tumor, but no excellently effective influence upon the life-span of the cases of malignant glioma. In the future, more effective and tumor-specific anticancer agents or combination with other available techniques (immunological, radiological or nuclear, and physical-chemical, etc.) will potentiate our method.

E-8. Chemotherapy of Brain Tumor. The Uptake of $^3$H-Methotrexate and $^{14}$C-Bleomycin in Mouse Glioma

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As the maximum effects of chemotherapeutic agents would be considered to occur when they concentrate preferentially in the tumor, it was felt that a knowledge of the uptake and distribution of the drugs by malignant gliomas might improve their clinical usefulness. This study was initiated to determine the uptake and distribution of Methotrexate and Bleomycin in mouse glioma after intravenous or intrathecal administration, and to estimate the effectiveness of these drugs by various routes of
administration for treatment on the patients with malignant glioma.

Brain tumors were induced in male mice of strain ddN of approximately 5 weeks old and weighed 15 gm. by intracerebral implantation of 20-methylcholanthrene pellet of approximately 1 mgm. in weight. Tritiated Methotrexate ($^3$H-MTX) (0.05 mCi/mgm.) was injected intravenously (1.78/gm. of body weight) or intrathecally (0.187/gm. of body weight) into mice bearing an induced brain tumor. The mice were bled to death at various hours after injection and the distribution of $^3$H-MTX was determined by counting of radioactivities in tissue and by radioautography (freeze dried, embedded in Epon). The $^{14}$C-Bleomycin A$_2$ ($^{14}$C-BLM) (7.52 $\mu$Ci/mgm.) was intravenously injected (0.1 mgm./gm. of body weight) to mice with malignant glioma. The distribution of $^{14}$C-BLM in organs were determined by radioactivity at two hour after the administration. In order to know the ratio of inactivation of $^{14}$C-BLM in glioma, distribution of $^{14}$C-BLM in sub-cutaneously transplanted gliomas was measured by the radioactivity and the antibacterial activity by the thin layer disc method using B. subtilis as the test organism.

Glioma was induced in 31 mice at 9.2 months on average after the implantation of methylcholanthrene pellet, and used in this study. They were very similar histologically to the human malignant astrocytoma or glioblastoma. Sixteen mice with induced intracranial fibrosarcoma, 15 mice with induced fibrosarcoma in the scalp and subcutaneously or intracerebrally transplanted gliomas were also used in this study.

The amount of $^3$H-MTX taken up by the gliomas was considerably high and from 2.5 to 13 times more than that of the surrounding normal brain tissue. The uptake of $^3$H-MTX by gliomas at 24 hours after intrathecal administration is higher than that obtained after intravenous injection, though the dosis of the drug administrated was one tenth of that of intravenous injection. The concentration ratio between glioma and brain tissue ranged from 5 to 11. The high concentration of $^{14}$C-BLM in gliomas was observed (approximately 37/gm. of wet tissue), and it was assumed that the two third of $^{14}$C-BLM remained in active form in glioma. The uptake of $^3$H-MTX by intracerebrally transplanted glioma differed from that of primary glioma, and was rather similar to that of subcutaneous fibrosarcoma.

From the data following conclusions were made:

1) Methylcholanthrene induced gliomas would be useful for the study on chemotherapy of brain tumor.
2) Intrathecal administration of Methotrexate may be more-effective than intravenous administration on some kind of glioma.
3) Bleomycin may have cytostatic effect on malignant glioma.