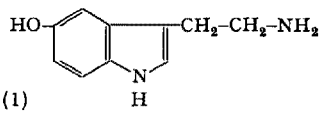
Gute Strahlenschutzwirkung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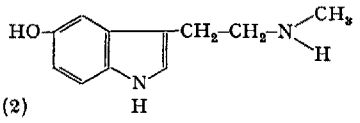
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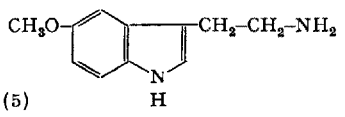
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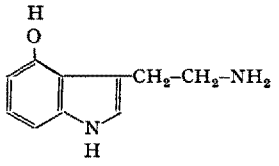
Schwache Strahlenschutzwirkung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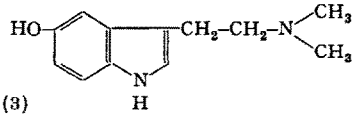
Keine Strahlenschutzwirkung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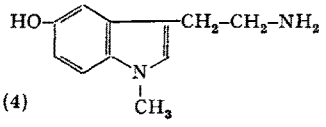
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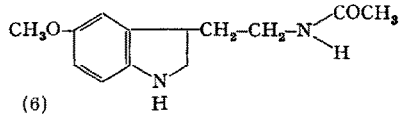
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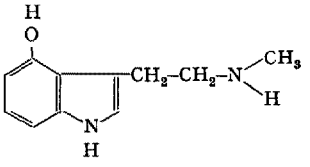
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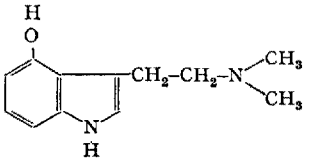
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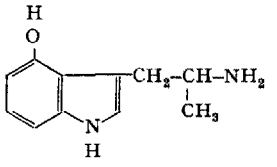
(10)

rung. Diese geringe schützende Aktivität des 4-Hydroxytryptamins geht aber sowohl nach Methylierung oder Dimethylierung des endständigen Stickstoffs als auch nach Substitution einer Methylgruppe in Stellung α völlig verloren.

Dabei scheint uns wesentlich, dass die Strahlenschutzwirksamkeit der substituierten Oxyindolderivate keine strenge Parallelität zu deren pharmakologischem Charakter aufweist[10]. Dies gilt insbesondere auch für die quantitative Wirkung der von uns verwendeten Substanzen am isolierten Rattenuterus[11].

Unsere Befunde scheinen geeignet, den strahlenbiologischen Wirkungsmechanismus des Serotonins genauer zu definieren. Wir werden darüber andernorts im Rahmen weiterer experimenteller Ergebnisse berichten.

Summary. Mice receiving a lethal dose of whole body irradiation are protected by 5-methoxy-tryptamine or 5-hydroxy-ω-N,N-monomethyltryptamine to the same extent as by serotonin. Other derivatives of oxytryptamine have only slight or no protective properties against irradiation.

P. DUKOR und R. SCHUPPLI

Dermatologische Universitätsklinik Basel, 16. März 1961.

[10] J. R. VANE, Brit. J. Pharmacol. *14*, 87 (1959). – M. J. GREENBERG, Brit. J. Pharmacol. *15*, 375 (1960). – H. WEIDMANN und A. CERLETTI, Helv. physiol. Acta *18*, 174 (1960).

[11] M. TAESCHLER, persönliche Mitt.

Catalase Synthesis and Destruction in Starvation[1]

In starvation[2] and in the cachexia of the tumor-bearing host[3,4] there is a marked reduction in many of the proteins of the various organs and tissues of the body. Biochemists have been intrigued by this observation but have lacked specific tools with which to elucidate the mechanism by which such reduction takes place, namely whether it results from an increased rate of breakdown or a decreased rate of synthesis of the respective proteins.

Methods have been developed recently in our laboratory[5,6] for determining in the living animal the rates of synthesis and destruction of a single protein, the enzyme catalase. The methods are based on the use of one of two drugs, namely 3-amino-1,2,4-triazole (AT) and allylisopropylacetamide (AIA). AT acts by irreversibly inhibiting

[1] Presented in part at the Fifth International Congress on Nutrition, Washington (D.C.) September 1960.

[2] L. L. MILLER, J. biol. Chem. *172*, 113 (1948).

[3] J. P. GREENSTEIN, *Biochemistry of Cancer* (Academic Press, Inc., New York 1954).

[4] M. RECHCIGL, Jr., F. GRANTHAM, and R. E. GREENFIELD, Cancer Res. *21*, 238 (1961).

[5] V. E. PRICE and M. RECHCIGL, Jr., Fed. Proc. *19*, 49 (1960).

[6] V. E. PRICE, M. RECHCIGL, Jr., and R. W. HARTLEY, Jr., Nature *189*, 62 (1961).

catalase without interfering with its resynthesis, while AIA acts by blocking the synthesis of new catalase. In the present work AT was used to destroy the catalase following which a comparison was made of the rates by which the activity of the newly synthesized catalase returned to the plateau value, in starved and in normally fed animals.

Methods. Male Sprague-Dawley rats with an average weight of 205 g at the beginning of the experiments were used throughout. The animals were kept in wire cages with screen bottoms and were allowed to eat and drink *ad libitum*. The composition of the stock diet has been described previously[4]. The animals were divided into four main groups. Two of the groups were injected intraperitoneally with AT, at a level of 1 g/kg of body weight, and the two remaining groups were kept as controls. 18 h after AT administration the food was removed from one of the control and one of the AT groups.

At various points during the experiment 5 rats in each of the four groups were killed by decapitation. The livers were removed and homogenized in a Waring blendor with 50 vol of ice-cold distilled water. Catalase activity was determined on 50 µl aliquots of homogenates, using the modification[7] of the spectrophotometric method of BEERS and SIZER[8]. A continuously recording spectrophotometer[9] with a log-absorbance attachment permitted accurate and rapid assays in less than 1 min using relatively low concentrations of substrate (0.01 *M* H_2O_2).

Results and Discussion. The total liver catalase activities of starved and fed animals, with and without AT, are shown in Figure 1. It can be seen that the total liver catalase fell off sharply soon after starvation was begun, both in the control animals and in those which received AT. The AT curve shows that there was actually less catalase being synthesized within the liver.

During starvation, however, the weight of the liver fell rapidly, to $^1/_2$ and $^1/_3$ of normal size in five and ten days, respectively. Therefore when the values are expressed in terms of units per g of liver, as shown in Figure 2, nearly the same rates of catalase synthesis and destruction are observed during the first five days of starvation as in the control animals. From semilogarithmic plots of these data and equations presented previously[6], it could be calculated that during each hour approximately 4.5 units or 25 µg of catalase were being synthesized per g of liver, and that 2.2% of the catalase molecules present were being destroyed.

During the first five days of starvation, therefore, the rate of catalase synthesis per g of liver proceeded as rapidly as in the controls, but since the livers were becoming progressively smaller in size there was less total catalase being synthesized. Since during starvation[10] there is known to be a marked loss of the liver RNA which is essential for protein synthesis, it may be inferred from these data that in the early stages of starvation the animal may control the rate of catalase synthesis by progressively decreasing the number of synthesizing units in proportion to the liver size, but that those synthesizing units which remain may be operating at full activity.

After five days, the starving animal enters a second phase in which the rate of catalase synthesis per g of liver starts to fall, and this continues progressively until death of the animal. It remains to be determined whether this fall in the catalase activity results from a deficiency of certain nutrients or whether it represents a death of liver cells.

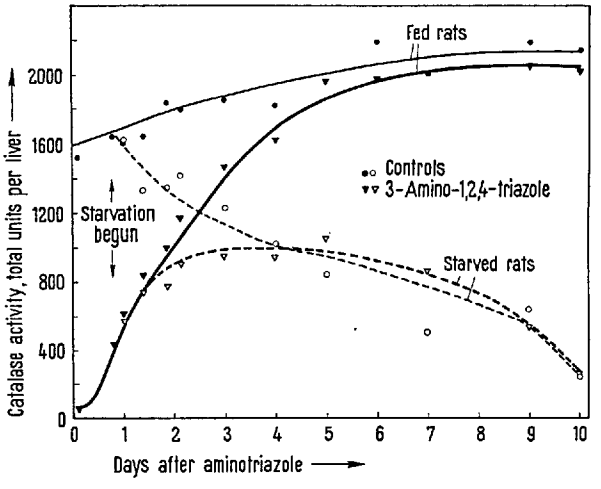

Fig. 1. Liver catalase activity of normal and starved rats following the injection of 3-amino-1,2,4-triazole.

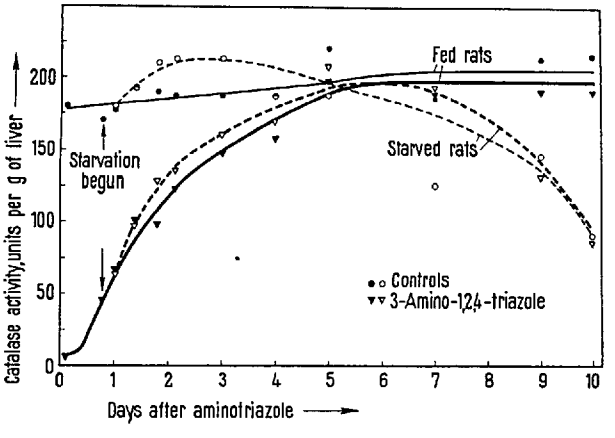

Fig. 2. Liver catalase activity of normal and starved rats following the injection of 3-amino-1,2,4-triazole.

Zusammenfassung. In der Leber hungernder Ratten verliefen Auf- und Abbaugeschwindigkeit der Katalase während der ersten 5 Tage im wesentlichen wie bei den Kontrolltieren. Durch die Verkleinerung der Leber wurde bei den Hungertieren total weniger Katalase in derselben Zeitspanne synthetisiert. Nach 5 Tagen fiel die Geschwindigkeit der Katalase-Synthese pro g Leber allmählich bis zum Tod der Tiere ab.

M. RECHCIGL, Jr., and V. E. PRICE

Laboratory of Biochemistry, National Cancer Institute, National Institutes of Health, Bethesda (Maryland), March 13, 1961.

[7] R. E. GREENFIELD and V. E. PRICE, J. biol. Chem. *220*, 607 (1956).
[8] R. F. BEERS, Jr., and I. W. SIZER, J. biol. Chem. *195*, 133 (1952).
[9] Cary Model No. 11-MS recording spectrophotometer, Applied Physics Corporation, Pasadena (California).
[10] H. W. KOSTERLITZ, J. Physiol. *106*, 194 (1947).