mm into the arachnoid space. The tube and needle contained a fine silver wire stylet, and the top of the needle was closed with a cork. The needle was fixed in place with dental caulking substance and acrylic material (Fig. 1). Thus the tube was vented to the cerebrospinal fluid bathing the cerebral cortex.

For intraventricular implantation (*4*), a metal cannula specially made for this purpose (*3*) was screwed into the hole instead of the tube and needle. The cannula was likewise fixed in place with dental caulking substance and acrylic material.

A drug was not administered until 1 week after the tube or the cannula was implanted. The volume of the drug did not exceed 0.2 ml, and the *p*H was controlled. For study of the distribution of the drug, each dog was sacrificed after a single experiment and 0.2 ml of aniline blue dye was given through the tube or cannula. With intra-arachnoid injection, this dye distributed over the entire hemisphere, but was concentrated in an area about 1 cm^2 around the tip of the tube. The exact distribution depended on the direction of the tube. Intraventricular injection, however, distributed the dye throughout the ventricular system of the brain, as was reported by Kumagai *et al.* (*3*).

Results on 21 dogs (8.6 to 14 kg) were selected for this report. Morphine, amobarbital, or imipramine were administered to these dogs.

Intra-arachnoid injection of 2 mg or 4 mg of morphine HCl (three dogs) provoked no marked response except frequent scratching of the head, which suggested itching or irritation. However, 2 mg of morphine HCl injected into the lateral ventricle (three dogs) evoked, in order: licking, vomiting, defecation, signs of fear, restlessness, drooping hind quarters, profuse salivation, exophthalamus, and ceaseless pacing. Complete loss of appetite was also noticed. These symptoms started within 1 minute after the injection and continued for 6 hours. Analgesia was not found.

Intra-arachnoid injection of 50 mg of amobarbital sodium (three dogs) produced variously no change, slight motor ataxia, or a decrease of activity. An additional injection (100 mg) given 1 hour later (two dogs) caused moderate motor ataxia and muscle weakness, especially of the hind quarters. The ataxia and weakness of muscles began after 10 minutes and continued for 20 minutes. An intraventricular injection of 50 mg of the drug (three dogs) produced within 1 minute licking, vomiting, and defecation, followed by coughing, sneezing, hiccoughing, motor ataxia, and head drop (like that produced by curare). About 10 minutes after injection the animal in prone position pedaled with all legs for 2 minutes, and for the next 7 hours the dog had no appetite, wandered continuously, panted, and barked more than usual. In one experiment 10 minutes after the injection, respiration ceased for 10 minutes. The animal was readily maintained by artificial respiration and seemed conscious throughout.

No unusual behavioral change was noticed after intra-arachnoid injection of 6 mg or 12 mg of imipramine HCl (three dogs). However, intraventricular injection of 2.5 mg (three dogs) caused vomiting and defecation within 1 minute. During the 2 hours after the injection, the following abnormal behavior was observed: slight motor ataxia, barking, twitching of the neck muscles, and behavioral depression. The depression continued for 7 hours. In another experiment in which 6 mg of the drug were injected (three dogs), depression was more marked, with slowed motor activity, drowsiness, and lack of response to previously recognized stimuli.

Thus, the behavioral effect obtained by intra-arachnoid injection differed from those obtained by intraventricular injection, the former method producing little response to the three drugs tested. However, not all drugs produced such slight response by the intra-arachnoid injection. For example, potassium chloride or acetylcholine chloride induced marked behavioral depression, and strychnine sulfate provoked generalized convulsions (*5*).

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Are New Neurons Formed in the Brains of Adult Mammals?

Abstract. In an autoradiographic investigation, the production of brain lesions in rats was combined with intracranial injection of thymidine-H^3. Nuclei of numerous glia cells were found labeled in brain regions associated with the traumatized areas. In addition, some neurons and neuroblasts showed labeling, suggesting the possibility of proliferation of neurons in adult rats.

It is commonly stated that in higher vertebrates neogenesis of nerve cells is restricted to the early stages of embryonic development. This belief is based on the observation that neurons with mitotic figures are absent in the central nervous system of most higher vertebrates. However, this does not definitely rule out the neogenesis of neurons in the adult, for new neurons might arise from nondifferentiated precursors, such as ependymal cells. After multiplication, such embryonic cells could differentiate and thus add new neurons to the existing population. This hypothesis can be tested by administering to animals thymidine-H^3, a specific precursor of the chromosomal DNA, and so labeling the proliferating cells. That tritiated thymidine is, indeed, incorporated exclusively into nuclei of dividing cells was shown by several investigators by means of fine-resolution autoradiography (*1*).

In a pilot experiment, which was designed to test simultaneously the kinetics of glial proliferation after brain trauma, bilateral electrolytic lesions were produced stereotaxically in the lateral geniculate body in ten young adult Long-Evans hooded rats. The insulated hypodermic needle used to produce the lesion was employed for the unilateral injection into the lesion area of 50 μc of thymidine-H^3 (specific activity 5.21 c/mmole; total volume of aqueous solution 0.05 ml). Pairs of animals were then sacrificed 1 day, 1 week, 2 weeks, 1 month, and 2 months after the operation by cardiac perfusion with 10-percent neutral formalin. After paraffin embedding, 5-μ thick coronal sections were cut from a block extending from the mesencephalon to the rostral diencephalon. The deparaffinized sections were coated with Ilford G-5 nuclear emulsion, dried, and exposed for 2 months. The exposed slides were then developed and stained with gallocyanin chromalum. Several sections were soaked, before being coated with nuclear emulsion, in a 0.05-per-

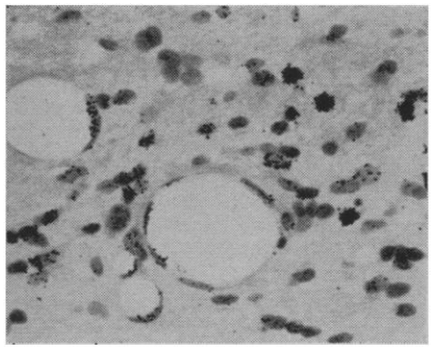

Fig. 1. Radioactive labeling of glia and vascular cells in the visual radiation of a rat in which bilateral destruction of the lateral geniculate body was combined with injection of thymidine-H^3; animal was sacrificed 2 months after operation. Stained with gallocyanin chromalum after autoradiographic exposure and development (only nuclei of glia cells stained) (about × 380).

cent solution of deoxyribonuclease in 0.003*M* $MgSO_4 \cdot 7H_2O$ to test the DNA-specificity of the retained label in the tissue.

In all sections studied, numerous glia cells showed uptake of the radioactive material and the reduced silver grains were in general localized within the nuclei of glia cells. The majority of labeled glia cells was found in the areas of the lesions (both on the injected and opposite sides of the brain) and in regions known to have intimate connections with the traumatized lateral geniculate bodies. These latter included the visual radiation, the lower layers of the visual cortex, the pretectal region, the optic tract, and the brachium of the superior colliculus. As described elsewhere (*2*) the technique proved useful in investigating the extent, kinetics and various other aspects of glial proliferation. In addition to the numerous labeled glia cells, which presumably underwent proliferation in response to the lesions, a few labeled glia cells, some labeled neuroblasts, and also labeled nuclei of some neurons were observed in brain regions not necessarily associated with the lesion area. Digestion with deoxyribonuclease removed the label. In systematic scanning of two coronal sections through the thalamus in several animals (with survival periods following lesion and administration of thymidine-H^3 ranging from 1 day to 2 months) a varying number (6 to 36 in single sections) of mildly or intensely labeled neurons and neuroblasts were observed. Most of the labeled neurons were of the stellate type; in the cortex a few labeled pyramidal cells were also seen (Figs. 1 and 2).

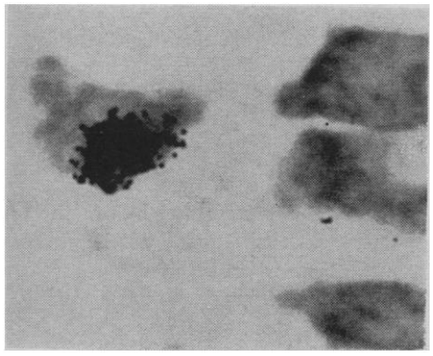

Fig. 2. Radioactive labeling of a neuron in the cerebral cortex of a rat which was sacrificed 1 month after the operation (about × 1170).

This indicates that new neurons may come into existence in the brain of adult mammals, at any rate in such forms as the rat. If the general observation is valid that mitotic figures are absent in the brain of adult mammals, these findings might suggest that the labeled neurons were formed from undifferentiated cells which divided mitotically during the period at which the administered thymidine-H^3 was available. The presence of labeled neuroblasts, mostly in fiber tracts, would support such a process of neurogenesis.

Koenig (*3*) observed the retention of some label by glia cells after administration of C^{14}-labeled adenine and orotic acid and extraction of RNA, and he suggested that this may be due to a slow turnover (that is, metabolic instability) of DNA. The plausibility of this conclusion, which was based on an indirect method of DNA labeling, was questioned by Hughes (*4*) on the basis of contrary direct evidence. The intense labeling of numerous glia cells, and some nerve cells, after as short a survival period as 1 day, also speaks against such an interpretation. The other possibility is that the uptake of thymidine observed in this study was due to some induction effect either by the lesion or by the injected thymidine. Extracerebral injection of thymidine-H^3 would be a better procedure to test whether turnover of this DNA precursor occurs in the normal brain. In fact, Schultze and Oehlert (*5*) and Messier and Leblond (*6*) reported no uptake of thymidine-H^3 by neurons after intraperitoneal injection of this substance into adult rodents. As the blood-brain barrier retards the penetration of most nucleotides, the dose of thymidine-H^3 used in these studies may have been too low to label neurons. Experiments are in progress in our laboratory to determine whether neurons take up systemically administered larger doses of thymidine in normal animals (*7*).

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Papova Virus Group

Abstract. The papilloma, polyoma, and vacuolating agents seem to form a natural group of tumor viruses, for which the name papova virus group is proposed. Members of the group have the following properties: 45 mμ diameter, deoxyribonucleic acid core, 42 capsomeres, absence of essential lipids, thermal resistance, slow growth cycle with multiplication within the cell nucleus, and tumorigenicity.

In the course of the work in this laboratory with papilloma (wart) virus of man (*1*), polyoma virus of mice (*2*), and vacuolating virus of monkeys (SV_{40}) (*3*), I have been made conscious of the similarities in properties between each of them and papilloma virus of rabbits (*4*). This has led me to group these viruses together in the pa'po'va virus group, the name being derived from the first two letters of each virus name: *pa*pilloma, *po*lyoma, *va*cuolating, in the order in which the viruses became known. The properties of the four members of the group are listed in Table 1. The list is less complete for