pected to occur. In fact, the average circulation time between capillaries in the hand and forearm and the veins in the antecubital fossa is probably well below 15 sec. The half-life of bradykinin in the circulation has been calculated to be some 30 sec[10]; so most of the kinin which is formed in the capillaries should still be found in the venous blood. If kinin should be formed in the extravascular space, where the plasma substrate comes in contact with the cells, as suggested by LEWIS[11], the amount which reaches the larger venous trunks would be smaller.

Kinins appear to have a role in vasodilatation occurring within the pancreas and the salivary gland[2,3,6], but even in those cases where the evidence seems strongest, there are some doubts. For instance, SCHACHTER[12] has shown that in the guinea-pig, salivary kallikrein will not form kinins with its own plasma.

The above results show that kinins are found in the circulating blood of normal individuals. The levels are low, 1 U/100 ml of blood (0.1 mcg bradykinin), and near the limit of sensitivity of the method employed, but high enough to have physiological implications. Since the kinin content of the arterial blood is comparable to the venous, plasma kinins appear to be formed within the circulating blood[13].

Résumé. Le contenu en «kinines» du sang veineux ou artériel humain équivaut à 0.1 mcg de bradykinine par 100 ml. Le contenu des veines du pli du coude n'augmente pas pendant la vasodilatation thermique ni pendant le travail des muscles de l'avant-bras.

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DNA Synthesis in Glial Cells during Nerve Regeneration

In a series of experiments HYDÉN et al. have demonstrated that the metabolic processes in the nerve cell and the surrounding glial cells are interrelated[1]. During nerve regeneration the total amount of proteins and ribonucleic acid per nerve cell increases[2]. Tracer studies have shown an increased incorporation of lysine[3,4] and of orotic acid[3] per nerve cell in regenerating hypoglossal neurons. The present study demonstrates that changes also occur in the surrounding glial cells during nerve regeneration.

The glial cells surrounding the neurons belonging to the hypoglossal nucleus in rabbits weighing 1.5–1.6 kg were studied. The hypoglossal nerve on the right side was crushed with cooled forceps, where it intersects the *musculus digastricus*. Before the experimental procedure was carried out, a cannula was implated with its tip in the *cisterna magna* according to a technique described by KOELLE and KOENIG[6]. Through this cannula radioactive precursors were injected intracisternally. The DNA synthesis in the glial cells during nerve regeneration was studied with H^3-thymidine by autoradiography. Each rabbit received a total of 200 μc H^3-thymidine (Schwarz lab., sp. act. 3.0 C/m*M*) divided into four equal doses 24, 22, 20 and 18 h before sacrifice at 9 p. m. Carnoy fixed sections through the *nucleus hypoglossus* in the *medulla oblongata* were extracted with 0.2 *N* perchloric acid at 4°C for 5 min and then thoroughly rinsed in water before coating with the autoradiographic emulsion (Ilford, K2) according to a slightly modified technique described by KOPRIWA and LEBLOND[6]. Some slides from each animal were incubated with deoxyribonuclease according to EDSTRÖM et al.[7] before coating with the emulsion. After exposure for eleven days the autoradiographs were developed and stained through the emulsion with toluidine blue at 4.0 and mounted. The number of glial nuclei with more than four grains over the nucleus was calculated in the same region of *nucleus hypoglossus* at different postoperative intervals (Table I).

Results. During the second to the sixth postoperative day there is an intensive DNA synthesis in the glial cell population on the regenerating side compared to the unoperated side. On the third postoperative day around 10% of all glial cells in the regenerating nucleus are labelled. In all animals one or less than one labelled glial nucleus is

Table I. The number of H^3-thymidine labelled glial nuclei per section on the regenerating and control side of *nucleus hypoglossus*. Rabbits were injected intracisternally four times: 24, 22, 20, and 18 h before sacrifice

Days after operation	1	2	3	6
Regenerating side	2.2	9.6	22.3	8.7
Control side	1.0	0.6	0.1	0.1

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observed on the unoperated side. No increased DNA synthesis can be seen in the interfascicular glial cells along the hypoglossal axons outside the regenerating nucleus. During this period with increased DNA synthesis mitotic figures can be found in the glial cells. In animals killed at 9 p.m. on the fourth postoperative day around one mitotic figure can be seen per section in the regenerating nucleus, and this corresponds to 2–3 mitotic figures per 1000 glial cells. The endothelial cells in the regenerating nucleus also show a DNA synthesis of nearly the same order as the glial cells.

In a second series material from a study of RNA synthesis in the regenerating *nucleus hypoglossus* was used. The experimental technique was exactly the same, but the tracers administered intracisternally were H^3-adenine and H^3-cytidine, which were given in daily injections at 9 p.m. during four days before sacrifice. The animals were sacrificed at 9 p.m. on the fifth day after the first injection. A total of 740 μc H^3-adenine and 300 μc H^3-cytidine was given in each experiment. The Carnoy fixed sections were incubated with ribonuclease in ammonium bicarbonate buffer according to EDSTRÖM[8] for 3×30 min at 37°C. Some sections were incubated after this extraction with deoxyribonuclease according to EDSTRÖM[7] for 3×60 min. The autoradiographic procedure was exactly the same as in the first series and the exposure time was kept constant for all sections, which made it possible to compare the DNA synthesis in four-day intervals from the second to the thirty-sixth postoperative day (Table II). All glial nuclei with ribonuclease resistant labelling extractable with deoxyribonuclease giving more than 10 grains in the autoradiographic emulsion over the nucleus were counted as labelled. This second series demonstrates that the DNA synthesis in glial cells rapidly decreases after the first postoperative week, and after the second postoperative week there is no significant difference between DNA synthesis on operated and unoperated sides. In all experiments the increase in DNA synthesis was restricted to the regenerating nucleus.

Table II. The number of labelled glial nuclei per ribonuclease treated section on the regenerating and control side of *nucleus hypoglossus*. Rabbits were injected with H^3-adenine and H^3-cytidine on four successive days and sacrificed 24 h after the last injection

Days after operation	6	10	14	20	28	36
Regenerating side	24.5	9.4	4.0	0.5	1.0	0.7
Control side	1.9	1.7	2.5	0.5	0.3	0.2

The morphological glial changes during and after the period with DNA synthesis in the regenerating nucleus were studied with Cajal's gold sublimate method for astrocytes, Tsujiyama's method for oligodendroglia, and Hortega's silver carbonate method for microglia. The astrocytes show a remarkable hypertrophy in the regenerating nucleus and this astrocytic reaction begins on the third day after nerve crushing and reaches its maximum during the ninth and fourteenth days. After the third week the astrocytosis rapidly decreases and 90 days after the nerve crush the astrocytosis in the regenerating nucleus is negligible. The microglial cells change less dramatically and the maximal microglial response is found between the third and fifth postoperative weeks. In the oligodendroglial cell population no significant changes can be seen during regeneration.

A detailed account of the experiments will be published later.

Zusammenfassung. Autoradiographie von Gliazellen, welche regenerierende motorische Nervenzellen umgeben, ergab eine stark erhöhte DNA-Synthese in den Gliazellen zwischen dem zweiten und sechsten Tag nach dem Nervenschaden. Morphologisch erscheinen typische Gliaveränderungen mit hochgradiger Hypertrophie der Astrocyten in der zweiten und dritten Woche nach der Operation.

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Protein Synthesis in the Early Stages of Liver Regeneration

A literature survey of radioisotopic investigations during regeneration after partial hepatectomy shows some lack of information on the behaviour of protein synthesis early after liver lobectomy, before significant tissue restoration occurs.

We refer in particular to the first post-operative day, when, compared to normal controls, generally only small changes have been reported in amino acid incorporation into regenerating liver proteins[1].

However, it is evident that active synthesis of proteins, most likely enzymes, necessary to trigger the later increase of the liver parenchyma, must take place at a molecular level long before the time the hepatic cells seem to be metabolically inert.

Such phenomena may in fact have been missed in previous researches either because of the tendency to take the regenerating liver for biochemical investigations long after the partial hepatectomy, when the growth rate has reached a maximum, or because the investigations are mainly carried out on the whole cell protein instead of on protein from subcellular fractions.

Some data supporting the above views may be derived from the research by several authors showing that, during the so-called pre-synthetic period, lasting from zero to 18 h after surgery, the apparently quiescent liver cell already synthetizes the enzymes necessary for nucleic acid replication. Generally, these investigations have been devoted more to the mechanism of the nucleic acid production and its inhibition by ionizing radiation than to

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