# GLIOBLASTOMA MULTIFORME

## REVIEW OF 219 CASES WITH REGARD TO NATURAL HISTORY, PATHOLOGY, DIAGNOSTIC METHODS, AND TREATMENT

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IT IS a curious fact that our current neurosurgical literature exhibits a striking paucity of articles about our greatest problem: glioblastoma multiforme.[1,4–10] While the contemporary literature on cancer swells to an overabundance, our "cancer" of the nervous system appears to receive scant attention—certainly not through complacency. Since communication is a leaven of ideas, the present one is offered with that intent. Harvey Cushing continuously recorded his experiences with various types of intracranial tumors, culminating in the great meningioma monograph, with Louise Eisenhardt.[3] In the preface to his *Intracranial Tumours*[2] he stated, "The laying bare of one's mere mortality percentages, however, is only a start toward what will ultimately be called for: namely, figures relating to the expectancy of life of those who have survived tumor extirpations. And still more important would be figures for each kind of tumor which would show the percentage of surviving patients whose wage-earning capacity has been restored by operation and for how long a time." It is for this purpose that this study was undertaken.

### MATERIAL

The 219 cases collected here comprise all the verified cases of glioblastoma multiforme seen at the New Haven Hospital during the period 1924–1952. The microscopic sections were reviewed and the diagnosis was verified. A number of doubtful cases were discarded. We are grateful for the valuable assistance of Dr. Louise Eisenhardt and Dr. Elias Manuelidis in reviewing the microscopic sections when the diagnosis was questionable.

Aside from histological verification, the cases are not selected in any sense. Some of the patients were never seen by a neurosurgeon. Those who came to operation were treated by many different surgeons, many of them residents. The time span represents an entire generation during which many surgical advances came into being, including the blood bank, fluid replacement in its modern sense, and antibiotics.

The follow-up is complete on all of these patients. All have died. Autopsies were done on 105 of the 219, and the findings are known in all but 1 case, in which the autopsy was performed at another hospital.

## METHOD

For this statistical survey the hospital charts, microscopic sections, autopsy protocols, and records of the hospital Tumor Registry were used as sources of information. Using a code suitable for transferring the information to IBM punch cards, 50 different items were recorded.* The cards were run through an IBM card counting sorter, permitting computation and correlation of various factors.

## AGE INCIDENCE

The age at onset of symptoms is presented in Fig. 1. Two-thirds of the patients were in the fifth and sixth decades. The youngest was 12 years old, and the oldest 73. There were only 2 patients below the age of 20, and 2 over 70.

## SEX INCIDENCE

The present series consists of 127 males, or 58 per cent, and 92 females, or 42 per cent. This difference suggests that there might be something in the female endocrine makeup which serves as protection against the occurrence of this tumor. If this were the case, one would suppose that the incidence of glioblastoma might be particularly low in the group of females with actively functioning ovaries.

To examine this question the state of ovarian function was tabulated in the 73 cases of females in which this information was available. None of these patients was prepubertal, 39 per cent were in the reproductive period, while 60.3 per cent were menopausal or postmenopausal. However, in the third and fourth decades, corresponding to the reproductive period, the incidence was greater in females than in males. Also, the peak incidence for both sexes is in the fifth and sixth decades, which corresponds to the menopausal or postmenopausal period of females (Fig. 1). The evidence fails to support a significant correlation between the state of ovarian function and the incidence of glioblastoma.

## TOTAL DURATION OF DISEASE

The survival curve is seen in Fig. 2. Total duration is defined as the time from the appearance of the first symptom until death. At the end of 7 months, 50 per cent of the patients were dead while 67 per cent failed to survive 1 year. Another 22 per cent died during the second year. The remaining 11 per cent lived for periods of 2 to 5 years.

The age of the patient seems to have little effect on the duration. When divided into 3 groups consisting of those under 30, those from 30 to 49, and those 50 and over, the survival curves for the 3 groups are not strikingly different (Fig. 3). The course of the oldest group is slightly more rapid, perhaps a reflection of the fact that these older patients are poorer surgical

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FIG. 1.

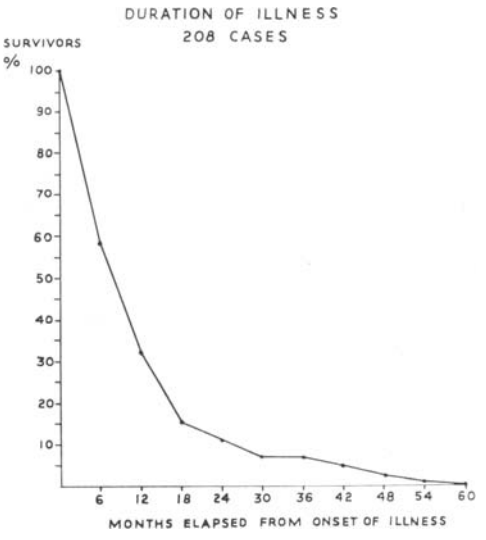



FIG. 2.

risks. In any event, the disease does not run a more rapid course in younger patients, as is often the case with some other neoplasms.

The survival curves of the male and female groups are almost identical. Among the females, there is no significant difference between the survival rates of the reproductive group and the menopausal-postmenopausal group.

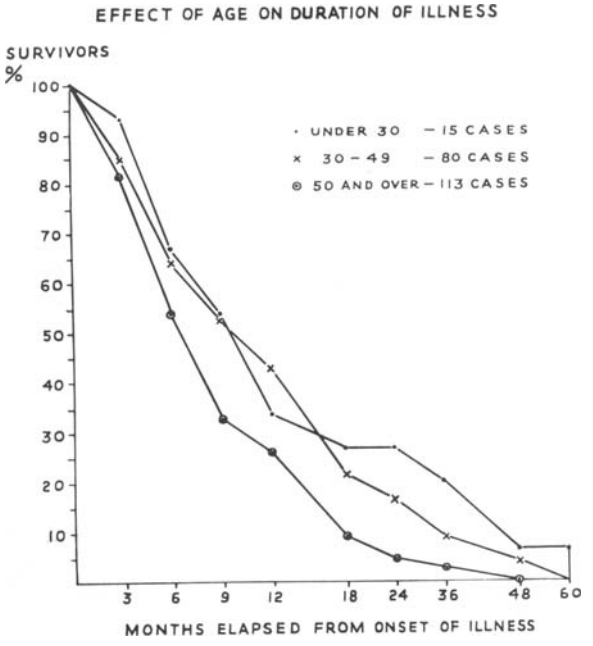



FIG. 3.

## DURATION OF SYMPTOMS

The duration of symptoms prior to the time of diagnosis was usually rather brief. The duration was less than 6 months in 70 per cent of the patients, while 83 per cent had a history of less than 1 year. It is worth noting, however, that 17 per cent in this series had histories of over a year's duration: 10 per cent between 1 and 2 years, and the remainder from 2 to 5 years. The patient with the longest history was a 28-year-old woman who was admitted in extremis, 7 months pregnant, with a 5-year history of generalized seizures. She died before treatment could be instituted.

## SYMPTOMATOLOGY

It is well known that the symptomatic onset of glioblastoma multiforme may be extremely abrupt, simulating a vascular accident. This type of apoplectic onset was noted in only 8 of these patients. In 2 cases the mode of onset is not known, while in the remainder it was gradual.

TABLE 1

*Symptomatology*

| | Present (Per Cent) | Initial Symptom (Per Cent) | Chief Complaint (Per Cent) |
|---|---|---|---|
| Headache | 86 | 37 | 35 |
| Mental change | 47 | 7 | 3 |
| Nausea, vomiting | 45 | 0 | 1 |
| Motor | 44 | 3 | 5 |
| Visual | 39 | 5 | 2 |
| Altered consciousness | 39 | 3 | 7 |
| Gait disturbance | 35 | 2 | 0 |
| Cranial nerve* | 35 | 4 | 1 |
| Personality change | 34 | 7 | 1 |
| Seizures | 32 | 16 | 10 |
| Aphasia | 32 | 5 | 4 |
| Sensory | 23 | 4 | 1 |

* Not including optic nerve.

The symptoms complained of are listed in Table 1, with data also on the frequency with which each was the initial symptom and the chief complaint. Headache is the leading symptom by a wide margin in all 3 categories. Approximately a third of the patients had seizures and in half of these it was the initial complaint.

## FAMILIAL INCIDENCE

Of 163 cases in which a family history was recorded, only 3 were positive for brain tumor. The type of tumor is not known in any of these.

## COINCIDENCE WITH OTHER NEUROLOGICAL DISEASE

The history of each of these patients was examined to see whether glioblastoma multiforme tends to be associated with any other neurological

disease. The following associations were noted: 1 patient had von Recklinghausen's disease; 17 gave a past history of head injury; 9 had various psychiatric diseases, including 1 with mental deficiency; 2 had epidemic encephalitis, 1 having Parkinsonism as a sequel, the other seizures; 1 case each of the following: chorea plus a "stroke," migraine, Bell's palsy, meningitis. There is nothing to suggest that any of these were more than chance associations.

## INCORRECT DIAGNOSIS

An initial diagnosis other than brain tumor was made in 25 instances as follows: 7 cases were initially diagnosed as cerebral thrombosis; 3 were thought to be psychiatric problems; 4 were labeled epilepsy; 3 patients were thought to have subdural hematoma, and another a subcortical hemorrhagic cyst of traumatic origin—a diagnosis made at the operating table; 2 patients were thought to have encephalitis. The following erroneous diagnoses were made once each: alcoholic neuritis, Sydenham's chorea with Bell's palsy, poliomyelitis, paresis, porencephaly, and "chronic progressive encephalopathy."

In 5 instances a brain tumor other than glioblastoma was diagnosed: 3 astrocytomas, 1 meningioma, and 1 metastatic tumor.

## DIAGNOSIS

It is of interest to inquire into the usefulness of various diagnostic studies performed on patients suspected of having a brain tumor.

*Lumbar Puncture.* Lumbar puncture was done in 122 of the 219 cases. Of this number there were 2 fatalities directly attributable to the lumbar puncture. The pressure was recorded in 112 cases. Of these, the pressure was elevated above 180 mm. of water in 90 (80 per cent). Of 79 cases in which the cerebrospinal fluid protein was determined, it was elevated above 45 mg. per cent in 60 (76 per cent). The cell count was determined in 96 cases. More than 5 white cells per c. mm. were present in 23; 30 showed the presence of red cells, while 52 had normal cell counts. Out of 66 cases in which pressure, protein, and cell count were all recorded, only 4 showed normal values for all 3 determinations.

Based on this experience, the cerebrospinal fluid in a case of glioblastoma multiforme is very likely to be abnormal in some respect. The information obtained, however, is nonspecific and is gained at the risk of a mortality rate of almost 2 per cent for the procedure of lumbar puncture.

Many of these lumbar punctures were performed by other services before the patient was referred to us, and a good many were done during the early years. Our present attitude is that lumbar puncture should be reserved for those cases in which the diagnosis is in considerable doubt and when it appears that valuable information of benefit to the patient can be thus obtained.

*Roentgenograms of the skull* are taken routinely. The results of this

examination are recorded in 191 of our cases. Abnormalities were present in 59 per cent; 32 per cent showed a pineal shift, 26 per cent had changes secondary to increased intracranial pressure, 2 per cent showed abnormal calcification, while 9 per cent had various other abnormalities. In addition to being "positive" in a respectably high percentage of cases, the roentgenograms of the skull may give information of specific diagnostic value. The presence of a mass lesion and its lateralization are often disclosed.

TABLE 2

*Results of air studies*

| | Pneumoencephalogram | Ventriculogram |
|---|---|---|
| Number done | 19 | 135 |
| Result unknown | 3 | 4 |
| Result known | 16—100% | 131—100% |
| Localizing | 3—18.7% | 101—77.1% |
| Nonlocalizing | 13—81.3% | 30—22.9% |
| Indeterminate | 2—12.5% | 2— 1.5% |
| Abnormal, nonlocalizing | 3—18.8% | 2— 1.5% |
| Lateralizing only | 0— 0% | 6— 4.6% |
| False localization | 0— 0% | 5— 3.8% |
| Inadequate filling | 8—50.0% | 15—11.5% |
| Total abnormal | 6—37.5% | 114—87.0% |
| Fatalities | 1— 5.3% | 0 |

*Electroencephalography* was done in 90 cases. Of these 93 per cent were abnormal in some respect and only 7 per cent normal. Abnormality without localization occurred in 10 per cent; 49 per cent localized the lesion correctly while an additional 24 per cent gave a localization in the wrong lobe of the brain, yet close enough to be of some value; 9 per cent lateralized the lesion correctly without localizing it. In 1 case there was a localization in the wrong hemisphere. The figures speak for themselves. The electroencephalogram is without question a valuable diagnostic tool.

*Air Studies.* Short of surgery, the ultimate means of confirming the diagnosis of tumor and localizing the lesion has been an air study. The results of pneumoencephalography and ventriculography are compared in Table 2. Because the risk of a simple lumbar puncture is compounded in the pneumoencephalogram it is our present policy not to do this procedure knowingly in cases of tumor. Only a small number were done in this series. One out of 19 resulted in a fatality. Because of the small numbers involved the figures admittedly do not bear much weight. The results in this series, at any rate, were quite poor.

The yield of useful information from ventriculography is quite high, with accurate localization in 77 per cent. This appears particularly noteworthy since the series includes our early experiences with the procedure. In most

instances ventriculography was followed by craniotomy the same day. Any fatalities that might have followed were therefore scored against the craniotomy. The fact that no localization was obtained in 23 per cent of the cases emphasizes the importance of having an accurate history and neurological examination before becoming committed to surgery.

*Arteriography* was performed in only 21 cases, this series antedating the present vogue for this procedure. Of these 11 were abnormal; 10 (48 per cent) localized the lesion while 11 did not. Of those that failed to localize, 1 was lateralizing only, 2 were indeterminate, and 8 were inadequately filled. All were carotid injections. Bilateral studies were done in only 1 case, which was indeterminate. There were no fatalities. With the development of new techniques such as the use of the seriograph the future of arteriography is no doubt brighter than these results would indicate.

## TREATMENT

*Surgery.* Surgical treatment was employed in 183 of 219 cases. Patients with craniotomy and tumor removal limited to biopsy are considered as surgically treated, as the procedure probably had some influence on the subsequent course. A patient with needle biopsy via a burr hole, however, is considered untreated. Of the 36 untreated patients, 4 were dead on arrival at the hospital, 15 were undiagnosed prior to death, 10 were diagnosed but died before treatment could be instituted, while 7 were judged inoperable.

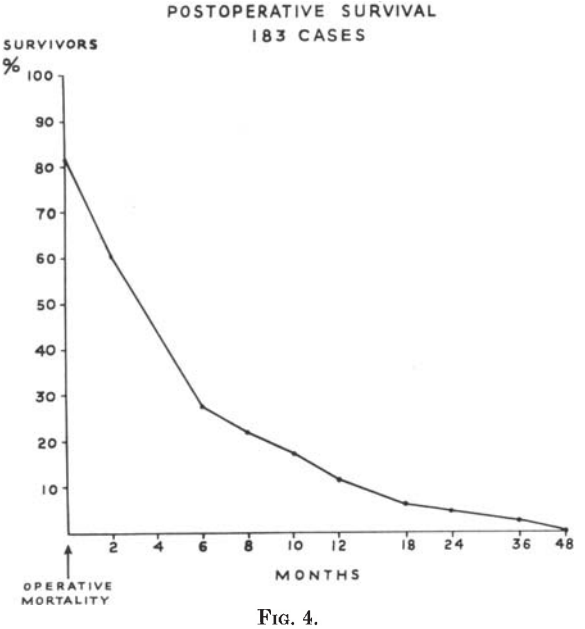



FIG. 4.

The postoperative survival of the 183 surgical cases is presented in Fig. 4. The operative mortality was 18.5 per cent, operative deaths being arbitrarily defined as any that occurred within 1 week of operation. About

50 per cent of the patients were dead within 3 months, almost 75 per cent within 6 months; 13 per cent survived over a year postoperatively. The longest survival was 48 months. In those cases in which more than one operation was performed the survival is computed from the date of the first procedure.

A single operation was done on 155 patients, 26 had two, 1 had three, while 1 had five procedures. Only actual attacks on the tumor are included in these figures. Procedures such as re-elevation of a bone flap for postoperative clot are not included.

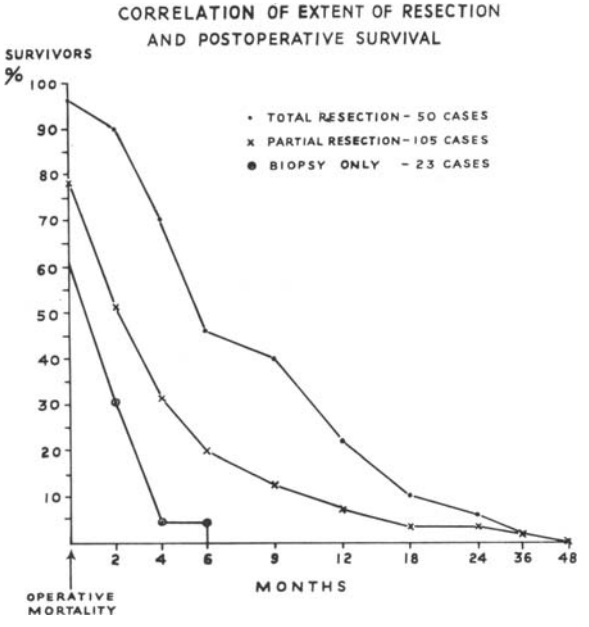



FIG 5.

The technique of the surgical attack upon brain tumors varies considerably, being governed by the various factors that determine operability—such as anatomical site and size of the tumor, the general condition of the patient, the neurological deficit—and also by the philosophy of the surgeon. We felt that it would be of interest to compare the results of various techniques. Based on the details reported in the surgeon's operative note, it has been possible to divide the cases into groups according to the extent of tumor resection, the type of external decompression, and the type of internal decompression.

With respect to the extent of tumor resection, it was possible to classify 178 of the cases; 50 patients had a grossly "total" removal of tumor in the estimation of the surgeon, 105 had a partial removal, while in 23 cases the tumor removal was limited to a biopsy. The survival curves of these 3 groups are presented in Fig. 5. The striking difference in operative mortality and

extended survival is quite apparent. It is clear that complete removal of all visible tumor tissue, if it can be accomplished, will give the patient the best chance of survival. However, it is obvious that the opportunity for carrying out such a "total" resection is limited by the various factors previously noted.

The type of decompression was noted in 176 cases; 51 patients had none, 95 had a small decompression, usually subtemporal, and 30 had a large decompression with removal of the bone flap. The first two groups had operative mortality rates of 17.6 per cent and 14.7 per cent respectively, with little

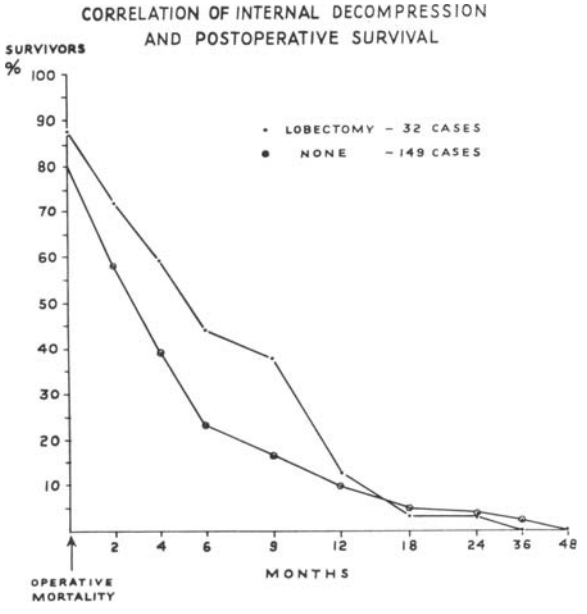



FIG. 6.

difference in the survival rates. The group with large external decompressions did not fare so well, having an operative mortality of 30 per cent and all the patients dead within 1 year. Removal of the bone flap in this clinic is reserved usually for patients with brain swelling or an inoperable tumor. The procedure undoubtedly enables many patients to survive a crisis and may prolong life a few months. The figures merely reflect the poor prognosis of the group of patients selected for removal of the bone flap.

Some degree of internal decompression accompanies any tumor removal, but occasionally a massive internal decompression is achieved by means of partial lobectomy. Out of 181 patients classified, 26 had a lobectomy incidental to removal of the tumor. Another 6 had a lobectomy in addition to the tumor removal, making a total of 32 lobectomies. The remaining 149 patients did not have a lobectomy. Comparison of the survival curves of the 2 groups (Fig. 6) indicates that the patients with lobectomy enjoyed a considerable advantage for the first 9 months. From 12 months on the 2

groups were quite similar. Our comments regarding "total" removal of visible tumor apply equally well here.

The evidence presented indicates that the most radical surgical procedure consistent with maintaining neurological function will accomplish the most for the patient in terms of survival. The more radical procedures also have a lower operative mortality.

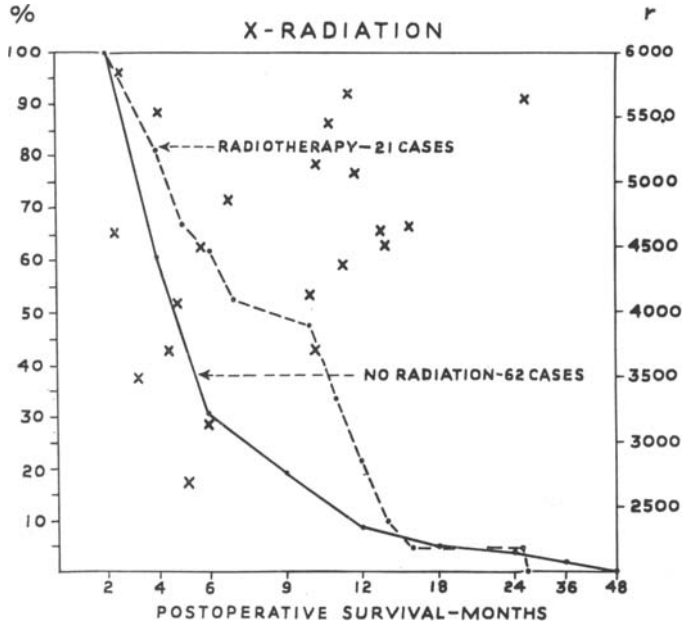



FIG. 7. Comparison of postoperative survival of 21 patients who completed radiotherapy within 60 days after operation with that of 62 patients who had surgery alone and were alive 60 days after operation. x indicates survival of each radiotherapy case plotted against tumor dose in r.

## RADIOTHERAPY

Radiotherapy was used in 47 patients of whom 41 completed the prescribed course; 39 of these had surgical resection of the tumor, 1 had only a biopsy, and 1 had no surgery at all. Treatment was given at various times in the course of the disease, some patients being treated late in their course because of a symptomatic recurrence. It was possible to select a group of 21 patients all of whom completed their radiotherapy within 60 days after operation. The dose of radiation in these cases varied between 2700 and 5900 r tumor dose. In Fig. 7 the postoperative survival of these patients is compared with a group of 62 patients who had surgery alone and who were alive 60 days after operation. It is apparent that during the first 12 months there is a significantly greater percentage of survivors in the radiated groups. After the first year, however, the difference disappears. The radiation dose of each of the treated patients is plotted against the survival time.

Among the patients surviving less than 9 months there is a wide range of dosage. With a single exception, those surviving 9 months or more received over 4000 r tumor dose. The results of routine postoperative radiation in this small series indicate that a worth-while prolongation of the palliative effects of surgery may be obtained. We propose to use radiotherapy more generally in the future than was the case in this series.

## THE EFFECT OF TREATMENT ON TOTAL DURATION OF ILLNESS

Sufficient information was available on 178 patients receiving the various types of treatment discussed above and on 30 patients receiving no treatment at all to allow us to compare these two groups.

Comparison of the duration of illness between the treated and untreated groups (Fig. 8) reveals a considerable difference in the number of survivors during the first year. We have seen that two-thirds of the postoperative

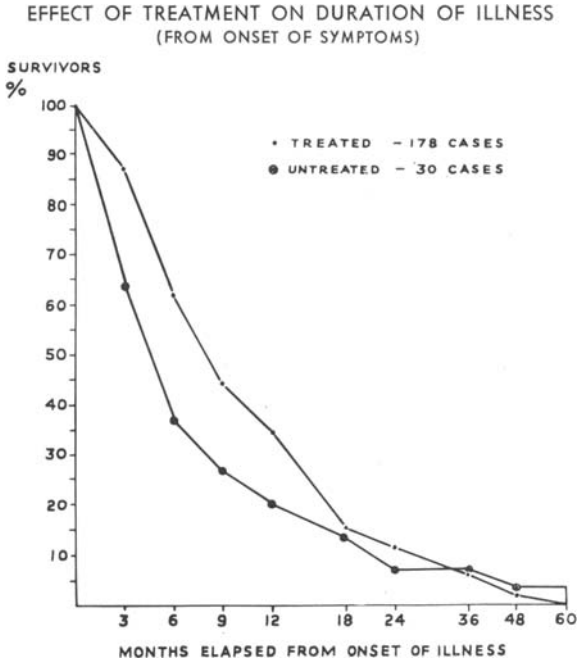



FIG. 8.

survivals are less than 6 months, the average being closer to 3 months. This extra 3 to 6 months seems to correspond to the early difference between the treated and untreated groups. It is of considerable interest that after the first year the percentage of survivors in the two groups is roughly the same. It would appear that the occasional long postoperative survival is because of the fact that the tumor happens to be a slow-growing one. An equal percentage of patients with untreated tumors last just as long.

## POST-TREATMENT COURSE

Since all the presently known forms of treatment for glioblastoma are merely palliative, we cannot be satisfied with mere prolongation of life, laudable though it may be. It is pertinent to inquire also into the disability remaining after treatment. Of 172 treated patients whose disability status is known, 27.3 per cent died within 2 weeks of treatment, 33.1 per cent were left with severe disability, including such conditions as unconsciousness, hemiplegia, etc.; 27.3 per cent had slight disability, not requiring constant nursing care. Only 12.2 per cent were able to resume a useful occupation. We might say that 40 per cent had reasonably good results: slight or no disability.

## RECURRENCE OF SYMPTOMS

If a patient is to benefit from treatment, how long can we expect this benefit to last? A recurrence is defined for our purposes as the development of symptoms indicative of progressive disease. We were able to document the question of recurrence in 143 of the 184 patients treated. There was no remission in 60 per cent. The deaths following treatment are included in this number. Only 27 per cent of the patients went 3 months without a recurrence; 15 per cent passed the 6 months' mark, while only 5 per cent went a year. The longest interval recorded was 29 months.

## STATUS AT DEATH

As mentioned above, all of the 219 patients in this series are dead. In the cases in which the patient survived treatment, 130 deaths were from the tumor; 47 patients died during treatment or within 2 weeks; 35 died untreated. Death occurred in 3 cases from unrelated causes with tumor present; 4 patients died with the status of the tumor unknown. None of the patients died of an unrelated cause with no evidence of recurrence: there were no cures.

## PATHOLOGY

In tabulating the various morphological characteristics of these tumors we have taken as our example in each case the first specimen obtained, usually a surgical specimen, but in some cases the autopsy specimen. This method offers the advantage of a uniform approach to each case, avoiding the dubious process of deciding which specimen is most representative in those cases in which serial specimens were available.

The primary site of the tumor is indicated in Table 3. There was a slight preponderance of tumors in the right hemisphere over the left. Growths arising primarily in midline structures were relatively rare.

The gross characteristics of 200 tumors are presented in Table 4. Most common were solid tumors, although cysts occurred frequently. Areas of necrosis were quite common (52 per cent), as were small scattered hemorrhages (40 per cent). Four of the tumors presented as solitary cysts with a

TABLE 3

*Primary site of tumors*
*218 cases*

| | |
|---|---|
| Right hemisphere | 109 |
| Left hemisphere | 91 |
| Midline structures | 18 |
| Frontal lobe | 50 |
| Frontal-temporal | 5 |
| Frontal-parietal | 8 |
| Temporal lobe | 47 |
| Temporal-parietal | 18 |
| Parietal lobe | 42 |
| Parietal-occipital | 9 |
| Occipital lobe | 8 |
| Occipital-temporal | 4 |
| Occipital-temporal-parietal | 5 |
| *Diencephalon, corpus striatum | 14 |
| *Brain stem | 5 |
| *Corpus callosum | 5 |

* Includes combined sites.

mural nodule, resembling astrocytomas. In only 6 cases was there grossly visible calcification (2 per cent of the roentgenograms of the skull in this series showed abnormal calcification).

The microscopic details of glioblastoma multiforme are well known. In establishing the diagnosis the criteria which we weighted most heavily were pleomorphism, proliferation of the intima of blood vessels, and the presence of mitotic figures. Unless at least two of these could be demonstrated the tumor was excluded from the series. The frequency of the various microscopic characteristics is given in Table 5.

The predominant type of cell was tabulated in 204 cases; 174 tumors presented a mixed picture with no single type of cell predominating. In 15

TABLE 4

*Gross pathology of tumors*
*200 cases*

| | |
|---|---|
| Solid tumor | 119 |
| Cyst | 77 |
| Solitary cyst with mural nodule | 4 |
| Small hemorrhages | 80 |
| Massive hemorrhage | 4 |
| Necrosis | 104 |
| Calcification | 6 |

TABLE 5

*Microscopic pathology of tumors*
*206 cases*

| | |
|---|---|
| Pleomorphism | 203 |
| Multinucleated giant cells | 174 |
| Mitoses numerous | 147 |
| Mitoses rare | 52 |
| Proliferation of vascular intima | 197 |
| Overgrowth of vascular adventitia | 67 |
| Blood vessels numerous | 190 |
| Necrosis | 193 |
| Pseudopalisades | 92 |
| Hemorrhage | 129 |
| Calcification | 14 |

tumors the predominant cell was the fibrillary astrocyte, in 7 it was the protoplasmic astrocyte, in 6 the spongioblast, and in 1 the astroblast.

It is commonly believed that the presence of mitotic figures indicates a more malignant or rapidly growing tumor. If this were true, one would suppose that the tumors with the most mitotic figures would be the most rapidly progressive. To test the validity of this assumption we compared the total duration of illness in a group of 142 patients with tumors having numerous mitotic figures with a group of 54 patients with tumors having rare or no mitotic figures. Interestingly enough, the survival curves for the two groups were almost identical.

## SUMMARY

An unselected series of 219 cases of glioblastoma multiforme has been reviewed from the standpoint of natural history of the disease, diagnostic studies, treatment, and pathology.

*Natural History.* The sex incidence was 58 per cent males and 42 per cent females.

The age incidence was greatest in the fifth and sixth decades.

The total duration of the disease was under a year in 67 per cent of the cases; 11 per cent of the patients, however, lived 2 to 5 years. The duration was not related to the age or sex of the patient.

The duration of symptoms prior to diagnosis was less than 6 months in 70 per cent of the cases but 17 per cent of the patients had histories longer than a year.

The frequency of various symptoms is tabulated. Headache was most common. Seizures occurred in a third of the cases and were the initial symptom in half of these.

There was no evidence of familial incidence nor of a relationship with any other disease of the nervous system.

*Diagnostic Studies.* The cerebrospinal fluid is almost always abnormal in some respect. There was a mortality rate of 2 per cent for the procedure of lumbar puncture while the information gained was nonspecific. Routine use of this procedure is not recommended.

Roentgenograms of the skull were abnormal in 59 per cent of the cases.

Electroencephalograms were abnormal in 93 per cent and localized the lesion correctly in 49 per cent of the cases.

Pneumoencephalograms were done only 19 times with 1 fatality. The lesion was localized in only 3 cases.

Ventriculograms gave a correct localization in 77 per cent of 135 cases.

Arteriography was performed in only 21 cases with 48 per cent successful localization.

*Treatment.* There were 183 patients treated surgically, with an operative mortality of 18.5 per cent. Average postoperative survival was about 3 months. The more radical surgical procedures, including "total" removal of the tumor and lobectomy, offered the best prognosis with regard to operative mortality and survival time.

Of 47 patients receiving radiotherapy, 21 received a course of 2700–5900 r tumor dose completed within 60 days after operation. This group showed a significantly higher percentage of survivors during the first year when compared with a group who had surgery alone.

The effect of all present forms of treatment is to prolong life by 3 to 6 months. Long-term survivals are just as common among untreated patients as those treated.

Postoperative disability tended to be great. Only 40 per cent of the patients had slight or no disability.

There was no remission of symptoms in 60 per cent of the cases. Only 15 per cent of the patients went 6 months without a recurrence. There were no cures.

*Pathology.* The anatomical site, and gross and microscopic characteristics of these tumors are tabulated.

The number of mitotic figures seen is shown to bear no relationship to prognosis.

## REFERENCES


1. Busch, E., and Christensen, E. The three types of glioblastoma. *J. Neurosurg.*, 1947, *4:* 200–220.
2. Cushing, H. Intracranial tumours. Notes upon a series of two thousand verified cases with surgical-mortality percentages pertaining thereto. *Springfield, Ill.: Charles C Thomas,* 1932, xii, 150 pp. (see pp. vii–viii).
3. Cushing, H., and Eisenhardt, L. Meningiomas. Their classification, regional behaviour, life history, and surgical end results. *Springfield, Ill.: Charles C Thomas,* 1938, xiv, 785 pp.
4. Davidoff, L. M., and Feiring, E. H. "Circumscribed" glioblastoma multiforme. *J. Neuropath. clin. Neurol.*, 1951, *1:* 161–167.
5. Davis, L., Martin, J., Goldstein, S. L., and Ashkenazy, M. A study of 211 patients with verified glioblastoma multiforme. *J. Neurosurg.*, 1949, *6:* 33–44.
6. Farr, L. E., Sweet, W. H., Locksley, H. B., and Robertson, J. S. Neutron capture therapy of gliomas using boron$^{10}$. *Trans. Amer. neurol. Ass.*, 1954, 110–112.
7. Maxwell, H. P. The incidence of interhemispheric extension of glioblastoma multiforme through the corpus callosum. *J. Neurosurg.*, 1946, *3:* 54–57.
8. Murray, M. R., Peterson, E. R., Hirschberg, E., and Pool, J. L. Metabolic and chemotherapeutic investigation of human glioblastoma in vitro. *Ann. N. Y. Acad. Sci.*, 1954, *58:* 1147–1171.
9. Netsky, M. G., August, B., and Fowler, W. The longevity of patients with glioblastoma multiforme. *J. Neurosurg.*, 1950, *7:* 261–269.
10. Sachs, E. The problem of the glioblastomas. *J. Neurosurg.*, 1950, *7:* 185–189.