saline or of 1 ml of the NaOH solution of pH identical with that of diazoxide solution (pH 11.6). The mean values of the control group (without any injection), after saline and after NaOH were 0.53%/mg, 0.61%/mg and 0.68%/mg respectively.

Discussion and conclusions. FREGLY[1] proved in rats fed with an iodine defficient diet and treated chronically with hydrochlorothiazide, a decrease of the thyroid uptake of radioiodine. This effect is considered to be a probable result of an increased excretion of the iodine. The decrease of the uptake was found in euthyroid patients treated with chlorothiazide[2]. However, the acute administration of hydrochlorothiazide to euthyroid persons did not influence the thyroid radioiodine uptake[3].

In our experiment diazoxide in the administered dose in 1 i.v. injection was able to decrease significantly the thyroid uptake of radioiodine in rats. The mechanism of this effect of diazoxide, which is no diuretic agent, is unknown. It is of interest that diazoxide in the same dose increases the blood flow through the thyroid gland of rats (as indicated by the uptake of radioactive rubidium ^{86}Rb) in the first minutes after the i.v. injection[4]. The elucidation of the presented effects of diazoxide on the thyroid gland and their possible interrelations are a subject of further study.

Zusammenfassung. Es wird über eine signifikante Hemmungswirkung von Diazoxide (Hyperstat Schering) auf die Radiojodspeicherung in der Ratten-Schilddrüse berichtet. Während die Kontrollen einen Mittelwert der Radiojodspeicherung 0,65%/mg zeigen, beträgt er nach i.v. Injektion von 5 mg Diazoxide 0,49%/mg.

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[1] M. J. FREGLY, J. Toxicol. appl. Pharmacol. *8*, 558 (1966).
[2] J. H. NODINE, in, *Edema* (Eds J. H. MOYER and M. FUCHS; Saunders, Philadelphia 1960), p. 678.
[3] D. E. SCHTEINGART and M. PERLMUTTER, Am. J. Med. Sci. *239*, 571 (1960).
[4] J. KAPITOLA, unpublished results.

The Early Effects of low DDT Doses on the Nervous System in Animal Experiments

All over the world DDT is one of the most widely used pesticides[1]. Beyond its useful properties, however, it is harmful to fish, warm-blooded animals and even to man[2,3]. In Hungary the amount of DDT accumulated in human fatty tissue is nearly as high as that measured in the U.S.A.[4,5]. KEMÉNY and TARJÁN[6] have demonstrated that even small amounts of DDT might have blastomogenic effects. These findings induced us to elucidate the smallest DDT dose, which, on passing by way of food into the organism, might affect the activity of the nervous system. By demonstrating early symptoms, more serious damage might be prevented. We also wanted to get information about the site of action in the nervous system, about which great discrepancies can be found in the literature[7].

In the present experiments 237 male white Wistar rats weighing 100–130 g each were used. Besides controls, the animals were divided into groups consuming daily, 40, 20, 10, 5, 2.5, 2, 1 and 0.5 mg DDT/kg body weight. Chronic cerebral cortical electrodes were implanted in 77 rats. Then in a state of rest and under loading by means of rhythmic light flashes, EEG recordings were taken at regular intervals from the alert animals moving about unrestrictedly. The curves were evaluated by an analogous electronic computer[8].

For the determination of the site of action before starting the experiment, and on the 3rd, 10th, 17th, 24th and 31st day of DDT administration, 50% of the animals were narcotized with pentobarbital, acting chiefly on the brainstem[9], and the rest with chloralhydrate, acting mainly on the cortex[10], in order to observe which hypnotic would be antagonized by DDT. The time between injection of the narcotic and disappearance of certain position reflexes, as well as the corneal reflex, then the time during which these reflexes could not be elicited, and finally the total time of sleeping were measured in the different groups. The values obtained were evaluated by the 'Gier' electronic digital computer of the Central Statistical Office, performing variation analyses and 'repeated comparison' calculations after SCHEFFÉ[11].

When DDT was applied in an amount of 40 mg/kg body weight, the amplitude, as well as the frequency of the resting EEG activity, increased from the third day. In response to 20 mg the amplitude increased from the third day, and the frequency in the fourth week. In animals treated with 10 mg the frequency did not change, while the amplitude increased measurably from the tenth day above that of the controls. The resting electrical activity of the animals ingesting 5 mg DDT did not change.

When rhythmic flashing-light loading was applied to the rats fed 20, 10 and 5 mg DDT (the group fed 40 mg

[1] W. EICHLER, Biol. Rundschau *3*, 227 (1965).
[2] L. F. STICKEL, W. H. STICKEL and R. CHRISTENSEN, Science *151*, 1549 (1966).
[3] F. A. GUNTHER, *Residue Reviews* (Springer, Berlin 1964), vol. 6, p. 165.
[4] J. Sós, Egészségtudomány *10*, 88 (1966).
[5] A. DÉNES and R. TARJÁN, *The Accumulation of DDT in Food and in Human Fatty Tissues* (Paper on the Conf. of Nutr. Res., Budapest 1964).
[6] T. KEMÉNY and R. TARJÁN, Experientia *22*, 748 (1966).
[7] W. J. HAYES, in *DDT* (Ed. P. MÜLLER; Birkhäuser Verlag, Basel 1959), vol. 2, p. 11.
[8] I. FARKAS, I. DÉSI and L. GARAMSZEGI, Orv. és Technika *4*, 11 (1966).
[9] P. B. BRADLEY and B. J. KEY, Electroenceph. clin. Neurophysiol. *10*, 97 (1958).
[10] B. ISSEKUTZ, Gyógyszertan (Pharmacology) Eü. Kiad. Budapest, 631 (1963).
[11] H. SCHEFFÉ, *The Analysis of Variants* (J. Wiley, New York 1959), p. 477.

Changes in depth and duration of sleep in different animal groups on the 17th day of DDT administration

DDT administration mg/kg body weight	Cervical reflex				Labyrinth reflex				Corneal reflex				Total sleeping time	
	I		II		I		II		I		II			
	A	B	A	B	A	B	A	B	A	B	A	B	A	B
20	5.0[a]	2.5	15[b]	56.0[b]	22.1[b]	3.6	5.6[b]	49.6[a]	80[a]	8.0	3.5[b]	37.3[b]	20[b]	86.4[a]
10	3.9	2.7	22[b]	64.6[a]	5.8	3.33	20.3[b]	55	20.9[a]	13.8	7.1[b]	34	27.4[b]	81.3[a]
5	3	2.7	32.4[b]	77.5	3.4	2.7	27.7[b]	71.1	23.3[a]	12.1	12[b]	25.3	36.6[b]	99.8
2.5	3.0	2.6	38.6[b]	112.2	4.9	3.0	35.2[b]	92.7	23.9[a]	16.7	13.9[b]	65.2	47.7[a]	124.6
Control	2.7	2.6	100	108.1	3.6	2.7	92.7	101.8	8.5	10.7	72.0	57.8	107.4	131.7
2	4.6	3.8	130.0	136.0	4.5	3.8	106.6	136.0	11.3	15.5	56.3	57.3	143.6	135.7
1	4.1	3.4	135.4	135.5	4	2.4	125.1	130.5	17.0	16.4	64.3	69.6	165.8	149.2
0.5	7.26	5.2	172.8	119.5	7[b]	5.2	140.3	119.5	18.1	8.5	79.1	77.0	198.1	129.1
Control	3	4.5	172.8	125.3	3	3.5	151.5	125.6	14.6	6.6	78.5	61.8	174.0	133.3

I, time between injection of the narcotic and disappearance of the reflex in min. II, time between disappearance and appearance of the reflex in min. A, animals under pentobarbital narcosis. B, animals under chloralhydrate narcosis. [a] $p < 0.05$, [b] $p < 0.02$. In the groups of 20–2.5 mg and of 2–0.5 mg DDT the experiments were performed in 2 series. In both cases statistical calculations were carried out on the basis of the values of the experimental animals and those of their own controls.

was not observed), disorders were found indicating an increase in the irritability of the central nervous system.

A rhythmic light irritation of certain frequency causes driving in the electrical activity of the brain, and the brain waves follow this rhythm. In the progress of time, the experimental animals followed more and more kinds of frequency, and those treated with 20 mg followed the most. But even the animals treated with 10 and 5 mg DDT followed 20% more of all kinds of the flashing-light frequencies examined, even on the third day.

The effects of pentobarbital and chloralhydrate were differently influenced by DDT. First of all pentobarbital was antagonized. The dosages of 20, 10 and 5 mg DDT/kg body weight on the third day and that of 2.5 mg on the tenth day decreased markedly the deepness and duration of sleep, which showed a close dependence on the dose. The greater the DDT dose in any rat group, the later disappeared and the sooner reappeared the position and corneal reflexes after injection of the hypnotic. The more deep sleep was proved by the disappearance of the given reflex, the greater was the time difference between controls and experimental animals.

The above DDT dosages did not notably influence the duration of the chloralhydrate narcosis. The DDT doses of 2, 1 and 0.5 mg/kg body weight did not affect the influence either of pentobarbital or chloralhydrate. It seems, therefore, that under the given experimental conditions 2.5 mg/kg body weight was the smallest dose causing estimable functional changes in the nervous system (Table).

During the experimental time of 30 days, other signs of poisoning did not appear. The movement of the animals remained coordinated, both on flat surfaces and in climbing tests. Ataxy[12] taken for one of the earliest signs of DDT poisoning did not develop at 20 mg or lower doses. In response to 40 mg, slight ataxy could be observed.

DDT produced an excitation focus in the brain-stem. According to several authors, in response to DDT acetylcholine accumulation[13] takes place. The changes in EEG and sleeping observed in our experiment after DDT administration are very similar to the acetylcholine-produced symptoms in the nervous system[14]. It is therefore possible that one basic cause of the symptoms in the nervous system is the effect produced by acetylcholine on the brain-stem accumulating there in response to DDT administration.

The effect of small DDT doses in food by which the irritability of the central nervous system is increased calls our attention to the fact that even low DDT levels might produce functional disorders in the nervous system. These alterations in themselves might not yet be called serious, but they show that the normal equilibrium between the nervous system and its environment is disturbed, and on continuation of this injurious effect lasting damage might probably occur.

Zusammenfassung. Es wurde bei Verabreichung eines mit 40–0,5 mg DDT/kg Körpergewicht vermischten Futters an Ratten festgestellt, dass 40 und 20 mg DDT die Frequenz und Amplitude, 10 mg nur die Amplitude des spontanen EEG erhöht. Bei Verabreichung von 5 mg waren, bei stroboskoper Belastung, die Veränderungen noch sichtbar. Dosen zwischen 20 und 2,5 mg verminderten die Dauer und Tiefe der auf den Gehirnstamm als Angriffspunkt wirkenden Nembutalnarkose. Dosen von 2 bis 0,5 mg blieben wirkungslos. Die Vermutung wird ausgesprochen, dass sich durch DDT im Gehirnstamm ein Irritationsherd im Zusammenhang mit der Anhäufung von Acetylcholin bildet.

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[12] M. KHAIRY, Q. Jl exp. Psychol. *11*, 84 (1959).

[13] G. B. KOELLE, in *Handbuch der experimentellen Pharmakologie* (Eds A. HEFTER and W. HEUBNER; Springer, Berlin 1963), vol. 15, p. 741.

[14] V. G. LONGO, *EEG Atlas for Pharmacological Research* (Elsevier, Amsterdam 1962), p. 130.