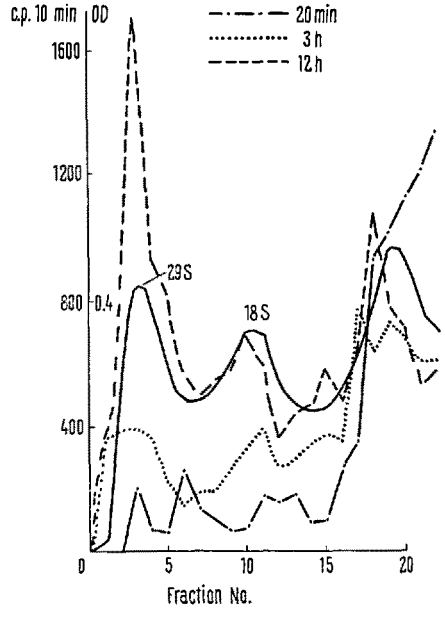
Labelling of Ribosomal RNA Peaks in the Liver of Rats After Administration of Tritiated Fluorouracil

HEIDELBERGER et al.[1] have shown that 5-fluorouracil (FU) is incorporated into liver ribonucleic acid (RNA). Labelled FU, given to mice, was recovered from the nucleic acids as labelled FU and only small amounts in other bases[2,3]. FU is also incorporated into poliovirus RNA[4] and tobacco mosaic virus RNA[5].

We have studied the effect of FU on the labelling of rat liver with cytidine-^{3}H[6,7]. The RNA labelling decreased after moderate doses of FU but was well recognizable in the ribosomal RNA peaks after 3 and 12 h. Very high doses of FU seemed to depress the RNA labelling almost completely, but characteristic ultrastructural alterations were obtained in the liver nucleoli, which also increased in size[8]. As the ribosomal RNA is considered to be elaborated in the nucleolus, the FU may be considered to interfere with the synthesis of ribosomal RNA. It was therefore considered to be of interest to investigate whether labelled FU labels ribosomal RNA.

Experiment. Six male white rats, weighing about 45 g each, were fed on a protein-free diet[9] for 4 days, starved for 24 h and killed at about 10.00 on the fifth day. The animals were given an i.p. injection of 23 μc 5-fluorouracil-6-T (580 mc/m*M*, the Radiochemical Centre, Amersham, England) per g body weight 20 min, 3 h or 12 h prior to sacrifice. RNA was extracted and, after high speed centrifugation, analyzed for UV-absorption and radioactivity as described elsewhere[7]. Due to the low labelling, counts/10 min were recorded.

Results and discussion. The results are given in the Figure. At 20 min there was low labelling without distinct peaks. At 3 and 12 h there was heavy labelling over the ribosomal RNA peaks. Since it has previously been shown (see introduction) that FU is incorporated as such into RNA and not converted into other bases, at least to any appreciable extent, the present results suggest that FU is incorporated into the ribosomal RNA of the liver of rat. Studies are planned to examine whether there are any differences in the half-life of RNA containing FU and its behaviour in different cell components, as compared with normal RNA[10].



Sedimentation patterns of RNA from the livers of rats labelled with 5-fluorouracil-6-T. Faster moving components are to the left. c.p. 10 min, counts per 10 min; OD, optical density at 2537 Å.

Zusammenfassung. Nach i.p. Injektion von 5-Fluorouracil-^{3}H wurde bei Ratten zu verschiedenen Zeiten die RNS-Neubildung der Leber bestimmt. Die Resultate sprechen dafür, dass Fluorouracil in die ribosomale RNA der Leber eingebaut wird.

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[1] C. HEIDELBERGER, Prog. Nucl. Acid Res. *4*, 1 (1965).
[2] C. HEIDELBERGER, N. K. CHAUDHURI, P. DANNEBERG, D. MOOREN, L. GRIESBACH, R. DUSCHINSKY, R. J. SCHNITZER, E. PLEVEN and J. SCHEINER, Nature *179*, 663 (1957).
[3] N. K. CHAUDHURI, B. J. MONTAG and C. HEIDELBERGER, Cancer Res. *18*, 318 (1958).
[4] W. MUNYON and N. SALZMAN, Virology *18*, 95 (1962).
[5] M. P. GORDON and M. STAEHELIN, Biochim. biophys. Acta *36*, 351 (1959).
[6] R. WILLÉN and U. STENRAM, Archs Biochem. *119*, 501 (1967).
[7] U. STENRAM and R. WILLÉN, Z. Zellforsch. mikrosk. Anat. *82*, 270 (1967).
[8] U. STENRAM, Z. Zellforsch. mikrosk. Anat. *71*, 207 (1966).
[9] U. STENRAM, Acta anat. *26*, 350 (1956).
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Effect of Cortical Spreading Depression on Norepinephrine-H3 Metabolism in Brain Stem

Alterations in the content of the biogenic amines in the cerebral hemispheres have been reported after lesion or stimulation of brain stem structures[1–4]. In contrast, ADLER et al. (1965) report that serotonin and noradrenaline levels in the brain stem were not changed 7 days after the surgical ablation of frontal or posterior cortical lobes[5], but DONOSO and STEFANO found that bilateral spreading depression of the cerebral hemispheres caused a significant lowering of the noradrenaline content of the hypothalamus[6].

Spreading depression may be produced by the local application of various chemical, electrical or mechanical stimuli to the cerebral cortex[7]. It is characterized by the attenuation of normal cortical rhythm which propagates outward from the local site of application but does not pass to the opposite hemisphere[8]. The present paper describes the changes in the metabolism of i.c. administered norepinephrine-H3 in rat brain stem associated with cortical spreading depression induced by the application of potassium chloride.