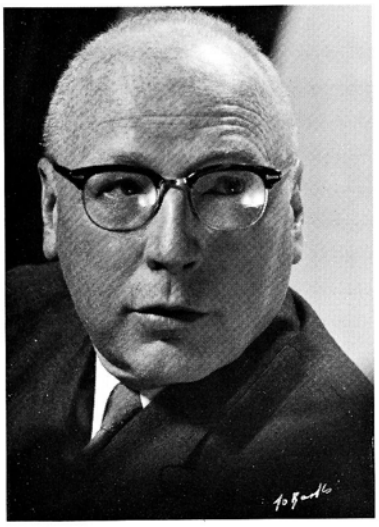


JUAN M. TAVERAS, M.D.

Professor of Radiology, College of Physicians and Surgeons, Columbia University, New York. Dr. Taveras is a graduate of the University of Santo Domingo, Dominican Republic. He is a frequent contributor to the medical literature and a recognized teacher of diagnostic radiology.

HARRY M. ZIMMERMAN, M.D.

Chief of Laboratory Division of the Montefiore Hospital of New York. Dr. Zimmerman is a graduate of Yale University. He is a notable neuropathologist, author of a book and of numerous contributions to this branch of our knowledge. He was guest of the College of American Pathologists.



PAUL C. BUCY, M.D.

Professor of Surgery, Northwestern University Medical School, Dr. Bucy is a graduate of Iowa State University. He has had a distinguished academic career as a surgeon and as a teacher of neurosurgery.

1. *Medulloepithelioma of the Left Cerebral Hemisphere*

Contributed by R. PÉREZ-TAMAYO, M.D., H. NEUSTEIN, M.D. and G. ENGLUND, M.D.,

Denver, Colorado

THE PATIENT was an 11-year-old boy in July, 1961, when he presented fainting spells followed by severe frontal headaches, vomiting and progressive lethargy. Physical examination revealed no neurologic signs. The cerebrospinal fluid was bloody and xanthochromic; the proteins were 160 mgm per cent, sugar 58 mgm per cent. An EEG was reported normal.

Dr. Taveras: The single posteroanterior film of the skull contains air in the ventricles; only the two lateral ventricles are filled with gas. Because of rotation it cannot be stated whether the asymmetry noted in the configuration of the two lateral ventricles is simply due to the rotation or whether it may be associated with the patient's condition. There is no gas visible in the third ventricle and none is seen in the aqueduct and fourth ventricle; the lateral ventricles are moderately dilated.

The lack of air in the third ventricle and in the cavities below the third ventricle in this single film is not necessarily significant, but the fact that it was stated on the history would indicate that there is an obstructive lesion in these portions of the ventricular system. It is, of course, not possible to state whether the lack of filling is due to a mass within the ventricle or ventricles or whether it is produced by compression and obstruction from a lesion adjacent to the passageways. The lack of any neurological findings would be in favor of an intraventricular type of tumor. Of the intraventricular tumors we should consider ependymomas of the third ventricle or of the fourth ventricle and, because of the presence of evidences of bleeding in the cerebrospinal fluid as indicated by the history, the possibility of a papilloma of the choroid plexus is a strong probability. From the evidence at hand, it is not possible to tell whether the lesion was in the third ventricle or in the fourth ventricle. Assuming that the statement that "the ventriculogram failed to fill the third and fourth ventricles" is correct, we would have to place the lesion in the third ventricle. Statistically, ependymomas and choroid papillomas are less common in the third ventricle than in the fourth ventricle but this would certainly not militate against the tumor being in the third ventricle. About one-sixth of the choroid papillomas occur in the third ventricle, although I have never seen one there myself.

In conclusion, we are dealing here with a lesion which is apparently producing obstruction to the flow of cerebrospinal fluid possibly in the third ventricle but at least in the aqueduct or fourth ventricle which later metastasized to the spinal subarachnoid space. This will make it one of the few neoplastic types which would do so in childhood; medulloblastoma, cerebellar sarcoma, choroid plexus papilloma, ependymoma, and pinealoma. I favor papilloma of the choroid because of the xanthochromic spinal fluid.

Dr. Taveras' impression: PAPILLOMA OF THE CHOROID PLEXUS.

Roentgenologic Impressions Submitted by Mail

Ependymoma, 3d ventricle	33
Pinealoma, 3d ventricle	17
Tumor of choroid plexus	15
Thalamic tumor	11
Various tumors	9
Cyst of 3d ventricle	5
Others	15

Dr. Taveras: I was leaning on the side of papilloma of the choroid plexus because of the bloody cerebrospinal fluid; but I suppose any intraventricular tumor could bleed at any time. Pinealoma is a fairly common tumor of the third ventricle and it could do the same thing. The possibility of a thalamic tumor should be considered because there is this apparent elevation of the atrium and there is also the obstruction of the third ventricle. However, in thalamic tumors only the posterior two-thirds of the third ventricle are usually obstructed, and there will be some air in the anterior third of the third ventricle. In fifty-two thalamic tumors we had in the Neurological Institute in the period of fifteen years we found that the third ventricle was visible in all, either partially or completely, with evidence of displacements and deformities and, in some cases, obstruction of the posterior portion but with dilatation of the anterior portion of the third; so, if we take the history as given—that there was no filling of the third ventricle—I would think that a thalamic tumor would be unlikely. I thought that the degree of ventricular dilatation would probably be greater than the one we see here, for a colloid cyst, which is the cyst *par excellence* of the third ventricle.

Dr. Regato: Dr. S. M. Jones, of Lubbock, Texas, submitted an impression of tumor of the left third ventricle; Dr. J. R. Galloway, of Albuquerque, offered a thalamic tumor. Dr. W. Kraemer, of Knoxville, Tennessee, preferred suprasellar craniopharyngioma. Dr. C. E. Shopner, of Oklahoma City, favored an ependymoma.

Operative findings: On July 4th, 1961, a Torkeldson's procedure, a bilateral ventriculo-cysternal shunt, was successfully carried out. On July 15th a needle biopsy was done which was unsatisfactory but appeared sufficient for a diagnosis of brain tumor.

Dr. Zimmerman: This tumor has an epithelial appearance and is distinctly papillary with pseudo-acinus formation here and there. It is abundantly supplied with blood vessels and large venous lakes. Some of these have ruptured to produce extensive hemorrhage. The stroma of the tumor is composed of neurogenic tissue and is not mesodermal. The papillae, however, which are lined by a single layer of cuboidal or columnar cells, contain blood vessels and fibrous strands to form central cores. Many of the tumor cells are in mitotic division. The cells have a strong resemblance to those which line the medullary canal of the embryo and they are also like the cells which cover the surface of the choroid plexus. There are neither cilia nor blepheroplasts at the free ends of the tumor cells. The best descriptive term for this neoplasm is, therefore, medullo-epithelioma.

This tumor should be distinguished from the ependymoma which has rosette formations. In one type of ependymoma, the rosettes have a solid structure, their cells are pear-shaped, and the cellular processes form a tangle in the center of the rosette or are attached to the adventitia of a blood vessel. In the second type of tumor, true acini are formed and are lined by ependyma-like cells which usually have cilia and blepharoplasts. The medullo-epithelioma is readily distinguished from the so-called medullo-blastoma whose cells form occasional pseudo-rosettes. The medulloblastoma has very little glial or mesodermal stroma, and is

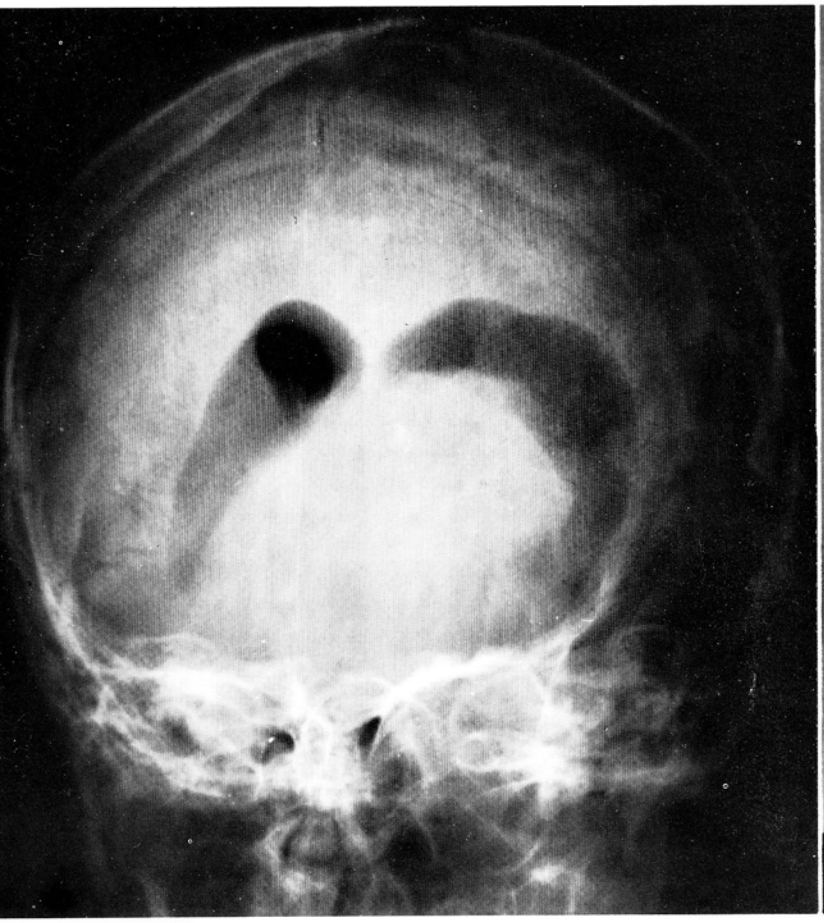


Fig. 1—Ventriculogram showing filling of lateral ventricles.

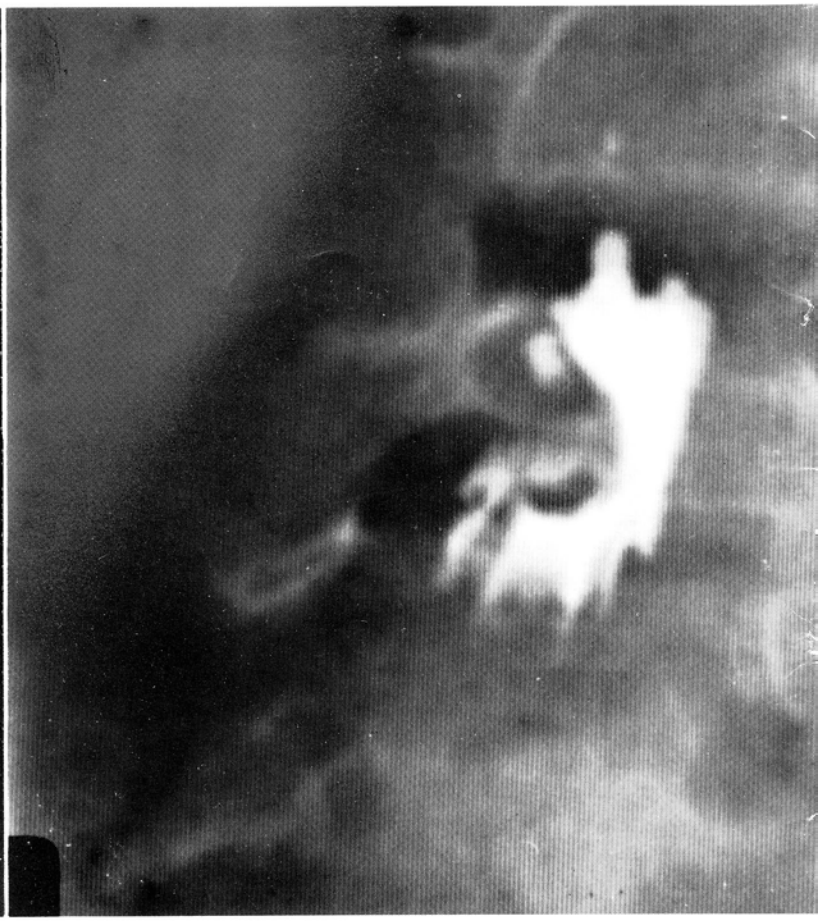


Fig. 2—Myelogram showing a lumbar defect due to metastatic tumor.

quite probably a neuroblastoma. It resembles rather closely the neuroblastomas of extracranial origin. Finally, the medullo-epithelioma should be distinguished from the choroid plexus papilloma. This tumor lies within the ventricular system, most often the fourth ventricle, and is attached to or replaces the choroid plexus. It is readily identified as a rather large papillary structure which is non-invasive of the neural parenchyma. The papillae contain connective tissue cores and are lined by columnar cells whose free margins often contain cilia. In rare instances the papilloma of the choroid plexus undergoes malignant change, when it becomes invasive and resembles papillary adenocarcinomas of extracranial origin.

Medullo-epithelioma is a tumor of childhood, which fact is important in distinguishing it from metastatic adenocarcinoma.

Dr. Zimmerman's diagnosis: MEDULLO-EPITHELIOMA.

Histopathologic Diagnoses Submitted by Mail

Malignant ependymoma	85
Pineal tumor	20
Medulloblastoma	11
Carcinoma, choroid plexus	10
Papilloma, choroid plexus	9
Hemangioblastoma	4
Others	21

Dr. Zimmerman: True pinealomas are exceedingly rare. Other tumors like teratomas may occur in the pineal gland but they are really not of pineal structure. They are the same teratomas that are found in other organs of the body. And then there are tumors that resemble the dysgerminomas that have been recognized in recent years as frequently occurring in the pineal and are mistakenly called, therefore, "pinealomas". Frequently these tumors may also involve the *tuber cinereum* and the stalk of the infundibulum and sometimes the pituitary gland as well; they are very frequently associated with signs of precocious puberty. These are dysgerminomas, not pinealomas; I have seen a number of them that involved the *tuber cinereum* without involving the pineal. There are, of course, a group of tumors in the pineal that are of glial origin. I have seen a number of astrocytomas, for example, of the pineal gland. Therefore I tend to be puritanical in my diagnosis of pinealomas and like if possible to call the tumor by the cell-type which forms the neoplasm rather than its location in the pineal. What I have said just now about pinealomas, and this may be subject to argument, applies as well to so-called thalamic tumors. I don't know what a *thalamoma* is: it is sometimes made up of astrocytes, in which case it is an astrocytoma, and sometimes of spongioblasts, in which case it is probably a glioblastoma multiforme, and you may have other types of tumors in that location. The neuroradiologist, seeing only masses, do well enough to be able to localize the tumor within an organ, and if they can localize it within the thalamus it is perhaps all that can be done and all that should be expected of them. But the pathologists see the histological structure of these tumors and they must do a little bit better than merely calling a tumor of the thalamus as a specific entity.

A diagnosis of malignant ependymoma I would have to go along with if by that term you mean what I mean by the term medulloepithelioma. There is really no difference and I am willing to accept that as the equivalent. Hemangioblastoma just never occurred to me. I do not believe that any of these epithelial-like cells can be mistaken for endothelial cells and although the tumor is vascular I do not believe in any way that it should be confused for a hemangioblastoma. The third ventricle colloid cyst, arises from choroid plexus, although there is a disagreement of opinion about that. Many talk in terms of a paraphysial origin for the colloid cyst of the third ventricle, but they are tumors usually only of the size of a grape which do not invade the tissue and therefore there is no intervening neural stroma. There is a capsule of connective tissue lying on the inner surface by a layer of cells usually single in type; occasionally two or three cells in thickness. Many of the cells have cilia and many of the cells of the colloid cyst of the third ventricles contain vacuoles in the cyto-

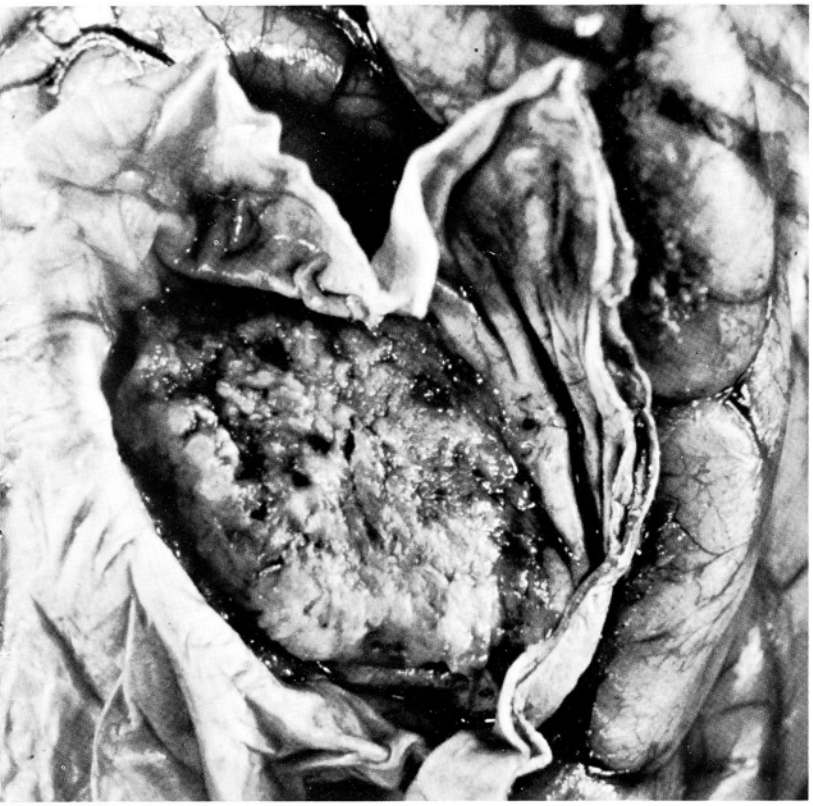


Fig. 3—Gross appearance of tumor on left cerebral hemisphere.

plasm, giving evidence to the fact that it is these cells that secrete the so-called "colloid" which fills the lumen of the cyst. There is no colloid in this case; there is no single-cell layer of the cyst cavity and so pathologically I think the diagnosis cannot be entertained of a colloid cyst of the third ventricle in this case.

Dr. Regato: Drs. N. Puente-Duany, of Salem, Virginia and R. Willis of Cornwall, England, submitted malignant ependymoma. Drs. D. S. Russell, of Surrey, England, and M. Wheelock, of Chicago, suggested papilloma of the choroid plexus. Dr. R. Delcourt, of Brussels, preferred carcinoma of the choroid plexus. Dr. J. P. Ray, Jr., of Lubbock, Texas, contributed a diagnosis of medullo-epithelioma.

K. J. Zülch, M.D., Cologne, Germany (by mail): Papilloma of the choroid plexus with malignant transformation (carcinoma). This is an alveolar and villous tumor with unilaminar very actively proliferating epithelium. The relation to the brain tissue is not clearly seen; the metastatic nature of the growth should be considered.

Subsequent history: The spinal fluid pressure remained elevated; the mental and motor status deteriorated. The patient was submitted to irradiation through two lateral fields 6 x 6 cm in diameter, with Cobalt-60; total dose was approximately 2750 roentgens in 28 days in a cerebral mid-plane, from July 12 to August 8th, 1961. This followed by rotation therapy with Cobalt 60 with an additional dose of 3200 roentgens on the axis of rotation in 22 days from August 9th to August 30, 1961. The patient improved and was discharged walking on parallel bars.

In October, 1961, the patient presented pain on the anterior aspect of the thighs and right sided paralysis without sensory loss. A suprapubic cystostomy was done. The myelogram revealed the presence of a defect in the lumbar spine and the patient submitted to radiotherapy.

On October 25th, 1961, a lumbar laminectomy was done. It revealed the presence of an extra- and intradural vascular growth with a granulomatous appearance between L4 and S2. A microscopic diagnosis of ependymoma was rendered. Because of suspicion of choriocarcinoma, the tissue was assayed for gonadotropins which were found in dilution of 1:1000. The patient had been submitted to lumbar irradiations which were in course but were interrupted for the myelograms, again for the laminectomy and finally discontinued in favor of chemotherapy in view of suspicion of choriocarcinoma. He received a total dose of 3,000 roentgens to the lumbar spine in about 28 days with the above interruptions. He was then submitted to Actinomycin, Chlorambucil and Methotraxate during November and December, 1961. There was some additional improvement, but his condition rapidly deteriorated and he expired on February 11, 1962.

Autopsy revealed a hemorrhagic mass in the left cerebral hemisphere arising from and obliterating the 3rd ventricle. Tumor was found along the needle tract of the biopsy. No residual tumor was found in the lumbosacral spine.

Dr. Taveras: Of the tumors that are capable of producing metastases by way of the cerebrospinal fluid, the most common is the medulloblastoma and then the ependymoma or the ependymoblastoma. The pinealomas, however, and the choroid plexus papillomas are also capable of seeding through the cerebrospinal fluid. The medulloepithelioma or malignant ependymoma would of course make the appearance of metastases in the subarachnoid space an expected or common finding. There are differences among the neuropathologists as to what they consider the incidence of medulloblastomas called malignant ependymomas by others.

Pinealomas rarely metastasize to the cerebrospinal fluid in a diffuse manner. We reviewed a total of 78 tumors of the third ventricle, of which a little over a third were pinealomas, and of those we found only five ectopic pinealomas. I have never seen diffuse subarachnoid metastases from a tumor which had been called pineal teratoma or belonging to this group of tumors. We are left then with the possibility of considering choroid plexus papillomas. I personally have not seen diffuse seeding of choroid plexus papillomas in the lumbar subarachnoid space although I have seen quite a few tumors of the other types—medulloblastoma and ependymomas, and I have also seen astrocytomas; in the final analysis almost any tumor of the central nervous system is capable of seeding by way of the subarachnoid space, and a good number of these tumors which are discovered as metastatic in the subarachnoid space in the spinal canal turn out to be astrocytomas or glioblastomas.

Dr. Bucy: We are dealing with a young boy who, in addition to the signs of increased intracranial pressure and episodes of loss of consciousness, has a bloody cerebrospinal fluid. We can rule out the possibility of bleeding due to a traumatic tap because of the fact that the fluid was also xanthochromic, which would indicate that the blood had been there for some time prior to the puncture. There are not many tumors that involve the central nervous system which produce blood in the cerebrospinal fluid. Whenever we get blood in the cerebrospinal fluid all of us are inclined to ask "Is this a vascular condition—not a tumor, strictly speaking? Are we dealing with an aneurysm or are we dealing with an arteriovenous malformation?" Had I seen this patient, one of the first things I should have wanted in the way of a diagnostic procedure would have been an angiogram, to see if there was any evidence of vascular anomaly. I would point out that as accurate a preoperative diagnosis as possible is very important in this case. Doctor Taveras has mentioned the possibilities that one might be dealing with a tumor which arose in the thalamus and which occluded a third ventricle, rather than a tumor lying in the third ventricle. This is an important distinction from a surgical standpoint. Or on the other hand, a benign cyst lying relatively freely in the third ventricle; or even a tumor of the choroid plexus lying within the third ventricle. Certainly the method of handling this case clinically would have been entirely different. A benign cyst should have been attacked directly and removed with an excellent chance that the patient would have made a complete recovery. Instead it was concluded that such was not the case, that

the tumor was one which could not be satisfactorily attacked directly, and therefore a procedure was used which it was hoped would in some measure relieve the patient's symptoms but not cure him. In other words, a surrender was made to this tumor right at the start from a clinical standpoint. The Torkeldson operation is purely a by-pass procedure, by means of which with rubber tubes one can drain the fluid from the lateral ventricle into the cisterna magna, and thus by-passing the obstructed third or fourth ventricle or the aqueduct as the case may be. The tumor in this instance was attacked only by radiation therapy, and although improvement resulted as is often the case with brain tumors, cure by such means is an impossibility. It would be much better if the tumor had been removed if for no other reason than to establish a diagnosis and thus to deal as intelligently as possible with it . An effort was made to supply this deficiency by means of a needle biopsy. So far as I am concerned this is an entirely unsatisfactory procedure. It is rare that one obtains tissue which is completely diagnostic and furthermore this is a procedure which is not without its own danger, particularly in a patient who has already bled from his lesion. The danger of producing another and perhaps even more serious hemorrhage than the one which he has already had is one which you cannot dismiss.

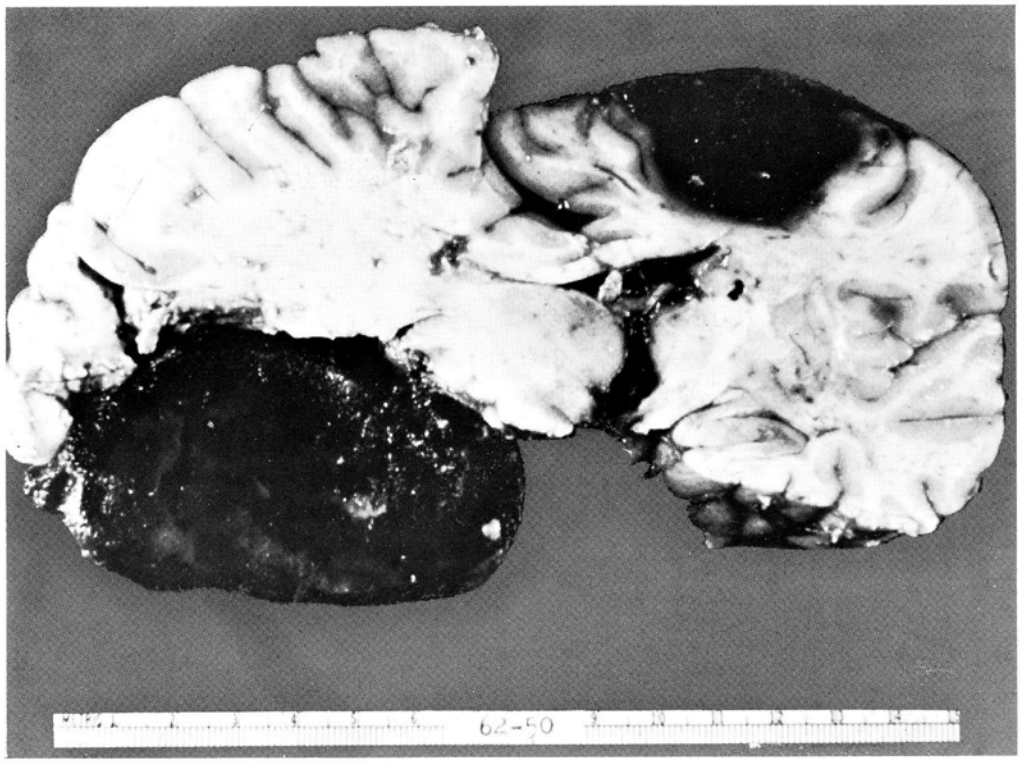
The appearance of another tumor in the lumbar spine raises the possibility that this tumor has seeded through the cerebrospinal fluid into the spinal canal. This occurs most frequently with medulloblastomas or sarcomas of the cerebellar meninges, but may occur with other tumors. Medulloepitheliomas are relatively rare tumors—so rare in fact, that it is not possible to form a very accurate picture of their clinical course or their natural history. Although I do not know I would freely admit the possibility that a medulloepithelioma might metastasize in this fashion. But there are two other possibilities here: we have the possibility that we are dealing with an entirely different tumor. I can cite for you instances of patients who have had two and even three separate tumors of their central nervous system entirely different in type and apparently completely unrelated. This is a possibility, perhaps a remote one here. There is another possibility that this was not a primary tumor of the central nervous system at all, but a metastatic tumor from some other part of the body which had metastasized to the brain and had also metastasized to the lumbar portion of the spinal canal. This possibility is raised by the diagnosis, suggested here, of choriocarcinoma. Choriocarcinoma is a rare tumor, so far as the nervous system is concerned. There are several interesting points in connection with choriocarcinoma. In my own experience, metastases of choriocarcinoma to the brain have all occurred in young women following pregnancy. Choriocarcinoma is one of the tumors which involves the brain which bleeds. Very often the metastases of choriocarcinoma are mistaken, not for tumor, but for a spontaneous intracerebral hemorrhage, so the fact that this patient had bled raises an interesting point in this connection. As far as central nervous system tumors is concerned, there are no particular racial differences except in two instances. One, are the tumors of the pineal region (I didn't say "pineal tumors"); these tumors occur far more in the Orient than they do in this part of the world. The Japanese state that twenty percent of all their cranial tumors are tumors in the pineal region; we see nothing like such an incidence in this part of the world. Choriocarcinoma has a very definite racial incidence: whereas choriocarcinomas are relatively rare in this part of the world, they are common in Indo-China.

Dr. Regato: I would like to make three observations: first of all, in spite of the interrupted treatment that this patient received, the tumor was sterilized in the lumbar spine and was not found there at autopsy. Another is that medulloblastomas in particular are not impossible to cure by radiotherapy; in fact, there is plenty of evidence that they have been cured by this means, depending of course on their degree of extension and dissemination through the spinal canal. Thirdly, the gonadotropins dilution that was found on this child 11 years of age could be explained physiologically and I think that was recognized by the contributors.

H. K. Giffen, M.D., Omaha, Nebraska: I notice Doctor Zimmerman detests the term "pinealoma" on the basis that it is in but not of the pineal. By the same line of thinking does he throw out the term "brain tumor"?

Dr. Zimmerman: The term "brain tumor" is used with the understanding that it is an enormous group of different type of neoplasms which, when identified should be called by their definitive name rather than by "brain tumor". The treatment of brain tumors is a totally different thing depending on whether you are dealing with meningiomas or cere-

Fig. 4—Hemorrhagic tumor obliterating the left third ventricle.



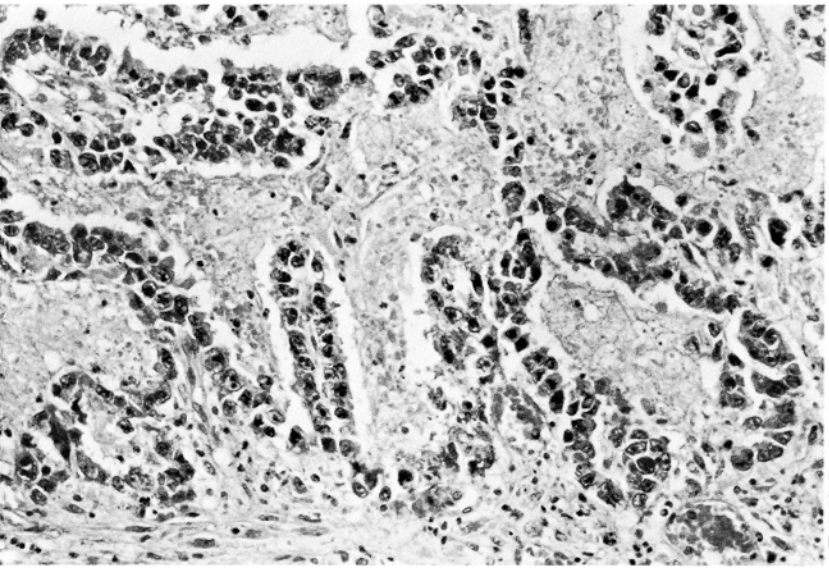


Fig. 5—Papillary structure of medullo-epithelioma. The stroma between papillae is composed of neural tissue, but within papillae there are blood vessels and connective tissue fibers. The free margins of the cuboidal cells contain no cilia and there are no blepharoplasts within the cellular cytoplasm. (H & E, x 180).

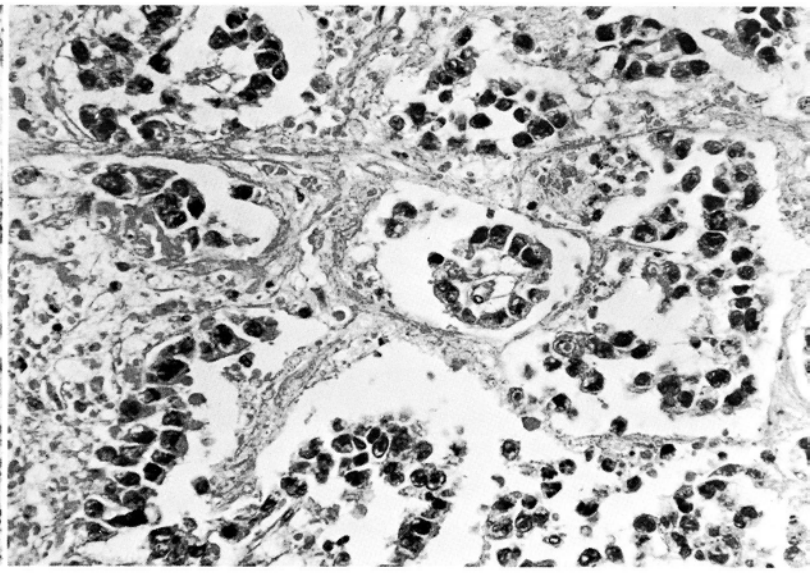


Fig. 6—Pseudo-acinar structure of medullo-epithelioma (H & E, x 250).

bellar sarcomas or glioblastoma multiforme or astrocytomas, etc.

A. E. Cyrus, M.D., Milwaukee, Wisconsin: I note a great deal of emphasis was placed on the glial fibrils amidst the tumor. Were these glial fibrils considered a part of the host or gliosis in response to the invasion or maturation potential of the medulloepithelioma?

Dr. Zimmerman: These are glial fibers which are in part the hosts and in part the reaction to the tumor itself and because of their large component they are probably the same kind of glial fibers that one sees in ependymoma in general. For example, I do not know of any ependymoma (and this is even more true of the spinal ependymomas than of the cerebral) in which an astrocytic gliogenous component is absent, and it helps us determine the nature of the tumor by finding the astrocytic component in all ependymomas, including this group which I think is the malignant ependymoma or medulloepithelioma.

Howard Ball, M.D., San Diego, California: Is the cytologic study of the spinal fluid a helpful procedure in any of these cases?

Dr. Zimmerman: Every once in a while one of my assistants or technicians see bizarre elements in the spinal fluid; we then check and discover that these represent really neoplastic cells, and nearly always the tumor turns out to be either a medulloblastoma or an ependymoma seeding along the cerebrospinal fluid pathway. Unfortunately, we have not been doing this routinely in all tumors. We find that approximately one percent of all our gliomas have tumor cells in the spinal fluid: this is not an encouraging experience. We feel that there are better methods of making intracranial tumor diagnosis than by examining cerebrospinal fluid. However, it ought to be done and perhaps every once in a while a tumor that is not picked up in any other way might be picked up by cerebrospinal fluid examination.

Dr. Bucy: I think that this is a very much neglected form of examination which can be very valuable. We have not looked often enough and carefully enough to be sure. There are instances in which this is the most significant way of making the diagnosis and there are also instances in which a good cytologist will also make the diagnosis of the type of tumor which is present. I would urge you all to encourage the development of this form of diagnosis.

Ruheri Pérez-Tamayo, M.D., Denver, Colorado: I would like to make one comment on the technical approach to radiotherapy of tumors of the brain: the attempt to treat a tumor of the brain with a small field after an exploration has been done is doomed to failure unless the entire skull is included in the field of treatment.

Dr. Regato: This is a point that is very well taken. This patient was irradiated with fields of 6 x 6 cm for a lesion that, as we saw, was beyond that size. The failure of radiotherapy which is due to technical error or lack of understanding of the possibilities of therapy should not be blamed on radiotherapy itself.

James R. Galloway, M.D., Albuquerque, New Mexico: I thought this was a pinealoma invading the thalamus. I wondered if in the asymmetry in the roentgenogram you considered that the bulging in the region of the thalamus was due to rotation. Do you believe that this amount of mass can be entirely explained on that basis, or that the tumor must have invaded the thalamus to present this mass? I would like to know if in any of the pinealomas invading the thalamus that you have seen the third ventricle was not filled.

Dr. Taveras: The patient had no localizing neurologic findings at the time and I think that the invasion laterally may have occurred between the initial treatment and the final autopsy examination. Unless we have a straight film, one should not make a statement as to this apparent elevation of the atrium such as was seen here. If we have a tumor of the third ventricle it could definitely invade and the invasion would ordinarily be in the region of the thalamus, but the evidence that we had was insufficient for me to arrive at that conclusion.

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2. *Magnocellular Glioblastoma*

Contributed by D. L. Alcott, M.D. and J. J. McCort, M.D., San José, California

THE PATIENT was a 60-year-old woman in July, 1962, when she complained of fronto-occipital headaches. There was early papilledema and general motor weakness more marked on the left side.

Dr. Taveras: The films presented are those of an anteroposterior and a lateral film made in the early arterial phase which demonstrate the presence of a marked shift of the anterior cerebral vessels to the left of the midline. The configuration of the shifted anterior cerebral vessels presents a relatively rounded appearance. The bifurcation of the carotid siphon is possibly slightly displaced downwards and backward and the initial portions of the anterior and middle cerebral arteries seem to be displaced downward. In the lateral projection it is noted that the anterior opercular branches of the middle cerebral artery are slightly displaced backwards and downward. The ophthalmic artery is not enlarged and I cannot trace branches coming off this artery.

The appearance is that of a frontally-placed space occupying mass. The decision will be between an intracerebral mass such as a glioma or an extracerebral lesion such as a meningioma. I cannot visualize any branches of the ophthalmic artery which might supply the meninges of the anterior fossa of the skull and I see no filling of the middle meningeal artery channels that would assist me in arriving at a histological diagnosis or, at least, at the exact location of the lesion, whether intra- or extracerebral. If supplied by the middle meningeal channels or by meningeal branches of the ophthalmic artery, the lesion would more likely be an extracerebral tumor. There is slight irregularity along the inner table of the skull in the frontal region and two diploic venous channels are visualized in this region but these are not sufficient to arrive at a diagnosis of meningioma. In the arteriographic film of the frontal projection, there is a relative increase in density of the right side in the inferior frontal region. However, there is a slight rotation of the skull to the left, that is, with the face towards the left, which would ordinarily make the right frontal region slightly denser than the left side and, therefore, this observation may not be a valid one.

In conclusion, I would say that we are dealing here with a right frontal neoplasm of unknown type or location as to its intra- or extracerebral position. Some features suggest that it could be a meningioma in the anterior frontal region but the evidence is not sufficient.

Dr. Taveras' impression: RIGHT FRONTAL NEOPLASM OF UNKNOWN TYPE.

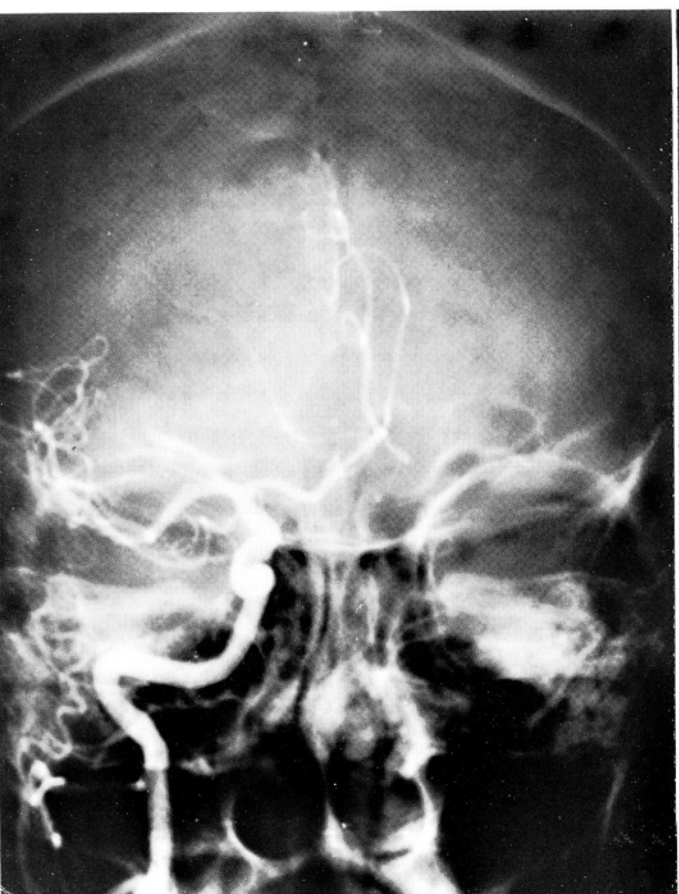
Roentgenologic Impressions Submitted by Mail

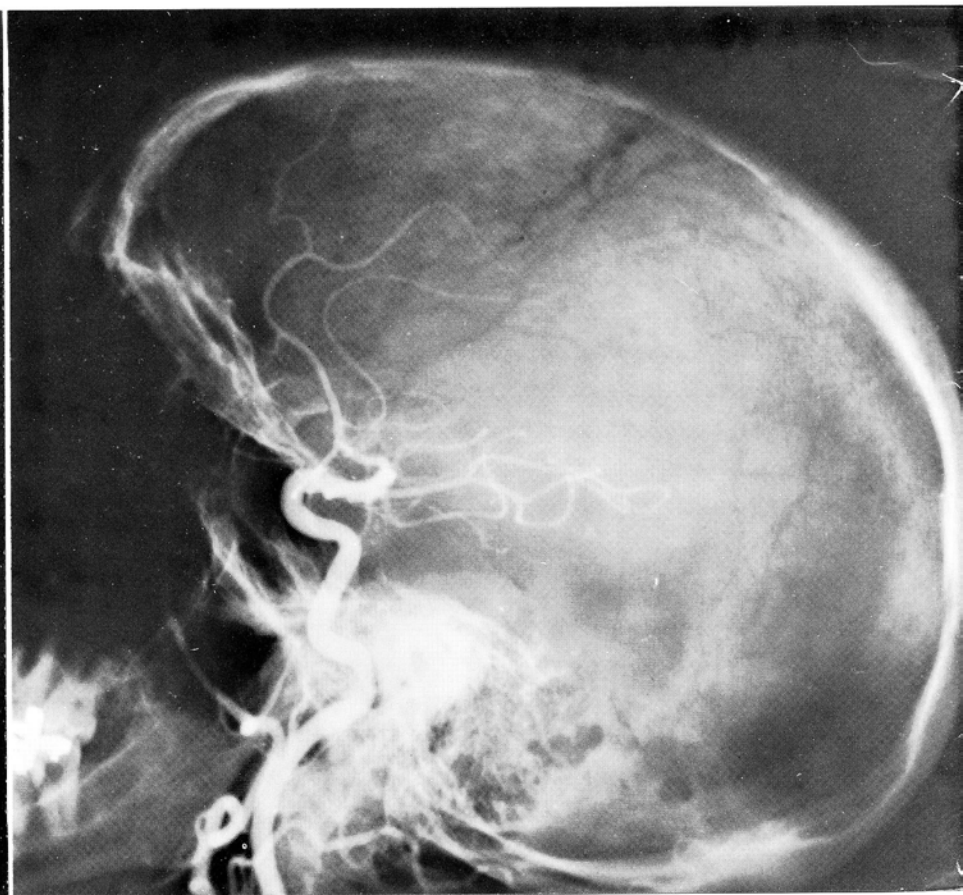
Right frontal lobe tumor	39
Right parietal tumor	17
Glioma	16
Meningioma falx cerebri	5
Subdural hematoma	4
Others	15

Dr. Taveras: For the reason that I have already given —that is, the lack of depression of the angiographic Sylvian point and the fact that the pressure appears to be on the anterior aspect of the Sylvian triangle would indicate to me that this is not a parietal tumor. Since most intracranial tumors belong in the glioma group, one may not be too far off when one says "glioma" but I am much against this attitude because our purpose is twofold: to localize a lesion anatomically, and to attempt to indicate whether this lesion is intra-axial or extra-axial. I feel that there is not sufficient evidence to suggest the diagnosis of meningioma of the false cerebri; moreover, the meningiomas of the false cerebri in

Fig. 1—Angiogram in early arterial phase showing marked shift of the anterior cerebral vessels to the left of the midline.

Fig. 2—Arteriogram showing slight backward displacement of the anterior opercular branches.





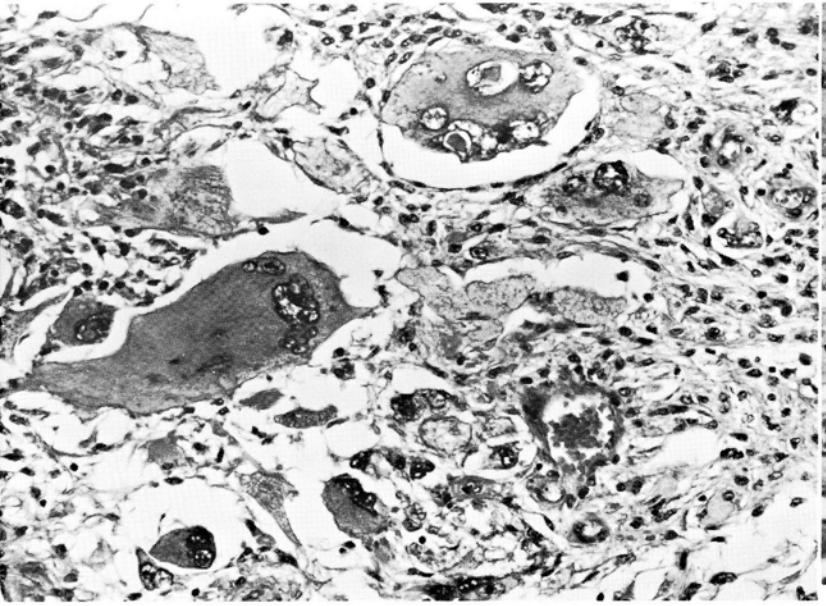


Fig. 3—Photomicrograph of huge multinucleated tumor giant cells in magnocellular glioblastoma. (H & E, x 180).

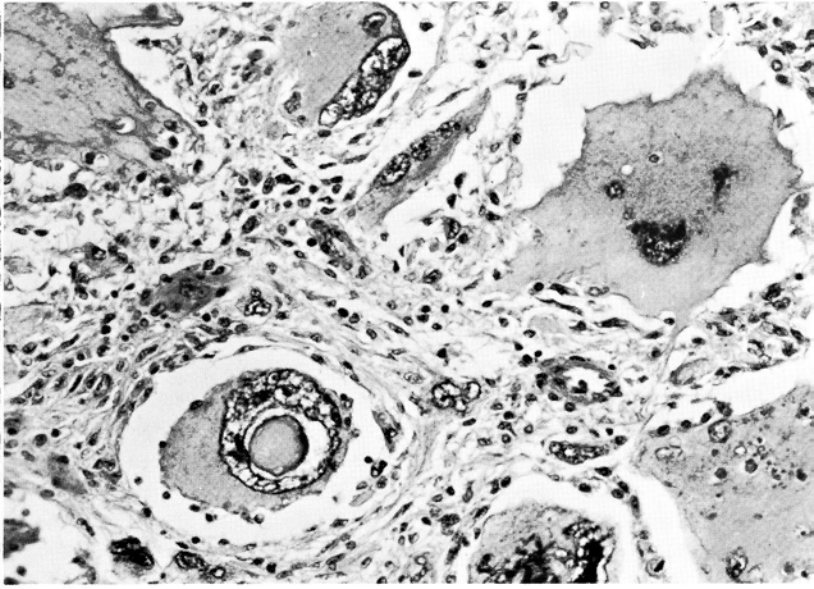


Fig. 4—Intranuclear inclusion body in one of several giant tumor cells. The smaller cells are astrocytes. (H & E, x 180).

the frontal region produce a depression of the knee—that is, the point where the pericallosal artery turns around the genu of the corpus callosum. Also, these meningiomas usually depress this portion of the artery, as it was not the case here. In the angiographic films there was nothing to indicate that this was a subdural hematoma.

Dr. Regato: Drs. H. Hauser, of Cleveland, and J. Lemon, of Denver, submitted an impression of glioblastoma of the fronto-parietal region. Dr. P. Swenson, of Columbia, South Carolina, diagnosed a parietal mass, either a glioma or a subdural hematoma.

Operative findings: On July 18, 1962, a right frontal lobectomy was done for removal of tumor therein. The specimen measured 7 x 6 x 5 cm; it appeared as normal brain with hemorrhage beneath arachnoid space. There were denser areas of whitish tissue.

Dr. Zimmerman: This neoplasm has a most dramatic appearance by virtue of its many huge multinucleated tumor cells; these vary enormously in shape and size and nuclear content. Some contain many small nuclei and others may harbor one or more huge, hyperchromatic and bizarre nuclei. Occasionally there are large eosinophilic, spherical inclusions within nuclei. The tumor is circumscribed but not encapsulated. It consists also of smaller cells which have multipolar processes and are identifiable as astrocytes.

Part of the tumor is necrotic and contains kariorrhectic nuclei and polymorphonuclear neutrophilic leukocytes. On the margins of the tumor there are noted small perivascular collections of lymphocytes, a finding often seen in glioblastoma multiforme.

There is no other tumor in the nervous system that has quite this characteristic appearance. A mesodermal origin for the tumor can be excluded with the aid of silver impregnation for reticulin fibers. Such fibers do not permeate the neoplasm but are rather confined to the immediate vicinities of blood vessels. Although Zülch presently considers this neoplasm a sarcoma, the majority of neuropathologists classify it as a magnocellular glioblastoma.

Dr. Zimmerman's diagnosis: MAGNOCELLULAR GLIOBLASTOMA.

Histopathologic Diagnoses Submitted by Mail

Glioblastoma multiforme	41
Giant-cell glioblastoma	38
Monstro-cellular sarcoma	30
Glioblastoma horribilis!	1
Astrocytoma, grade IV	19
Metastatic tumor	8
Others	11

Dr. Zimmerman: I see no objection to calling this a glioblastoma multiforme because I too think it is a malignant tumor of glial origin, but in the average glioblastoma multiforme we do not see quite as many multinucleated cells: that is why these poetic names as giant cell glioblastoma and monstrocellular glioblastoma have been invented; there is really no way that I can dispute this diagnosis because there is no way to prove whether one of these giant cells has arisen of glial or of mesodermal origin. Grade IV astrocytoma is the classification that is commonly employed practically synonymously with the diagnosis of glioblastoma multiforme, and if you like to grade gliomas on the basis of malignancy, I see no objection to it. By habit, and age perhaps, I have been sticking to one classification, but I see no objection to the other one. This is not a metastatic tumor because I cannot imagine where this type of tumor would be primary in; even the giant-cell tumors of the thyroid are never quite so gigantic.

Dr. Regato: Dr. M. Berthrong, of Colorado Springs, diagnosed astrocytoma grade VI. Dr. D. S. Russell, of Surrey, England, made a diagnosis of giant-cell glioblastoma or monstrocellular sarcoma of Zülch. Dr. K. J. Zülch, of Cologne, Germany, diagnosed monstrocellular sarcoma and stated that he does "not believe that this is a giant-cell glioblastoma": unlike Dr. Russell, he does not seem to believe that these two terms are interchangeable.

Dr. Bucy: I should like to emphasize one point which Doctor Taveras made: the diagnosis of subdural hematoma on the basis of cerebral angiography is one of the most definite diagnoses which is possible with this technique. So far as treatment of glioblastoma multiforme is concerned, I have completely changed my opinion and my attitude over the years. There are those who would do a needle biopsy, and if this confirms their clinical impression of a glioblastoma multiforme they would do nothing further. There was a time when I accepted this nihilistic attitude; today I would disagree completely. Life unfortunately is a fatal disease. All we can hope to do is either to prolong life or make people more comfortable or both. I think as physicians and surgeons this is our obligation and responsibility. I am convinced that by dealing as radically as possible with these malignant tumors, short of increasing the patient's disability, and I think this is important, we can make these patients more comfortable, their post-operative recovery more rapid, and their lives longer than if we leave the tumor alone. In many instances these people go for one, two and three years in relatively good health, able to carry on their occupations and to remain with their family; I am convinced that this is worthwhile.

Donald L. Alcott, M.D., San Jose, California: I checked the records this last week. The patient was seen October 11th at which time the hemiparesis was diminishing and she had function in all of the muscles on the left side, estimated at about 25%. She had apparently a disturbing functional overlay.

Leo Lowbeer, M.D., Tulsa, Oklahoma: Would Doctor Zimmerman let us in on the secret of how he manages to make two special stains like a phosphotungstic acid and reticulin stain on only one unstained section.

Dr. Zimmerman: The secret is very simple. After seeing that the Wilder reticulin was negative I decolorized the H & E preparation and stained it with phosphotungstic acid-hematoxylin.

Dr. Regato: Apropos of stains, I have a statement from Dr. Dorothy Russell that may interest you: "No self-respecting pathologist should be expected to make confident diagnosis in problematic cases from a single H & E preparation." I have met, occasionally, people who did not have respect for pathologists but I never met a pathologist who was not self-respecting!

John Kepes, M.D., Kansas City Kansas: In addition to the very characteristic histological appearance, there is something about the gross and biological behavior of these tumors that sets them apart from the rest of neoplasms of the brain. Doctor Zimmerman already mentioned that the average survival period is somewhat longer, even twice as long, as in the average glioblastoma. In the cases I have seen there was a gross appearance that was rather characteristic: they are often quite firm. Many of them are so circumscribed that the surgeon feels that he may be dealing with a metastatic carcinoma. Also, there is a false hope of complete removal at the time of surgery which is denied by the microscopic findings. Certainly the cells look terrible, no matter how terrible they look, they are less dangerous than the small-cell glioblastoma which has many more mytotic figures. It is my feeling that those big cells are degenerative cells, sort of burned-out monsters that are unable to cope with the competition. Some of the giant cells impregnate beautifully with Cajal but the reticulin fibers are restricted to the blood vessels. Up to this point I had a feeling that the teachings of Doctor Zülch were actually wrong until I ran into two cases of true giant-cell fibrosarcomas of the brain. I was satisfied that they were actually sarcomas and I think Doctor Kernohan had the same experience: in his series published in CANCER there are a few cases where the reticulin stain is rather convincing. Whereas the majority of these cases are giant-cell glioblastoma we should keep an open mind and accept at least a few cases of true sarcoma of this variety.

Dr. Zimmerman: I agree fully with the first remarks which Doctor Kepes made, mainly that these tumors in the gross have a certain circumscribed appearance almost as if they are distinctly separate from the adjacent brain tissue, and this is one of the characteristic features of giant-cell tumors. There is one disturbing feature about this apparent circumscription, and that is that in spite of the removal of the tumor it invariably ends fatally just as the glioblastoma multiforme does. I know of no case that was cured by surgical removal. I have seen a so-called "multicentric glioblastoma multiforme" in which there were two or three widely disseminated primary foci of tumor in the brain: one part looked exactly like this giant-cell tumor and appeared circumscribed, and the other two nodules in the opposite hemisphere looked like typical glioblastoma multiforme.

Thomas K. Craigmile, M.D., Denver, Colorado: I wonder if Doctor Zimmerman could comment briefly on the validity or accuracy of diagnoses made from needle biopsies; how often when a more adequate specimen is subsequently available is the original pathological diagnosis proved erroneous?

Dr. Zimmerman: When Doctor Bucy was a neuropathologist he did not examine cerebrospinal fluid for cells in order to make the diagnosis; *now* he wants the neuro-

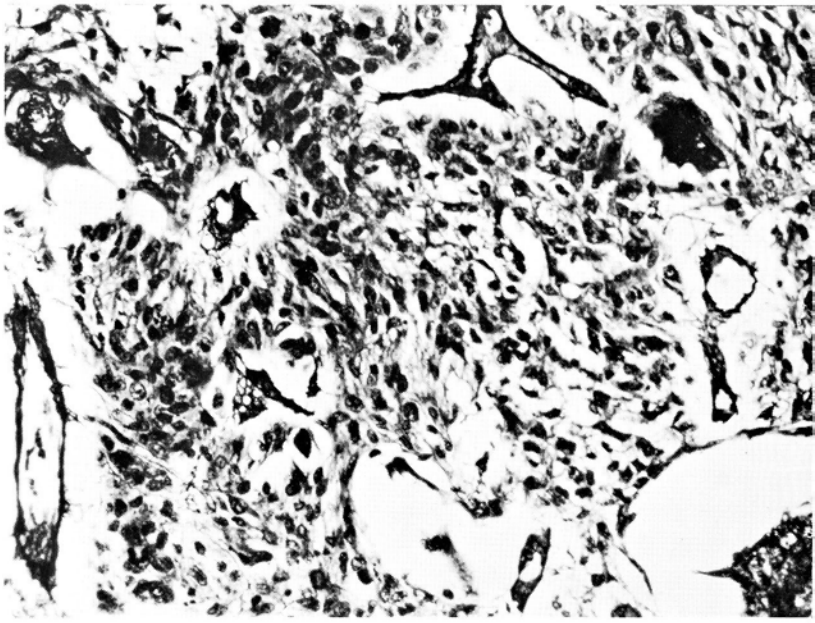


Fig. 5—Photomicrograph of magnocellular glioblastoma showing reticulin fibers only around blood vessels. (Wilder silver impregnation, x 180).

pathologists to do it. It is a difficult job to examine cells in the spinal fluid and the results are usually unrewarding, but I agree fully with him that the occasional positive case pays you back for all the trouble that you have taken and so I advocate it even though I know that you will do perhaps a hundred examinations on a hundred patients and find only one or two positive ones. This I have already found to be the case in my experience. As regards needle biopsies: If this is the best you can do of course you have to resort to it. In general it is much more difficult for us to make accurate diagnoses with needle biopsies of the brain than with needle biopsies let us say, of breast, or of the prostate, or of the liver. In the brain it is much more difficult, but I have had sufficient numbers of rewarding experiences to say that if you cannot do an open biopsy for one or another reason, and remove a larger chunk of tissue, then you have to resort to the needle and you must try to make the diagnosis with it and you will succeed in a fairly good percentage of cases. Scherer has always emphasized the fact, and I concur completely, that the diagnosis of a brain tumor is difficult even with a single large sample from one part of the neoplasm. I have had experiences repeatedly where the surgeon sends us five grams of tissue, which all of us would consider satisfactory, in which I see only astrocytoma; then, four or five months later, the patient is back with a huge bulging mass and the re-operation discloses a glioblastoma multiforme: I have always taken the attitude that in all probability I didn't get an adequate sample rather than that the surgeon's scalpel stirred up a benign astrocytoma to make of it a malignant glioblastoma multiforme. There are some neuropathologists who feel that the latter can happen, but from years of experience of my own I cannot agree with that. The smaller the sample, the less apt are you to get a representative section, and for this reason again I would urge to try to get a better sample if you possibly can do it. But there are cases where you cannot get even a needle biopsy. It is fashionable even for some neurosurgeons not to attack surgically any so-called "pinealoma" but to irradiate them without further diagnosis. I have lamented this, privately, without telling it to my neurosurgical friends, because I always like to see confirmation of tumors under the microscope. Nonetheless, I know that it cannot always be done and in some cases needle biopsy is the best you can do.

Leroy J. Miller, M.D., Albuquerque, New Mexico: I would like to make a comment on Doctor Bucy's remark that he has made complete about-face and prefers to attack glioblastomas with major craniotomy. This, of course, would depend on the state in which the patient gets to the neurosurgeon. The great majority of patients get to the neuro-

surgeon when it is far beyond his capacity to do very much for them, regardless of the type of tumor, because a rapidly progressive tumor and edema make most of the patients a rather poor risk. If the patient appears in good enough physical condition, I would agree. However, when a patient is badly debilitated and a diagnosis can be made by taking an adequate specimen of tumor either through a bur hole or by whatever satisfactory means are possible, I think that one should be satisfied with this diagnostic procedure and withdraw. We are treating human beings and we must show them the treatment we would want ourselves under the same circumstances.

Dr. Bucy: There is no disagreement between us. However, over the past thirty years there has been a great change in the diagnostic ability of the medical profession so far as brain tumors are concerned. When I began doing neurological surgery thirty-four years ago, 85% of our patients with brain tumor came to us with choked disc; today less than 30% do, because the medical profession have become able to recognize these tumors at a much earlier stage than they formerly did. Our patients are not getting to us in the debilitated serious state that you implied, and I think, in time, they will come still earlier.

A. E. Cyrus, M.D., Milwaukee, Wisconsin: I have had the occasion to see four of these tumors and three of them were in females. In the females, one was below puberty and the other two were post-menopausal: is there any relationship between these monstro-cellular alterations and steroid therapy in some form and age?

Dr. Zimmerman: I cannot remember whether or not the twelve-odd cases that I have seen received any of the therapy that you indicate. My feeling is that the tumor behaves very much like glioblastoma multiforme in general. It occurs usually in the aged rather than in the young. It involves men somewhat more commonly than women. I do not believe that there is any real distinction in the incidence of the two types of glioma in the human.

Karl T. Neubuerger, M.D., Denver, Colorado: We should call it glioblastoma "horribile" rather than "horribilis." Doctor Scherer wrote a very excellent paper, forgotten by most, in which he stated that in 40% of all gliomas there are variable features, such as glioblastoma multiforme, oligodendroglioma, etc. I think fifty or more years ago a paper by Meyer was written on giant-cell gliomas in German. I wonder if Doctor Zimmerman is familiar with that, and whether the gliomas he described then resemble what we have seen in this case.

Dr. Zimmerman: Doctor Neubuerger, both the French and the Germans have been using names of a similar type for this type of tumor. It is the same tumor that we are now dealing with.

Editor's Note: In April, 1963, this patient was reported receiving physical therapy at home; her condition was apparently stationary.

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3. Astrocytoma of the Fourth Ventricle

Contributed by P. W. Gikas, M.D. and R. Rapp, M.D., Ann Arbor, Michigan

THE PATIENT was a 35-year-old man in July, 1958, when he gave an 8 year history of intermittent throbbing headaches extending to the nape of the neck. The pain had become excruciating; it was worse in the morning and it was aggravated by coughing and strain. There was a history of skull fracture in 1950. On examination there was papilledema, right temporal hemianopsia, and spinal fluid rhinorrhea. The EEG suggested abnormality of the left temporal region; the spinal fluid proteins were 19 mgm per cent.

Dr. Taveras: Two films are offered for examination, one a lateral view of an angiogram made in the arterial phase only. This presents signs of ventricular dilatation. There are no abnormal arteries. The anterior choroidal artery is not remarkable in its appearance. The other film is a lateral view taken during ventriculography with a vertical beam and the patient's head on its side. The lateral ventricle which is visualized (probably the right ventricle since this film is marked "left" indicating that the left side of the head is probably against the film) is markedly dilated. There is no gas present in the 3rd ventricle, but this is not necessarily significant in a film made with the patient lying on his side.

In examining the appearance of the skull on this lateral view, it is noted that the sella turcica is markedly enlarged, the upper portion of the dorsum sellae is eroded and has completely disappeared, the anterior clinoid processes are thin and apparently spread and there is bone destruction involving the posterior portion of the floor of the anterior fossa on both sides. These findings are usually associated with long-standing increased intracranial pressure with marked enlargement of the lateral ventricles as well as of the third ventricle. There is also evidence of an old, unhealed, fracture of the skull in the parietal region.

In the differential diagnosis one would consider conditions which cause ventricular dilatation of an extremely marked degree, of long-standing, involving both lateral ventricles and probably also the third ventricle. A dilated third ventricle is capable of producing compression of the optic chiasm and hemianopsia. However, in view of the previous history of fracture, it is possible that the temporal hemianopsia of the right eye and the spinal fluid rhinorrhea are related to the trauma. Cerebrospinal rhinorrhea is occasionally seen in patients with pituitary adenomas due to erosion of the floor However, in this instance, the sella turcica presents more the appearance of erosion from above than

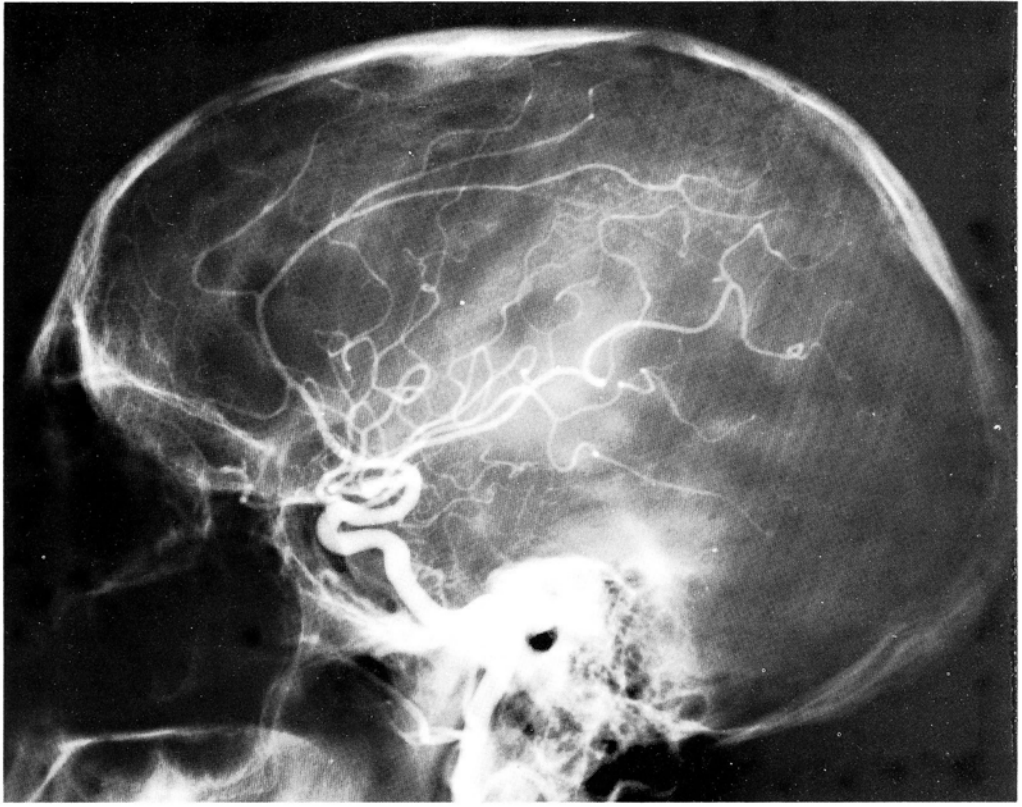

Fig. 1—Angiogram in arterial phase showing signs of ventricular dilatation but no abnormal arteries.

erosion from within and, moreover, the degree of ventricular dilatation is so extreme that it is beyond that which is seen even rarely in cases of pituitary adenoma with suprasellar extension. In the latter case, I would also expect that the degree of involvement of the optic chiasm and consequent visual loss would be much greater; the same would apply to craniopharyngioma.

In conclusion, I believe that we are dealing here with an obstructive lesion probably in the region of the aqueduct of Sylvius and this could be produced either by aqueduct stenosis without tumor or by a peri-aqueductal glioma. In view of the patient's age, a diagnosis of simple aqueduct stenosis should be made with caution. Post-traumatic gliosis in the peri-aqueductal region or possibly granular ependymitis resulting from hemorrhage into the ventricles with secondary ependymal changes should also be considered. A slowly growing lesion more distally placed, at the level of the fourth ventricle, or in the cerebellum may also produce similar findings.

Dr. Taveras' impression: Aqueduct stenosis probably due to a PERIAQUEDUCTAL GLIOMA.

Roentgenologic Impressions Submitted by Mail

Colloid cyst of 3d ventricle	25
Tumor of the posterior fossa	15
Subdural hematoma	14
Hydrocephalus	7
Malignant tumor	13
Others	25

Dr. Taveras: There is absolutely no basis for making a diagnosis of colloid cyst of the third ventricle; I would have considered that as an unlikely possibility. I shy away from diagnosing simply a tumor of the posterior fossa as a bad radiological diagnosis. The posterior fossa is the most difficult area for the neurosurgeon to attack and it is incumbent upon us, radiologists, to define the exact location of the tumor in the posterior fossa. Is it cerebellar? If so, is it on the right, on the left or in the midline? Is it superior or inferior? Is it anterior to the brain stem, anterior to the aqueduct and fourth ventricle? Is it intrinsic within the brain stem or extrinsic? If it is within the brain stem, is it to the left or to the right or in the midline? Or is it high or low in the extra-axial region? That is, is it a pure angle tumor in this relatively accessible position, or is it much higher up in the intradura, and if it is in the intradura, is it anterior in the midline, anterolateral, lateral, posterolateral or posterior? These are extremely important things to indicate. The diagnosis of tumor of the posterior fossa should be avoided and more specific localizing diagnoses should always be attempted from the observation of findings on the radiographs, and from specific views in certain positions to rule out each one of these locations.

A diagnosis of hydrocephalus is an extremely poor diagnosis to make because it has no meaning. Is it hydrocephalus of communicating or non-communicating type? Was the obstruction in the third ventricle or in the aqueduct?

Dr. Regato: Dr. R. E. Graf, of Denver, offered an impression of colloid cyst of the third ventricle. Dr. H. Hauser, of Cleveland, suggested fracture of the cribiform plate and hydrocephalus. Dr. P. J. Hodes, of Philadelphia, was concerned with the appearance of the sella turcica and suggested the possibility of a pituitary tumor decompressing itself into the nasopharynx. Dr. B. L. Pear, of Denver, also thought of a pituitary adenoma.

Surgical findings: On July 16th, 1958, a sub-occipital craniotomy revealed a tumor about 5 cm in diameter arising from the region of the obex on the right side of the fourth ventricle and extending to the level of C2. The anterior portion was incompletely excised. The tumor measured 1.3 x 2.5 x 5 cm, it was gray-white with a warty surface and contained a bright yellow fluid.

Dr. Zimmerman: The tumor appears to lie wholly within the fourth ventricle and at one point is attached to or is an integral part of the choroid plexus of this cavity. It has a distinctly lobular appearance, is relatively acellular, and has a dense fibrillary stroma which can be proved to be of glial origin with special stains such as phosphotungstic acid-hematoxylin. The cells are small and are noted to give rise to the glial fibrillary stroma. They occur in clusters but form no distinctive pattern.

Part of the tumor is abundantly supplied with blood vessels. Some of these appear to be reduplicated and suggest angiomatous malformations. The walls of others are abnormally thickened. Discrete but rather large zones of calcification also form part of the tumor.

Tumors of the nervous system perhaps more than those of other organs are often distinctive and diagnoseable from

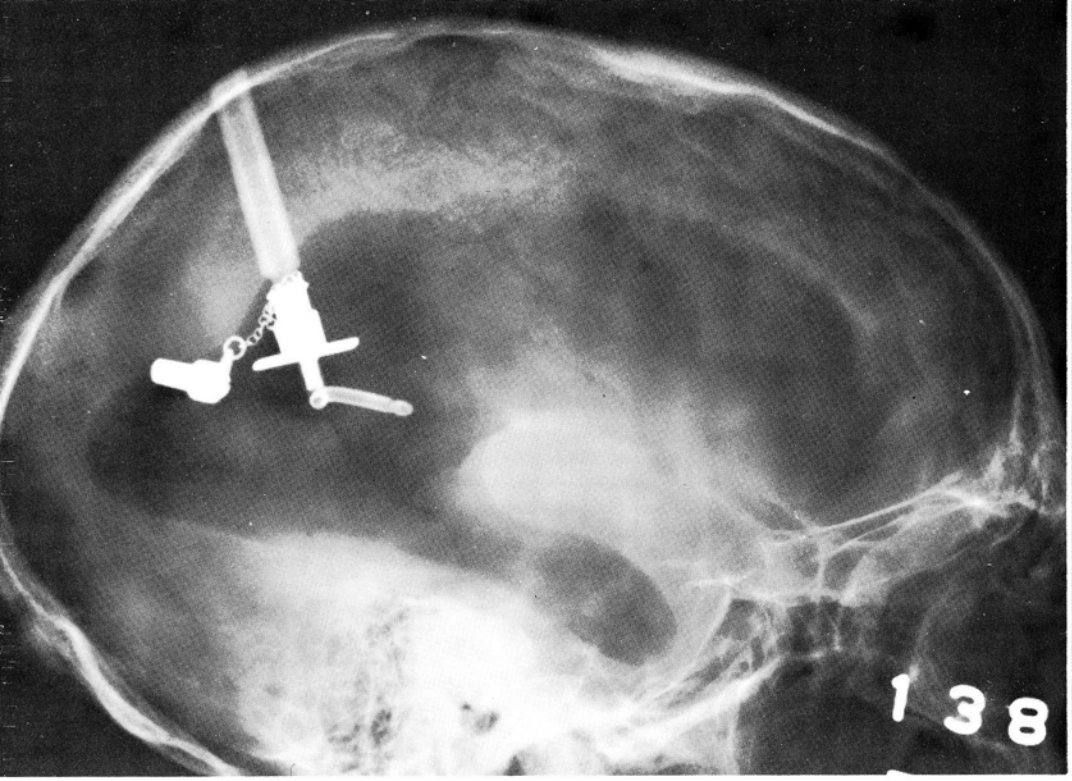

Fig. 2—Ventriculogram with patient in lateral decubitus showing marked dilatation of a lateral ventricle (probably the right).

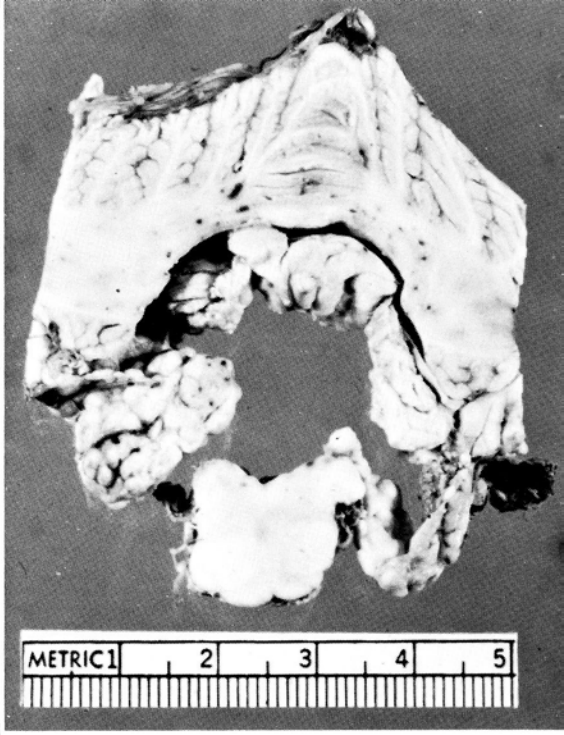

Fig. 3—Post mortem appearance of brain in cross section.

their macroscopic appearance. This tumor is an example of this rule. Its firm, gray, lobulated appearance and its attachment to the choroid plexus suggests one of two possibilities in diagnosis: one is an hamartoma, and the other is an astrocytoma. Actually, as may be true in this case, an element of harmatoma is often present in the astrocytoma wherever it occurs in the nervous system.

Dr. Zimmerman's diagnosis: ASTROCYTOMA in fourth ventricle.

Histopathologic Diagnoses Submitted by Mail

Subependymoma (astro-, glio-)	55
Astrocytoma	26
Meningioma	34
Neurilemoma, neurinoma	30
Others	9

Dr. Zimmerman: The vast majority of participants correctly diagnosed this tumor; correctly by my lights. It is true that some meningiomas are part of, or attached to the choroid plexus. In man, as well as in the cat, there occasionally occur intraventricular meningiomas which are part of a tumor of the choroid plexus. In general there are two things that I demand before I make a diagnosis of meningioma; one is the arrangement of meningocytes to form whorls and the other is at least one psammoma body. If I cannot find whorls and psammoma bodies, I would be exceedingly hesitant to diagnose any intracranial tumor as a meningioma. The astrocytoma, because it lies next to the choroid plexus, may have one or more psammoma bodies because normal choroid plexuses do have them; because of this I require that the psammoma body be in the tumor portion and not in the normal choroid plexus. I anticipated that some of you might make this diagnosis; I did the decolorized P.T.A.H. stain to prove that these fibrils are not mesodermal fibrils but really represent glial fibrils.

I agree that the fibrous character of this tumor should make one think of neurilemoma. However, if one saw the gross appearance (and this is why it is so important to know the gross in neuropathology) one would see that the tumor was not connected in any way with a cranial nerve fiber; this almost immediately rules out a neurilemoma except for the rare instance where a central neurilemoma is present. There are a few patients, usually young, who have peripheral neurofibromatosis and also a so-called cerebral neurofibroma; if that is the case, you ought to locate somewhere an arrangement of the nuclei of these cells, which I think are astrocytes, in a pseudo-palisade formation, or actually in a genuine palisade, which is the hall mark of a neurilemoma. If you cannot find this pseudo-palisading, or genuine palisading of nuclei, then you must find other evidences. For example, old blood pigment. It is amazing how many neurilemomas contain within them the blood pigment from old hemorrhage. This is so well known that the fact of hemorrhage in acoustic neurinomas is discredited as evidence of head trauma. Perhaps 80% of all the neurilemomas that I have seen contain old blood pigment and it is characteristic of the tumor rather than of trauma. If you cannot find that, then you ought to find some evidence of foam cells containing lipids; in nearly all acoustic or other neurilemomas you find large macrophages containing fatty sudanophilic material; if you cannot find that then you ought to find some cyst formation, because many of the neurilemomas degenerate in the center to produce cystic spaces filled with fluid.

Dr. Regato: Drs. I. Costero, of Mexico City, and R. Willis, of Cornwall, England, also made a diagnosis of astrocytoma. Drs. D. S. Russell, of Surrey, England, and J. Minckler, of Denver, offered subependymoma. Drs. G. Vogt-Hoerner, of Paris and E. F. Geever, of New York, preferred acoustic neurinoma. Dr. J. Butler, of Tachikawa, Japan, made a diagnosis of neurilemoma.

This slide was examined at the AFIP (Accession No. 893503) and the following report was given by Dr. W. E. Haymaker in December, 1958: The tumor is composed of clusters of small cells embedded in a dense mass of fibers. In some clusters the cells are fusiform; the nuclei are small, dark and round to oval in shape. No mitotic figures are apparent; no true pallisading patterns of nuclei or verocay bodies are seen. The neoplasm has a lobular appearance as a result of separation and encirclement of the cellular clusters by the fibrillary matrix. The tumor has one small cystic area and focal areas of calcification. Vascular channels are fairly abundant; many show thickening of their walls without endothelial proliferation. In our opinion this tumor is a subependymal glomerate astrocytoma which originated in the lateral recessus of the 4th ventricle.

K. J. Zülch, M.D., Cologne, Germany (by mail): This is a special form of ependymoma seen mainly in the fourth

ventricle. This degenerative form was first described by Giampalmo and illustrated by Scheinker in his book as well as by myself. Scheinker's view that this is an independent entity is tenable; I rather believe with Giampalmo that the pattern results from pressure atrophy and sclerosis in an ependymoma of the fourth ventricle. In some fields the usual architecture of ependymoma is faintly visible.

Subsequent history: Post-operatively the patient required a tracheostomy and frontal trephines to relieve cerebro-spinal pressure. He hemorrhaged from a duodenal ulcer and had a subtotal gastrectomy; he developed pneumonia and expired on November 28, 1961.

Autopsy revealed extensive bilateral pneumonitis and evidence of residual tumor bilaterally in the 4th ventricle.

Dr. Bucy: Doctor Taveras has drawn your attention to the fact that this patient is said to have had a right temporal hemianopsia; it is perfectly obvious that this tumor did not give rise to this neurological defect. What did? The trauma has been cited as a possibility. A lesion of the optic radiations in the temporal lobe or in the occipital region or in the lateral geniculate ganglion would have produced an homonymous hemianopsia and not a right sided one. This can only have arisen from either a lesion in the right optic nerve or in the right eye. We have not been told from the autopsy examination whether or not such a lesion was found.

Of considerable interest is the cerebrospinal fluid rhinorrhea; this could have been due to the cranio-cerebral trauma. There is the possibility, as Doctor Taveras pointed out, that the fracture had created a defect which was not complete, and that later, with the increased intra-cranial pressure and the hydrocephalus, this defect was broken through and the cerebrospinal rhinorrhea developed. Patients with long standing chronic, increased intracranial pressure may develop a cerebrospinal fluid rhinorrhea spontaneously, without any trauma, due to a rupture through the thin cribriform plates or through a small perforation in the region of the sella turcica.

Doctor Zimmerman has pointed out that we are dealing here with an essentially benign tumor. The results of surgery of neurologic tumors are most brilliant in the case of benign tumors of the posterior fossa. If we are to obtain satisfactory results these tumors must be extirpated completely. It is probable that in this case a complete extirpation was not possible. Did the patient make a neurological recovery? Was he perfectly well during this interval and, had he not developed a duodenal ulcer which bled, would he have continued well for a long period of time? These are things we do not know.

Paul W. Gikas, M.D., Ann Arbor, Michigan: As it is often the case, the surgeon sent this material with very little history and asked for a frozen section. On frozen section it was called "acoustic neurinoma". The pathologist was influenced probably by the reported location of the tumor; on the permanent sections it was called again an acoustic neurinoma; it wasn't until Doctor Webb Haymaker's remarks were received from the A.F.I.P. that we realized that this was indeed a different neoplasm. One of the striking features of this neoplasm is that the cells, the astrocytes, occur in clusters and aggregates, and this is an important clue. However, on frozen section if the quality is not good it could be confused with a Verocay body; I think that was the error in our case.

As for the follow-up, I would like to quote from a summary I have here: Post-operatively the patient required a tracheostomy because of inability to handle secretions and also re-opening of the wound with bilateral frontal trephines on July 21st, 1958, to relieve an elevated cerebrospinal fluid pressure. He then did well until the 28th of that same month, when he developed gastrointestinal hemorrhage, requiring 21 units of blood in a 36-hour time period. An emergency celiotomy was performed, an acute duodenal ulcer was found and treated with partial gastrectomy and vagotomy. The patient was discharged on September 9th, 1958, asymptomatic except for several post-operative neurologic residuals. He was readmitted on September 25th, treated for serum hepatitis and discharged on October 15, 1958. Headache and ataxia increased over what they were during the post-operative period and the recurrent cerebrospinal fluid rhinorrhea and bursts of anger resulted in re-hospitalization in January of 1961 when the Holter valve procedure was done. He was found to have optic atrophy then. He did poorly for a time, requiring revision of the valve and a tracheostomy; he aspirated several times with resulting pneumonia. He was discharged improved in May, 1961. In the ensuing months he was hospitalized three times for pneumonia and intermittent signs of increasing cerebrospinal fluid pressure, with rhinorrhea. He had difficulty swallowing and aspirated frequently; the ataxia increased, and finally he succumbed in November of 1961. This patient was discussed at length at our Tumor Board, particularly with the idea of re-operating upon him, since we realized at that time that this was histologically a benign tumor, the decision was made not to re-operate. As to the condition of the optic nerve, nothing was noted at the autopsy; we did not find the fracture either perhaps because we did not look hard enough.

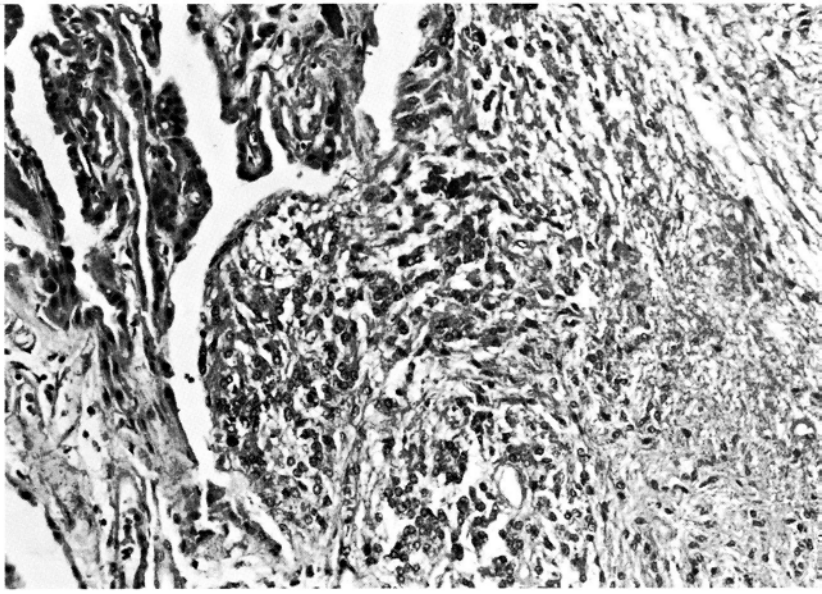

Fig. 4—Photomicrograph of astrocytoma attached to choroid plexus (H & E, x 180).

Philip J. Hodes, M.D., Philadelphia, Pennsylvania: I have seen craniopharyngiomas decompress into the nasopharynx, and I was hoping to learn that this is what had happened. I still cannot understand this optic atrophy; I don't believe anyone can gainsay the possibility that a traumatic opto-chiasmatic arachnoiditis might not have complicated this entire picture and that this man may not have had any trouble for a longer period of time.

Dr. Zimmerman: Have you ever seen an internal hydrocephalus with a herniation of the floor of the third ventricle downwards producing atrophy of the optic nerve or of the chiasm or both?

Philip J. Hodes, M.D., Philadelphia, Pennsylvania: In the cases which were a subject of the paper that we wrote on herniations we did see it. The unilaterality, however, is the thing that bothers me.

Dr. Taveras: If the third ventricle pressure upon the chiasma were the cause of this, there would have been diminished acuity bilaterally with perhaps some degree of optic atrophy and I would have expected more diffuse findings rather than those localized to the right temporal field.

Richard Lende, M.D., Denver, Colorado: It could be the anterior part of the third ventricle catching the chias-

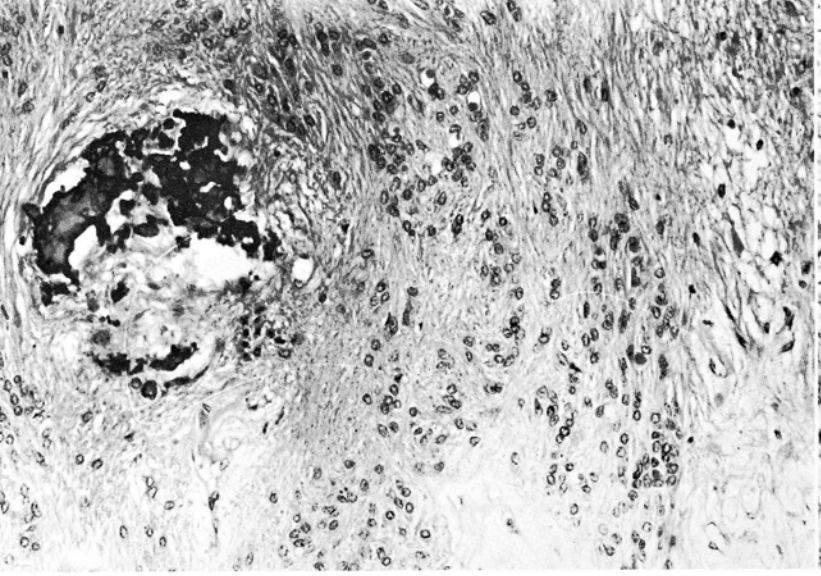

Fig. 5—Fibrillary astrocytoma in the 4th ventricle. Note calcification. (H & E, x 180).

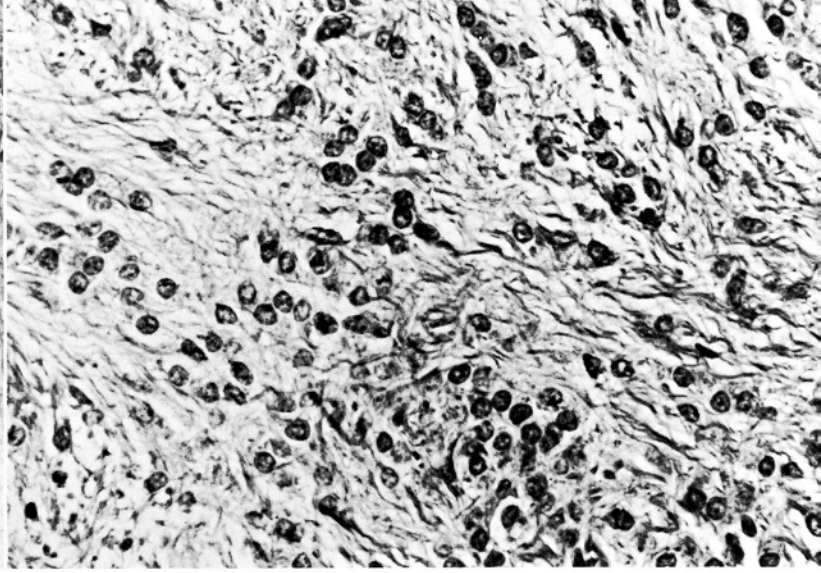

Fig. 6—Photomicrograph of astrocytoma showing interlacing glial fibers. (Phosphotungstic acid-hematoxylin stain, x 450).

matic region between it and the carotid artery. Harvey Cushing once wrote a paper on this subject describing binasal and also temporal defects, unilateral or bilateral, resulting from tumors in the posterior fossa that are not in the region of the chiasma.

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4. *Glioblastoma Multiforme of the Temporal Lobe*

Contributed by S. M. Grant, M.D., Los Angeles, California

THE PATIENT was a 65-year-old man in December, 1961, when he developed weakness of the left arm and leg. Physical examination revealed spasticity of the left upper and lower extremities as well as left homonymous hemianopsia. The blood ammonia was 1,170 mcgr per cent.

Dr. Taveras: The films consist of a frontal and a lateral view of an arteriogram made in the later arterial phase; they demonstrate the presence of moderate to marked elevation of the middle cerebral artery branches involving more the mid and posterior portion of these vessels but extending also to a portion of the horizontal segment of this artery. There is depression of the posterior cerebral artery in its anterior aspect involving also the posterior aspect of the posterior communicating artery. The anterior choroidal artery is also displaced downward and forms an arc concave upward. There is prominence of the lenticulostriate arteries which are not particularly displaced but there appears to be some enlargement of the posterior choroidal artery arising from the posterior cerebral artery.

In the frontal projection there is a displacement across the midline of the anterior cerebral vessels involving more markedly the proximal portion of the anterior cerebral artery than the distal portion. This is not uncommon in cases of temporal lobe masses.

The findings are consistent with a mass lesion involving the entire temporal fossa but more markedly the mid and posterior portions of this area of the skull. Again, it would be advantageous to determine whether we are dealing here with an intra- or an extracerebral mass. The appearance suggests an intracerebral mass because there is "draping" of one branch of the middle cerebral artery which actually goes through the area of maximum displacement in a downward and posterior direction. This would not be the case if the lesion was extracerebral and the entire temporal lobe was displaced upward. In addition, the anterior choroidal artery appears to be displaced downward which, again, would not be the case in an extracerebral type of lesion which should ordinarily be attached to the temporal fossa. The downward displacement of the anterior choroidal artery possibly also involving the posterior communicating and posterior cerebral arteries suggests a downward transtentorial herniation accompanying the mass.

In conclusion, there is a mass lesion involving the mid and posterior temporal region on the right side with an accompanying hippocampal herniation involving the anterior portion of the hippocampal gyrus. The lesion is most likely intracerebral.

Dr. Taveras' impression: INTRACEREBRAL TEMPORAL TUMOR with downward transtentorial herniation.

Roentgenologic Impressions Submitted by Mail

Metastatic temporal tumor	31
Sphenoidal ridge meningioma	19
Temporal tumor	18
Parietal glioma	4
Tumor corpus callosum	3
Others	29

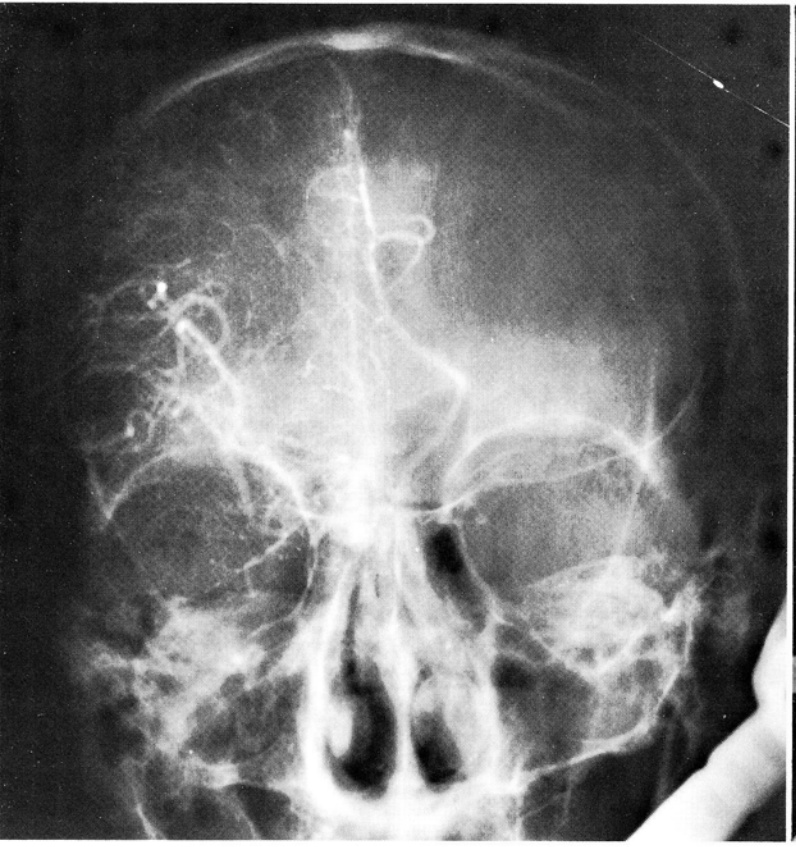

Fig. 1—Arteriogram in later arterial phase showing displacement across the midline of the anterior cerebral vessels.

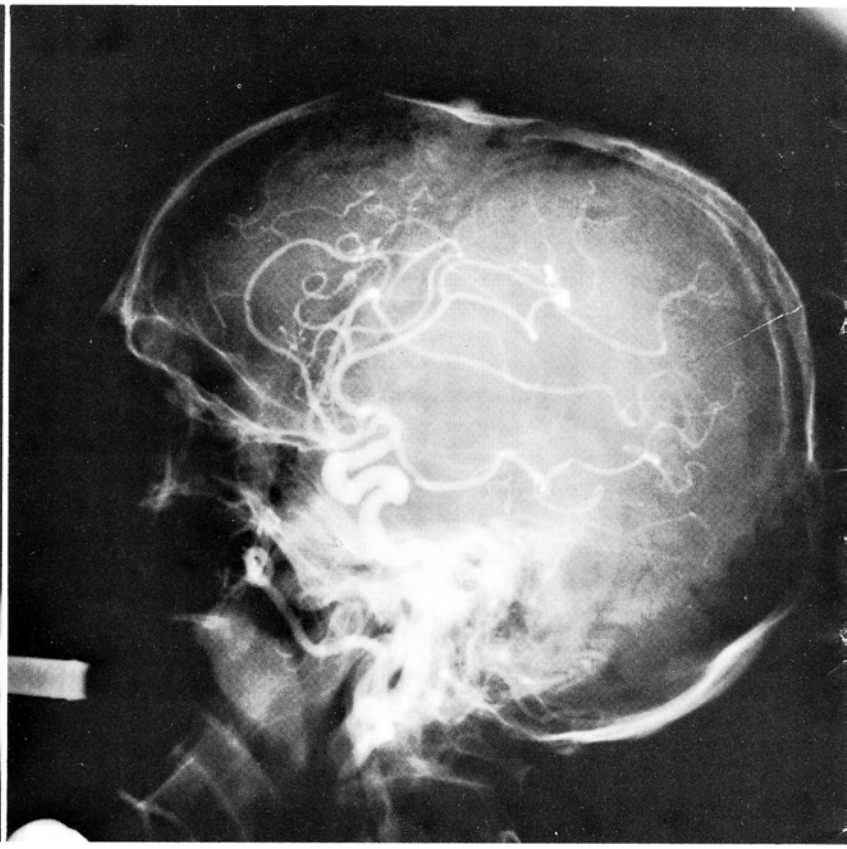

Fig. 2—Arteriogram in later arterial phase revealing elevation of the middle cerebral artery branches and depression of the posterior cerebral artery.

Dr. Taveras: The diagnosis of metastatic temporal tumor was made probably because of the 1170 micrograms per cent of blood ammonia. I have not been able to find any condition of the brain that would do this; I thought that perhaps we were dealing here with an intracerebral hemorrhage in a patient with liver disease due to interference with the blood clotting mechanism. However, the history was not that of an apoplectic episode and therefore I thought that we were dealing with a neoplasm. Sphenoid ridge meningioma is one thing that you could not diagnose from this examination, the reason being that the sphenoid ridge meningioma is anteriorly situated in the temporal fossa, and it is the posterior two-thirds of the temporal area that are involved, not the anterior third. I do not know how it is possible to make a parietal glioma out of this angiogram. There is clear elevation of the middle cerebral group and of the angiographic Sylvian point and there is no reason for saying that this is a supra-Sylvian tumor, such as a parietal tumor would be. This is clearly an infra-Sylvian mass. I don't know why a tumor of the corpus callosum should be mentioned.

Dr. Regato: Drs. T. O. Gabrielson, of Ann Arbor, Michigan, and J. A. Campbell, of Indianapolis, suggested metastatic tumor of the temporal lobe. Dr. W. F. Kraemer, of Knoxville, Tennessee, offered a glioma of the temporal lobe. Dr. J. R. Galloway, of Albuquerque, also made a diagnosis of tumor of the temporal lobe with uncal herniation. Dr. B. L. Pear, of Denver, favored a meningioma of the sphenoid wing.

Operative findings: On December 9th, 1961, while performing the arteriography, the patient had a needle biopsy which revealed a malignant tumor. On December 3rd, 1962, a right temporal craniotomy was done and uncovered a tumor extending 7 cm from the surface of the brain; it was gray, firm and non-vascular. The specimen was 8 x 3.5 x 3.5 cm; on cut section there were hemorrhagic areas.

Dr. Zimmerman: This neoplasm is characterized by the following features: There is great cellular pleomorphism; many tumor cells are multinucleated and are of giant size; there are numerous cells in mitotic division; somewhat spindle-shaped cells are arranged in groups to form pseudopalisades around central zones of necrosis; large parts of the tumor are replaced by dense, acellular, pink-staining zones. With special staining methods the latter are shown to be of mesodermal origin. Thus, a tumor which has most of the ear-marks of a malignant glial neoplasm contains distinctly mesodermal elements. It is true, of course, that some malignant gliomas are in reality mixed tumors and are in part sarcomas. Feigin and his associates, among others, have called attention to this phenomenon. In the present case, however, there is no clear-cut evidence that the dense stroma is part of a sarcomatous tumor. It is much more suggestive of the replacement fibrosis which is seen in tumors that undergo extensive necrosis. Actually this is not an uncommon finding in many cases of glioblastoma multiforme and is especially frequently encountered in this class of glioma following x-radiation.

Dr. Zimmerman's diagnosis: GLIOBLASTOMA MULTIFORME.

Histopathologic Diagnoses Submitted by Mail

Glioblastoma multiforme	39
Astrocytoma, grade IV	10
Malignant meningioma	31
Metastatic carcinoma	18
Various sarcomas (angio, fibro, rhabdo)	24
Mixed glioblastoma and sarcoma	11
Others	28

Dr. Zimmerman: Some of you called this a glioblastoma multiforme which is what I thought, with the reservation that there was too much stroma. Grade IV astrocytoma is the equivalent of glioblastoma multiforme. The diagnosis of malignant meningioma I take issue with. If one had heard Doctor Taveras say that this was an intrinsic tumor of the temporal lobe, the diagnosis of meningioma should have been made with a good deal of caution. However, neither you nor I knew the exact location of this tumor at the time we submitted our opinions. Meningioma came to mind because many of you recognized the fact that there was a dense stromal element, just as I did. Unfortunately that is not enough for a diagnosis of meningioma; one should

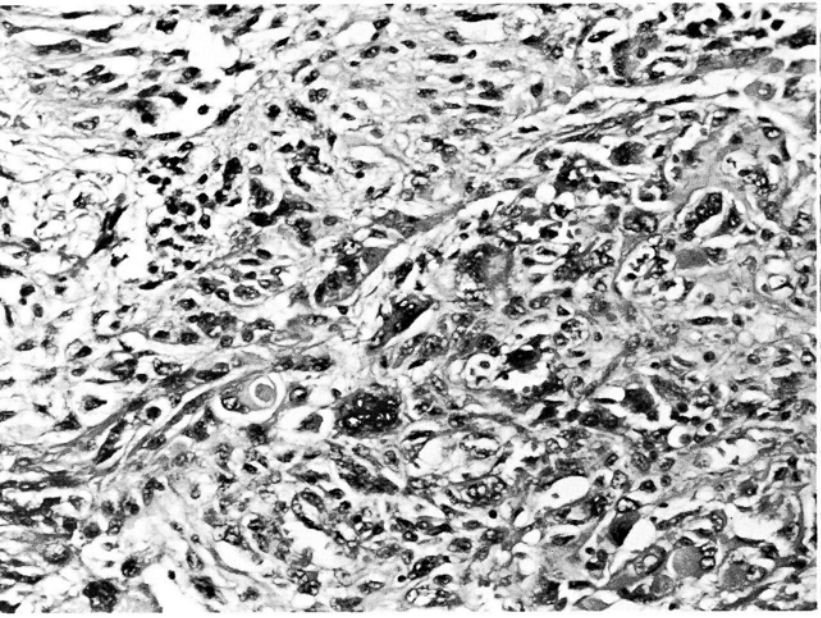

Fig. 3—Photomicrograph of glioblastoma multiforme showing cellular pleomorphism (H & E, x 180).

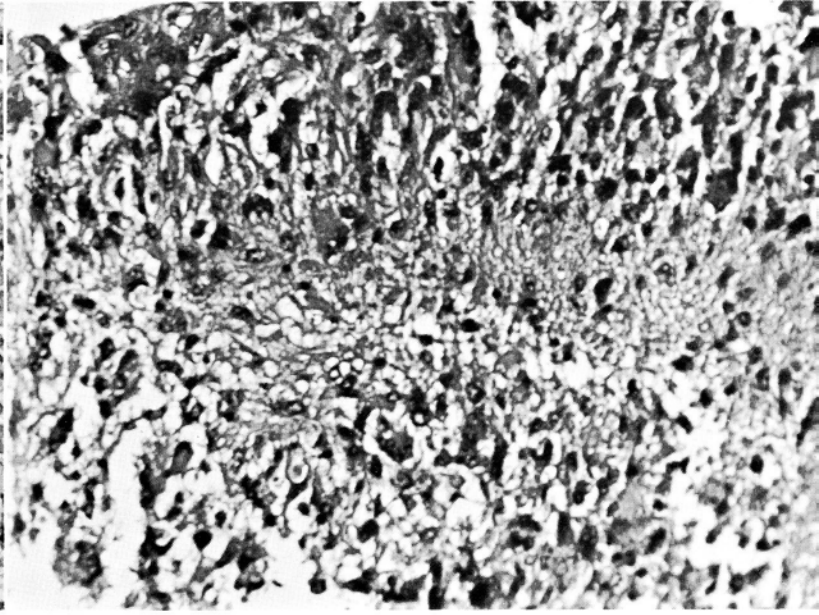

Fig. 4—Spongioblasts forming a pseudopalisade around an amorphous acellular zone (H & E, x 225).

insist on typical whorl formation or psammoma bodies, or both, before making a diagnosis of meningioma; these two elements are totally absent in this tumor. In many glioblastomas multiformes, especially in those having large zones of necrosis, it is common to encounter a mesodermal stroma, a reactive fibrosis, which is what I took this connective tissue to represent in the present tumor; secondly, in patients with glioblastoma multiforme who are irradiated, one encounters subsequently, and at post mortem, large zones of fibrosis as a reparative process, so that the presence of mesodermal tissue alone does not necessarily indicate a meningiomatous origin. In several hundred cases of meningioma that I have now seen, from various parts of the neuraxis, I have only encountered three malignant meningiomas; this is at variance with what is reported by others. The presence of an occasional bizarre cell in a meningioma does not mean that it is malignant; the fact that the tumor tends to recur commonly does not mean necessarily that it is malignant. Incomplete removals of meningiomas are often followed by recurrence; this happens with many other benign tumors. The fact that meningiomas have a proclivity to eroding the internal lamela of the skull, pressing into the diploic sinuses, eroding the outer table of the skull and presenting even in the scalp does not make it a malignant neoplasm. Benign tumors elsewhere will do the same thing, if pressing upon adjacent immovable tissue like bone. What one has to find are numerous mitoses, bizarre cells, massive zones of necrosis, and preferably, not local invasion but distant metastasis. If you use these criteria for malignant meningiomas, you will find that they are exceedingly uncommon. In view of the cells that are so characteristically gliogenous in type, the diagnosis of a meningioma of a malignant type can be eliminated. I cannot find any cells at all that I would call epithelial and therefore I do not believe that one can say this represents a metastaic carcinoma. Those who thought of sarcoma as the most important element in this tumor I cannot find any fault with, because perhaps their slides did indeed have large portions of sarcoma, and if so, the diagnosis can be justified on that basis; but I can hardly believe that there wasn't enough gliogenous tissue in the section to warrant your ignoring it completely.

I would insist on being shown a cell which contains striations and if you cannot find it, then it isn't a rhabdomyosarcoma. I don't know how one comes to a diagnosis of angiosarcoma in this case, because I didn't see that the tumor is very vascular.

Dr. Regato: Drs. E. Saxen, of Helsinki, and A. O. Severance, of San Antonio, also made a diagnosis of glioblastoma multiforme. Dr. J. B. Frerichs, of El Paso, offered angioendothelial sarcoma. Drs. W. J. Frable, of Chicago, and D. S. Russell, of Surrey, England, preferred a diagnosis of mixed glioblastoma and sarcoma.

K. J. Zülch, M.D., Cologne, Germany (by mail): The tumor consists in part of spindle-shaped cells forming a reticular pattern, and in part also of long spindle-shaped cells in long streaming bands. We find mitoses, necrosis and in one field also an angiomatous component. We have seen such tumors repeatedly within the brain or originating from the dura; it then shows signs of infiltration (see Handbuch der Neurochirurgie, figures 356, B and D). Unfortunately we have not been informed as to the site of origin; reticulin stains for intracellular fibers would be desirable.

In January, 1962, this slide had been submitted to Dr. D. S. Russell, of Durking, Surrey, England who wrote: "This is a remarkable tumor of glia and connective tissue; it could appropriately be called gliosarcoma. Both elements appear malignant and rather intimately mixed. I note with particular interest an area which seems to show cartilaginous transformation. The latter would suggest to me that the tumor was primarily a meningioma with the glial changes being secondary. But, it is difficult to accept this interpretation and I must hazard that the sarcomatous element is secondary."

In February, 1962, the slide had been submitted to Dr. L. J. Rubenstein, of New York, who wrote: "I would interpret this as a mixed glioma and sarcoma. An area of the sections suggest chondroplastic metaplasia similar to one of the cases that I reported in 1956. I have not observed this phenomenon in any of the mixed tumors I have met since."

Subsequent history: The patient improved and was discharged 6 weeks after operation; he expired four days later. Autopsy revealed a large recurrent gray mass 9 cm in diameter at the site of the excised tumor and pontine hemorrhages. The liver presented advanced cirrhosis.

Dr. Bucy: One must always be careful about belaboring the obvious; but this case is such an excellent example of the fact that dogs can have both lice and fleas. It is perfectly obvious that those who made a radiologic diagnosis of a metastatic tumor did so because of the elevated blood ammonia. This further evidenced the mistake which we must avoid, and which Doctor Taveras pointed out

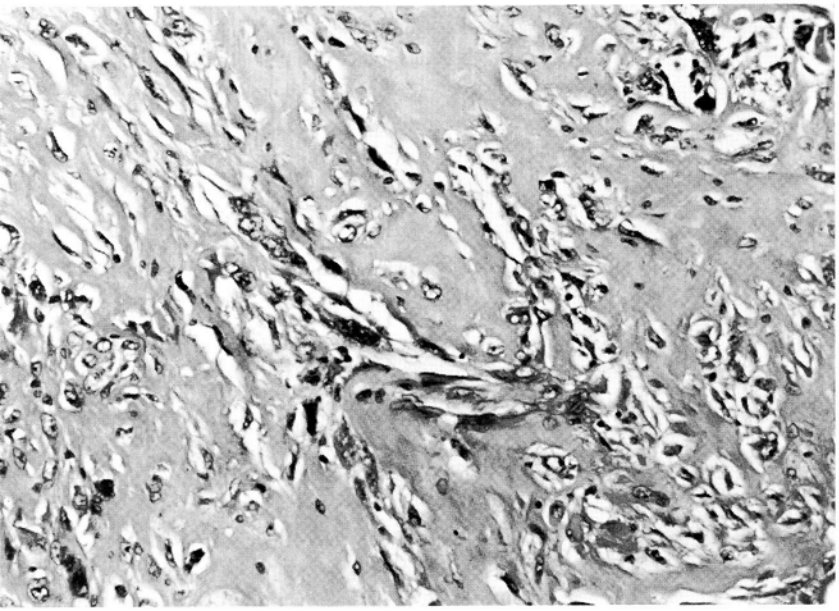

Fig. 5—Photomicrograph of dense collagenous connective tissue in glioblastoma multiforme (H & E, x 180).

earlier. We must make only radiological diagnoses from what we see in the films.

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5. *Meningeal Sarcoma*

Contributed by CAPT. T. J. BUTLER, MC, USAF, Tachikawa, Japan

THE PATIENT was a 19-year-old man in October, 1961, when he developed right frontal and superior maxillary pain accompanied by chills and malaise. A diagnosis of acute sinusitis was made. The pain recurred and was followed by blurred vision of right eye, stiffness of neck and vomiting. In December, 1961, he presented papilledema, but no sensory or motor changes. Blood chemistries were reported normal. The urine showed 30 leukocytes per high power. The spinal fluid presented 3 lymphocytes; total protein 9.7 mgm per cent, sugar 80 mgm per cent.

Dr. Taveras: The film consists of a frontal and lateral view of a ventriculogram. In the frontal projection there is a mild degree of ventricular dilatation slightly more marked on the left side. The third ventricle is not enlarged although it is somewhat irregular in contour. The parolfactory sulci are slightly prominent and slightly deformed; they also appear to be somewhat separated. In the lateral projection there is again noted a slight degree of ventricular dilatation. The surface sulci are not remarkable although it might be said that they are not narrow, some of the sulci in the frontal region are slightly wider than normal for a young man. In this lateral view, the contour of the inner aspect of the sella turcica suggests early evidence of increased intracranial pressure. No mention is made as to the patency of the aqueduct and fourth ventricle as well as to their outline. It is assumed, however, that they were patent because of the abundant amount of air in the subarachnoid space proceeding from this ventriculogram.

The appearance is that of a mild degree of ventricular dilatation with some prominent or slightly widened surface sulci particularly in the frontal region. There is no evidence of shift or localized deformity and no evidence of obstruction. One diagnosis that might be entertained with the clinical history as evolved in this patient would be an inflammatory process. However, there is nothing in the cerebrospinal fluid findings to support such a diagnosis. The sugar is normal, the protein is not elevated and the cells are not increased in number. The blurring of vision as described could be produced by increased intracranial pressure with papilledema. In addition, there appears to be some prominence or perhaps edema of the gyrus rectus on each side which could be producing pressure on the optic nerves and anterior aspect of the chiasm, particularly if they are herniated into the sella turcica. The most appealing diagnosis for this case would be that of pseudotumor cerebri. Some type of parasitic disease would appear to be unlikely in view of the normal cerebrospinal fluid findings in what clinically appears to be the acute stage of a disease process.

In conclusion, we are dealing here with a 19-year-old man without a demonstrable intracranial lesion on ventriculography who apparently presents edema of the gyrus rectus on both sides, with blurring of vision and evidence of early increased intracranial pressure radiologically. The findings do not support those of a brain abscess or another type of diffuse inflammatory or parasitic disease. I would entertain the diagnosis of pseudotumor cerebri (also called serous meningitis, meningeal hydrops and benign intracranial hypertension) in spite of the fact that the ventricles are slightly enlarged. In my experience, less than half of these cases have the classical "slit-like" ventricles.

Dr. Taveras' impression: PSEUDOTUMOR CEREBRI.

Roentgenologic Impressions Submitted by Mail

Brain abscess	41
Choriomeningitis	14
Encephalitis	9
Paragonimiasis!	1
I couldn't say!	1
Others	32

Dr. Taveras: There is no basis for making a diagnosis of brain abscess on these films. There was a good amount of fluid circulating freely in the subarachnoid space; I thought that meningitis probably should not be considered seriously in this case. This could be an encephalitic process; that is certainly a possibility, but I thought that this is probably a neoplasm, on account of the fact that this is a Cancer Seminar!

Dr. Regato: Dr. S. M. Jones, of Lubbock, Texas, offered a diagnosis of pseudotumor cerebri. Dr. J. R. Gallo-

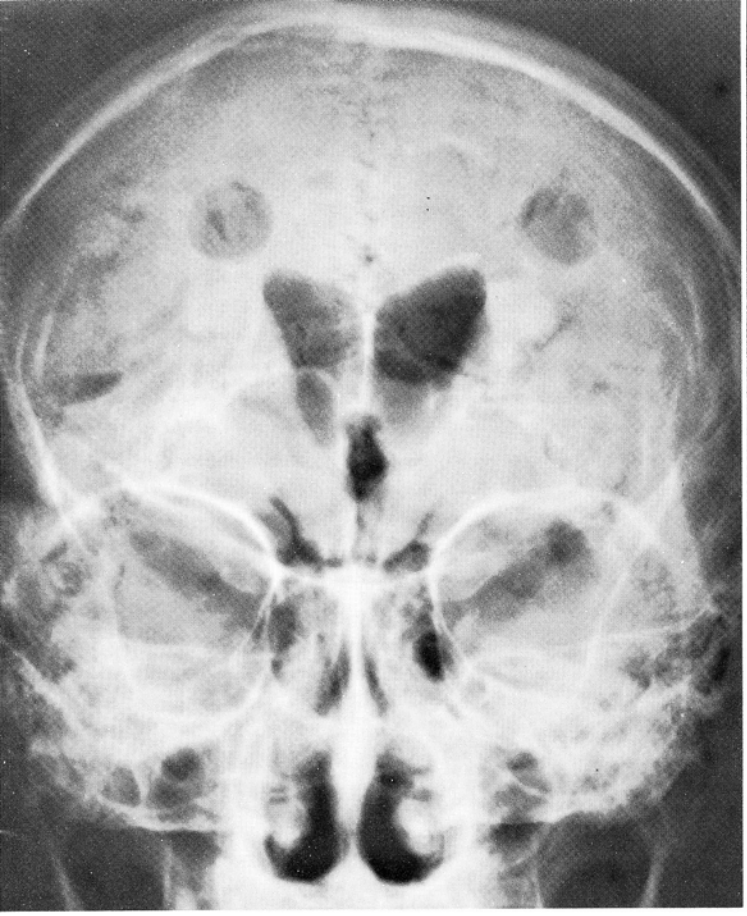


Fig. 1—Ventriculogram showing mild ventricular dilatation, more marked on the left.

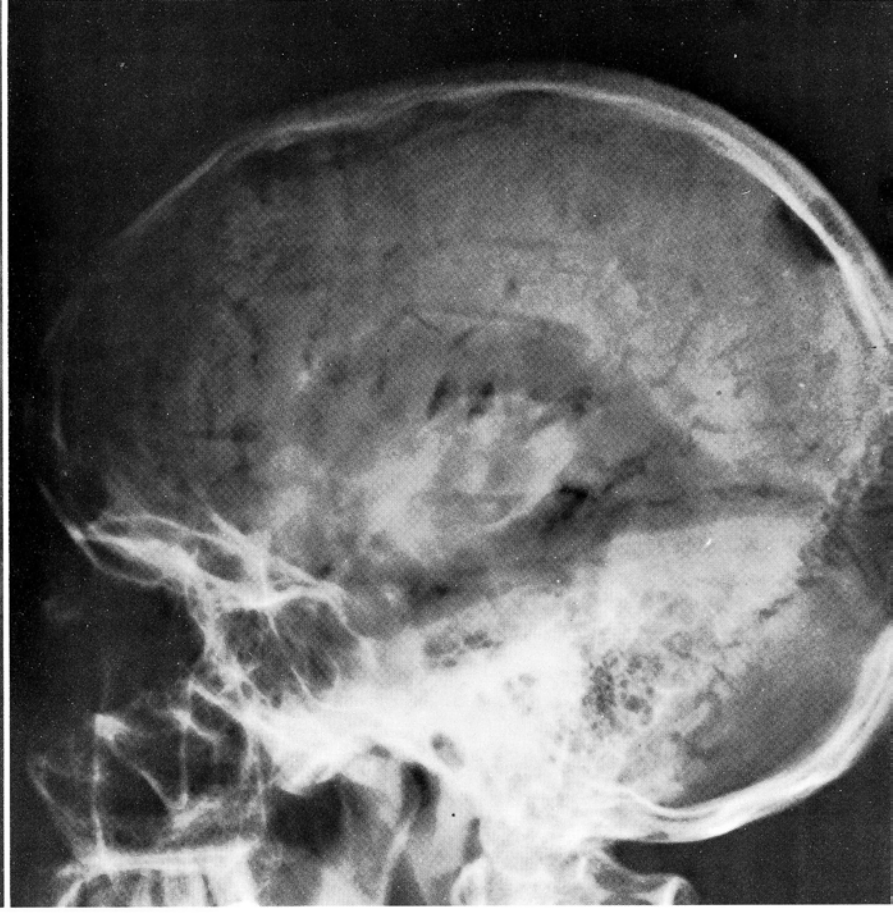


Fig. 2—Ventriculogram with mild ventricular dilatation. The inner aspect of the sella turcica suggests intracranial pressure.

way, of Albuquerque, preferred a sub-frontal abscess. Dr. R. E. Graf, of Denver, suggested a diagnosis of encephalitis.

Operative findings: On December 9th, 1961, a sub-occipital craniotomy was done. Marked enlargement of both cerebellar hemispheres was found with easy bleeding. A biopsy was done, the wound was closed and the patient was returned to the ward; he became comatose and died on December 12th, 1961, on his third post-operative day.

Autopsy failed to reveal any tumor in any and all organs examined. There were prominent hemorrhages associated with destruction of cerebellar tissue. The brain showed patches of subarachnoid discoloration, particularly on the lateral aspects of the frontal and temporal lobes; the same was present on the surface of the pituitary and spinal cord.

Dr. Zimmerman: This tumor presents an interesting problem. It is confined entirely to the cerebral leptomeninges and extends to the underlying cerebral cortex only along the Virchow-Robin spaces. The membrana limitans, in other words, acts as a strict barrier to this obviously malignant neoplasm. The individual tumor cells have a rather uniform appearance. The nuclei are the most prominent feature of the cells which, however, are seen to have short stubby processes when examined with higher magnification. The cells are present in great profusion and at first blush do not appear to have a distinctive pattern, but actually they do tend to form long parallel straight or curved rows. There is active cellular division and there is a rich reticulin stroma in the tumor. Even if one discounts some of the silver-impregnated mesenchyme in the leptomeninges as part of a non-specific reaction to tumor on the part of the pia-arachnoid, it is nevertheless obvious that the reticulin stroma is being produced by the tumor cells.

There is no really serious problem in classifying this neoplasm as a sarcoma. Its precise site of origin, however, is difficult to determine in the absence of evidence of tumor elsewhere in the brain and its coverings or even extracranially. It is indistinguishable from the so-called cerebellar sarcomas which are probably of leptomeningeal origin. There is no reason of course, why the same type of tumor may not arise from the cerebral leptomeninges, but it is a fact that the cerebellar meninges are much more frequently involved by this type of tumor than are the cerebral meninges. It is conceivable that there is actually in this case a site of origin in the posterior cranial fossa and that the microscopic preparation represents a cerebral meningeal metastasis. One cannot also, of course, exclude an extracranial site of origin in this case. The so-called reticulum cell sarcoma may have the appearance presented by this tumor.

Dr. Zimmerman's diagnosis: MENINGEAL SARCOMA

Histopathologic Diagnoses Submitted by Mail

Leptomeningeal sarcomatosis	85
Medulloblastoma	26
Lymphosarcoma	20
Cerebellar (parithelial) sarcoma	15
Hemangioblastoma	6
Metastatic tumor	6
Others	18

Dr. Zimmerman: In the gross photograph you can see some of the vertebral arteries with very little evidence of anything in the subarachnoid space. There is some laceration as one sees following the operative removal of a tumor. I presume that the hemorrhagic lesion that can be seen is either due to the removal from the calvarium at post mortem or is secondary to the trauma of the operative procedure. There is nothing in the section of the frontal lobes that gives you any clue as to the nature of the tumor. I could not make a diagnosis either of cerebral swelling, as one sees in pseudotumor cerebri, or of encephalitis; but it is notoriously true that one can see histologic evidence of encephalitis, when to the naked eye it is invisible.

I cannot agree with the diagnosis of medulloblastoma for the reasons I have already discussed. In medulloblastoma you do not get the reticulin stroma that I have shown

with the Wilder silver impregnation method; there is no stroma other than the natural occurring stroma in the medulloblastoma. I cannot object too vigorously to a diagnosis of lymphosarcoma, although I personally feel that these are not lymphocytes; the cells are not shaped like lymphocytes and they do lay down the reticulin stroma. I think it is a sarcoma of meningeal origin. I presume that people who call this "perithelial" refer to the papers that some years ago Percival Bailey published; he attempted to account for the presence of cerebellar sarcomas and suggested that either the meninges, or the connective tissue of the Virchow-Robin spaces in the cerebellum itself as a possible site; and he, or someone else suggested the term "perithelial" to indicate the Virchow-Robin space connective tissue. I do not think that it is a metastatic tumor. The proof would be the evidence that this tumor did not occur extracranially; we now have a large number of them in which no extracranial tumor was found. I might add that this type of cerebellar sarcoma is the only intracranial neoplasm that commonly metastasizes extracranially without the intermediary of a neurosurgeon. I have never seen a glioma which metastasized spontaneously extracranially; it was always in an operative case that I have seen it. But this type of sarcoma in about one-third of all cases does apparently metastasize extracranially and I have seen it in the lung; in one instance, on the basis of a bone marrow biopsy we made the correct pre-operative diagnosis of cerebellar meningeal sarcoma. It does not surprise me that no cells were found in the spinal fluid; we have ten of these tumors in which the spinal fluid was examined prior to operation and not in a single instance did we pick up loose tumor cells; the tumor is so coherent that loose cells rarely if ever are seen in cerebro-spinal fluid. Also, in contrast to some of the gliomas and especially the neurilemomas, the relatively low protein level is not a very surprising finding. I think in most cases you would find some elevation, but every once in a while one of these tumors has a normal protein level in the spinal fluid.

Dr. Regato: Drs. V. M. Areán, of Gainesville, Florida, J. Ewart, of Tachikawa, Japan, and M. Navarro-Roca, of New York, also made a diagnosis of meningeal sarcoma. Dr. D. S. Russell, of Surrey, England, submitted meningeal metastasis from a medulloblastoma. Dr. J. D. Rice, Jr., of Colorado Springs, suggested meningeal meningiomatosis but felt that meningeal metastasis from an unsuspected primary should be ruled out.

K. J. Zülch, M.D., Cologne, Germany (by mail): The slides contain a piece of cerebral cortex with a cellular tumor in the leptomeninges. The cells resemble those of a medulloblastoma possibly metastatic. But primary meningeal sarcomatosis must also be considered: a decision is only possible on the basis of detailed gross description. Special stains could reveal reticulin fibers which are not present in medulloblastoma.

Dr. Bucy: In connection with the microscopic picture, Doctor Zimmerman has not said anything about what has always seemed to me to be a common characteristic of the diffuse leptomeningeal sarcomas: the invasion of the tumor down the perivascular sheathes from the surface of the brain; one sees this so frequently that it becomes an easily distinguishing mark in most of them. In making a diagnosis of pseudotumor cerebri we are not making a diagnosis at all; we are merely giving evidence of our ignorance; we do not know what is wrong with the patient and we are only saying that he presents symptoms which we commonly see with an intracranial tumor which we are unable to find.

This was not spinal fluid which was examined but ventricular fluid. The protein reported here is perfectly normal for ventricular fluid; and the finding of only three

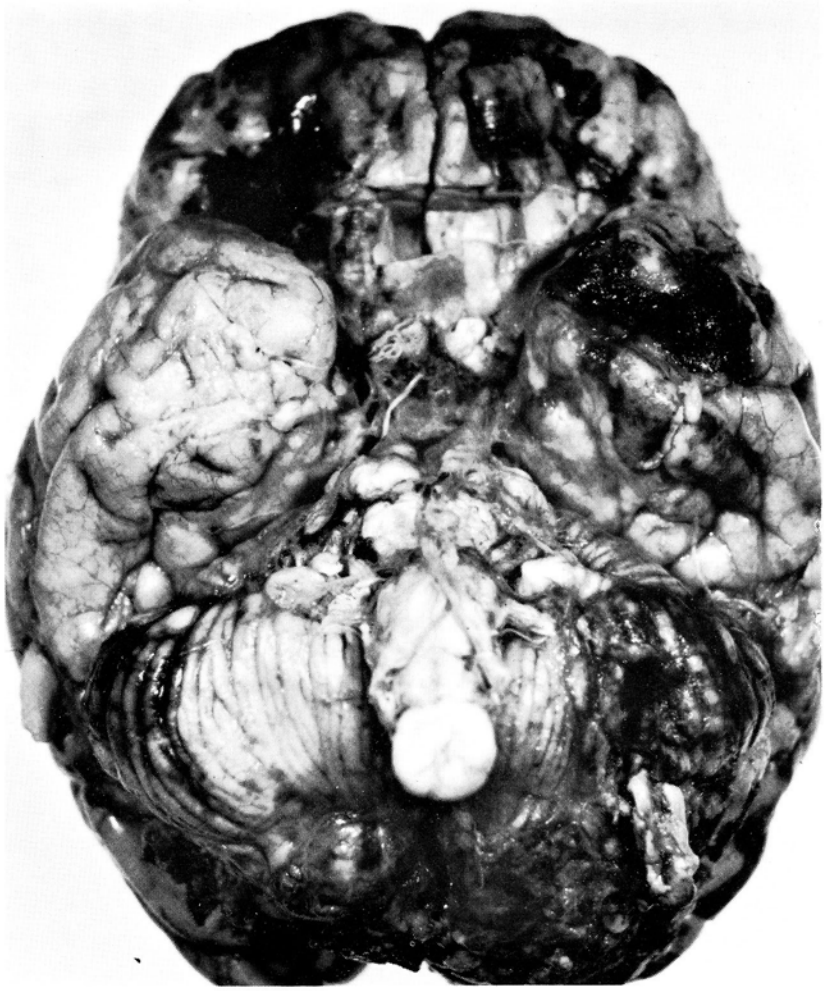


Fig. 3—Gross appearance of brain at autopsy.

lymphocytes likewise fits that picture. I believe that this fluid was obtained when the ventriculogram was made and, therefore, this report is not comparable to what we would have had had the spinal fluid been examined.

I would agree that on occasion what one calls a pseudotumor cerebri is associated with enlarged ventricles, but this is not the case usually. Unfortunately, if one operates upon a patient with a diffuse sarcomatosis of the meninges, or even removes the brain at autopsy, he frequently does not recognize the pathology which is present. One does not see a gross tumor and the slight clouding of the meninges is not always apparent to such superficial examination.

From an examination of the spinal fluid we have had a positive cytologic diagnosis of the presence of a sarcoma of the meninges in several instances. It is exactly in the situation which is presented here that I would recommend that a very careful cytologic study of the spinal fluid be made. I cannot explain why our experience in this regard has been different from Doctor Zimmerman's. I am sure that his examinations have been made as carefully as ours.

Mark Wheelock, M.D., Chicago, Illinois: I would like to ask Doctor Zimmerman one simple question, only because we prefer to look upon this as lymphosarcoma or reticulum-cell sarcoma. Is he able to differentiate always with accuracy between the so-called diffuse leptomeningeal sarcomatoses and those from a widespread or disseminated lymphosarcoma which has involved the meninges?

Dr. Zimmerman: I can only tell you that it is not possible to be certain in anything like 100 per cent of the cases that one is dealing with a cerebellar leptomeningeal tumor that has diffusely spread. I could also tell you that reticulum-cell sarcoma looks just like this and conceivably may be a difficult differential diagnosis to make. In this instance I was certain enough of it to have brought along

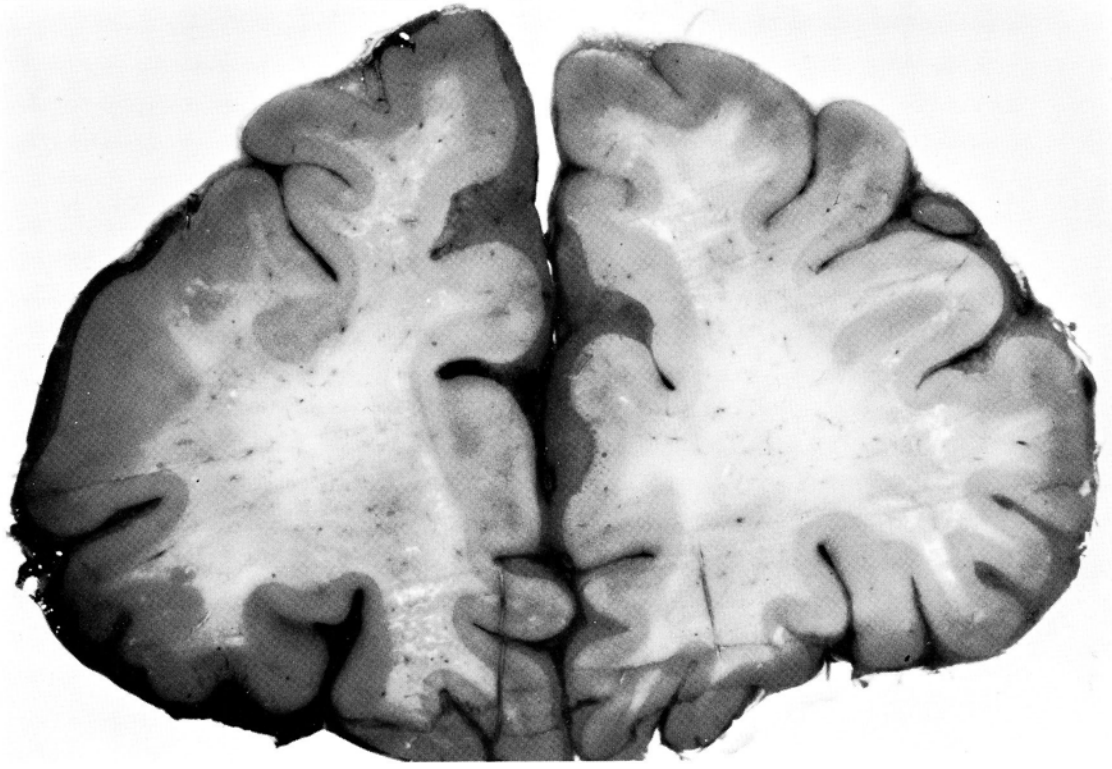


Fig. 4—Cross section of the brain.

the slide which I have shown you without knowing anything about the primary site as found at operation.

Thomas K. Craigmile, M.D., Denver, Colorado: Did you, Doctor Taveras, believe that these sutures were separated and what do you believe is the oldest age at which separation of sutures is seen?

Dr. Taveras: I did not believe this was so. I have seen, however, what I would call slight separation of the sutures in teen-agers between 15 and 20 years of age, always in very long-standing cases; but ordinarily sutural separation is not seen after 12 or 13 years of age. This is not a pronounced enlargement, but the ventricles are a little on the large side, that is, certainly not small.

Kenneth M. Earle, M.D., Washington, D.C.: We reviewed the case at the AFIP; we have had a great deal of trouble with tumors of this sort in the last few years; there are several hundred in our collection and we are beginning to re-study them. Most of these cases come to us labeled "medulloblastoma" but someone is worried particularly because they have occurred in a young adult. We believe that in most cases we can differentiate this group from the classical medulloblastoma. We can tell when we are dealing with a medulloblastoma of a child because it does not have the reticular pattern, but there are cases where we have not been able to make this differential. We have seen a rather diffuse reticular pattern in medulloblastomas which have spread into the leptomeninges although this pattern was not present in the primary tumor; this has caused great strife in our own group where we could not agree among ourselves. Conversely we have seen those occurring in young adults with a distinct reticular pattern in the primary tumor, which is often a solitary nodule over the cerebellum, but not in its spread: so we are in a state of confusion. I discussed this with Doctor Kernohan this week. Some of these tumors have a good prognosis. We have seen young adults with a solitary mass of this sort over the cerebellum, which when removed and then irradiated did not show implantation for years. Doctor Kernohan says he has one that went for fifteen years; I have personally followed one, a physician, who is alive and practicing four years after removal of such a tumor. In my experience all of these cerebellar sarcomas have eventually implanted in the sub-

Fig. 5—Photomicrograph of meningeal tumor invading cerebral cortex by extension along Virchow-Robin spaces (H & E, x 180).

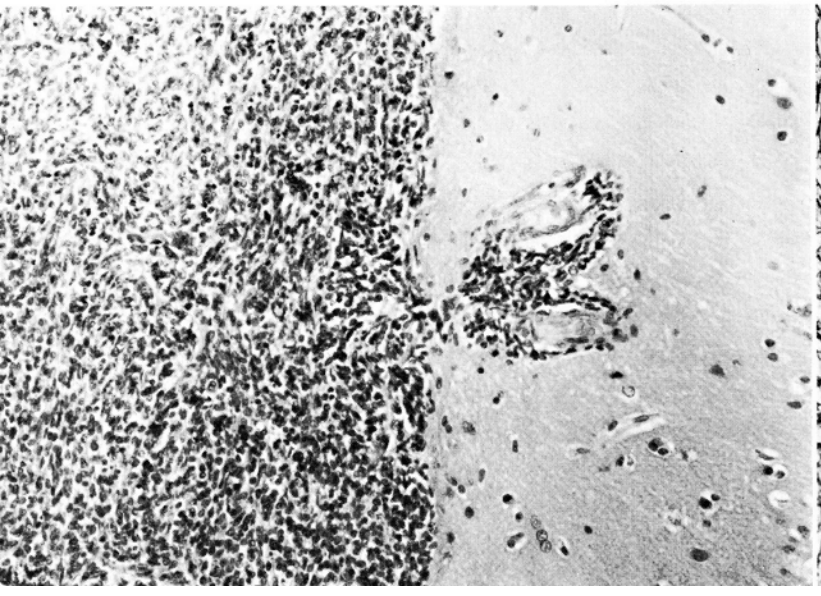
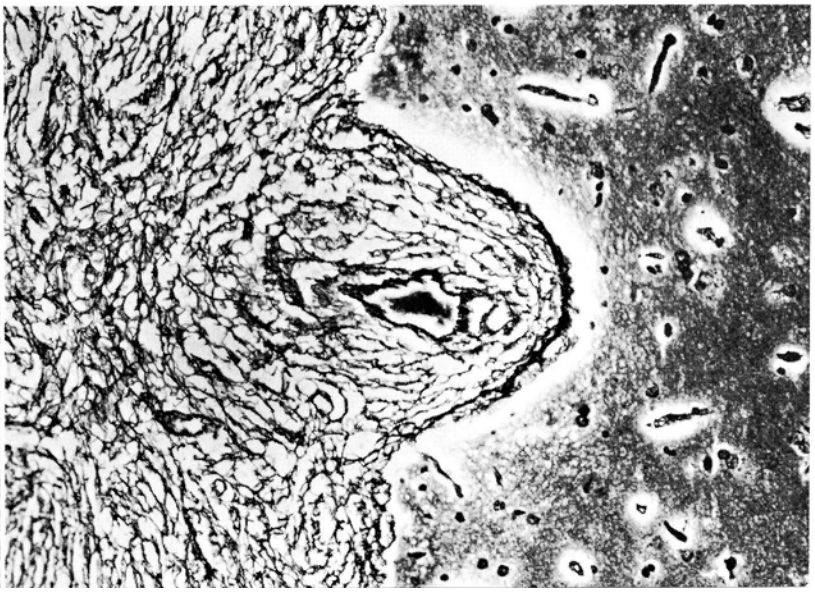


Fig. 6—Tumor in cerebral meninges showing rich formation of reticulin fibers (Wilder silver impregnation, x 180).



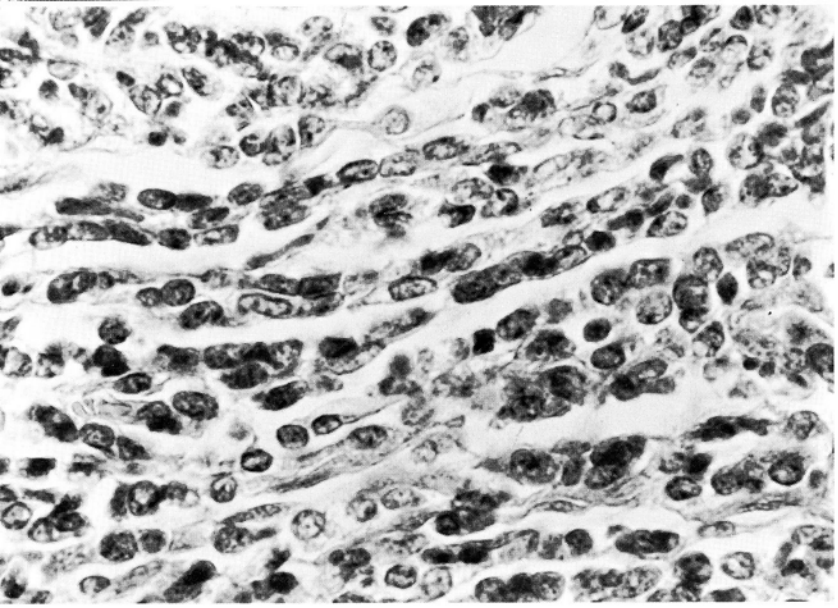


Fig. 7—Photomicrograph of meningeal sarcoma to show parallel arrangement of tumor cells and delicate connective tissue stroma (H & E, x 720).

arachnoid space, and I believe that is their natural behavior, but they seem to have a better prognosis than the medulloblastoma.

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6. *Metastatic Carcinoma of the Thyroid in the Left Parieto-occipital Region*

Contributed by M. Velasco-Suárez, M.D. and I. Costero, M.D., Mexico, D.F.

THE PATIENT was a 47-year-old woman in January, 1962, when she presented a large tumefaction of the left parieto-occipital region of three years duration. There was diminution of strength in the lower extremities and parasthesias of the left lower extremities. On examination there was an infected ulceration of the overlying scalp. There was no papilledema. The patellar reflexes were diminished on the left side and there was a questionable Babinski. The diminution of strength of the lower extremities was not accompanied by marked muscular atrophy. The EEG suggested a lesion in the left parieto-temporal region.

Dr. Taveras: The submitted films consist of an anteroposterior and a lateral view made during the late arterial phase of a cerebral angiogram. In the later projection there is noted a large area of bone destruction in the parietal region on the right side and evidence of displacement of the branches of the middle cerebral artery around the area of bone destruction. Through the radiolucent area there are noted some vascular shadows which have the appearance of veins rather than arteries although they could be enlarged arteries. In the frontal projection there is evidence of increased vascularity within an area measuring about 4 cm in diameter vertically and transversely towards the intracranial cavity from the inner table of the skull. By putting the film on a bright light it is noted that some vascular channels are seen to cross through the area of the outline of the skull and to extend into a flat soft tissue mass on the outer aspect. The appearance is that of a destructive bone lesion which is evidently invading the brain in view of the fact that vessels can be seen to cross from the cranial cavity out towards the extracranial portion of this mass. The differential diagnosis lies between a meningioma, a metastatic tumor of the skull secondarily invading the brain, or another type of local lesion such as an epithelioma of the scalp secondarily invading the bone and the intracranial cavity. Meningiomas are capable of producing these identical findings with the exception of the skin ulceration described in the history which is rather rare in meningiomas. The skin ulceration is, of course, possible following an injury to a meningioma which extends outwardly. Metastatic lesions which involve primarily the bone only rarely extend intracranially to invade the brain tissue. However, it is possible for a metastatic lesion which arose primarily in the meninges, to grow in both directions towards the brain and towards the outside thus producing bone destruction and invasion of the scalp. This is an unusual combination of circumstances although with the frequency of metastatic disease, no doubt this is not rare. The most appealing diagnosis would appear to be that of a primary epithelioma of the scalp which has grown to involve the bone and later to grow intracranially and to invade the brain. There is nothing on these films that would contradict that possible diagnosis. The configuration of the skull defect is unusual for meningioma and it is more likely due to metastatic disease or malignant involvement by epidermoid carcinoma.

Dr. Taveras' impression: EPITHELIOMA OF THE SCALP SECONDARILY INVADING THE SKULL AND BRAIN.

Roentgenologic Impressions Submitted by Mail

Meningioma	31
Carcinoma of scalp	18
Metastatic carcinoma	9
Meningeal sarcoma	7
Hemangioendothelioma	7
Others	27

Dr. Taveras: I feel that meningioma would be rather unlikely. There were venous channels within the area of the tumor which filled in the early arterial phase; meningiomas don't usually do that. In the second place, ulceration in meningiomas is rather unusual. Metastatic carcinoma is the second most likely possibility but the metastasis should

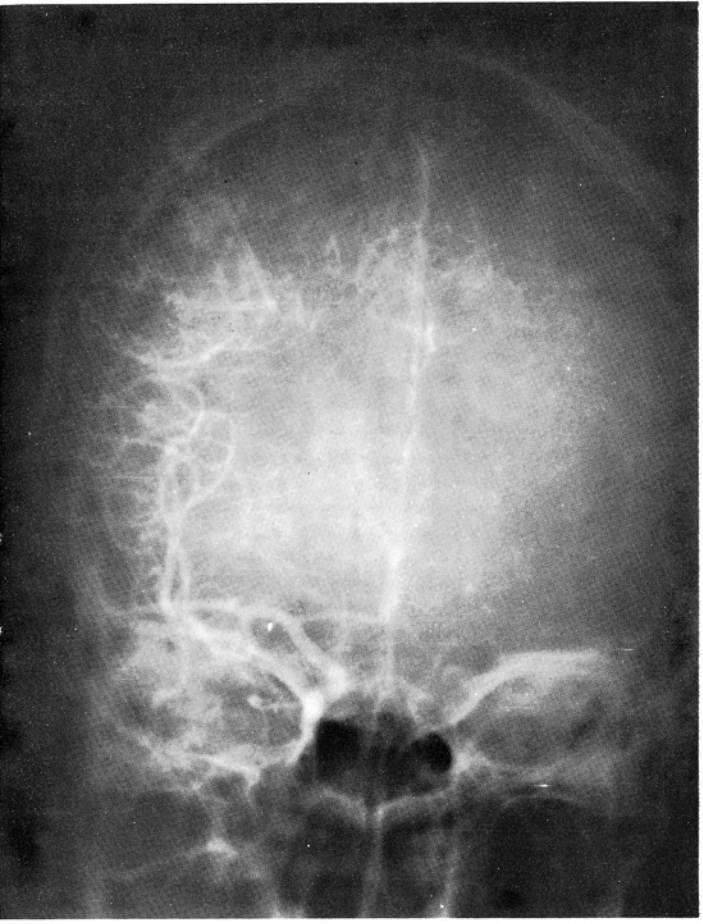

Fig. 1—Arteriogram in late arterial phase showing evidence of increased vascularity in the area adjacent to the tumefaction of the skull.

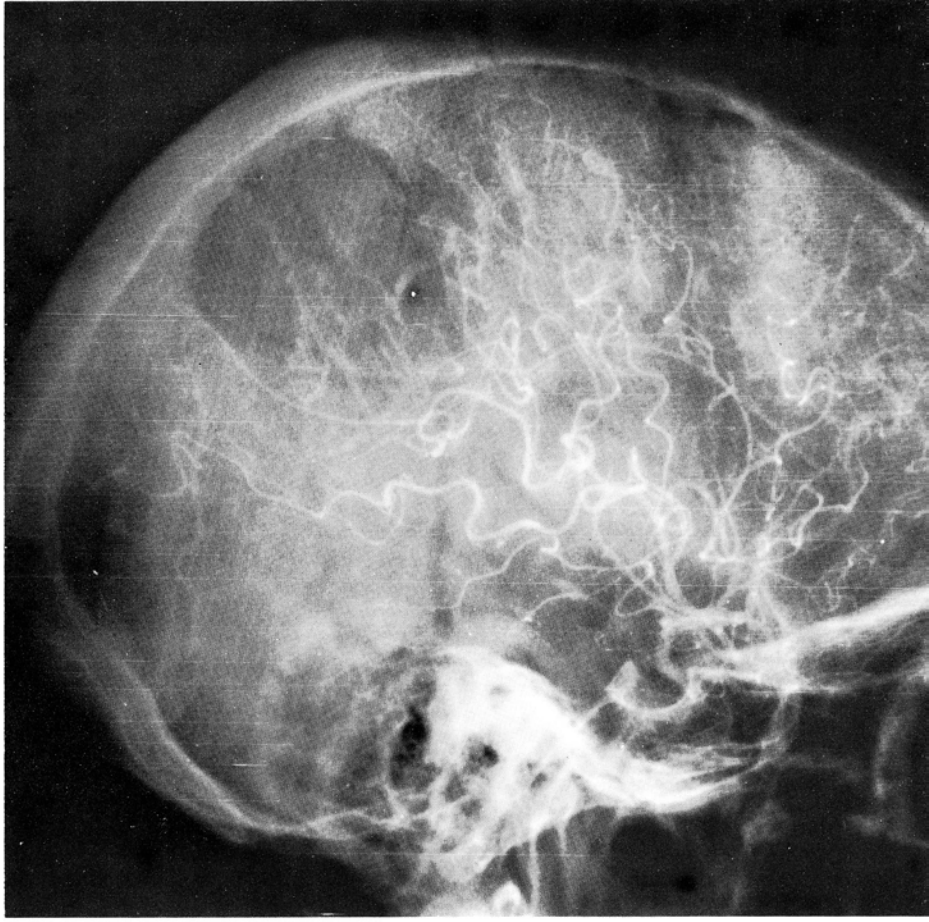

Fig. 2—Large area of bone destruction in the parietal region and displacement of the branches of the middle cerebral arteries around the defect.

have been in the meninges rather than in the skull bones themselves. Meningeal sarcoma is another possibility, but these are rather rare tumors and there was no bone reaction such as you see in meningeal sarcomas. I have seen a number of meningeal sarcomas with only clean cut bone destruction so I would not be able to rule out this possibility on the basis of the evidence. I don't know why we would suggest hemangioendothelioma on the basis of the film.

Dr. Regato: Drs. J. Lemon, of Denver, and H. Hauser, of Cleveland, also suggested a carcinoma of the scalp with osteomyelitis. Dr. J. W. McMullen, of Colórado Springs, and Dr. P. C. Swenson, of Columbia, South Carolina, suggested a metastatic carcinoma.

Operative findings: On February 7th, 1962, the mass was excised with the underlying and surrounding 8 cm fragment of the cranial wall. The tumor was twice as large inside as outside the skull. Hemostasis was difficult and had to be carried out with tantalum plate.

On February 16th, 1962, the patient was discharged in good condition. In July she was in an automobile accident and injured her knee; the roentgenogram revealed a fracture of the femur which was thought to be due to the presence of metastases and submitted to radiotherapy. She was reported well on September 27th, 1962.

A retrospective review of this patient's history revealed that she had had a thyroidectomy 9 years previously, but no tumor had been suspected.

Dr. Zimmerman: This tumor has a disarmingly benign appearance on microscopic study. It is composed of cuboidal cells containing small, round nuclei and forming acini. Many of the acini contain colloid. The conclusion is mandatory that the tumor represents thyroid gland, but its position within the skull and its benign appearance justifies some hesitation in diagnosis. Nevertheless, precisely this type of thyroid tumor, so benign looking, has been described as favoring metastases within the calvarium and its contents. This point was stressed in the chapter on Metastatic Neoplasms in our Atlas of Tumors of the Nervous System.

Dr. Zimmerman's diagnosis: METASTATIC THYROID CARCINOMA.

Histopathologic Diagnoses Submitted by Mail

Metastatic thyroid tumor	101
Ependymoma	24
Pituitary adenoma	10
Parathyroid adenoma	5
Sweat gland tumor	4
Others	7

Dr. Zimmerman: The vast majority thought as I did that this represented a metastatic thyroid tumor. Ependymoma is ruled out on the basis of the fact that no ependymoma secretes a deep pink staining colloidal-like material into the acini; and ependymomas that form this kind of acinar structure are lined by ciliated epithelium and not this low cuboidal type of epithelium. I cannot understand which of the three types of pituitary adenoma these participants had in mind who diagnosed this lesion. It is certainly not a chromophobe adenoma; it isn't an eosinophilic adenoma and it certainly isn't a basophilic adenoma. The pars intermedialis—the part that is lined by cuboidal epithelium and does secrete a colloidal substance—may certainly produce locally an adenoma which is not malignant, does not metastasize to the skull and doesn't produce erosion of bone and of the overlying connective tissue and epithelial lining of the scalp. I too for a moment thought of parathyroid adenoma. Superficially the non-colloid containing glands look a little like a parathyroid, but parathyroid adenomas which become malignant and then would metastasize to the skull are exceedingly rare. I have only seen one case myself: Doctor Castleman who probably has had the largest experience with these tumors in this country informed me that he had only seen six of them, and none metastasized

to the skull; they all invaded locally and metastasized to the lung by the blood stream. A sweat-gland tumor does not produce a colloidal secretion. The glands are smaller but the cells themselves are larger, are more granular and paler in color, and the lumens are filled with a very thin type of secretion, not this heavy type of pink staining colloidal material.

Dr. Regato: Most of the experts diagnosed metastatic carcinoma of the thyroid. Dr. R. A. Keffler, of Lubbock, Texas, suggested a parathyroid adenoma. Dr. L. Lowbeer, of Tulsa, Oklahoma, pointed at the possibility of a nodular hydradenoma of the scalp but concluded to a giant-cell glioblastoma. Dr. J. B. Frerichs, of El Paso, suggested a tumor of the sweat glands.

Dr. Bucy: If we need further evidence that our old criteria of a "five year" cure of malignant tumors is a false one, this case is certainly more evidence in that direction. Here we have nine years from this woman's thyroidectomy until this operation; three years after she first noted the swelling on her scalp.

Leo Lowbeer, M.D., Tulsa, Oklahoma: I think in my slide the colloid has been removed or the slide was understained with eosin because although I looked for colloid I couldn't find any. What is puzzling about this case, however, are the neurologic findings. I do not understand the changes in the left extremities with a left-sided tumor and a Babinski on the left side and a patellar reflex diminishing on the left side also.

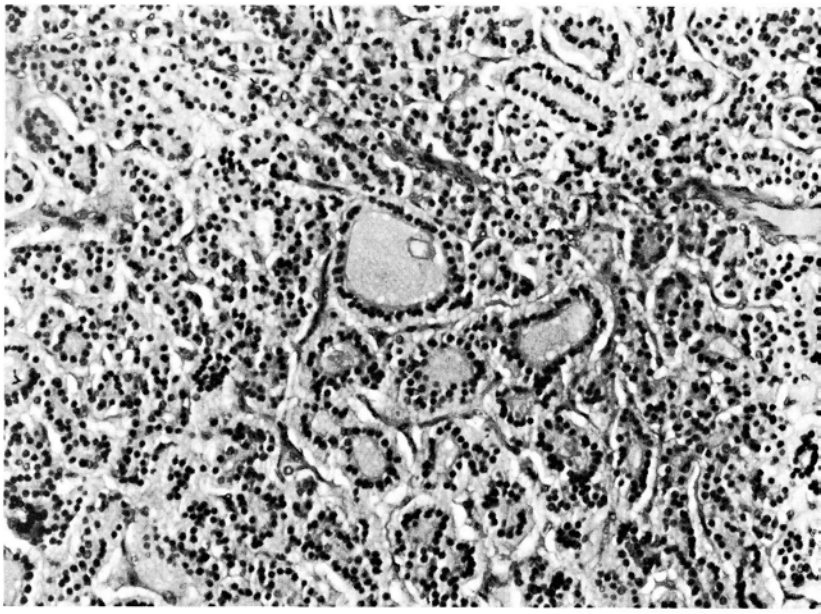

Fig. 3—Photomicrograph of tumor showing acinar structure. Some acini contain colloid (H & E, x 180).

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7. Chronic Subdural Hematoma (?)

Contributed by D. L. Alcott, M.D. and J. J. McCort, M. D., San José, California

THE PATIENT was a 50-year-old man in February, 1959 when he complained of symmetrical weakness and tremor of his arms. Physical examination revealed an abnormally large head and definite muscular wasting of all extremities but no sensory troubles.

Dr. Taveras: The presented roentgenograms consist of a frontal and lateral view of the skull. Both films demonstrate the presence of marked enlargement of the skull apparently in all diameters. There is evidence of erosion of the dorsum sellae indicating long standing increased intracranial pressure. There are many streaks of calcium situated bilaterally and apparently mostly at or near the surface of the brain.

The enlargement of the head would indicate a long-standing condition evidently going back to childhood. Inasmuch as the patient is now 50 years of age, it is obvious that it must be a very benign condition. The erosion of the sella turcica indicates that this lesion has been accompanied by long-standing increased intracranial pressure. A careful scrutiny of the calcium deposits shows that on the right side there is suggestive linear arrangement which describes a concave appearance. This configuration would be in favor of that which is seen in long-standing subdural hematomas which undergo calcification. On the left side this appearance cannot be discerned, but the configuration of the calcium shadows would not deny the possibility that they could be at or near the surface of the brain following the contour of the cerebral hemisphere. Between this and the inner table of the skull again a wide space is noted. The configurations just described would favor bilateral subdural collections of fluid which, if present since childhood, probably would now be subdural hygromas but which were evidently precipitated by subdural hematomas. Other conditions capable of producing similar findings are indeed difficult to find. Parasitic diseases should be mentioned, but the configuration does not suggest either cysticercosis or echinococchus cyst. Toxoplasmosis would be unusual with the apparent ability of the patient to function to the age of 50 years and with evidences of increased intracranial pressure. Other inflammatory conditions producing diffuse intracranial calcification such as cytomegalic inclusion disease fall in the same category as toxoplasmosis. The possibility of a diffuse teratoma of the cerebral hemispheres should also be included in the differential diagnosis although this entity is rather rare and it is doubtful that the patient would live to age 50.

In summary, we are dealing here with a 50 year old man with an extremely large head, scattered linear deposits of calcium apparently on the cortex of the brain and possibly, also, on the inner table of the skull against the dural surface. There is evidence of, in addition to the head enlargement, erosion of the sella turcica, which indicates increased intracranial pressure of long standing.

Dr. Taveras' impression: Chronic bilateral SUBDURAL HYGROMAS secondary to subdural hematomas.

Roentgenologic Impressions Submitted by Mail

Sturge-Weber	25
Toxoplasmosis	21
Endarteritis cerebri	9
Paget's disease	8
Histoplasmosis	6
Coccidiomycosis	5
Others	23

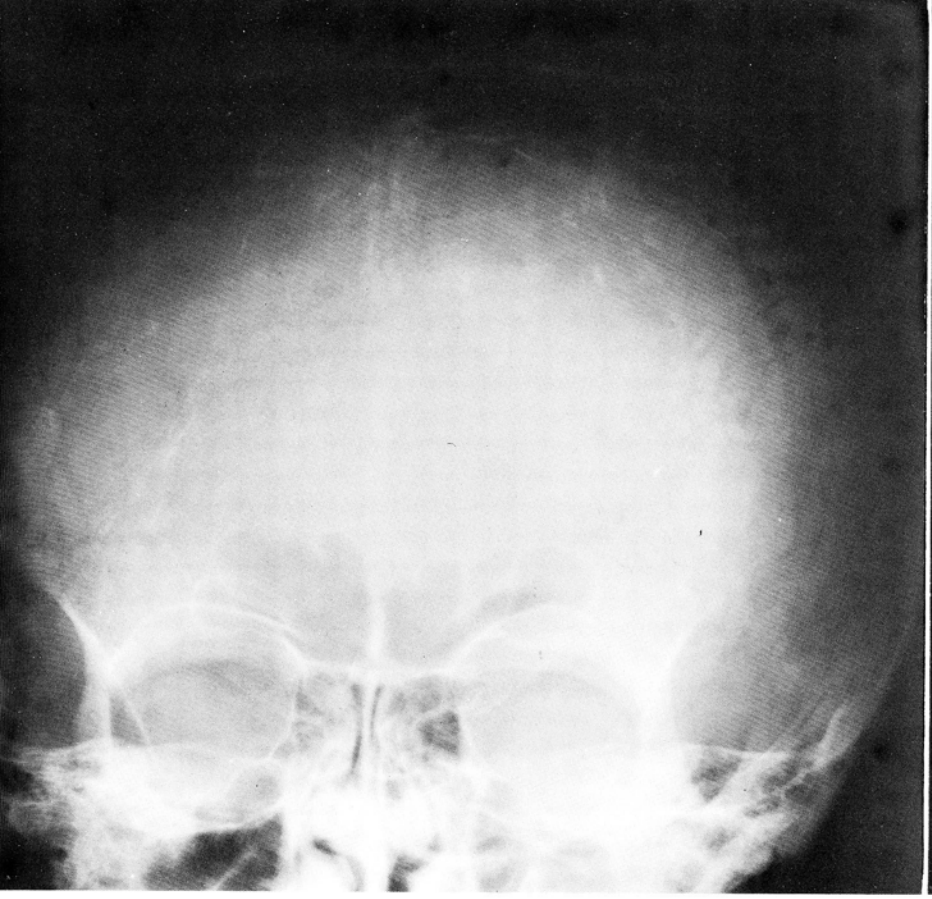

Fig. 1—Frontal roentgenogram showing marked dilatation of the skull. Streaks of calcium near the surface of the brain, bilaterally, are not well demonstrated in the photographic reproduction.

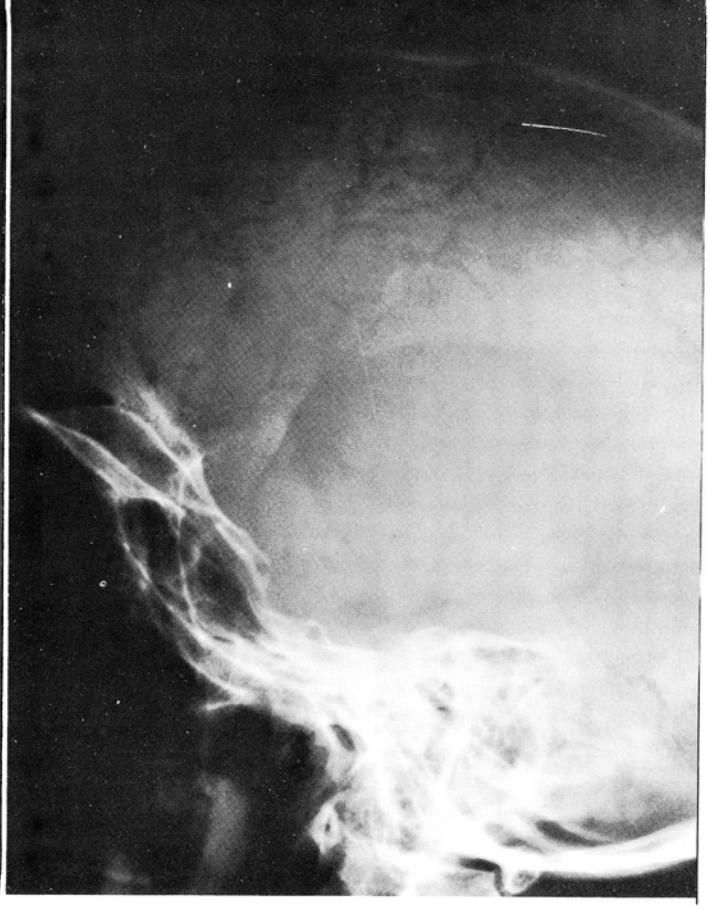

Fig. 2—Lateral roentgenogram shows erosion of the dorsum sellae.

Dr. Taveras: A diagnosis of Sturge-Weber would appear to be most unlikely from the evidence presented. These specks of calcium were linear and straight; they did reach the inner table at some points and not at other points particularly as seen in the frontal projection on the right side. The Sturge-Weber calcifications are usually convoluted and found in the great majority of instances in the posterior half of the hemisphere, although I have seen a few cases with calcifications anterior to the coronal suture. A toxoplasmosis would be most unlikely because although it may indeed cause this diffuse calcification I do not believe that it would have permitted this patient to function until he is 50 years of age. Penfield and Galen wrote a paper based on the history of a family where several members had a condition of diffuse cortical calcifications in the brain and biopsies yielded what they called an endarteritis cerebri; in the reported cases, however, the calcifications were globular, dense, speck-like, whereas here they were linear in configuration. There is no roentgenologic basis for defending a diagnosis of Paget's disease. The bones were not thickened so that the enlargement of the head could not be explained on the basis of the thickening of the bone. I think histoplasmosis causes calcifications in the lungs and spleen very commonly but I have not seen a documented case of histoplasmosis with diffuse calcifications in the brain. I would imagine that the calcium deposit would be speck-like rather than linear. I cannot see why anybody would make a diagnosis of coccidiomycosis, but perhaps someone has seen an appearance such as this that I am not familiar with.

Dr. Regato: Drs. H. Hauser, of Cleveland, T. O. Gabrielson, of Ann Arbor, and J. C. Lemon, of Denver, suggested a Sturge-Weber syndrome. Dr. P. J. Hodes, of Phliadelphia, favored a tuberous sclerosis; he stated that the patient's age rules out such diagnoses as toxoplasmosis and cytomegalic disease.

Subsequent history: A diagnosis was made of amyotrophic lateral sclerosis with pseudo bulbar palsy and hydrocephalus probably secondary to toxoplasmosis. The patient developed dysphagia and dyspnea; his general condition deteriorated and he expired on November 22nd, 1959.

Autopsy revealed a very thick dura mater. The brain was compressed medially. Between the dura and the arachnoid there was a thick yellow exudate. At the base of the brain the meninges were fused. Both cerebral hemispheres showed atrophy and in addition the left temporal lobe appeared hypoplastic.

Dr. Zimmerman: What information of a pertinent nature is supplied in this case is scant and some of it is misleading. For example, it is difficult to understand the significance of "an abnormally large head". Also, the statement that "scattered streaks of faint calcification over the calvarium, particularly on the right hemisphere," leaves the precise localization somewhat dubious. But it probably isn't important anyway.

The microscopic preparation can be reconstructed to represent two closely lying thick-walled arteries, each of which has been slit open and is therefore distorted. These vessels lie in areolar connective and adipose tissue. This, of course, eliminates the possibility of an intracranial situ for these vessels. It is much more likely that they are from the cervical region of the patient, and therefore it is suggested that one vessel represents the external, and the other the internal, carotid artery.

Since the vessel walls are greatly altered by atheromatous change (one of them contains some calcification in the media) it is difficult to identify either elastic tissue or smooth muscle fibers. These vessel wall constituents would have made indeed an absolute identification of these structures as blood vessels. Their absence made it seem momentarily possible that what looked like collagenous connective tissue structures represented the periosteum and dura of the skull. But the presence of atheromatous change in one of the vessels, tentatively identified as the internal

carotid artery, together with amorphous material which is quite probably thrombus, warrants the diagnosis of atherothrombosis of internal carotid artery.

Dr. Zimmerman's diagnosis: ATHEROTHROMBOSIS OF INTERNAL CAROTID ARTERY.

Histopathologic Diagnoses Submitted by Mail

Cyst (parasitic, epidermoid)	52
A-V malformation	24
Subdural hematoma	19
Meningeal carcinomatosis	8
Cavernous hemangioma	6
What hath God wrought!	1
Others	48

Dr. Zimmermans I, too, thought of the possibility of a parasitic cyst but I just cannot see any parasites, nor do I see an inflammatory process of a kind that would go with an old, long-standing cystic process. I do not know on what basis the diagnosis of arterio-venous malformation could be made on the slide that I received. I see nothing in my preparation that would even remotely suggest a carcinoma, nor can I see anything to suggest a cavernous hemangioma because these are probably thick-walled vessels.

Dr. Regato: Drs. G. D. Toll, of Denver, and K. J. Zülch, of Cologne, offered subdural hematoma. Drs. J. B. Frerichs, of El Paso, and R. Delcourt, of Brussels, preferred parasitic cyst. Drs. H. L. McGaffey, of Oklahoma City, and W. J. Frable, of Chicago, diagnosed epidermoid cyst.

Dr. Bucy: It struck me that in that lateral view of the skull there was a severe degree of platybasia. Was there a severe degree of platybasia with a malformation at the foramen magnum which resulted in the degree of hydrocephalus which this man had?

Dr. Taveras: Of course we had no basis for making the diagnosis of hydrocephalus. Platybasia of course is known to occur as a consequence of long-standing increase in the intracranial pressure starting in childhood.

Dr. Bucy: It is obvious that this man must have had sufficient weakness and atrophy in his extremities to let someone make the diagnosis of amyotrophic lateral sclerosis. This would suggest that he had severe involvement at least of the cervical portion of his spinal cord. Furthermore a diagnosis of pseudobulbar palsy was made, which would suggest either that he had severe involvement of his brain stem or of both cerebral hemispheres. And lastly he died with a dysphasia, also evidence that he had severe involvement of his brain stem. At autopsy we found a marked thickening of his dura mater as the most significant finding. A hypertrophic pachymeningitis is primarily and usually a disease of the cervical portion of the spinal canal; but it is not invariably limited to that area, for there have been many cases of hypertrophic pachymeningitis in which the condition has spread into the posterior fossa to involve the roots, if not the brain stem itself, and there have been cases in which it involved the dura mater over the cerebral hemisphere.

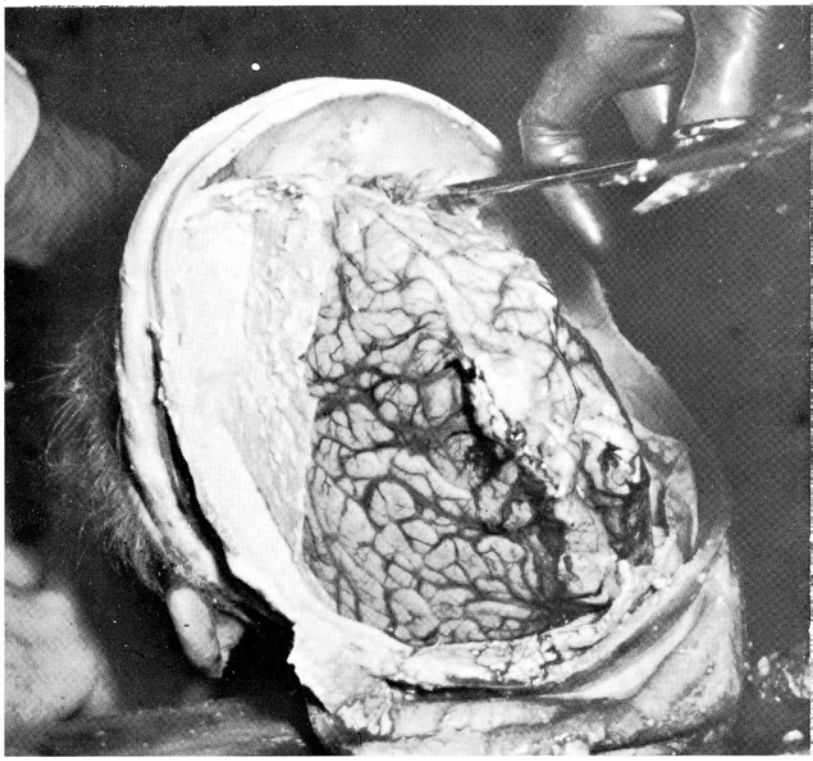

Fig. 3—Gross appearance of intracranial contents at autopsy.

D. L. Alcott, M.D., San Jose, California: It is our feeling that this did represent the dura. The diagnosis on the clinical grounds was made by Doctor Walter Freeman and he is a fairly eminent neurologist; he also saw the gross and I think even cut in the gross specimen and has reviewed the microscopic sections. As nearly as I can recall there was no evidence found to substantiate lesions in the brain stem or the cervical cord. We thought that this was a chronic calcifying subdural hematoma.

Editor's Note: A number of the slides distributed to the participating pathologists, including those sent to Dr. Zimmerman, were insufficient to establish a diagnosis; however, it was the opinion of Dr. Alcott, who contributed the case and performed the autopsy as well as of Dr. Zülch, of

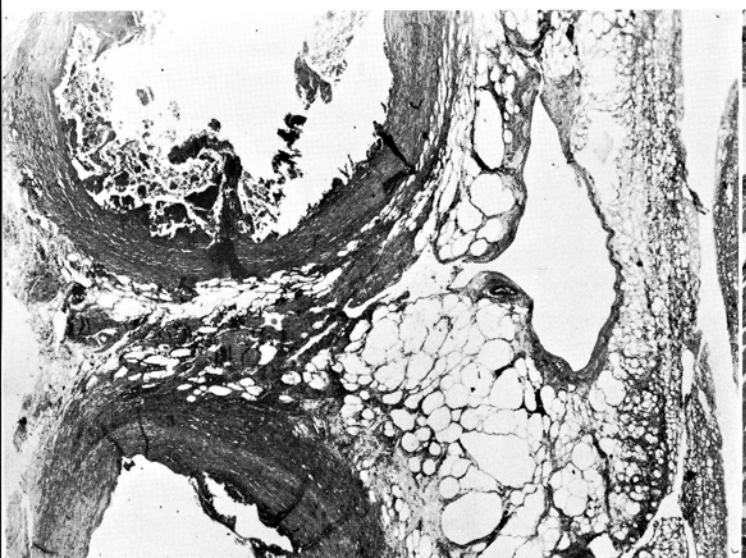

Fig. 4—Two adjacent thick walled blood vessels in areolar and adipose connective tissue. One artery is partially filled with atherothrombotic material. (H & E, x 20).

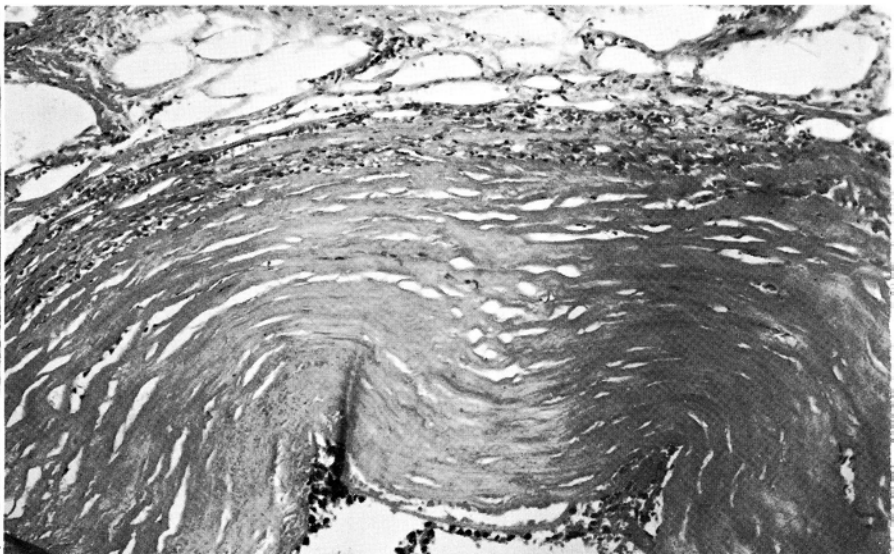

Fig. 5—Photomicrograph of thick, hyalinized structure which resembles a large vessel wall but which is purported to be dura. The kariorrhectic nuclei in the upper part of the micrograph lie either in the adventitia, if this is a vessel, or in the epidural space. This microscopic picture precludes a definitive diagnosis (H & E, x 120).

Cologne, Germany and Dr. Morgan Berthrong, of Colorado Springs, that they could make a diagnosis of subdural hematoma on the slides that they examined. In deference to them we have titled the presentation of this case as Subdural Hematoma; in deference to our eminent guest pathologist, Dr. Zimmerman, we have added a question mark!

Davidoff, L. M. and Dyke, C. G.: Relapsing juvenile chronic subdural hematoma. Bull. Neurol. Inst. New York, 7: 95-111, 1938.

8. Chromophobe Adenoma of the Pituitary

Contributed by J. M. VAETH, M. D. and O. N. RAMBO, M.D., San Francisco, California

THE PATIENT was a 25-year-old man in June, 1959, when he complained of severe frontal headaches of nine months duration; more recently he had noticed marked thirst and malaise. Physical examination revealed no neurological abnormalities.

Dr. Taveras: Two films taken following the ventricular injection of a moderate amount of gas, one made in frontal and one in lateral projection have been submitted. The film made in frontal projection shows a marked degree of bilateral, fairly symmetrical ventricular dilatation. The septum pellucidum is slightly tilted so that its lower portion is slightly further to the right than its upper portion. A small amount of gas is seen within the third ventricle which is markedly dilated and seems to contain a soft tissue mass within it. The lateral projection confirms the ventricular enlargement and, in addition, shows the presence of elevation of the floor of the lateral ventricle just behind the foramen of Monro. A soft tissue mass seems to be present in this region and there is a posterior margin to this soft tissue mass which suggests that it has a slightly lobulated smooth contour. A drop of air is seen in the suprasellar region but I cannot tell whether this is in the anterior third ventricle or in the subarachnoid space. The mass is on the posterior aspect of the foramen of Monro certainly, but whether it extends to involve the inferior anterior portion of the third ventricle cannot be stated from this film which was made with the patient lying on the side and using the vertical beam. Ordinarily, the anterior portion of the third ventricle is shown on films made in the supine position with the chin lifted using the horizontal beam. The lateral view of the skull also demonstrates evidence of long-standing increased intracranial pressure; the calcium outline of the sella turcica has disappeared completely and so has the calcium in the region of the planum sphenoidale and in the floor of the anterior fossa at least on one side.

The findings indicate the presence of a mass within the third ventricle. What is not clear is whether this represents a mass which is well localized involving the roof of the third ventricle or whether it occupies the entire third ventricle. The anteroposterior film made in the supine position indicates that at least some gas is capable of entering the anterior portion of the third ventricle and I would, therefore, assume that a good portion of the anterior aspect of the third ventricle is patent and not filled by a mass. Moreover, there is a fairly sharp posterior margin to the mass as traced down from the floor of the lateral ventricles into the area of the third ventricle which has a well-defined smooth circular contour. Because of the location, of this contour and the bulging into the floor of the lateral ventricles, I would favor a colloid cyst as the most likely possibility. The obvious differential diagnosis is between a colloid cyst and another type of third ventricle tumor. I do not believe that this represents a pinealoma because of the location of the portion of the mass that I can visualize although I am aware of the fact that some pinealomas may spread around the third ventricle and metastasize through the subarachnoid space. A diffuse glioma of the third ventricle is the other possibility, either an ependymoma or an astrocytoma. Colloid cysts are usually located on the superior wall of the third ventricle and in the posterior aspect of the foramen of Monro, they may bulge into the lateral ventricles and are rounded or slightly lobulated. They do not usually obliterate the anterior aspect of the third ventricle, but they may be adherent to one wall of the third ventricle.

Dr. Taveras' impression: COLLOID CYST OF THE THIRD VENTRICLE.

Roentgenologic Impressions Submitted by Mail

Craniopharyngioma	25
Pinealoma	21
Hypothalamic tumor	14
Pituitary adenoma	9
Cyst (colloid)	7
Others	23

Dr. Taveras: I did not think that this would be a craniopharyngioma of the ordinary type because it was a lobulated tumor high in the third ventricle and bulging into the lateral ventricles. About 75% of craniopharyngiomas have sufficient calcium in them to be shown radiographically; there was no calcification in this case. The lack of enlargement of the sella turcica does not necessarily militate against craniopharyngioma because a good proportion of them, particularly the ones that arise in the hypothalamus, are not accompanied by sellar enlargement; but I think this is certainly not a bad diagnosis. Pinealoma, that is a tumor of pineal origin, is also a good diagnosis because these tumors can spread into the third ventricle and also metastasize to the subarachnoid space; the pinealoma would ordinarily have the main mass posteriorly and metastasize forward, whereas in this case one could see a posterior margin to the mass; it is possible, although I considered it less likely. Hypothalamic tumor falls in the same category as craniopharyngioma of hypothalamic origin or a gliomatous type of tumor. Pituitary adenoma frankly did not occur to me, because I did not see sufficient changes in the sella turcica. I have seen pituitary adenomas grow high into the third ventricle, but they usually displace the third ventricle rather than invade it.

Dr. Regato: Drs. J. A. Campbell, of Indianapolis, and J. C. Lemon, of Denver, made a diagnosis of pituitary tumor. Drs. J. R. Galloway, of Albuquerque, and W. F. Kraemer, of Knoxville, suggested a hypothalamic tumor. Drs. R. E. Graf, from Denver, and P. J. Hodes, of Philadelphia, favored a pinealoma.

Operative findings: On May 12th, 1959, a bilateral Torkeldsen's shunt procedure was done. The lesion was judged surgically inaccessible. The patient was followed

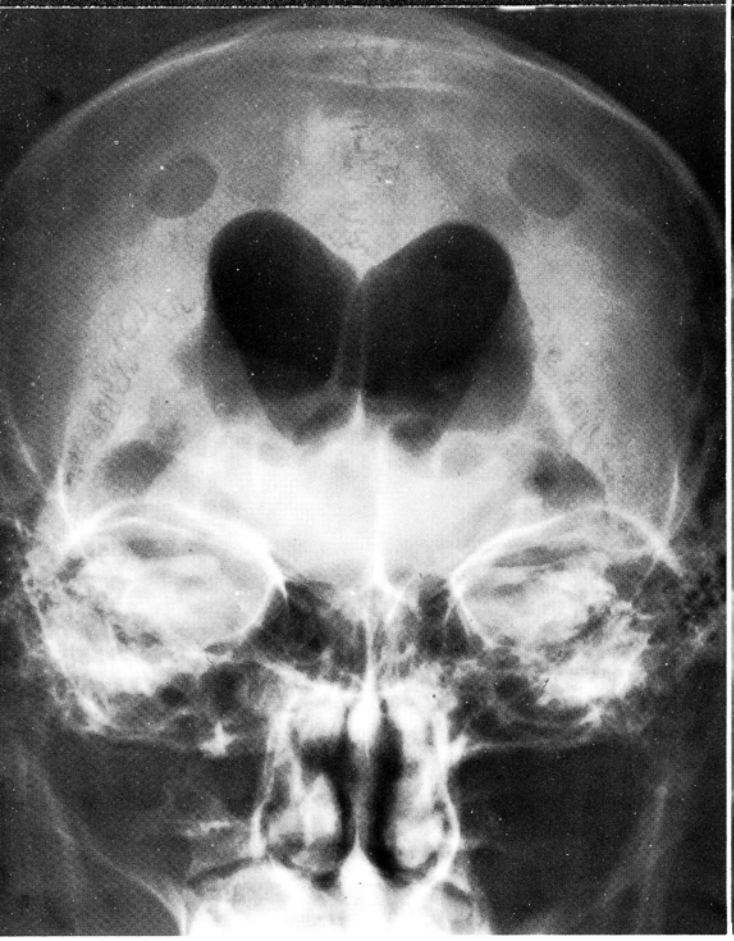

Fig. 1—Ventriculogram showing symmetrical ventricular dilatation and slight tilting of the septum pellucidum.

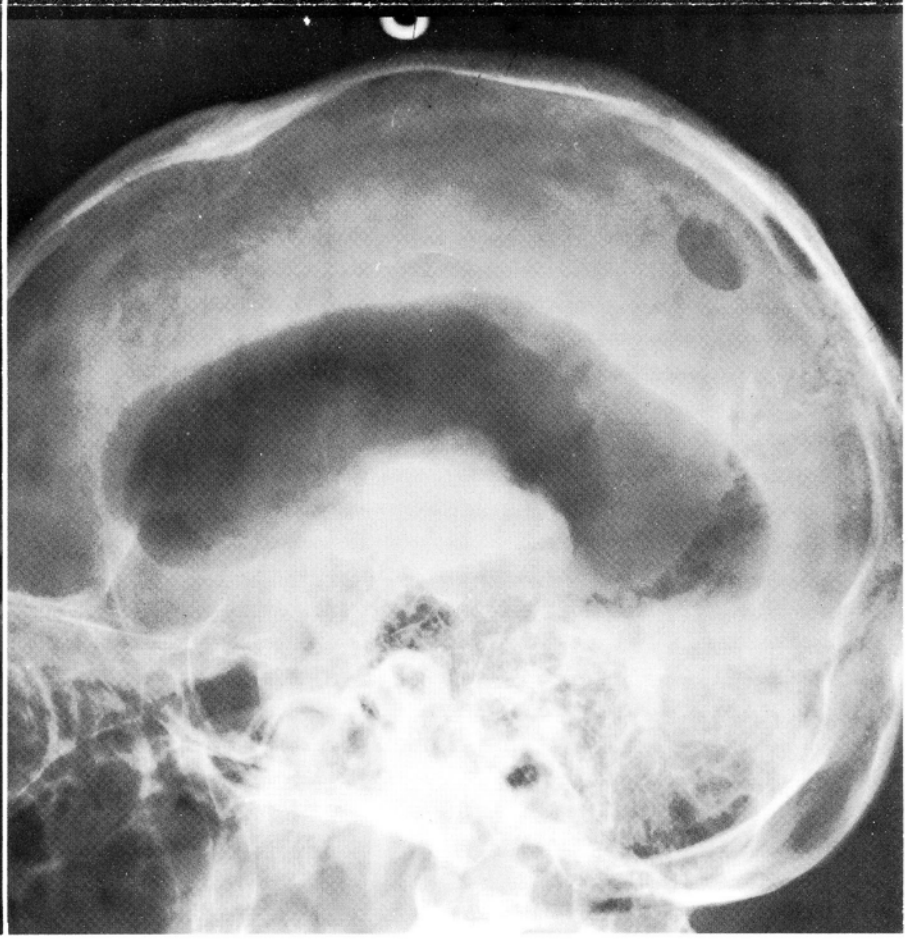

Fig. 2—Ventriculogram showing elevation of the floor of the lateral ventricle and a mass just behind the region of the foramen of Munro.

and he remained unchanged until May, 1962 when he began to lose his memory and the roentgenograms showed enlargement of the previously noted mass.

On May 16th, 1962, a right fronto-temporal craniotomy was done; upon entering the right lateral ventricle the tumor presented itself immediately beneath the wall; it was reddish in color and so soft that it could be removed by suction. There was minimal vascularity. Complete removal was not possible.

Dr. Zimmerman: The tumor cells in this case have a strikingly uniform appearance and are composed of sheets and clusters resembling the structure of an endocrine gland. The cells have scant cytoplasm and prominent small, round nuclei. They are identified as chromophobe cells of the pars anterior of the pituitary body. As is frequently the case in chromophobe tumors, there is extensive fresh hemorrhage. It is well known that the endocrinologically quiescent chromophobe adenomas often become clinically noticeable because of a sudden hemorrhage into them.

Dr. Zimmerman's diagnosis: CHROMOPHOBE ADENOMA of the pituitary body.

Histopathologic Diagnoses Submitted by Mail

Ependymoma	60
Chromophobe adenoma	53
Astroblastoma	10
Pinealoma	10
Meningioma	7
Malignant choroid tumor	6
Others	10

Dr. Zimmerman: I don't know on what basis a diagnosis of astroblastoma was made. Astroblastomas are cells with prominent, abundant cytoplasm as a rule. They look very much like the protoplasmic astrocytes and they tend to form collars or cuffs around blood vessels and their processes are attached to blood vessels. The more malignant type of astroblastoma made up of spongioblasts, which is a smaller cell than the protoplasmic astrocyte, also is characteristically a tumor that forms cuffs of many cells around blood vessels. I saw nothing like this nor do I see any processes at all in this chromophobe adenoma. This perhaps is again a good point to indicate that the term "pinealoma" is meaningless: this is not glioma of the pineal gland; it is not a dysgerminoma, for there are no large epithelioid cells mixed with clusters of lymphocytes, nor are there hair or teeth or other structures like one sees in a teratoma of the pineal, so what kind of pinealoma can it be? Only the clinical suggestion that the patient had diabetes insipidus made some of us think in terms of a so-called pinealoma, the dysgerminoma which frequently has a transplant on the tuber cinereum associated with this condition. Histologically it is a totally impossible diagnosis to make. Those of you who thought of meningioma I again want to warn: there are no cells forming whorls, onion-skin like arrangements of mesothelial cells around the center core, and there are no psammoma bodies in this tumor. A choroid plexus tumor forms papillary projections and they are quite a different type of structure than the one we see in this case.

Dr. Regato: Drs. A. O. Severance, of San Antonio, and D. S. Russell, of Surrey, England, also diagnosed a chromophobe adenoma; Dr. Russell suggested that ependymoma should be eliminated by special stains. Drs. L. Lowbeer, of Tulsa, and M. Wheelock, of Chicago, offered ependymoma.

K. J. Zülch, M.D., Cologne, Germany (by mail): This is an epithelial tumor with evenly distributed capillaries; occasionally we find radiating patterns suggestive of ependymoma. An exact diagnosis is impossible without description of where the growth came from and what was the condition of the sella turcica. Elsewhere the tumor is suggestive of chromophobe adenoma (see paper by Antoni who has described these relations).

Subsequent history: From June 4th to July 17th, 1962, the patient received a series of irradiations with Cobalt-60

through two lateral fields 8 x 8 cm in diameter: a total of 5,000 roentgens was delivered at the level of the tumor in 44 days. After three weeks of treatments his memory started to improve and was much better upon completion of treatments.

On September 17th, 1962, the patient complained of vomiting and lumbar pain. The spinal tap revealed fluid of yellow color with 5,000 red blood cells per mm^3 and no white cells; the pressure was 240 mm of water. He was discharged improved without further treatment. It was thought that the trouble was due to a non functioning shunt in the presence of an easily coagulating fluid. On October 15, 1962, there were no complaints and no neurological abnormalities.

Dr. Bucy: Here we have a tumor which could be dealt with reasonably well surgically even three years after the patient originally presented himself for treatment. I think that undoubtedly had he been operated upon in 1959 instead of 1962 it would have been even simpler. I would not wish to use a shunting procedure unless I was convinced that the tumor could not be attacked surgically because this is an unsatisfactory way of dealing with tumors of this sort. I, too, have had craniopharyngiomas with perfectly normal sella turcicas; sometimes even with a sella turcica which looked as if it had been flattened by pressure from above. I quite agree that it is not the usual thing and I would not make a diagnosis of pituitary adenoma here on the basis of the radiographic evidence presented, even though that is what the tumor ultimately turned out to be histologically.

There are those who believe that all pituitary adenomas should be treated by radiation therapy, and there are those who believe that they should first be attacked surgically. I have used both forms of treatment and I have returned to operating upon pituitary adenomas with visual disturbances because I think the results are better than when we have treated them initially with radiations. On the other hand I would insist that all of those patients with pituitary adenoma that I operate upon be given radiation therapy following the operation because if one fails to do this he will have a fair percentage of recurrences which will require additional treatment at a later date.

James P. Galloway, M.D., Albuquerque, New Mexico: This is another example of a tumor which could have been easily diagnosed if a pneumoencephalogram rather than a ventriculogram had been done initially. None of us would have missed this tumor. I called this a hypothalamic glioma and I would like to ask Dr. Taveras if in these tumors with the cistern encroached upon, can one differentiate between a tumor arising in the hypothalamic area and a solid tumor of the third ventricle?

Dr. Taveras: If the tumor is bulky enough the interpeduncular cistern will be encroached upon primarily by suprasellar tumors, as well as suprasellar extensions of intrasellar tumors. The encroachment however would present a lower margin which is convex caudally and therefore the usual diagnosis of a mass can be made. I am glad that you made the point that a pneumoencephalogram would have probably solved the problem here. I have refrained from talking too much about technique because in exercises such as these the films presented are only one or two and we are supposed to try to get out of the films whatever we can; but pneumoencephalography would have ordinarily been done here, not only to see the suprasellar region but also to visualize the fourth ventricle. We would have liked to see whether this tumor may have come up from behind and grown all the way into the third ventricle, such as we have seen, or whether the lesion was arising in the suprasellar area or the hypothalamic region, etc. We didn't even see the anterior portion of the third ventricle. There was evidence of some gas which was capable of going into the third ventricle but how much or how far down we had no idea. The encroachment on the interpeduncular system is common in tumors arising both in the suprasellar region or inside the third ventricle or the hypothalamus. In the hypothalamic and third ventricle tumors the cut-off of the cysterna interpeduncularis will be straight, whereas in the suprasellar tumors the cutoff will be curved and that will decrease as you go upwards toward the deeper portion of the interpeduncular cistern, but we saw no interpeduncular cistern here.

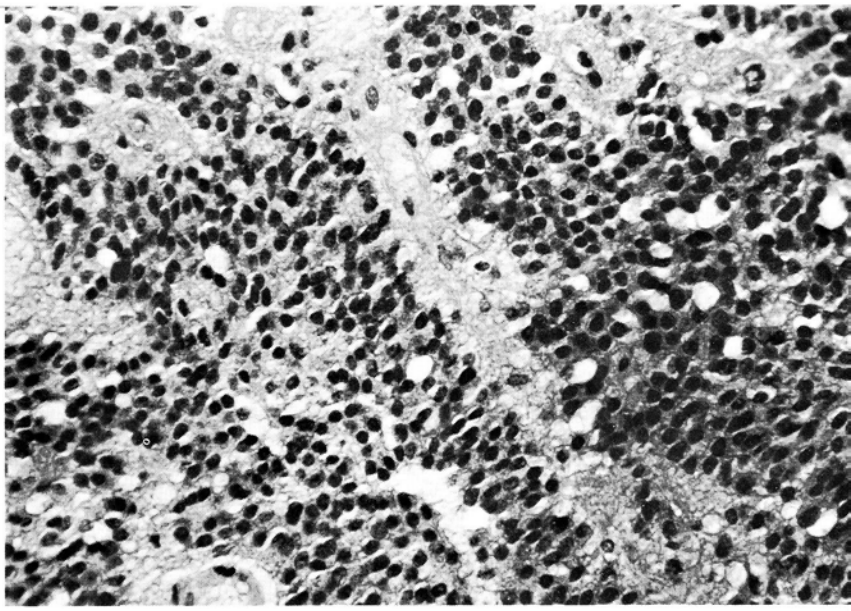

Fig. 3—Chromophobe adenoma of pituitary body. The cells have prominent nuclei and scant cytoplasm and are arranged as in an endocrine gland (H & E, x 275).

Karl T. Neubuerger, M.D., Denver, Colorado: Some ten or twenty years ago Antoni published a paper on "The Myth of Chromophobe Adenomas". He said that all chromophobe adenomas are actually gliomas of any nature. Would you like to comment on that?

Dr. Zimmerman: This is not a gliogenous tumor. I think it is a parenchymal tumor of epithelial structure and is the same type of cell which under various endocrinological stimuli may become eosinophilic at one time, or in the resting stage or chromophobe, or even on occasion may be basophilic. I am a little surprised that several other participants have handed in the diagnosis of ependymoma because there is a class of chromophobe adenoma of the pituitary that does tend to form a superficial resemblance to the type of acini that one sees in one form of ependymoma, but this was peculiarly lacking in this case.

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9. *Diffuse Astrocytoma or Gliomatosis Cerebri*

Contributed by K. W. Dumars, M.D. and J. D. Rice, Jr., M.D., Colorado Springs, Colorado

THE PATIENT was a 12-year-old boy in January, 1960, when he complained of difficulty in chewing, easy falling, shifting gait, diplopia, right side headaches and vomiting; the symptoms had been progressing for several months and had been accompanied by development of indifference and lethargy. Physical examination revealed general muscular weakness, nystagmus on lateral gaze, and paralysis of the soft palate. All reflexes were hypoactive. The EEG was reported within normal limits. The spinal fluid showed 26 lymphocytes, 27 mgm per cent of protein and 61 mgm per cent of sugar.

Dr. Taveras: The submitted films consist of a frontal and a lateral view of a pneumoencephalogram. The antero-posterior projection was made with the patient supine and the lateral projection was made with the vertical beam and the patient lying on the right side. There is no evidence of marked ventricular dilatation but the ventricles are probably slightly larger than usual for a 12 year old child. This history indicates a lesion situated in the posterior fossa, in the region of the pons and medulla. However, the films do not show the aqueduct or fourth ventricle. Moreover, there is no significant visualization of the pre-pontine space behind the clivus.

The findings, therefore, are not those which would lead me to an intelligent discussion of this case. In fact, the discussion will have to be based on the clinical findings and on the absence of certain findings on the pneumoencephalogram rather than on positive evidence. The symptoms and neurological findings as described could be due to involvement of the brain stem itself or they could be due to extrinsic involvement. A tumor within the brain stem would ordinarily produce backward displacement of the fourth ventricle and aqueduct with flattening of the anteroposterior diameter of the fourth ventricle and stretching of this structure which produces an increase in the transverse diameter of the fourth ventricle. A lesion in the subarachnoid space primarily would at least obliterate the air spaces around the brain stem. Of course, obliteration of the pre-pontine cistern can also be produced by a mass within the pons which projects forward so that this structure is in contact with the posterior margin of the clivus. The possibility of an intra-axial brain stem tumor would appear more likely because of the progressive nature of the clinical history and the absence of an elevation of the cerebrospinal fluid protein. In trying to work this possibility into the submitted films, there is no significant ventricular dilatation; this is in favor of a brain stem tumor. The visible portion of the aqueduct, the upper 3 mm, come down to a point immediately caudad to the region of the posterior commissure. This could be due to pressure on the aqueduct at this point. But, inasmuch as the film was made in the recumbent position with the patient lying on his side, this could also be a normal finding. The suprapineal recess

Fig. 1—Pneumoencephalogram in antero-posterior projection showing slightly enlarged ventricles.

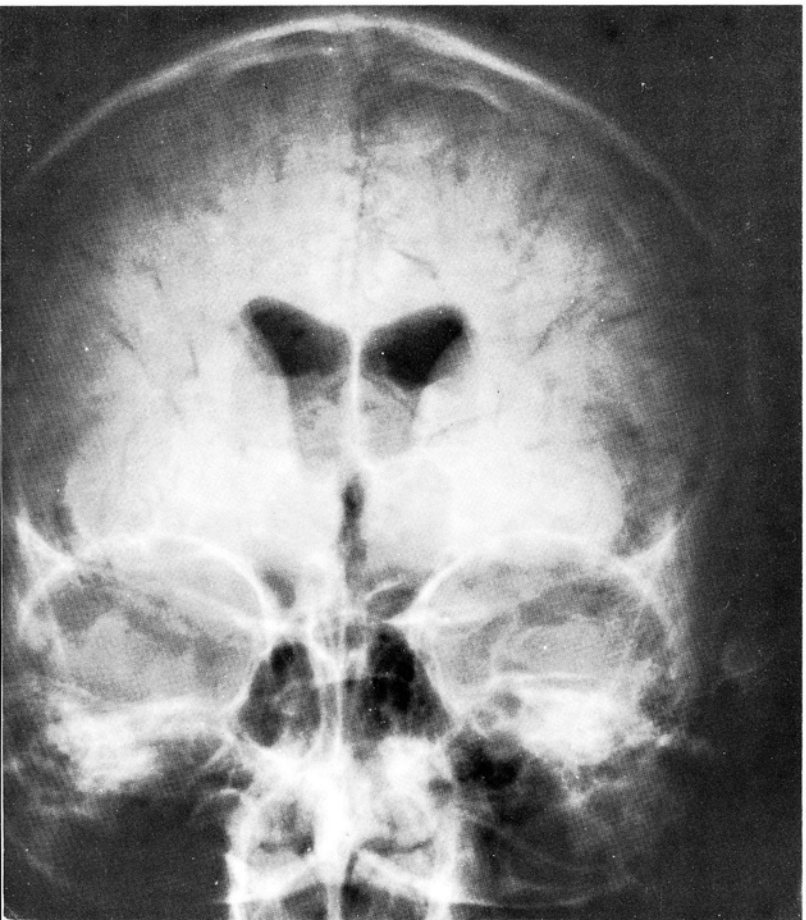
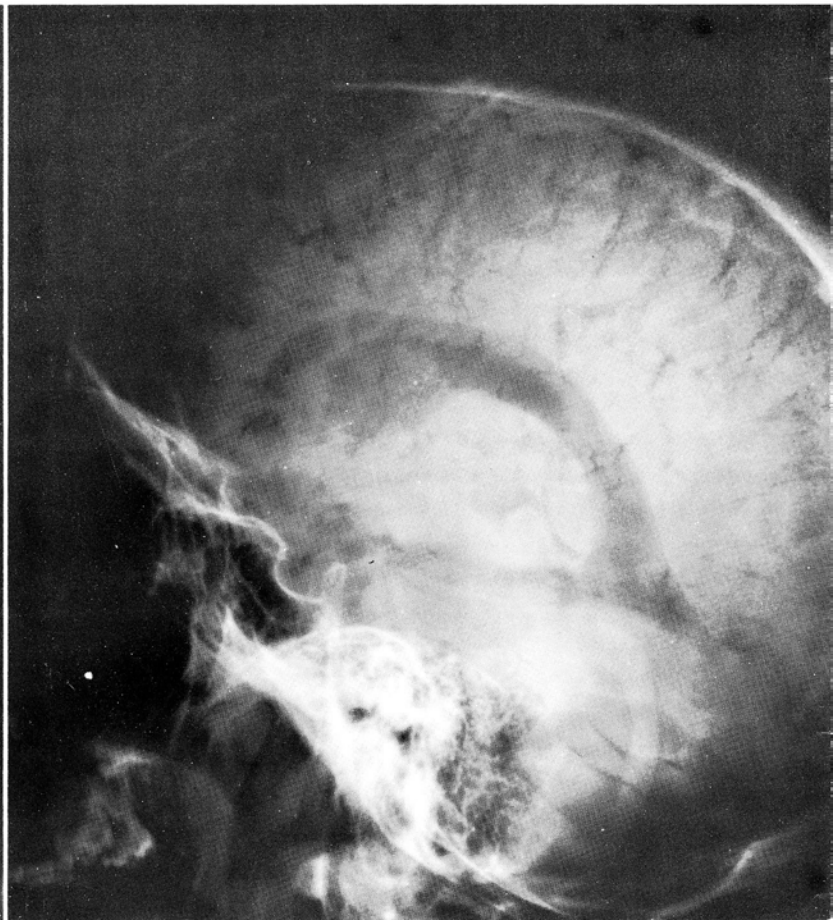


Fig. 2—Pneumoencephalogram failing to show the aqueduct or fourth ventricle.



is long and presents a configuration concave upwards. This is usually produced by the splenium of the corpus callosum and is of no significance.

In summary, this is a 12 year old boy with a progressive history of involvement of the brain stem. The pneumoencephalogram reveals only slight ventricular dilatation which is symmetrical and a tapering upper portion of the aqueduct which could be significant but is not necessarily so. The increase in cell count in the cerebrospinal fluid without elevation of protein would be in favor of the neoplasm being close to the wall of the ventricle.

Dr. Taveras' impression: INTRA-AXIAL BRAIN STEM TUMOR.

Roentgenologic Impressions Submitted by Mail

Pontine glioma	22
Encephalitis	19
Choriomeningitis	13
Cerebellar medulloblastoma	10
Guillain-Barré	8
Others	24

Dr. Taveras: When I say "brain stem tumor" I usually mean a tumor which involves the pons, the medulla and mid-brain but not necessarily all at the same time. If I am able to say that the tumor is in the pons extending into the mid-brain or the lower mid-brain or the thalamus this is more complete information; or the tumor can sometimes be demonstrated radiographically to extend into the medulla. In this case where we have no information roentgenographically speaking we would have to say simply "brain stem glioma". Encephalitis and choriomeningitis are not roentgenological diagnoses. I am not prepared to argue against cerebellar medullablastoma because I did not see the fourth ventricle and the aqueduct so I do not know whether they are or are not displaced; from the little that we saw it appeared that the aqueduct was going to be either in normal position or perhaps a little back but not forward of its normal position, so I would not consider this.

Dr. Regato: Dr. S. M. Jones, of Lubbock, Texas, and Dr. T. O. Gabrielson, of Ann Arbor, suspected a pontine glioma. Dr. P. J. Hodes, of Philadelphia, offered a diffuse glioma of the base of the brain involving primarily the pons.

Subsequent history: A diagnosis of syringobulbia was made. The patient developed paralysis of the 5th, 7th, 9th, and 10th cranial nerves and cerebellar symptoms; pain increased, the patient became comatose and he expired November 15th, 1960.

At autopsy sections of the brain failed to reveal gross evidence of tumor in either hemisphere.

Dr. Zimmerman: Two morphologically distinct cell types constitute this neoplasm. The one is composed of rather large cells with prominent cytoplasm and multipolar processes. These form interlacing fibrillary strands which are stained blue with phosphotungstic acid-hematoxylin. They belong to the astrocytic series of the glia. The other cell type is a much smaller cell and is grouped in clusters. Cells of this variety also give to interlacing fibrils and are likewise identified as astrocytes.

Many cerebellar astrocytomas are, of course, cystic, whereas this is a solid glioma. It is to be noted that the histologic characteristics of this neoplasm have no prognostic significance. The rate of growth is not related to the presence or absence of cysts.

An interesting feature in this case is the presence of clusters of small cells in the molecular layer of the cerebellar folia which resemble the small cell variety of astrocytes. These cells do not appear to be neoplastic and are interpreted as representing heterotopias.

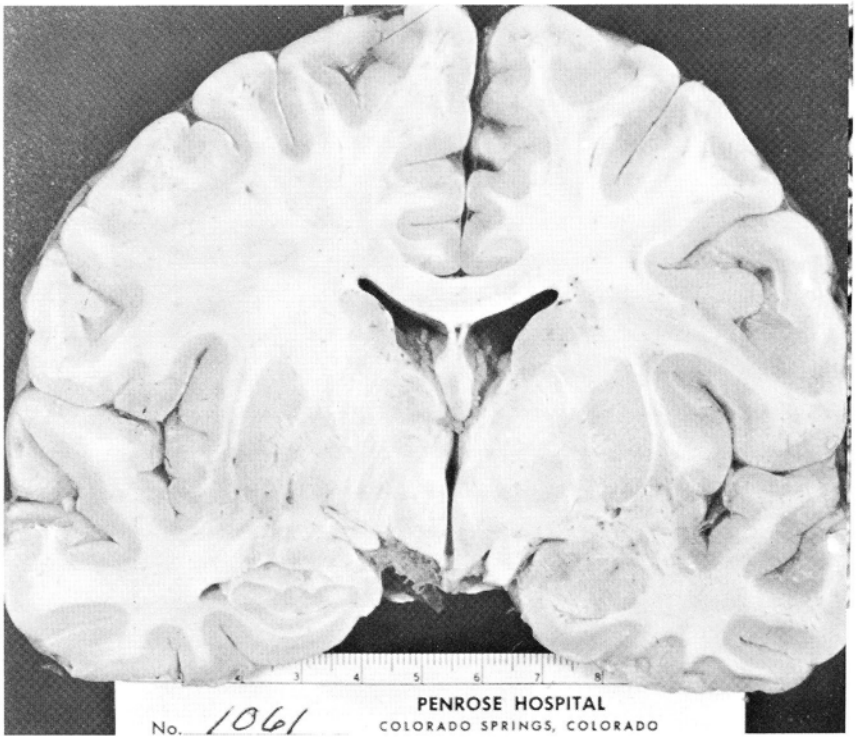


Fig. 3—Cross section of the brain. All sections, like this one, failed to show any gross evidence of tumor.

Dr. Zimmerman's diagnosis: CEREBELLAR ASTROCYTOMA.

Histopathologic Diagnoses Submitted by Mail

Astrocytoma (cerebellar)	111
Spongioblastoma	14
Gliomatosis cerebri	12
Oligodendroglioma	6
Medulloblastoma	3
Gangliocytoma cerebri	1
Nicht Klassifizierbar!	1

Dr. Zimmerman: I believe the diagnosis of spongioblastoma was made on the basis of the smaller cells that occurred in clusters. I think they are young astrocytes but after all a spongioblast is really a young, rapidly growing astrocyte. Spongioblastoma conveys the impression, to me at least, that it is a much more actively growing tumor than is the case in this instance and for this reason I favor the more benign astrocytoma rather than the spongioblastoma. One cannot find too great fault with those who decided that this was gliomatosis cerebri. They apparently are aware of the fact that histologically in other parts of the brain and the cerebral hemispheres clusters of tumor cells like those we saw in the cerebellum are also present. If that is the case then the diagnosis of gliomatosis or astrocytosis cerebri is perfectly all right, but I don't believe one could make that diagnosis on the basis of one section alone. Not by the wildest stretch of the imagination can I make a diagnosis of oligodendroglioma in this case; I saw no oligodendroglial cells at all. Medulloblastomas are tumors that do not lay down a stroma and they occur in areas in which neither mesoderm nor gliogenous stromal tissue proliferate. So that the extensive fibrillary appearance of this tumor would in my opinion be incompatible with the diagnosis of medulloblastoma.

Dr. Regato: Dr. D. S. Russell, of Surrey, England, diagnosed cerebellar astrocytoma, she pointed at the presence of numerous small foci of closely aggregated and less differentiated cells, together with the conspicuous development of sub-pial secondary formation of Scherer which suggest anaplasia. Dr. J. D. Rice, Jr., of Colorado Springs, made a diagnosis of gliomatosis.

K. J. Zülch, M.D., Cologne, Germany (by mail): The tumor cannot be classified with certainty. Large areas consist of long spindle cells with ample fiber production and also with large cytoplasmic astrocytes. One therefore could

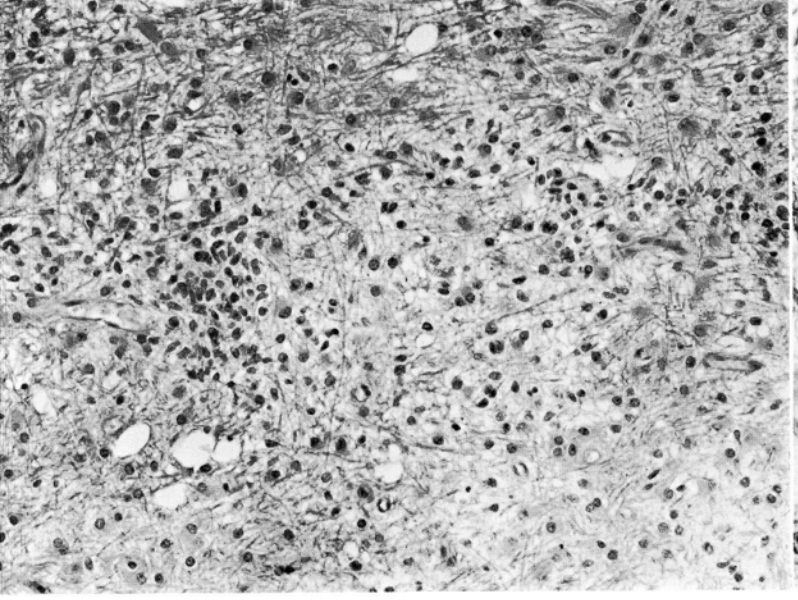


Fig. 4—Photomicrograph of cerebellar tumor. Two distinct tumor cell types are to be noted, one small and lying in clusters and the other large and having multipolar processes (H & E, x 180).

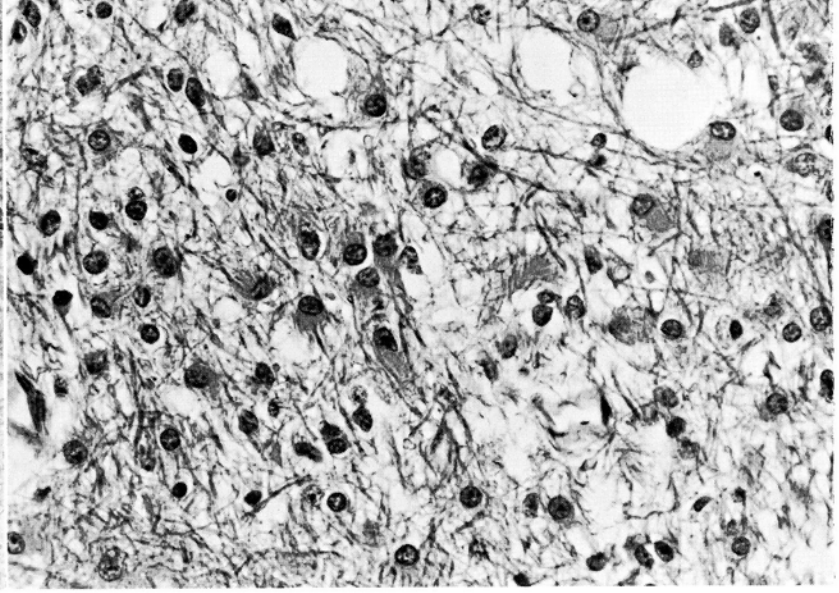


Fig. 5—Both large and small tumor cells produce glial processes (Phosphotungstic acid-hematoxylin stain, x 375).

think of a cerebellar astrocytoma with infiltrating growth. However, we find focal dense aggregations of undifferentiated cells that are rich in chromatin and show clearcut mitotic activity. This is a picture never seen in a cerebellar astrocytoma or spongioblastoma; *it does remind us of medulloblastoma.*

Dr. Bucy: If one is going to use air studies in the diagnosis of brain tumor he must make every effort to demonstrate and study the third and fourth ventricles. Just taking three or four pictures and being content with them is not enough. Spacial views must be taken and no one should be satisfied until he has made every effort to demonstrate this important part of the ventricular system.

There is no question from the case history that we are dealing here with a disease of the brain stem. Whatever disease there may have been in the cerebellum was of secondary importance. I would judge that in all probability the same type of neoplastic disturbance which is seen in the cerebellum might be found in the brain stem.

Certainly there was nothing to do done here from a surgical standpoint. Whether or not radiation therapy will help these people with neoplasms of the brain stem is a serious question. I have not been very impressed with the results of such therapy, and in those cases where it has been effective the results have been of relatively short duration.

Morgan Berthrong, M.D., Colorado Springs, Colorado: The only portions of the brain that did not show these changes were the cerebral gray matter and particularly both frontal cortices. Beginning anteriorly at the level of the anterior portion of the third ventricle and extending posteriorly and down the brain stem into the upper cervical cord exactly the same process that was demonstrated in Doctor Zimmerman's slides was found in our material. The greatest concentration perhaps was in the pons but the cerebellum was just an example and was equally good, histologically.

James Stephens, M.D., Denver, Colorado: Doctor Bucy's criticism was of course well taken. The initial diagnosis here was pontine glioma on clinical grounds, and at the time the pneumoencephalogram was done, the fourth ventricle and the aqueduct were demonstrated and were in normal position.

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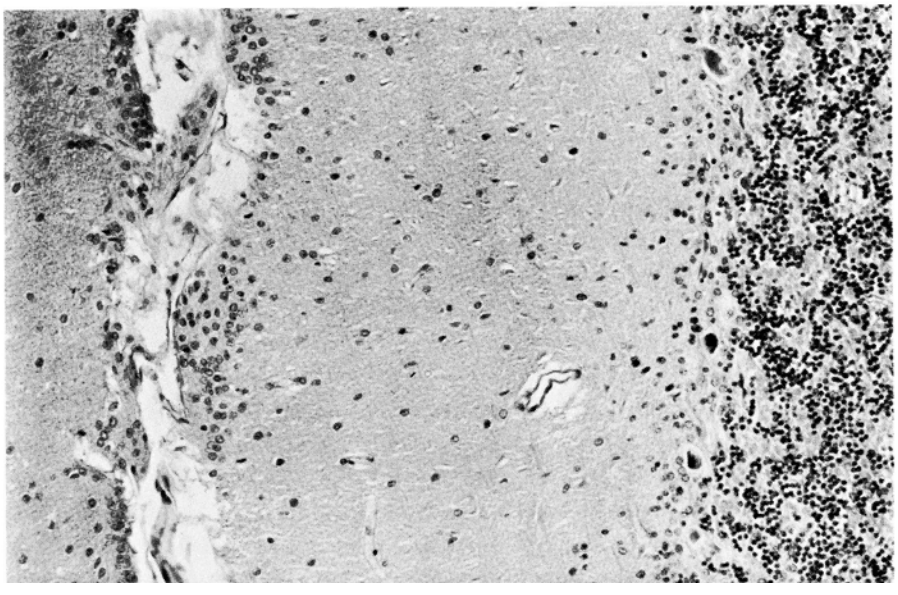
Fig. 6—Photomicrograph of cerebellar cortex to show groups of small round cells (astrocytes?) in subpial layer. These cells are probably not neoplastic and represent heterotopias (H & E, x 150).



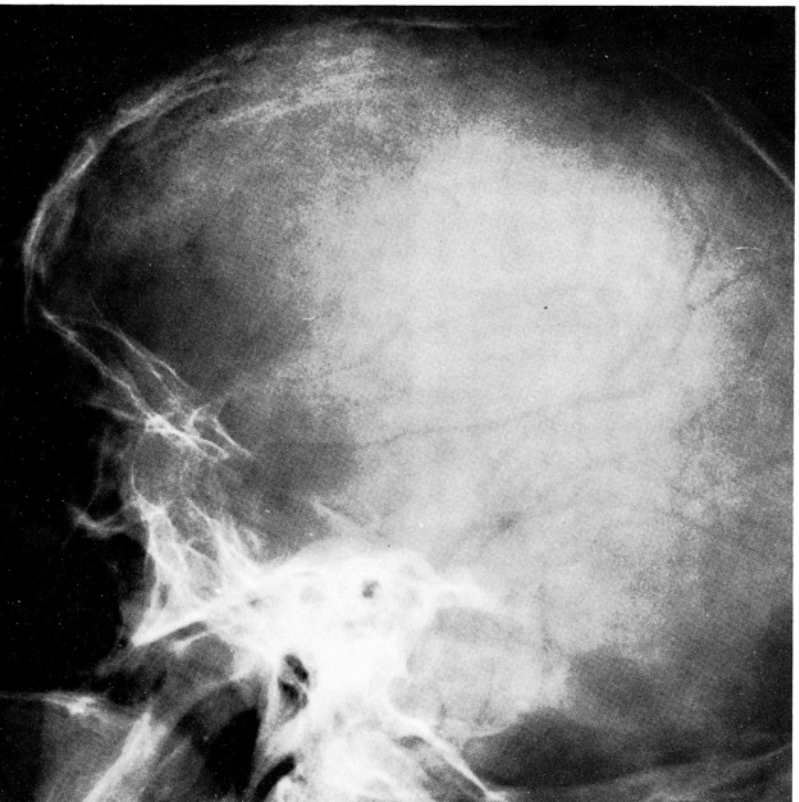
10. Eosinophilic Adenoma of the Pituitary with Sarcomatous Changes

Contributed by M. C. Wheelock, M.D., Chicago, Illinois

THE PATIENT was a 50-year-old woman in December, 1957, when she complained of frontal headaches and vomiting of two weeks duration. Twelve years previously she had received radiotherapy to the pituitary as treatment of acromegaly. Physical examination revealed paresis of the third, fourth, and sixth right cranial nerves.

Dr. Taveras: The submitted film consists of a single lateral view of the skull. The findings are those of destruction of the normal outline of the sella turcica. I cannot, on this moderately rotated lateral view, see any of the portions of the sella turcica including the anterior margin of this structure in the region of the tuberculum sellae or the floor or dorsum. A thin calcium line is seen to extend almost horizontally in front of the petrous pyramid at a point which might correspond to the top of the sella turcica, but whether this represents a portion of the sella or not cannot be discerned from this single film. The two shadows of the middle fossae on each side simulate the floor of the sella turcica but they are not a portion of this structure and should not be confused with it. On the other hand, there is a soft tissue shadow which occupies the entire area around the expected outline of the sella turcica obscuring the air content of the posterior ethmoid cells and of the sphenoid sinuses. A small curvilinear calcium shadow is seen just above the outline of the base of the petrous pyramid which could represent calcification within an old pituitary adenoma. There is another shadow within the confines of the sella turcica which could also represent calcification within an old tumor. The appearance of the skull is not particularly striking for acromegaly. There are only two remaining lower teeth and no upper teeth. The angle of the jaw is not particularly open and the mandible itself is normal in size.

Fig. 1—Roentgenogram showing destruction of the sella turcica.



The obvious question here is whether the previously treated lesion 12 years prior to this admission was actually a pituitary adenoma or whether it was another type of intrasellar or perisellar lesion. Another possibility is that it could be a meningioma in the parasellar region which responded somewhat to irradiation and did not continue to grow rapidly after that. Chordoma would seem to be unlikely because of the duration of the patient's history. Of course, if this patient had a pituitary adenoma previously it does not have to be an eosinophilic adenoma but it could be a chromophobe pituitary adenoma with superimposed acromegaloid features (the so-called mixed pituitary adenoma). No evidence of suprasellar extension with compression of the optic chiasm and visual disturbance is described in the history as given. The lack of signs of optic chiasm compression is in favor of an eosinophilic tumor, but chromophobe pituitary adenomas may grow towards the base of the skull and not project upwards towards the suprasellar region. It is probable that the strength of the diaphragma sella may be a determining factor in the direction in which the tumor will grow. If the sella turcica diaphragm is strong and presents a small opening in the region of the pituitary stalk, the tumor will tend to grow downwardly and destroy the floor of the sella turcica which will become considerably enlarged. Twelve years after having received treatment to the region of the sella turcica for a "pituitary adenoma" the patient comes in with signs of third, fourth and sixth cranial nerve involvement. This would indicate that there is at this time, involvement probably in the region of the cavernous sinus. The ophthalmic division of the fifth nerve also is in the wall of the cavernous sinus and it is not mentioned as being involved. This, however, does not rule out the presence of involvement of the cavernous sinus since the third and sixth nerves are apt to show evidences of compression or invasion earlier than the fifth nerve, as manifested by diplopia. The involvement of these nerves would indicate that there has been invasion of the cavernous sinus and the apparent soft tissue shadow which obscures the air contents of the sinuses, as described above, indicate that the tumor has also grown downward and forward from the sella turcica. The possibility of malignant degeneration should be considered under these circumstances. Another possibility to be considered is that of an unrelated tumor which might have been provoked by irradiation 12 years previously or it may be growing as an independent tumor. I see no evidence of encroachment on the soft tissues of the nasopharynx to justify the diagnosis of a nasopharyngeal tumor. The last possibility, that of a soft tissue tumor such as sarcoma, related to the previous irradiation should also be considered but I believe that this is quite rare. Therefore, I believe we are dealing here with a pituitary adenoma which may have become a

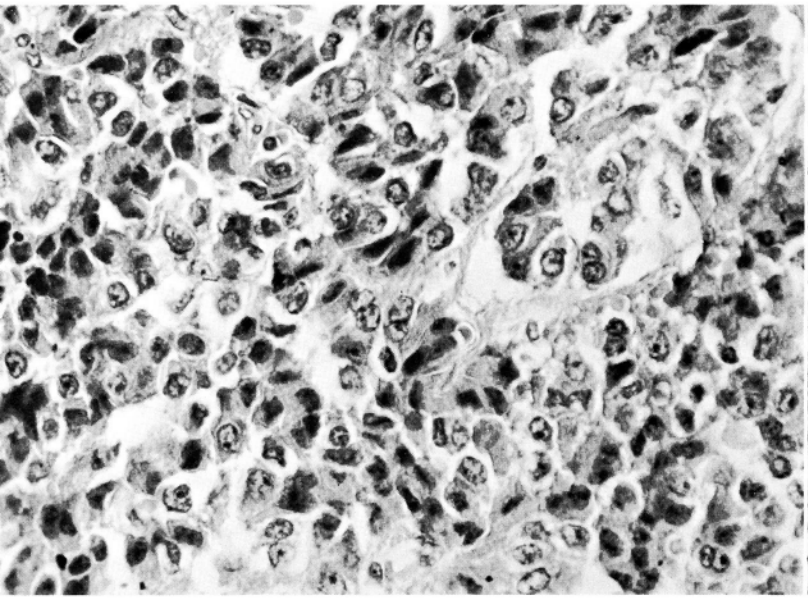


Fig. 2—Photomicrograph of large, deeply eosinophilic cells in pituitary adenoma (H & E, x 450).

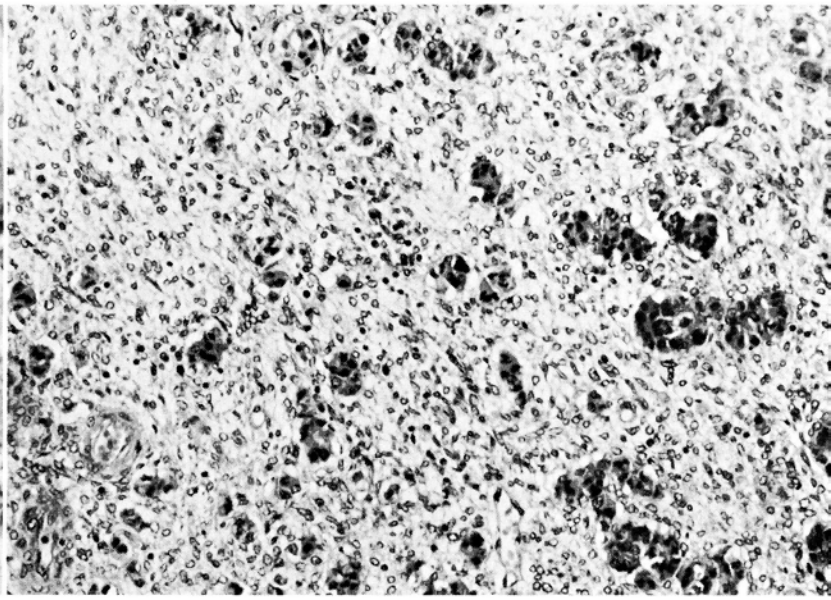


Fig. 3—In the same tumor, nests of gland-forming eosinophilic cells are separated by a cellular stroma of connective tissue. Many of these stromal cells are in mitotic division (H & E, x 180).

malignant adenoma in view of the multiple cranial nerve involvement. The episode which brought the patient to the hospital, that of frontal headaches and vomiting, may well have been related to a meningitis secondary to the tumor rupturing and invading the ethmoid and sphenoid sinuses with or without a preceding cerebrospinal fluid rhinorrhea. The possibility of infection of the meninges in these pituitary adenomas which tend to grow downwards, towards the sinuses, without significant intracranial extension, should always be kept in mind.

Dr. Taveras' impression: PITUITARY ADENOMA, possibly undergoing malignant transformation.

Roentgenologic Impressions Submitted by Mail

Pituitary adenoma	56
Chordoma	9
Meningioma	8
Various tumors	17
Others	19

Dr. Taveras: I have seen involvements of one nerve —the third, the sixth, in what proved to be pituitary adenomas; but involvement of all three nerves, apparently fairly profound, such as in this case I have not seen and I therefore will consider the diagnosis of just simple adenoma as most unlikely. Chordoma is another possibility; I thought that the type of growth and the configuration of the sella were against it. This patient was acromegalic so we thought that meningioma was less likely.

Dr. Regato: Dr. H. Hauser, of Cleveland, favored a recurrent pituitary adenoma. Dr. S. M. Jones, of Lubbock, suggested the possibility of a malignant pituitary tumor. Dr. P. J. Hodes, of Philadelphia, and Dr. B. L. Pear, of Denver, also suggested a malignant pituitary tumor.

Operative findings: On December 30, 1957, a right frontal craniotomy was done. A tumor was found in the pituitary area extending to the right and displacing the carotid laterally. The surface of the tumor was coagulated and an incision done: the tumor was fibrous in consistency and was gutted out. The fragments were mottled, granular and gray-brown in color.

Dr. Zimmerman: This remarkable tumor is in part composed of a classical eosinophilic adenoma. The large cells of this portion of the tumor have cytoplasmic bodies with prominent granules which are deeply eosin-staining. This type of tumor has long been associated with the clinical picture of acromegaly.

There is another part of the tumor, however, which presents a more difficult problem. In this portion of tumor, there are small nests of eosinophilic cells that represent the remnants of the original eosinophilic adenoma, but they are now embedded in a large stroma of fibroblastic cells and their processes. These look like fibroblasts and many are in mitotic activity. They can be identified as of mesodermal origin with special methods such as the Gömöri trichrome stain. In contrast to the eosinophilic parenchymal cells whose bizarre nuclei and nuclear division do not necessarily indicate malignancy, the mitotic activity and invasive behavior of the fibroblastic elements strongly suggest sarcomatous transformation. The presence of sarcoma in a pituitary tumor of benign type which has been irradiated is evidently rare but has now been noted in three previous cases by the present observer.

Dr. Zimmerman's diagnosis: EOSINOPHILIC ADENOMA OF THE PITUITARY BODY WITH SARCOMATOUS CHANGE IN STROMA

Histopathologic Diagnoses Submitted by Mail

Eosinophilic adenoma	117
Malignant pituitary tumor	30
Hitherto unobserved!	1
Others	5

Dr. Zimmerman: The majority agreed that this is an eosinophilic adenoma and I imagine that 30 participants were more impressed with the malignant component than with the eosinophilic adenoma, because I think both are present as you saw.

Dr. Regato: Dr. R. Delcourt, of Brussels, offered a diagnosis of malignant eosinophilic adenoma. Drs. M. Wheelock and M. H. Haber, of Chicago, favored a mixed glioma and adenoma. Dr. D. S. Russell, of Surrey, England, and Dr. M. Berthrong, of Colorado Springs, wondered if the stromal reaction could or not be a sarcoma and referable to previous irradiation; Dr. Russell could find no mitoses and only one giant cell, however.

Subsequent history: Following surgery the patient developed left sided Jacksonian epilepsy and 12 days after operation suddenly collapsed while being photographed.

Autopsy revealed a massive embolus of the pulmonary artery and right ventricle. Coagulated blood, necrosis and residual tumor were found in the pituitary. The adjacent bone was friable.

Dr. Bucy: Fortunately malignant transformation in pituitary tumors is rare, but every once in a while one does come along which invades the dura mater, invades the cavernous sinus, and then one has such difficulties as were present here.

In recent years the neurosurgeon's attitude toward the treatment of the eosinophilic adenoma has changed. In the past it has been the feeling that adenomas of the pituitary gland should be treated surgically only to save vision. In many instances one saw eosinophilic adenoma with severe

gigantism or acromegaly with no involvement of vision and therefore they were not operated upon and were, as in this case, treated with radiation therapy. With the introduction of various forms of replacement therapy, we are able to deal with patients who have had an extirpation of their pituitary gland and extensive extirpations of pituitary adenomas. It has become possible to remove these tumors more extensively, and in fact completely. If this is done early in a patient with acromegaly, before the bony changes become severe, it is possible to prevent further progress of the bony changes and even to reverse them to some extent. I realize that acromegaly is not a matter of life and death, but it certainly is a matter of great importance to these patients, and I believe that as time goes on we will attack these tumors of the pituitary gland very vigorously and probably follow the surgical treatment with radiation therapy.

I was not aware of the fact which has been brought out here that apparently the malignant transformation which can occur in these pituitary tumors may be secondary to radiation. Is that an established fact?

Dr. Regato: I am glad you asked, Doctor Bucy. I welcome the opportunity to repeat that "because you find toads after it rains, it has not necessarily rained toads." In this instance it remains to be proven that radiotherapy is the cause of this sarcoma. I would like to remind you of other well known facts, such as found in giant-cell tumors of the bone. Sometimes these tumors were irradiated and, when they recurred, evidence of malignancy was then found and blamed on the irradiation, but there are similar cases that recur after inadequate excision and nobody blames surgery for being carcinogenic. The clear fact is that they were malignant from the start and this was not recognized until the tumor recurred.

As a radiotherapist, I see no reason why a patient who is curable by a surgical procedure without mutilation or risk should have radiotherapy. Moreover, radiotherapy as applied to these tumors is often done without histologic evidence and may lead to circumstances in which radiotherapy is blamed for what was there in the first place. You advise that the patients receive radiotherapy post-operatively. When radiotherapy is effective post-operatively on the residual of the tumor it could also be equally effective, if done adequately, on the entire tumor. If the tumor is radio-curable it could have been cured as well without the surgical intervention but I personally prefer to treat patients on which I have histologic evidence.

Dr. Zimmerman: It is only fair to admit that one cannot say that it has been proved that these sarcomas are the result of irradiation. These are rare tumors: I have only seen three cases and Doctor Taveras two others; my three had been previously irradiated. I know of no sarcoma in that region in a non-irradiated patient. Altogether we could collect only a dozen cases and I don't know whether they all had received irradiation.

Dr. Taveras: The two cases I have seen had received irradiation ten years before or a little longer; I would like to point out that we have seen between 400 and 500 pituitary adenomas in the Neurological Institute of New York, and therefore the incidence is rather small; I think that the surgical mortality and morbidity far outweigh that type of malignant transformation.

Dr. Regato: If you find sarcomas of the pituitary only in patients who have been previously irradiated you have a strong circumstantial evidence. On the other hand there is no evidence in clinical medicine of any benign tumor that becomes malignant because of irradiation. Actually radiations are definitely cancerigenic on soft tissues, on bone, on the epithelia under special circumstances, usually when administered in short-term massive doses and when sufficient time has elapsed afterward, but there is not real evidence that any benign tumor becomes malignant because of irradiation.

Morgan Berthrong, M.D., Colorado Springs, Colorado: After irradiation, and particularly, say, of the oral cavity, we may see extraordinary spindle-cell change in what was squamous cell carcinoma. Doctor Zimmerman, do you think it possible that these spindle cells which you have considered a second tumor are actually spindle-cell changes in the previous adenoma cells?

Dr. Zimmerman: We judge malignancy by histological criteria, which are often fallacious. The presence of mitoses in pituitary adenomas, the presence of invasion locally, are not criteria for malignancy. In this case, however, as in the other two that I have had, the mitoses that are present, the evidence of the replacement of the gland structure itself and the evidence of invasion of the dura, etc., makes me suspect that it may be malignant. I wouldn't argue the point too strenuously in this particular case.

Arnold Greenhouse, M.D., Denver, Colorado: I had a case of a young lady with an eosinophilic adenoma of the pituitary who received irradiation and a few years later developed a very similar picture of very malignant sarcoma. She expired after two or three surgical interventions.

Mark Wheelock, M.D. ,Chicago, Illinois: You might like to know that we submitted this material to Doctor Kernohan and he came to more or less the same conclusion that we did, that is, that this was definitely an eosinophilic adenoma but he leaned more toward it being a glioma of the posterior lobe, rather than a sarcomatous reaction due to the irradiation.

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II. *Meningioma*

Contributed by S. M. LeBer, M.D., Edmonton, Alberta, Canada

THE PATIENT was a 48-year-old woman in April, 1961, when she noticed tremors, and later weakness of the left arm and leg. Physical examination revealed a hyperactive left patellar reflex and an equivocal Babinski on the left. There was also some diminution of movements of the left shoulder, elbow, and left lower extremity.

Dr. Taveras: The submitted film consists of a single lateral film of a right carotid angiogram made in the mid arterial phase. There is a rather obvious, slightly lobulated well-circumscribed collection of vessels in an area measuring almost 6 cm in diameter high up in the brain, touching the inner table of the skull in the frontoparietal region. The lesion probably straddles the posterior aspect of the frontal lobe and the anterior aspect of the parietal lobe. There is obvious blood supply of this mass by an enlarged posterior internal frontal branch of the anterior cerebral artery and possibly, also, by post-rolandic branches of the middle cerebral artery. A prominent posterior branch of the superficial temporal artery which goes over the edge of the tumor is visualized. Inasmuch as this branch is considerably larger than the anterior branch arising from the same trunk of the superficial temporal artery, I would consider that there is an increased blood flow through this posterior branch as compared to the anterior branch. Although I do not trace direct vessels from the temporal artery branch in question, to the tumor, the increased flow through it would lead me to believe that there must be flow from the external carotid into the tumor area. The middle meningeal artery branches are not well defined in this film, at least two branches are seen to ascend towards the area of the tumor but they are not particularly enlarged. Displacement of branches of the middle and anterior cerebral artery around this mass are seen which are of secondary importance for diagnosis in view of the marked density of the tumor mass.

An anteroposterior film of a ventriculogram was also submitted and this demonstrates the presence of a shift of the septum pellucidum and third ventricle towards the left with a greater shift of the upper portion of the septum pellucidum than of the lower portion. The right lateral ventricle is lower than the left. It is also noted that the lateral angle of the right ventricle has preserved its normal rounded configuration. On this film there is also noted a slight increase in density of the inner table of the skull at the center of a point approximately 4 cm from the midline in the parietal bone, on the right side. The above described findings would favor a tumor which is situated at or very near to the surface of the brain. The position as noted in the lateral view places the superior aspect of the mass immediately against the inner table of the skull and the ventriculogram indicates that this is a tumor which is fairly

Fig. 1—Ventriculogram showing displacement of septum pellucidum and of the third ventricle towards the left.

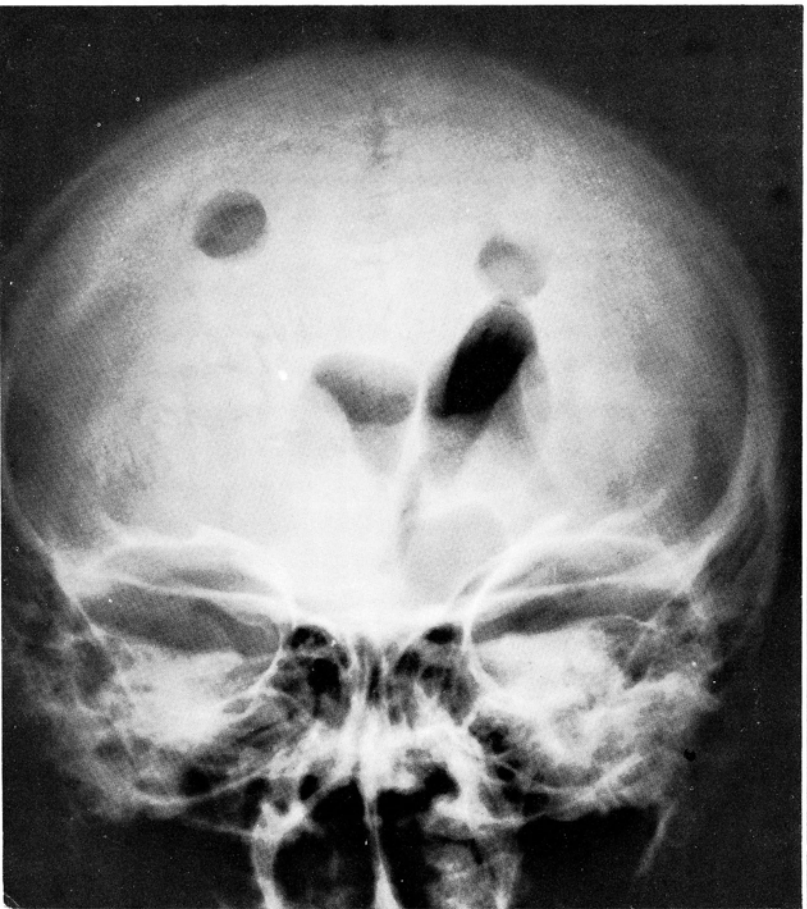
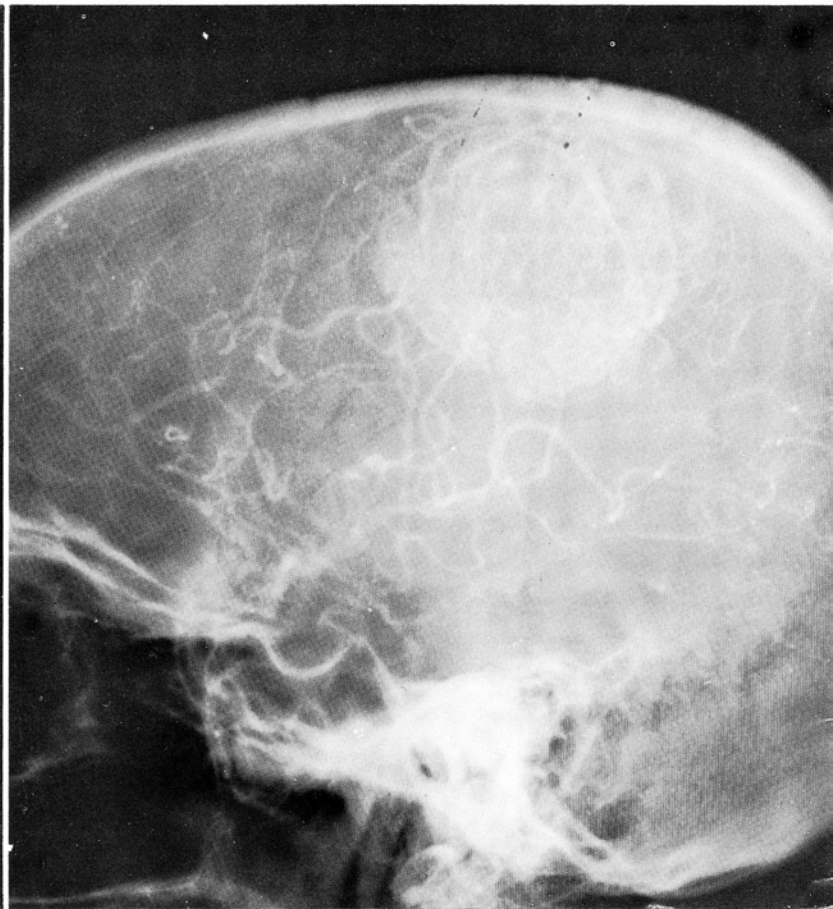


Fig. 2—Right carotid angiogram in mid arterial phase showing well circumscribed collection of vessels in the fronto-parietal region.



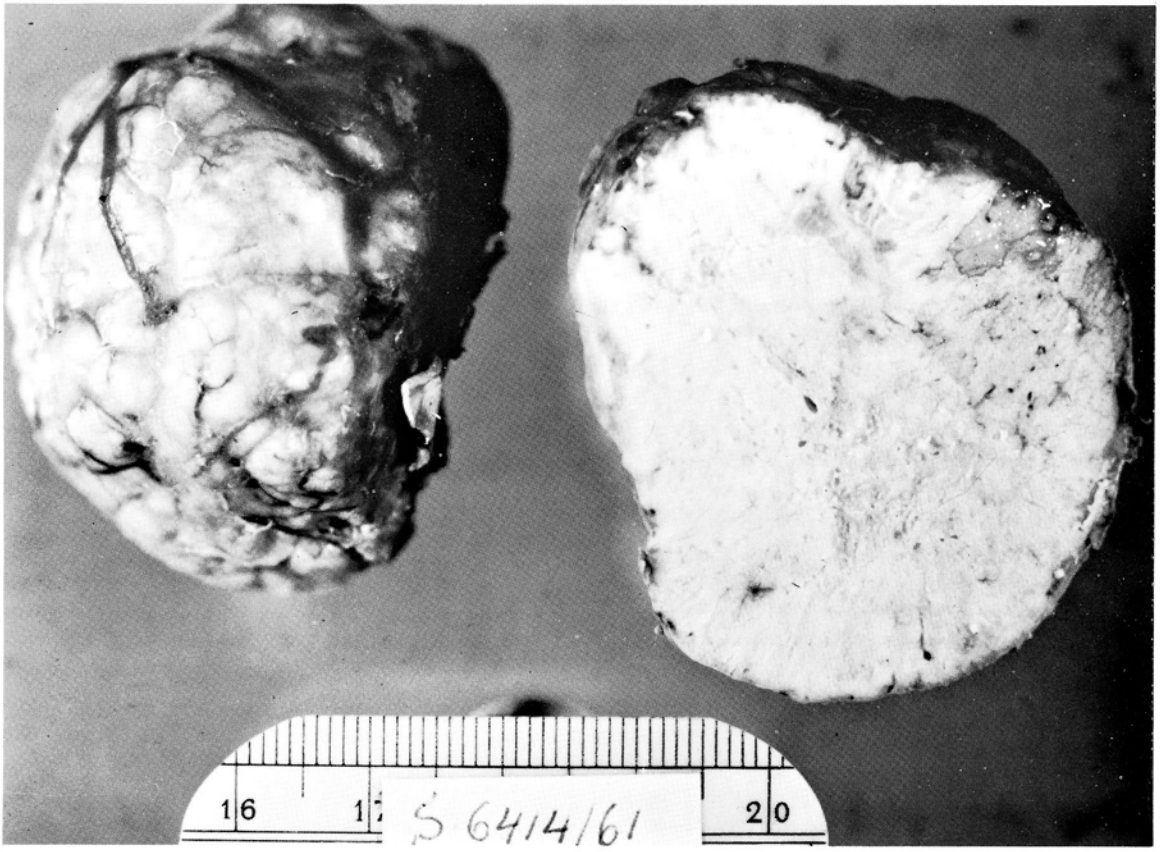


Fig. 3—Gross appearance of tumor, surface and cross section.

far removed from the ventricular wall in view of the fact that the lateral angle has preserved its normal rounded contour. Therefore, we would consider either a meningioma or a glioma which would be intracerebrally located on the surface of the brain and projecting inwardly from that point. The angiogram shows what appears to be a supply of the tumor by a superficial temporal artery. Unfortunately, this should always be considered as doubtful unless there is demonstrated evidence of bone involvement. Ordinarily, the superficial temporal artery does not become involved in the blood supply of a meningioma unless the tumor has invaded bone possibly to include the outer table. There is apparent bone involvement here as evidenced by the questionable slight hyperostosis on the inner table of the parietal bone seen in the frontal film. On the lateral view of the angiogram there are some large vascular channels overlying the posterior portion of the mass which I am not sure are venous or arterial. If they were venous, we would have to suggest that there is an increased speed of circulation through the tumor as compared with that of the rest of the brain. For adequate evaluation of this finding it would be necessary to have a serialogram to determine what the subsequent flow pattern is in the late arterial, intermediate and venous phases. Meningiomas can be supplied by branches of the internal carotid as well as by branches of the external carotid. When external carotid supply is demonstrated it is possible to state the neoplasm is either a meningioma or another type of tumor arising from the bone or meninges. Rarely a glioblastoma could invade the meninges and draw some blood supply from the meningeal arteries.

In summary, we have a 48 year old woman with a demonstrated neoplasm in the frontoparietal region high in the convexity. Because the neoplastic circulation is not adequately studied, or at least, if it was, only a single film is available for examination at the moment, it is not possible to make any further "sophisticated interpretation" of the nature of the tumor. The findings along the inner table of the parietal bone are not sufficiently well defined to make a definite diagnosis of meningioma.

Dr. Taveras' impression: High convexity, or parasagittal, superficially placed INTRACRANIAL NEOPLASM OF THE RIGHT FRONTOPARIETAL REGION.

Roentgenologic Impressions Submitted by Mail

Meningioma (parasagittal)	71
Glioma falx cerebri	9
Parietal tumor	8
Others	14

Dr. Taveras: Gliomas do not occur in the falx cerebri; meningiomas do. Parietal tumor is a very neutral diagnosis to make, particularly in the face of such a profound stain seen on the angiogram.

Dr. Regato: All of the participants mentioned in previous cases made a diagnosis of parasagittal meningioma.

Operative findings: On December 29th, 1961, a right lateral craniotomy was done. A firm tumor 5 cm in diameter was found in the right cerebral hemisphere, it was smooth and on cut section it was homogeneous and creamy pink in color: it was removed.

Dr. Zimmerman: The fact that the patient harboring this intracranial neoplasm is a female and has "a blush of vessels in the parasagittal area" on angiography strongly suggests a microscopic diagnosis of meningioma. On microscopic study the tumor has a lobulated appearance with a pink stroma in which are embedded oval nuclei frequently arranged in whorls. These nuclei are identified as belonging to meningocytes. The tumor is one of the more common types of meningioma. The whorl formation assures this diagnosis even in the absence of psammoma bodies which are often seen in this class of tumor.

Dr. Zimmerman's diagnosis: MENINGIOMA.

Histopathologic Diagnoses Submitted by Mail

Meningioma (meningothelial syncitial)	135
Neurilemoma	4
Others	6

Dr. Zimmerman: Neurilemomas do not form whorls. All of us stand on the diagnosis of meningioma.

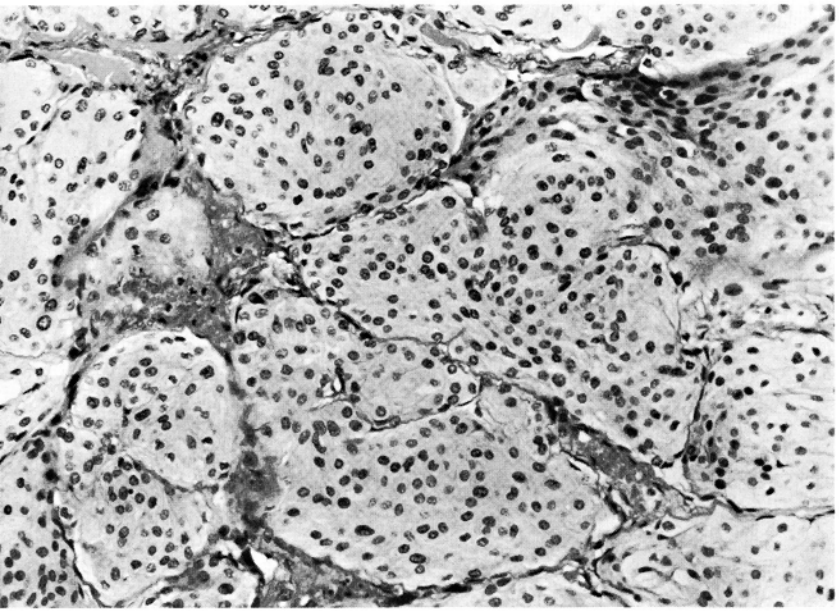


Fig. 4—Photomicrograph of meningocytes arranged in whorls (H & E, x 180).

Dr. Regato: All of the experts agreed on the diagnosis of meningioma except for secondary qualifying designations.

Subsequent history: This patient was examined by Dr. Vance MacDonald on October 15, 1962: she appeared to be getting along well; she was not complaining of headaches or difficulty with her vision, but manifested slight weakness of the left arm and leg. There was some secondary optic atrophy.

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12. *Ependymoma*

Contributed by E. Siqueira, M.D. and J. M. Budinger, M.D., Chicago, Illinois

THE PATIENT was a 14-year-old girl in April, 1960, when she gave a history of repeated episodes of convulsions, at week's intervals. Physical examination revealed complete left homonymous hemianopsia, bilateral choking, and optic atrophy. There was also impaired stereognosis of the left arm and hand and marked intentional tremor of the left side extremities. The EEG showed slow wave focus on the right parieto-occipital region.

Dr. Taveras: The submitted films consist of a frontal and a lateral view of an angiogram taken during the arterial phase. The lateral view demonstrates elevation of the middle cerebral artery branches which is more marked in its posterior aspect than it is in the anterior portion. The posterior cerebral artery is filled and it is noted that its posterior portion is crinkled, accordion-shaped. There is, proximal to the origin of the posterior communicating artery, another arterial branch which appears to arise from the internal carotid artery and is directed posteriorly and downward from this point. However, this arterial branch could equally well originate from the ascending branch of the superficial temporal artery which also passes through this area. I do not see evidence of destruction of bone but there is an area of radiolucency with ill-defined edges in the parieto-occipital region. In the frontal projection there is only slight deviation of the anterior cerebral vessels to the left of the midline which is questionable. There is lateral displacement of the angiographic sylvian point; that is, of the last branch of the middle cerebral artery to emerge from the sylvian fissure. There is a medial displacement of the posterior cerebral artery.

The findings are those of a mass lesion situated in the occipito-parietal region which extends forward and either invades or deforms the structures in the region of the thalamus. The mass is invading or arising from the occipital lobe region and is fairly far medial in location. It produces forward displacement of the medial posterior choroidal artery arising from the posterior cerebral artery and the posterior choroidal artery is rather large. The question here is what type of mass lesion are we dealing with. We assume that this is a neoplasm because of the way in which the history developed. If the branch mentioned previously as arising from the internal carotid artery is a true branch of this artery, it would be a meningeal branch of the internal carotid artery which is usually seen in tumors arising from the meninges and occasionally in tumors that invade the meninges secondarily, but the point from which it arises is above the intracavernous segment of the internal carotid artery and, therefore, it is probably not a meningeal branch of this artery.

There is another dense line which could represent a straight artery over the surface of the tentorium, that is, a tentorial meningeal artery, extending upwards and backwards just above the region of the lateral sinus groove. Under these circumstances we should suggest that this tumor could be a meningeal sarcoma of childhood as against that of an intracerebral gliomatous neoplasm. These neoplasms may invade bone and perhaps the area of radiolucency mentioned above in the parieto-occipital region represents an area of bone involvement. However, the findings are rather tenuous and no definite statements can be made.

In summary, we are dealing here with a 14 year old girl with a large tumor apparently arising in the occipital region and extending forward to invade or displace the thalamic portion of the brain as evidenced by the lateral displacement of the arteries in the region of the angiographic sylvian point. More films of the lateral serialogram are required to determine whether the branch apparently over the tentorium is indeed a meningeal branch supplying the tumor. If so, the diagnosis of meningeal sarcoma should be entertained. This type of tumor is not unduly rare in children. The profound neurological findings would be against the diagnosis of a simple meningioma and in favor of an invasive type of tumor.

Dr. Taveras' impression: RIGHT OCCIPITO-PARIETAL NEOPLASM, possibly a meningeal sarcoma.

Roentgenologic Impressions Submitted by Mail

Right temporal tumor	53
Parieto-occipital tumor	14
Ependymoma	8
Glioma	5
Others	19

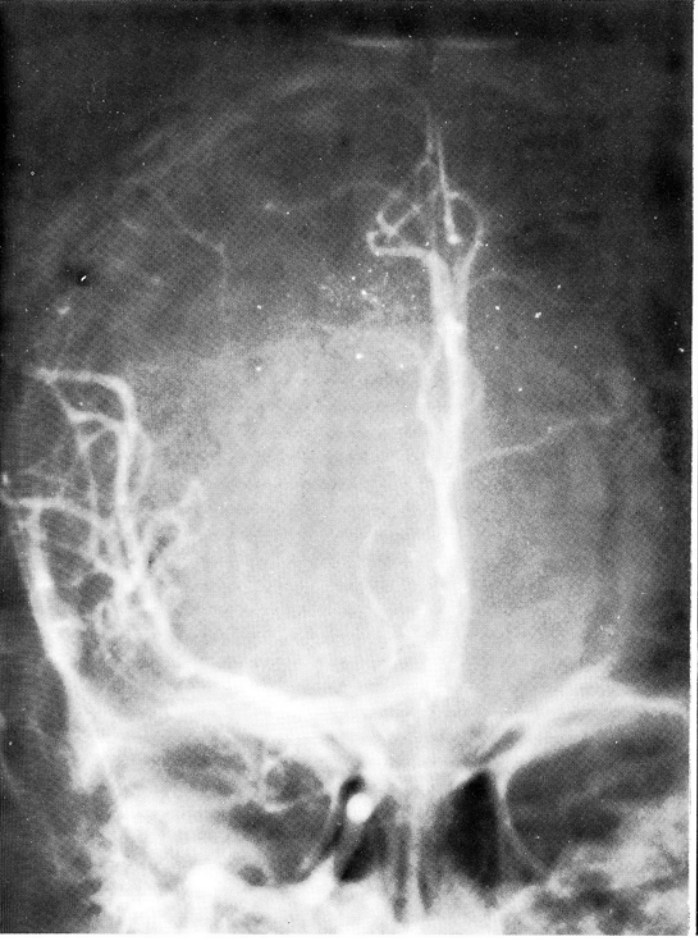

Fig. 1—Arteriogram on arterial phase showing lateral displacement of the last branch of the medial cerebral artery and medial displacement of the posterior cerebral artery.

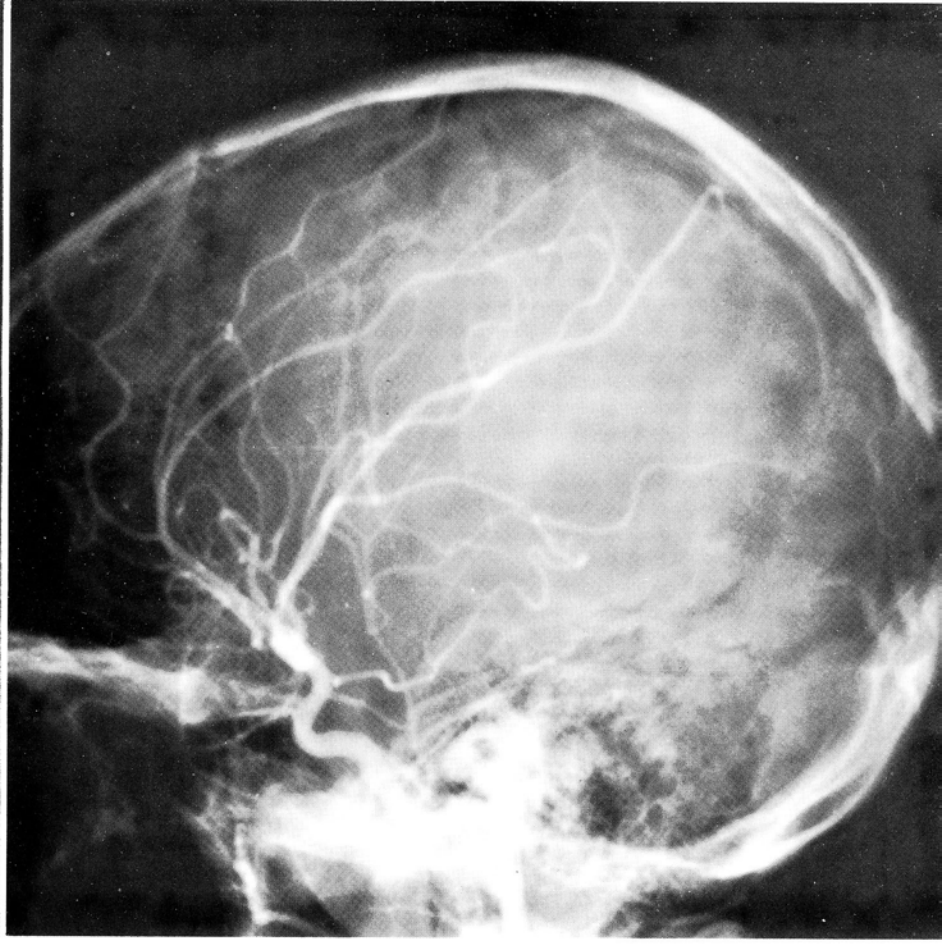

Fig. 2—Arteriogram showing elevation of the middle cerebral artery branches and an accordion-shaped posterior cerebral artery.

Dr. Taveras: I think we have enough evidence on the angiogram to indicate that this is not a temporal tumor. The telescoping of the branches of the parieto-occipital branches indicate that the tumor is in the occipital region. I see no reason for diagnosing ependymoma here; we have no evidence of any type, no abnormal tumor cloud or anything, that would lead us to make the histological diagnosis of ependymoma. The diagnosis of glioma I would not argue with, but our purpose radiologically is not to say that the patient has a glioma but that the patient has an occipito-parietal tumor, intracerebral, or secondarily invading the brain and extending forward to involve the thalamus.

Dr. Regato: Drs. J. C. Lemon, of Denver, J. A. Campbell, of Indianapolis, and P. J. Hodes, of Philadelphia, favored cystic astrocytoma of the right temporal lobe. Drs. R. E. Graf, of Denver, and J. W. McMullen, of Colorado Springs, made a diagnosis of ependymoma of the right temporal lobe.

Operative findings: On May 2, 1960, a right temporo-occipital craniotomy was done. A large tumor was found involving the right occipital and parietal lobes and extending also on the temporal lobe anteriorly. The tumor was removed piecemeal. A large amount of blood had to be transfused. At one point the tumor was adherent to the choroid but it was impossible to say whether or not it arose from that structure.

Dr. Zimmerman: There are, in reality, two distinctly different portions of tumor in this case. One consists of unipolar cells arranged in classical rosette formation around blood vessels. The apical processes of these cells point towards and probably insert in the adventitiae of the vessels. The cells are identifiable as of ependymal origin. The second portion of the tumor has tall columnar cells arranged in one or multiple cell layers on a basement membrane which rests on a vascular core of connective tissue. These cells are reminiscent of medullary epithelium, and the papillary arrangement of the tumor is suggestive of the neoplasm described in Case 1.

The proximity of the two variants of the tumor, which is obviously of ependymal origin, is of significance in calling attention to the fact that a single cell in all likelihood gave rise to both the mature ependymoma and the more malignant medullo-epithelioma. This cell, of course, forms the lining of the medullary canal in the embryo.

Dr. Zimmerman's diagnosis: EPENDYMOMA (with a component of medullo-epithelioma).

Histopathologic Diagnoses Submitted by Mail

Ependymoma (papillary, epithelial)	95
Malignant choroid plexus tumor	28
Chromophobe adenoma	10
Angiosarcoma	7
Others	5

Dr. Zimmerman: I haven't the vaguest idea how a tumor of the kind we have just seen could be diagnosed as a chromophobe adenoma. I cannot quite make out the reason for a diagnosis of angiosarcoma unless it is in the fact that in the course of some of these papillary projections, blood vessels of an adult, mature, type are present but you hardly can get any tumor in the brain without some blood vessels in it, and I do not believe that is of any significance. The other part which may have led to the suggestion of an angiosarcoma is the arrangement of the cells with their long axis perpendicular to the margin of the blood vessel wall; what I call the rosette formation perhaps some of you are calling perithelial sarcoma arrangement. If you think that is the case then how would you in the same tumor account for the definitely epithelial arrangement of that part of the tumor which I call "medullo-epithelioma"? I think that part of the tumor proves fairly conclusively that an epithelial-like cell is present in the

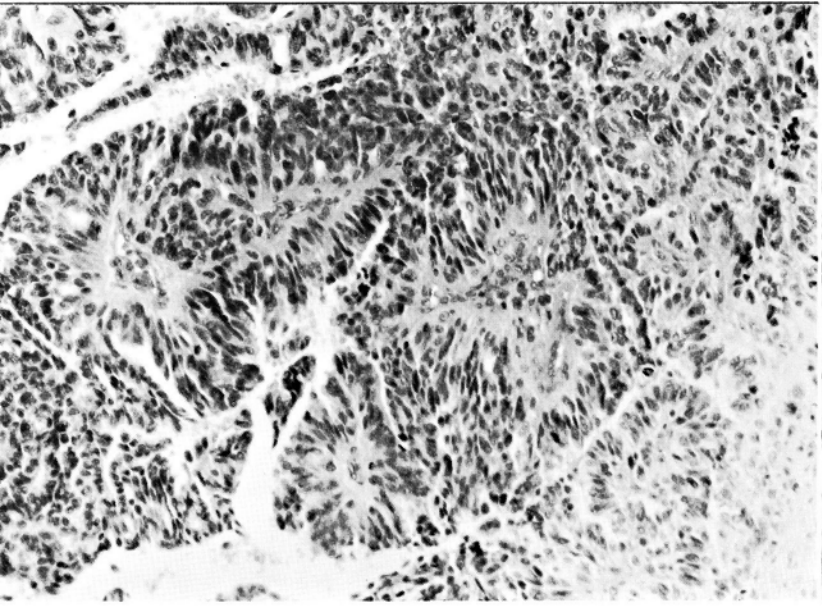

Fig. 3—Photomicrograph of pyriform cells arranged in rosettes around blood vessels, characteristic of ependymoma.

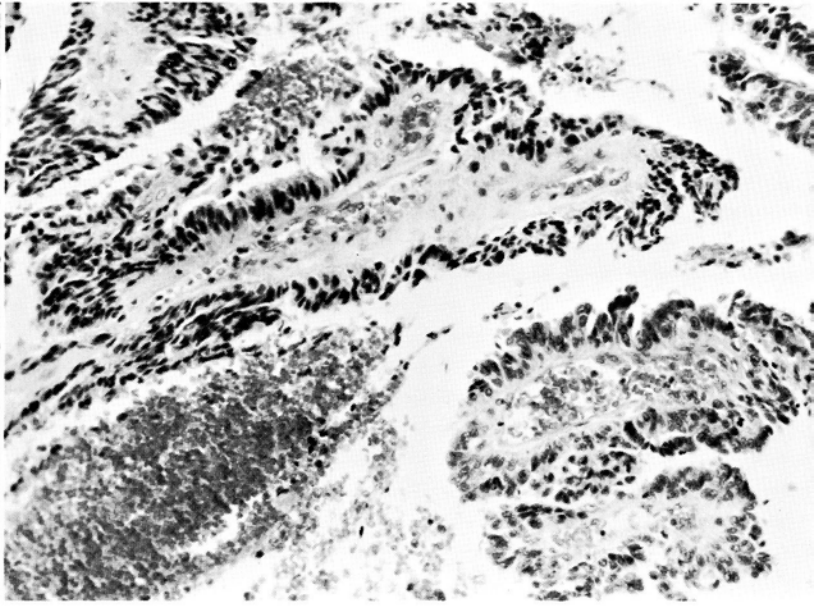

Fig. 4—Same tumor to show papillary structures. The rows of tumor cells rest on a basement membrane; the free margins of cells contain no cilia (H & E, x 180).

neoplasm. I end up again with the diagnosis of medulloepithelioma—a tumor which is predominantly and perhaps adequately diagnosed as an ependymoma. I want to further call your attention to the fact that, as I have said in the first case, the tumor cells of the ependymoma and the medulloepithelioma are derivatives of the primitive neural ectoderm which forms the lining cells of the ventricular system, namely, the ependyma, and which may give rise to a mature type of tumor like the rosette forming ependymoma, or to a more rapidly growing tumor in which bizarre cells are present, which we then call either malignant ependymoma or medulloepithelioma.

Dr. Regato: Dr. R. A. Willis, of Cornwall, England, and Dr. M. Berthrong, of Colorado Springs, diagnosed papillary ependymoma, but noted that it could also be an imperfectly differentiated papilloma of the choroid plexus. Dr. D. S. Russell, of Surrey, England, diagnosed a papilloma of the choroid plexus, possibly malignant. Dr. M. Wheelock, of Chicago, categorically designated it as a carcinoma of the choroid plexus.

K. J. Zülch, M.D., Cologne, Germany (by mail): This is a predominantly papillary tumor; in other places it is more trabecular but in many fields it is reminiscent of papilloma of the choroid plexus. The epithelium is mostly unilaminar although in some fields it is stratified and several groups of epithelial cells merge from solid tumor nests; in these nests there is some degree of pleomorphism and the same occurs in single cells in other locations. Mitoses are numerous. First of all I thought of a papilloma of the choroid plexus with malignant transformation; this diagnosis is compatible with the clinical information. But a differential diagnosis must be made with ependymoma of papillary-trabecular type, for this pattern often occurs in hemispheric tumors of children and presents rapid growth and mitoses.

Subsequent history: Following operation the patient did well for ten months. She then began to notice a decrease in sensory of the left hand and foot and later temporal headaches which progressed to left hemiplegia. A second craniotomy was done on February 13th, 1961, evidence of recurrence was found and a partial removal was carried out. Following operation there was a complete left hemiplegia with some spontaneous slight improvement in the following days. She was submitted to a course of roentgentherapy; a total of 3,200 roentgens were administered to each one of two lateral fields 7 x 7 cm in diameter in 28 days, from March 1st to March 28th, 1961, with 280 kv at 50 cm target-skin distance. The patient improved and did well until two months later, in May, 1961, when she had repeated seizures and recurrent intracranial pressure. She expired on February 6th, 1962. No autopsy was done.

Dr. Bucy: Fortunately most patients with ependymomas do better than this child and I suspect that the rapid recurrence here is related to these structures which Doctor Zimmerman has just shown you and which are related to medulloepithelioma. This is not a common location for an ependymoma; we see ependymomas in the cerebral hemisphere from time to time but the majority of them occur in the fourth ventricle. I think the difference here is the more malignant type of cell which occupied part of this tumor and which therefore accounts for the rapid recurrence and the patient's death.

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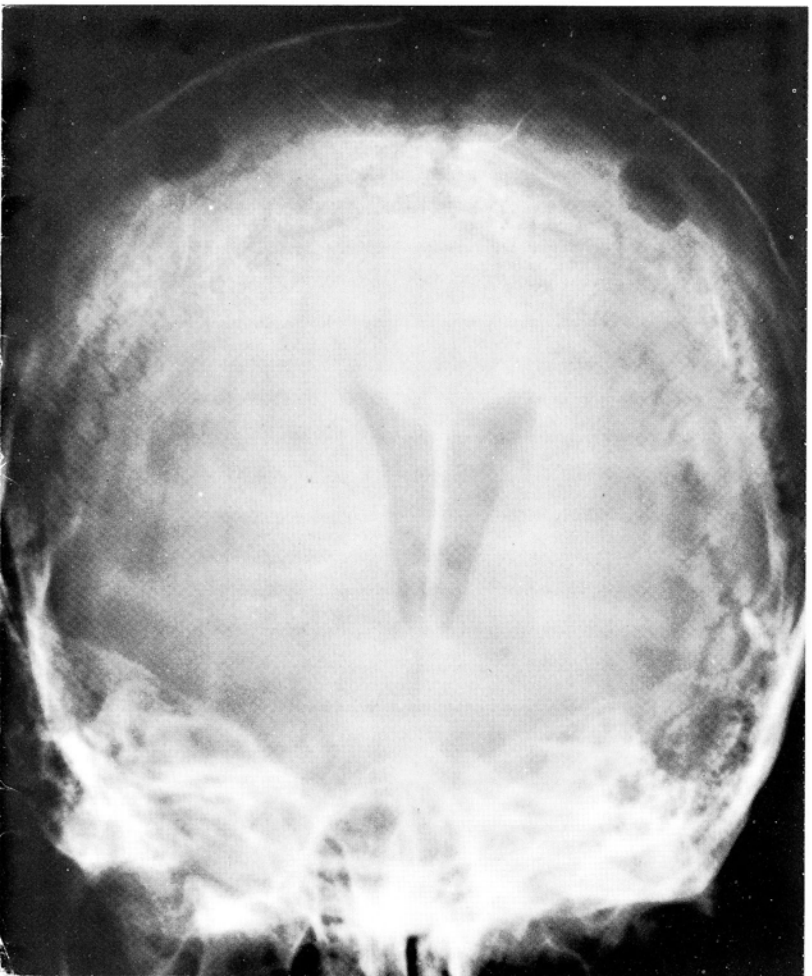
13. *Glioblastoma Multiforme of the Temporal Lobe*

Contributed by L. Lowbeer, M.D., Tulsa, Oklahoma

THE PATIENT was an 11-year-old boy in February, 1961, when he complained of bilateral retro-occular pain which increased over 18 months and had become constant and throbbing. This was accompanied by vomiting and there had been recent episodes of irrationality. When 3½ years old the boy was involved in an automobile accident which produced scalp lacerations and in which his father was killed. Physical examination revealed papilledema with retinal hemorrhage and weakness of the right sixth cranial nerve. The EEG showed a slow elevation of proteins in the spinal fluid.

Dr. Taveras: The submitted radiographic evidence consists of a single anteroposterior film of the skull following the introduction of air into the lateral ventricles through burr holes. There is filling of both lateral ventricles; the septum pellucidum is displaced to the left and there is no filling of the third ventricle. There is sharpening and slight elevation of the lateral angle of the right lateral ventricle and the anterior third of the body of the right lateral ventricle is slightly smaller than the left. The frontal horn of the right lateral ventricle appears to be intact although it is slightly smaller than the one on the left side. The appearance on this film suggests a mass situated in the temporal region. Examining this film further, it is noted that there is enlargement of the middle fossa on the right side. The middle fossa has become deeper and rounded in configuration.

Fig. 1—Ventriculogram showing displacement of the septum pellucidum to the left and some changes in the right lateral ventricle.



The findings indicate a tumefaction in the right temporal region which does not seem to extend into the frontal region because of the lack of deformity or compression of the right frontal horn. The elevation of the lateral angle of the lateral ventricle is typical of temporal lesions; it could also be seen in inferiorly placed frontal masses, but these would also produce changes in the frontal horn. The deepening and rounding of the middle fossa on the right side would confirm the presence of a mass here. In the differential diagnosis one should consider a neoplasm in the temporal lobe or temporal fossa and a chronic subdural hematoma. Some years ago, Davidoff and Dyke, described a syndrome which they called chronic juvenile relapsing subdural hematoma. Presumably these children had received an injury at some time in the past; a subdural hematoma, usually in the temporal region, was produced which did not lead to immediate attention but which, with the passage of time, became larger and produced enlargement of the middle fossa with elevation of the sphenoid ridge. Later, at the time of another, often trivial, injury, the child would develop marked symptoms with increased pressure and papilledema requiring immediate attention. The clinical history as described could well fit this syndrome, with the obvious differential diagnosis being a neoplasm. Temporal neoplasms only occasionally produce significant enlargement of the middle fossa, although a slight degree of enlargement is not uncommon.

Recapitulating, we have here an 11 year old boy who presents a history of 18 months duration leading to rather marked evidences of increased intracranial pressure but without any significant localizing neurological findings. The right sixth nerve palsy is probably associated with the increased intracranial pressure. The single ventriculogram is consistent with a mass in the temporal fossa and because of enlargement of the temporal fossa and slight thinning of the squamosal portion of the right temporal bone, I would suggest a long-standing non-neoplastic process, namely, chronic juvenile subdural hematoma, with neoplasm being the obvious second possibility.

Dr. Taveras' impression: Chronic juvenile SUBDURAL HEMATOMA, right temporal region.

Roentgenologic Impressions Submitted by Mail

Subdural hematoma	25
Frontal lobe tumor	19
Parencephalic cysts	18
Glioma	16
Temporal tumor	5
Others	17

Dr. Taveras: This is not a frontal lobe tumor because it does not produce any changes in the frontal horn itself; I think this is a most important thing to observe in a frontal lobe tumor. What in the world would make anybody make a diagnosis of porencephalic cyst when you don't see porencephaly? Glioma of the temporal lobe would be fine with me. Temporal tumor is the diagnosis that we should make, or temporal expanding lesion, which of course can be intratemporal or extratemporal.

Dr. Regato: Dr. H. Hauser, of Cleveland, Drs. P. S. Swenson, of Columbia, South Carolina, and J. W. McMul-

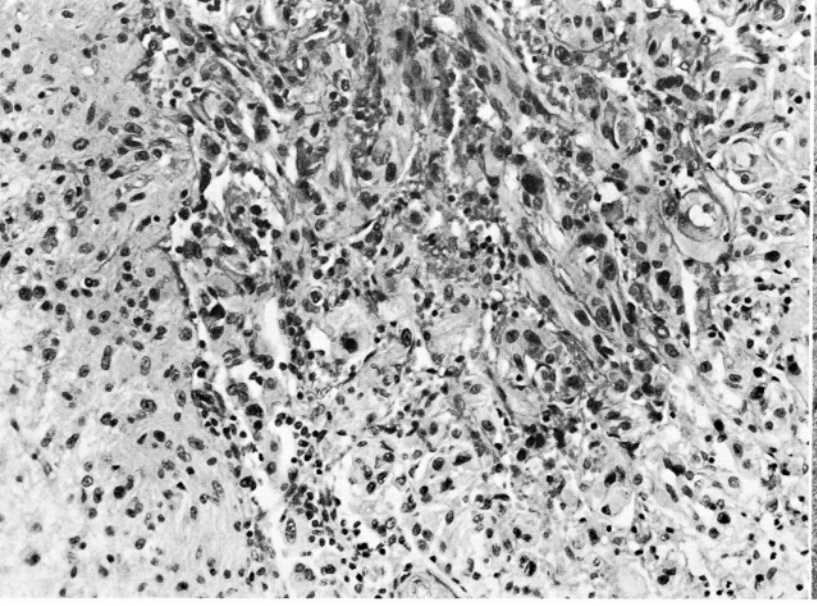


Fig. 2—Photomicrograph of meningeal tumor whose cells form vascular channels. There is gliosis in the subpial cortex (H & E, x 180).

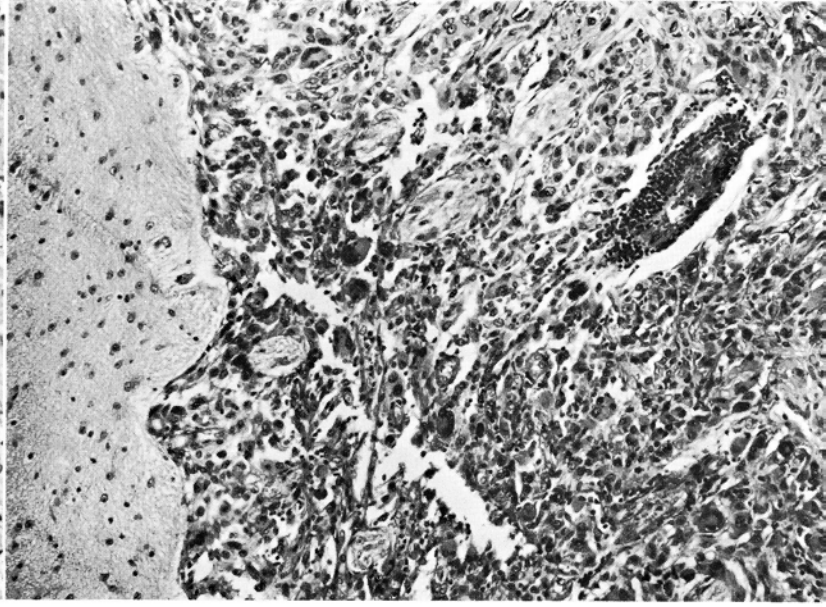


Fig. 3—Photomicrograph from one of the additional microscopic preparations sent by Dr. Lowbeer following the Seminar. This discloses an invasion of the cerebral leptomeninges by glioblastoma multiforme. The multinucleated tumor giant cells, the cellular pleomorphism and the perivascular lymphocytic cuffing make the diagnosis certain (H & E, x 120).

len, of Colorado Springs, also favored a subdural hematoma. Dr. J. R. Galloway, of Albuquerque, diagnosed an expanding lesion of the temporal lobe.

Operative findings: On February 7, 1961, a right temporal craniotomy was done. A large cystic tumor 6 cm in diameter was found involving the right temporal lobe; a large portion of the lobe was resected with the tumor. The surgical specimens measured 1.5 to 3 cm, they had a homogeneous whitish color without apparent differentiation between white and gray matter.

In spite of the devoted care of Dr. Berthrong and Mr. Barhite, we sent away a few slides in this case which did not show any part of the tumor. This may explain the confusion in findings and in the tabulation of diagnoses.

Dr. Zimmerman: The tumor seems to have its being in the leptomeninges which cover the cerebral cortex. To a minor extent only does it seem to invade the pia and infiltrate the cortical parenchyma. There is a gliosis in the superficial layers of the cortex which resembles the response of the neural tissue to an invading neoplasm. The tumor cells seem to form the walls of many channels, some of which contain red blood cells and some of which are empty. This portion of the meningeal tumor has a distinct hemangiomatous appearance. More solid nests of tumor cells have large cytoplasmic, pink bodies and prominent, large, vesicular nuclei with an occasional nucleolus. The cells resemble malignant endothelial elements such as are present in hemangioendotheliomas.

The presence of nuclei in mitotic division and the evidence of cortical invasion indicate malignant changes. Parenchymal hemangioblastomas, especially the cerebellar variety, are benign, non-metastasizing tumors despite their designation. The meningeal variety of this neoplasm may be malignant.

Dr. Zimmerman's diagnosis: MENINGIOMATOUS HEMANGIOBLASTOMA.

Histopathologic Diagnoses Submitted by Mail

Astrocytoma	45
Malignant meningioma	22
Glioblastoma	18
Gliosis	16
Rhabdomyosarcoma	8
Hemangioblastoma	7
Lowbeer's tumor!	1
Others	27

Dr. Zimmerman: I think many participants were impressed with the subpial astrocytic reaction, and although my interpretation is that this represents an astrocytosis and not a neoplasm, I cannot really insist that I am right and that those who thought otherwise are wrong. It is a malignant meningioma but of a type that tends to form blood vessels, and therefore I have called it a hemangioblastic type of malignant meningioma. I do not believe for a minute that this is a glioblastoma. In order to make a diagnosis of glioblastoma multiforme you should find a certain number of the following: you must find spongioblasts and there should be some evidence that these spongioblasts are arranged around central cores of necrosis in a pseudo-palisade formation; there should also be vascular endothelial proliferative changes, collections of lymphocytes around blood vessels, blood vessels which are thrombosed, large zones of necrosis, excessive pleomorphism and usually many cells in mytotic division and many multinucleated giant cells. You may not find in every glioblastoma multiforme all of these criteria but certainly there ought to be enough of them to make the diagnosis a plausible one; I see practically nothing of these criteria in the present case. I am in agreement with a diagnosis of gliosis if it refers to the subpial, parenchymal, part of the story. I question seriously if any of those who diagnosed this as rhabdomyosarcoma identified striations in the cytoplasm of these cells; without them I am at a loss to know how one could make the diagnosis.

Dr. Regato: Drs. M. Navarro-Roca and J. Martinez, of New York, diagnosed hemangioendothelioblastoma. Dr. D. S. Russell, of Surrey, England, suggested a glioma, probably gemistocytic astrocytoma. Dr. L. Lowbeer, of Tulsa, made a diagnosis of giant-cell glioblastoma and stated that Dr. Dorothy Russell was in agreement as was Dr. Earle, of Galveston. Dr. K. J. Zülch, of Cologne, Germany, suggested oligodendroglioma due to the presence of verrucous formations but admitted that the material was too scanty to be definite. Dr. R. Font-Menéndez, of Pittsburgh, diagnosed malignant meningioma.

This slide was submitted to the AFIP (accession no. 991279). In March, 1961, Dr. W. Haymaker wrote: "The sections reveal a neoplasm composed of pleomorphic cells, some of them giant and multinucleated, arranged in round clusters and associated with a very rich network of capillaries. In some areas the arrangement of the cells is epithelial, but in others the tumor cells are seen joining each other by processes. This is a malignant primary neoplasm and, although we favor the diagnosis of meningeal sarcoma, we cannot definitely exclude the possibility of a peculiar malignant glioma until we have made additional studies."

In November, 1961, Dr. R. L. Davis wrote: "Examination of the PTAH and Gömöri reticulin stained sections reveal features which suggest a meningeal sarcoma."

Subsequent history: One month after operation the patient was submitted to a series of Cobalt-60 irradiations. From March 7 to April 13, 1962, he was treated through two lateral fields 8 x 10 cm in diameter and received a total of about 4,600 roentgens at the level of the tumor area in 38 days.

On September 20, 1962, the patient was reported well, had no symptoms and was attending school.

Dr. Bucy: Doctor Zimmerman, did you make a reticulin stain of this tumor?

Dr. Zimmerman: Yes I did, although it is not a terribly satisfactory one because the tumor, as you see, is relatively small, and the underlying brain tissues extensive. Reticulin stain of the tumor is strongly suggestive of the type of stroma that you get supporting endothelial cells, and I would say it was positive for hemangioblastoma. But the rest of it which is astrocytic in type has no reticulin.

Dr. Bucy: And is not neoplastic?

Dr. Zimmerman: No, I don't think it is.

Dr. Bucy: I think you would agree that in this type of tumor the reticulin stain is particularly valuable, and that is why I asked what you had found with it. It seems to me that this is a type of tumor about which we have had a very imperfect understanding. In the past we have in general looked upon hemangioblastomas as being predominantly or perhaps exclusively cerebellar tumors. This is not true. There is a very definite group of these hemangioblastomas which occur in the cerebral hemisphere, and I think this is a very good example of that type of tumor. Doctor Taveras has told us that from the radiological evidence this is a tumor of long standing. As a matter of fact, in some instances calcium salts are deposited in these tumors and, of course, this indicates that they are of long standing. In general, as in this case, there have been large cysts in connection with these tumors. The actual tumor tissue is small, in some cases even smaller than here. I have operated upon one patient who had symptoms of 35 years' duration with a tumor of this type; this is the longest that I have seen, and this too I think is typical of this type of very slowly growing non-malignant tumor. If the tumor is completely removed the patient should be cured.

Leo Lowbeer, M.D., Tulsa, Oklahoma: I believe some of the difficulties originate simply from the fact that the material submitted to Doctor Zimmerman, as well as to the participants of the Seminar, did not represent the entire tumor; but as Doctor Zimmerman pointed out himself, it is a common experience in brain tumors that one cannot make a definitive diagnosis from one portion of the tumor. I would like for you to see six slides, they look very different, and particularly the reticulin pattern is very different. This one shows simply the general pattern of the tumor with a large blood vessel and markedly proliferated endothelial cells. These are some of the giant cells in almost syncytial bands. This other slide reveals areas from which the impression was gained that these are glial cells. This other is a reticulin stain and here the reticulin seems to be entirely confined to the large number of blood vessels, and in between there are large nests of syncytial cells which are obviously glial cells. In this other section the reticulin pattern is in that portion of the tumor which invaded the meninges; we had the definite impression that the tumor was in the brain as well as infiltrating the meninges. We see here some of the same phenomena which Doctor Zimmerman referred to as reactive astrocytosis, only we see a portion of the tumor which was in the brain itself.

Dr. Zimmerman: Well, it could very well be that I have been had! I assumed that slides that were sent were representative of the tumor under discussion, and if by design or inadvertence a section is sent me that doesn't represent the tumor, then I can only do the best I can by calling it as I see it. I would like the opportunity to study this evidence and see if I would revise my diagnosis. I am not one hundred percent convinced that it could not yet be a vascular tumor of endothelial origin, but it looks suspiciously like a gliogenous tumor.

A. E. Cyrus, M.D., Milwaukee, Wisconsin: This case caused me a great deal of difficulty and I ended up by making two diagnoses. Is there a difference in the cytoarchitectural pattern of a glioma when it is found deep within the parenchyma, as compared with other portions where it may come in contact with the pia?

Dr. Zimmerman: It is well known that gliomas, astrocytomas, medulloblastomas, ependymomas, and glioblastoma multiforme as they invade the leptomeninges cause proliferative changes so that there can be confusion between a mesodermal and a gliogenous tumor in the meninges. I only saw a minor fraction of brain tissue in this slide and saw a tumor involving essentially meninges; I had no idea that there was a bulk of involvement of the kind that Doctor Lowbeer showed with bizarre cells which look suspiciously like glial cells. He may be right that what I saw is a meningeal reaction to a tumor of glial origin which produced the vascular proliferative change in the other structures I have indicated. It is quite possible.

Editor's note: After the Cancer Seminar Dr. Lowbeer revealed additional details of the gross description of the tumor and submitted other slides to Dr. Zimmerman for study. Dr. Zimmerman wrote: "The invasion of the cerebral leptomeninges by glioblastoma multiforme is disclosed by these slides (Fig. 3). The multinucleated tumor cells, the cellular pleomorphism and the perivascular lymphocytic cuffing make this diagnosis certain."

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14. *Glioblastoma Multiforme of the Cerebellum*

Contributed by M. C. WHEELOCK, M.D., Chicago, Illinois

THE PATIENT was a 69-year-old man in September, 1961, when he presented personality changes accompanied by vomiting and weakness of the lower extremities. Physical examination revealed unsteady gait and hyporeactive reflexes. The EEG presented irregular slowing in all left side leads. The spinal fluid showed normal dynamics and chemistry. An angiogram was reported normal.

Dr. Taveras: The submitted film consists of a lateral view taken during the initial injection of a pneumoencephalogram which shows filling of the cisterna magna, the fourth ventricle, the aqueduct and the posterior two-thirds of the third ventricle. This film suggests that there is slight stretching of the anterior aspect of the aqueduct of Sylvius. On the inferior aspect of the third ventricle, over the area of the tegmentum of the mid-brain, just anterior to the entrance of the aqueduct, there is a slight elevation which is somewhat unusual. A very small amount of gas is seen to be present in one lateral ventricle.

The findings are somewhat suggestive of an increase in the size of the tissues anterior to the aqueduct and upper portion of the fourth ventricle. This might indicate the presence of a mass in the brain stem or anterior to the brain stem. If it were within the brain stem we would consider a neoplasm, either primary or metastatic, and if it were anterior to the brain stem we should consider, in addition to meningioma, the possibility of an aneurysm of the basilar artery. Inasmuch as no other films were given and that, in the history, it is not stated whether the negative angiogram was of the carotid or of the vertebral arteries, it is not possible to offer any diagnostic suggestions. Moreover, I am not sure that the displacement of the aqueduct is genuine and it is necessary to have air anterior to the pons to be able to measure the size of the soft tissue shadow of the mid-brain and pons to ascertain this fact.

Dr. Taveras' impression: No roentgenological diagnosis possible on this film alone.

Roentgenologic Impressions Submitted by Mail

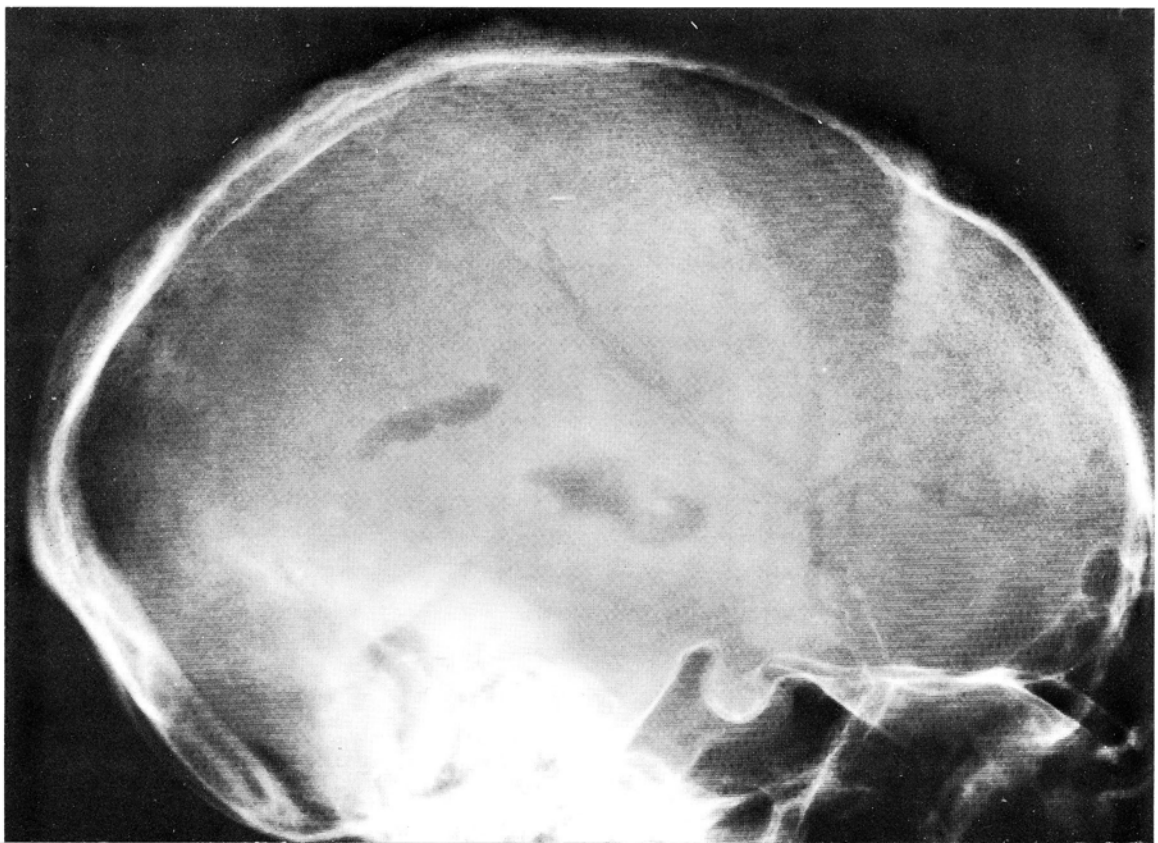
Arteriosclerosis	18
Tabes	16
Frontal lobe tumor	15
Tumor of posterior fossa	15
I capitulate!	1
Others	32

Dr. Taveras: This could be an aneurysm of the basilar artery but I wouldn't just diagnose arteriosclerosis. We see nothing on these films to permit us roentgenologically to make a suggestion of frontal lobe tumor.

I always refrain from making a diagnosis of just "tumor of the posterior fossa" because what the surgeon wants to know is whether the tumor is in the brain stem, or cerebellum, or extra-axial, etc. or anterolateral, etc. I think that there is probably a tumor of the posterior fossa but it should be in the brain stem.

Dr. Regato: Dr. S. M. Jones, of Lubbock, Texas, favored a gliomatosis cerebri of the left hemisphere. Dr. P.

Fig. 1—Lateral view during initial phase of pneumoencephalogram suggesting slight stretching of the aqueduct.



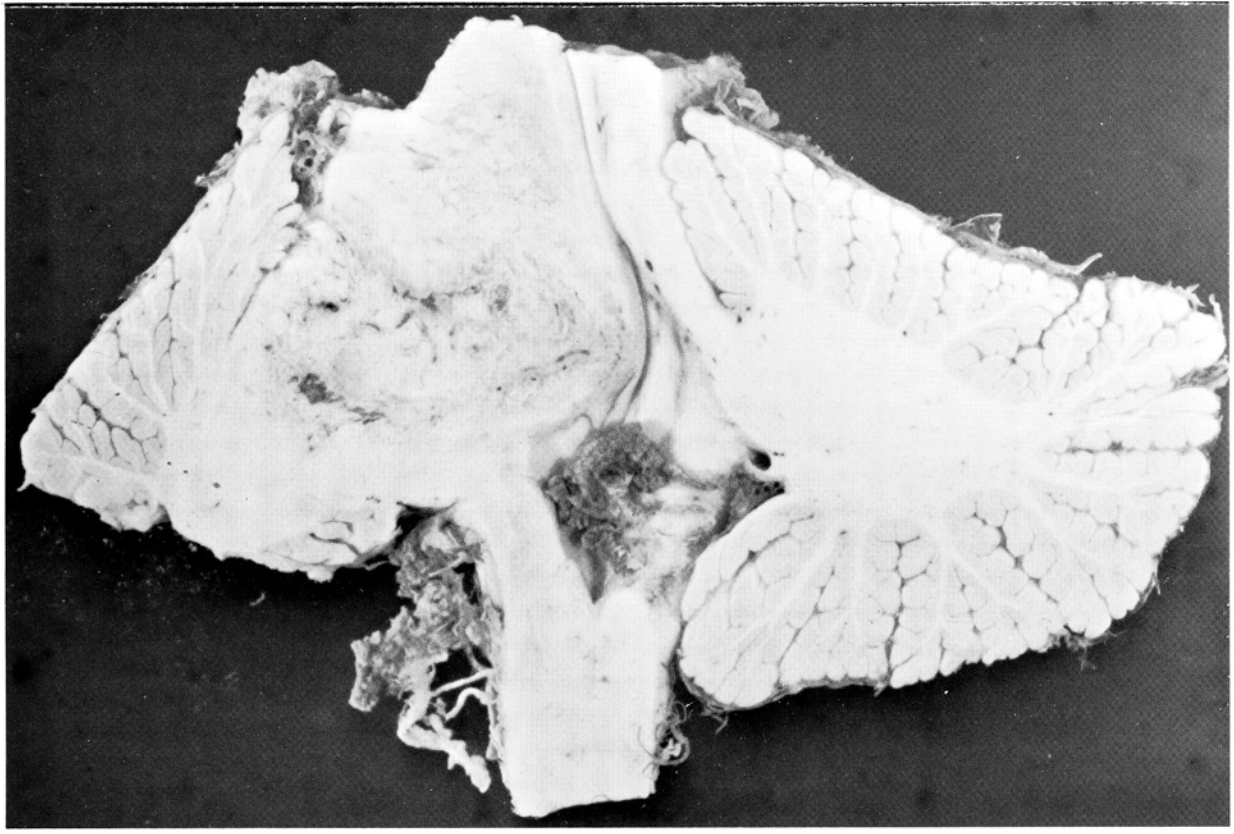


Fig. 2—Autopsy appearance of tumor infiltrating the pons.

J. Hodes, of Philadelphia, suggested a midbrain glioma encroaching on the aqueduct.

Subsequent history: A diagnosis of arteriosclerosis was made and the patient was given anticoagulants. A speech defect appeared, followed by progressive deterioration of the sensory and motor functions. He expired in January, 1962.

Autopsy revealed a poorly demarcated yellowish tumor infiltrating the left half of the pons, the brain stem and the left cerebral peduncle and extending anteriorly to the level of the optic chiasma. The fourth ventricle was distorted.

Dr. Zimmerman: This is not a common tumor of the cerebellum. It consists of very pleomorphic cells, many of which are in mitotic division and some have large bizarre nuclei. There is a considerable amount of hemorrhage and necrosis. Some blood vessels are thrombosed and many vessels disclose endothelial proliferative changes. Around a considerable number of vessels there are present cuffs of small dark cells which are identifiable as spongioblasts. On the other hand, adult protoplasmic and fibrillary astrocytes are also seen. One of the characteristic features of this tumor, which is obviously of glial origin, is the arrangement of numerous spongioblasts in pseudo-palisade formation around zones of necrosis.

Tumors of this malignant variety are frequently encountered in the cerebral hemispheres in patients of the older age group, especially males. In the cerebellum they are seen but infrequently.

Dr. Zimmerman's diagnosis: GLIOBLASTOMA MULTIFORME.

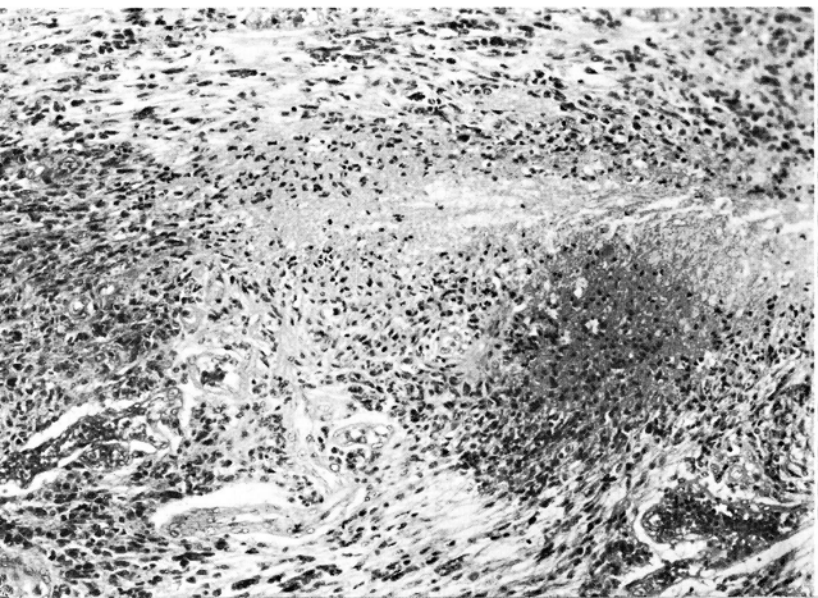
Histopathologic Diagnoses Submitted by Mail

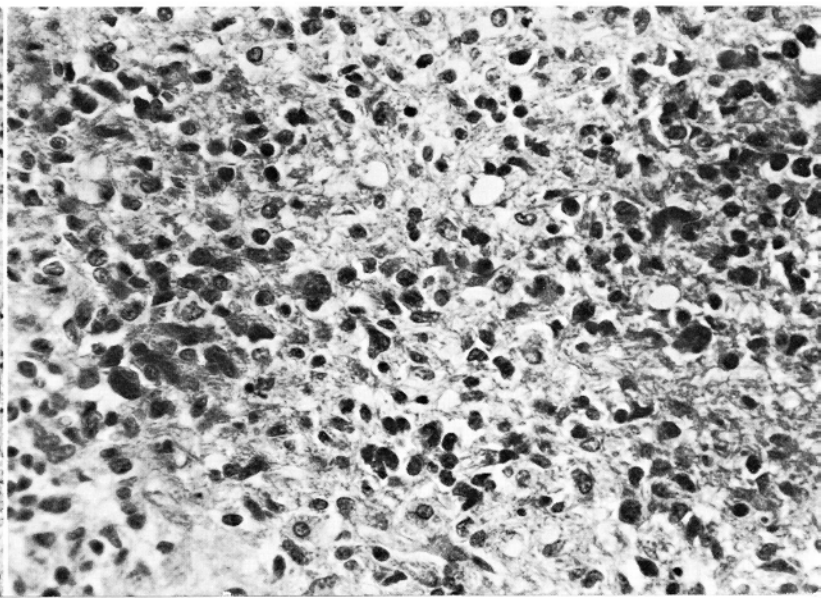
Astrocytoma (cerebellar)	67
Glioblastoma multiforme	58
Malignant meningioma	8
Carcinoma choroid plexus	4
Others	20

Dr. Zimmerman: I don't think these are mature adult astrocytes; (too much necrosis, too much vascular proliferation); unless you are of the Kernohan school and would

Fig. 3—Photomicrograph of tumor showing cellular pleomorphism, vascular endothelial proliferation, and zone of necrosis surrounded by spongioblasts—features of a glioblastoma multiforme (H & E, x 130).

Fig. 4—Cellular pleomorphism in same malignant glioma (H & E, x 350).





modify this by saying "astrocytoma Grade IV of the cerebellum" I wouldn't agree with you. It is not a benign tumor. I do not believe that a diagnosis of meningioma can be made in this case; malignant meningiomas are quite rare; I see no basis for making that diagnosis; this is a tumor that is obviously in brain parenchyma and is not a meningeal tumor invading brain. I cannot see where a choroid plexus tumor could even be suggested in this case.

Dr. Regato: Drs. M. Wheelock, of Chicago, J. D. Rice, Jr., of Colorado Springs, and K. J. Zülch, of Cologne, Germany, also diagnosed glioblastoma multiforme. Dr. R. Horn, of Detroit, suggested a collision tumor, part astrocytoma and part perithelial sarcoma. Dr. R. Willis, of Cornwall, England, and Dr. E. W. Koneman, of Billings, Montana, offered poorly differentiated astrocytoma.

Dr. Bucy: I should like to compliment both Doctor Taveras and Doctor Hodes on having made a remarkably accurate diagnosis on the basis of very little evidence. This case demonstrates how little in the way of accurately localizing neurological findings there may be in the presence of a very definite and sizable lesion. On the basis of the clinical evidence which is listed here I think no one could have made an accurate diagnosis of this tumor. Of course so far as therapy is concerned, there are no indications.

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15. *Cerebellar Ependymoma*

Contributed by S. M. LeBer, M.D., Edmonton, Alberta, Canada

THE PATIENT was a 17-month-old infant in May, 1960, when he sustained a fall from a swing. Shortly afterward, he presented vomiting, a staggering gait, and deviation of the head towards the right. Physical examination revealed papilledema and no other findings.

Dr. Taveras: The submitted films consist of a frontal and a lateral view made during ventriculography. Very small burr holes are present and it is probable that twist drills were used to facilitate the ventricular puncture. The frontal film shows a marked degree of bilateral ventricular dilatation slightly more marked on the left side. The septum pellucidum is thick and is in the midline. The third ventricle is markedly enlarged and also in the midline. This film was made in the supine position. The lateral view was made using the horizontal beam with the patient lying prone. The posterior portion of the third ventricle is well filled and the aqueduct is also shown. There is a soft tissue mass projecting into the mid-portion of the aqueduct from its ventral aspect and this mass is continuous down to the lower portion of the fourth ventricle. It is obvious that the fourth ventricle is enlarged and filled with an irregular mass. The tumor appears to occupy chiefly the anterior aspect of the fourth ventricle. No frontal film is available to determine how much increase in the width of the fourth ventricle is present. There is irregularity in the region of the floor of one lateral ventricle which could be produced by the choroid plexus. I do not believe that this represents a neoplastic mass within the lateral ventricle. There are apparently two silver clips in the posterior fossa seen both in the lateral and frontal views and I do not know just how they got there. Pantopaque was also used to outline the mass but the Pantopaque does not add any further information.

The findings are those of a mass lesion involving the fourth ventricle, chiefly along its anterior wall and extending upwards to involve the anterior aspects of the aqueduct. The most likely diagnosis would be an ependymoma, an astrocytoma or a medulloblastoma secondarily invading the fourth ventricular cavity. The degree of ventricular dilatation would be more in favor of an ependymoma or an astrocytoma invading the fourth ventricle, but does not necessarily exclude a medulloblastoma. The sella turcica is elongated and the sutures are slightly widened. Both of these can be manifestations of increased intracranial pressure. In view of the history of trauma we should consider the possibility of hematoma in the wall of the fourth ventricle but the degree of enlargement of this structure would be most unlikely with an acute history of hemorrhage. The possibility of a large vascular malformation occupying the floor of the fourth ventricle with large vein which has later bled is also to be considered. In this case perhaps cerebrospinal fluid changes would help in making a diagnosis but the cerebrospinal fluid findings have not been reported in the history.

Dr. Taveras' impression: NEOPLASM of the FOURTH VENTRICLE.

Roentgenologic Impressions Submitted by Mail

Medulloblastoma	29
Tumor posterior fossa	20
Dandy-Walker	9
Parencephalic cyst	5
Porencephaly	4
Others	31

Dr. Taveras: The diagnosis of medulloblastoma does not agree with the position of the tumor; the medulloblastomas produce forward displacement of the aqueduct and fourth ventricle; the ventricles are possibly a little bit too large also. I have the same objection as before to a diagnosis of tumor of the posterior fossa. Dandy-Walker is supposed to be a congenital atresia of the foramen of Magendie and Lushka which prevent the emptying of the fourth ventricle; this produces a huge fourth ventricle which

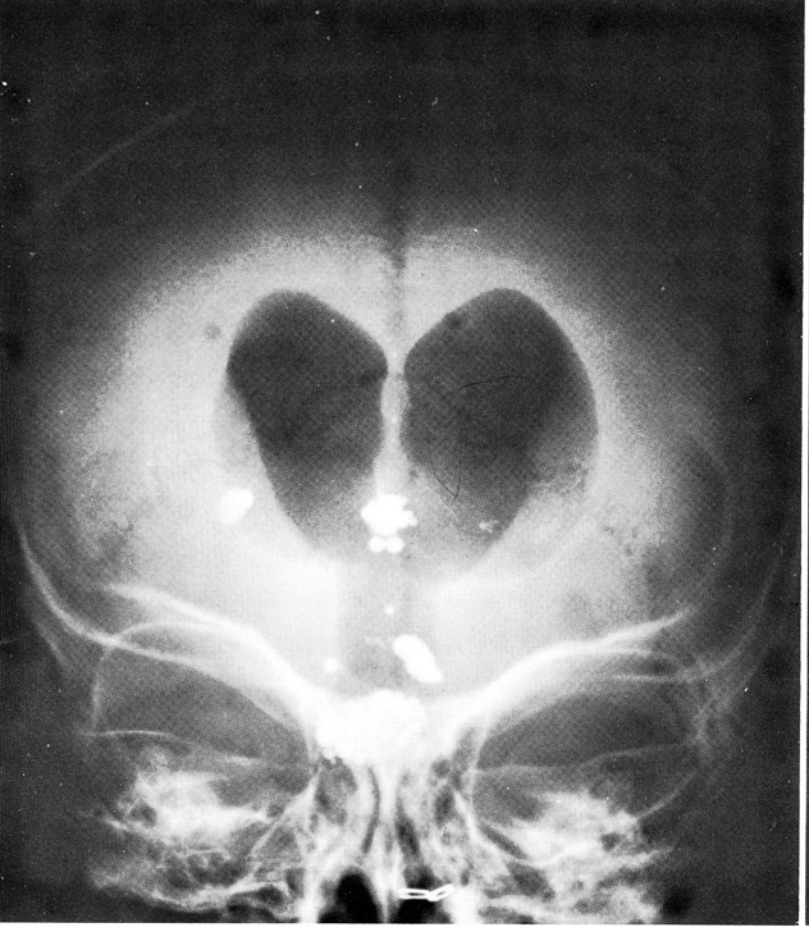


Fig. 1—Frontal view of ventriculogram showing bilateral ventricular dilatation and enlargement of the third ventricle.

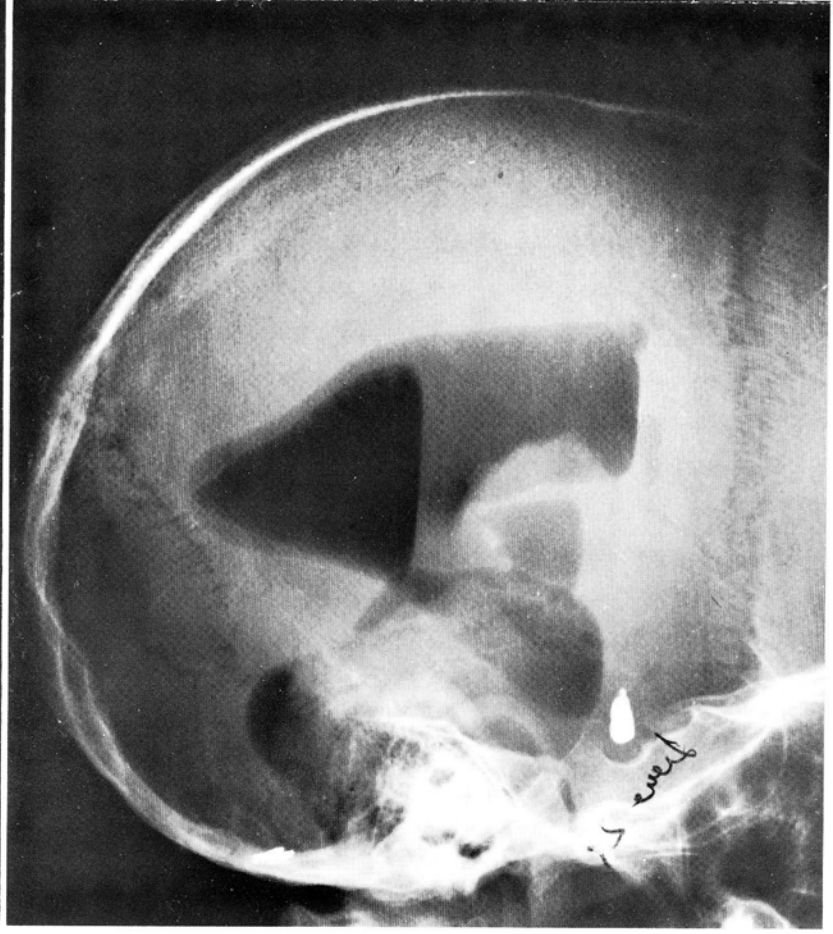


Fig. 2—Lateral view of ventriculogram showing well filled third ventricle and aqueduct and enlarged fourth ventricle.

herniates through the foramen magnum and may produce enlargement of the posterior fossa, but this is obviously not the case in this instance. I guess the diagnosis of porencephalic cyst may include a porencephalic cyst in the cerebellum, but I don't see any reason for that when we see an irregular mass within the fourth ventricle.

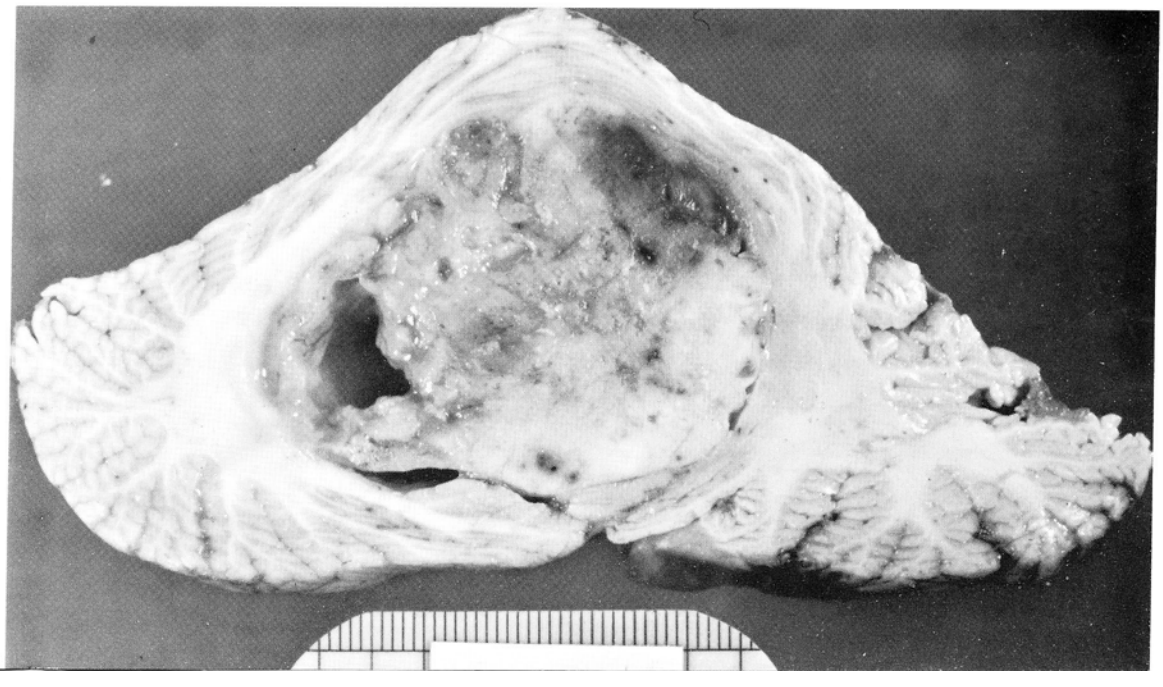
Dr. Regato: Dr. T. O. Gabrielson, of Ann Arbor, suggested a pontine tumor, probably a glioma. Dr. R. E. Graf, of Denver, favored a medulloblastoma.

Operative findings: On June 21, 1961, a sub-occipital craniotomy was done. The cysterna magna was found filled with a purplish-gray tumor which was rather soft and not particularly vascular. The tumor was mobilized and removed from the floor of the fourth ventricle which was almost completely filled by the mass; the attachment was not broad.

Dr. Zimmerman: The most distinguishing characteristic of this neoplasm is the presence of many scattered acinus-like structures lined by tall columnar cells of ependymal origin. These structures are strongly reminiscent of the central spinal canal of the embryo. They represent one variety of rosette commonly encountered in ependymomas.

The rosettes are interspersed with a loose fibrillary glial stroma in which are present small numbers of typical fibrillary astrocytes. This astrocytic portion of the tumor is another feature of ependymoma which, however, is un-

Fig. 3—Gross appearance of ependymoma in the fourth ventricle.



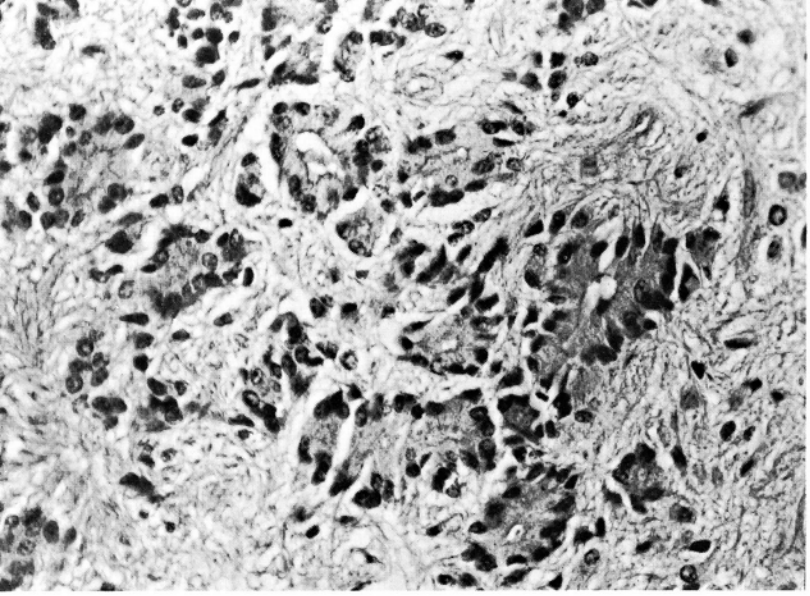


Fig. 4—Photomicrograph of cerebellar ependymoma showing tumor cells in acinar formations. The free cellular margins often have cilia and there are blepharoplasts in the cytoplasm near the free margins. The acinar structure is reminiscent of the central canal of the spinal cord (H & E, x 350).

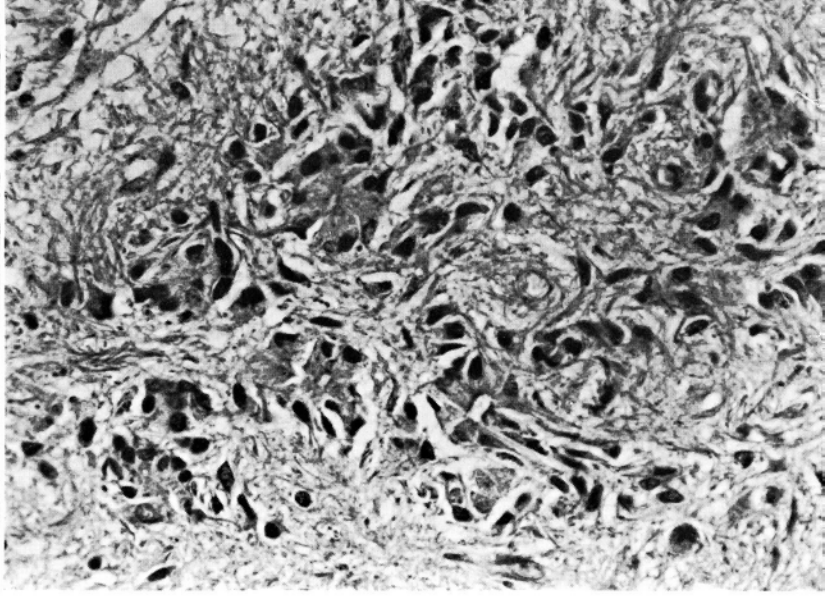


Fig. 5—The pyriform shape of the tumor cells forming acini is clearly shown (Phosphotungstic acid-hematoxylin stain, x 350).

questionably present more commonly in the spinal cord variety of this tumor than in the cerebral or cerebellar.

Dr. Zimmerman's diagnosis: CEREBELLAR EPENDYMOMA.

Histopathologic Diagnoses Submitted by Mail

Ependymoma	98
Medulloblastoma	33
Others	15

Dr. Zimmerman: A medulloblastoma forming genuine acini is not likely. I have already mentioned that at one center where I visited where they had eighty-six medulloblastomas listed, I found that half of them were ependymomas. I think that some of you are just grouping ependymomas and medulloblastomas into one category. I think that they can be separated histologically, that they can be separated prognostically, and perhaps even therapeutically.

Dr. Regato: All of the experts were agreed on a diagnosis of ependymoma.

Subsequent history: On June, 1961, the patient had recurrent headaches and the ventriculograms showed great dilatation of the ventricles. In December she became comatose and expired on December 28, 1961.

Dr. Bucy: The first paper on brain tumors which I ever wrote, in 1928, was about such a tumor. At that time, following the example of Percival Bailey, I called this tumor a "neuroepithelioma"; I don't think it matters greatly whether it is called a neuroepithelioma or an ependymoma. It is an ependymoma of a particular type, and if one wishes to give it a separate designation I see no harm in doing so. Unfortunately these tumors seem to occur in small children and the outlook is not good.

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Fig. 6—Photomicrograph of a portion of the same tumor which is composed of fibrillary astrocytes.