

Removal of ^{60}Co and ^{65}Zn from the Mammalian Body

The mobilization of both radionuclides by the Ca-chelate of diethylenetriaminepentaacetic acid (DTPA) is a well-established fact¹⁻³. The actual fraction of the body burden which can be removed, however, is relatively small. This is due to the fact that the coordination compounds formed by Zn and Co with endogenous ligands are rather stable and/or inert^{4,5}. The present study aims at the elucidation of the question whether a higher efficacy can be achieved with the Co- and Zn-chelates, respectively, i.e. by isotopic exchange.

Adult rats of the Heiligenberg strain were injected intravenously with carrier-free $^{60}\text{CoCl}_2$ or $^{65}\text{ZnCl}_2$. The body burden following the intraperitoneal administration of Ca-, Zn- and Co(II)-DTPA⁶, respectively, was determined and expressed as % of the radioactivity in control animals. Obviously, as can be seen from the Table, the principle of isotopic exchange is more effective than chelation.

Radioactivity of the whole body 48 h after the administration of the chelates. Averages of 5 (^{60}Co) and 6 (^{65}Zn) animals per group

Treatment	% of control (95% confidence limits)
200 μM $\text{Na}_3\text{Ca-DTPA}$ 6 h after ^{60}Co	90 (70–107)
200 μM $\text{Na}_3\text{Co-DTPA}$ 6 h after ^{60}Co	60 (50–71)
512 μM $\text{Na}_3\text{Ca-DTPA}$ 168 h after ^{65}Zn	91 (88–94)
512 μM $\text{Na}_3\text{Zn-DTPA}$ 168 h after ^{65}Zn	80 (77–83)

At this juncture, it may be mentioned that the apparent retention of ^{65}Zn observed after administration of Zn-DTPA labelled with $^{65}\text{Zn}^{7-9}$ is due not only to an instability of Zn-DTPA in the physiological milieu and a corresponding genuine Zn-retention. In view of the above mentioned findings, it is most likely that the isotopic exchange also in this case plays a significant role.

Zusammenfassung. Trägerfreies $^{60}\text{Co(II)}$ und ^{65}Zn wurden Ratten intravenös injiziert. Bei nachträglicher intraperitonealer Applikation der entsprechenden nichtradioaktiven und durch DTPA chelierten Isotope werden erheblich grössere Radionuclidmengen aus dem Körper ausgeschieden als nach Verabfolgung von Ca-DTPA. Isotopischer Austausch ist somit wirksamer als Chelierung.

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Urinary Excretion of 5-Hydroxyindole Acetic Acid by Smokers and Non-Smokers

It has been reported by SCHIEVELBEIN et al.¹ that liberation of serotonin from experimental animals and isolated organs can be produced by nicotine. These findings led the same investigators (SCHIEVELBEIN et al.²) to study the urinary excretion of 5-hydroxyindole acetic acid (5-HIAA), the principal urinary metabolite of serotonin, by human smokers and non-smokers. They reported a considerable increase in the urinary excretion by smokers in comparison to non-smokers as well as by non-smokers after smoking several cigarettes. As a consequence they suggest that in studies on serotonin metabolism it is essential to pay attention to smoking habits of the persons to be studied.

The results published were, however, based on very few observations with considerable individual variations, and consequently do not seem too convincing especially as far as the habitual smokers are concerned. Because of this a larger field survey study was undertaken to find some additional data. This problem seemed worth studying since a positive correlation between smoking and changes in tryptophan metabolism could possibly be related to the higher incidence of malignancies in smokers through the

fact that numerous internal carcinogenic substances could be produced in the organism as a consequence of changes in tryptophan metabolism (LEPPÄNEN and OKA³). After the material for this work was collected, DEGWITZ⁴ reported that in his studies no differences in the excretion of 5-HIAA by smokers and non-smokers was found and consequently he could not confirm the results of the authors mentioned.

The present material was collected from male heavy workers in a shipyard and metal industry, Pansion Telakka, Turku. All the workers (25 to 65 years of age) were given, after a normal working day in the middle of the week, two 50 ml bottles and a paper with instructions. They were asked to eat their normal daily food without any selection and to spend a normal life in every respect. On waking up next morning (6–6.30 a.m.) they were

- 1 H. SCHIEVELBEIN, E. WERLE, and W. JAKOBY, *Naturwissenschaften* 48, 602 (1961).
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asked to urinate in both of the bottles before eating, drinking or smoking. The workers brought the bottles with them to work where they were immediately collected (7.0 a.m.) and cooled. Every worker gave the following information: age, smoker or non-smoker, how many years smoked, and any medication during the last few days. The urinary 5-HIAA concentration was determined according to HANSON and SERIN⁵ as $\mu\text{M/l}$.

In the analysis of the material collected, it appeared that there were acceptable urinary samples from 72 non-smokers and 154 from smokers. All cases were discarded in which smoking was very small (less than 10 cigarettes per day) as well as those in which smoking had continued for less than 5 years or where any medication was involved. The Figure presents the distribution of the individual measurements. It appears that no clear differences can be seen between smokers and non-smokers. The mean in the non-smoker group was $4.51 \mu\text{M/l}$ and in the smoker group $4.57 \mu\text{M/l}$. The mean age of the non-smokers was lower but it does not affect the result since no age-dependent change could be demonstrated in either group. As can be seen in the Figure the range of the amount of urinary 5-HIAA is wide, being of the same great order as

that found by SCHIEVELBEIN et al.² and is partly due to the fact that no dietary limitations were required. It seems, however, reasonable to assume that the dietary habits (no data on this matter were collected) are about equal in both groups of workers, even while differences exist between individual workers. This assumption is taken to be valid in relation to the quality of food eaten as well as the amount of urine excreted (only the concentration of 5-HIAA was measured). Consequently the present result is taken to mean that there is no difference in the concentration or amount of 5-HIAA excreted in the urine by habitual smokers and non-smokers.

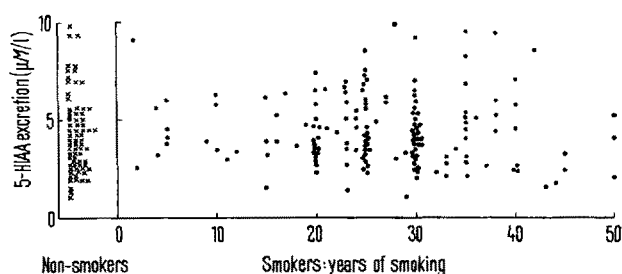
This result demonstrates that the habitual smokers studied have fully adapted to the nicotine effect so far as excretion of 5-HIAA is concerned. Our results do not confirm those presented by SCHIEVELBEIN et al.² in the case of habitual smokers, but are in full agreement with those of DEGWITZ⁴. As to the effects of inhaled nicotine on the tryptophan metabolism through the serotonin pathway, it seems that at least this metabolic pathway is not deranged.

Zusammenfassung. Die Ausscheidung von 5-Hydroxy-indoleessigsäure im Harn von Rauchern und Nichtrauchern wurde untersucht. Die individuellen Ausscheidungswerte variieren sehr erheblich in beiden Gruppen, doch konnte keine Differenz zwischen den Mittelwerten der beiden Gruppen gefunden werden.

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⁵ A. HANSON and F. SERIN, *Lancet* 1955 *ii*, 1359.



The Release of Dopamine from the Putamen

The neostriatum contains the highest concentration of dopamine of any region of the mammalian brain^{1,2}, and inasmuch as its metabolic product noradrenalin is present only in much smaller amount, the suggestion has been made that dopamine itself may be of importance to the functions of the nuclei concerned³.

Although its concentration there is very much less, the substantia nigra also contains appreciable amounts of dopamine^{1,2}. Basing his conclusion on these facts, HORNYKIEWICZ² has argued for the existence in the extrapyramidal motor pathways of neurones liberating dopamine as a synaptic transmitter substance. ANDÉN et al.⁴ and BERTLER et al.⁵ have provided evidence for dopamine-containing neurones whose cell bodies lie in the pars compacta of the substantia nigra and whose axons form bundles in the crus cerebri and run in the internal capsule to reach the neostriatum.

McLENNAN⁶ demonstrated an increased output of dopamine from the caudate nucleus in response to stimulation of nucleus centralis centralis (centromedianus) of the thalamus. Using a similar method it has now been shown that stimulation of the substantia nigra brings

about a marked increase in dopamine output from the putamen.

Methods. A push-pull cannula⁷, the outer tube being No. 22 S.W.G., was placed stereotactically in the putamen of cats lightly anaesthetized with pentobarbital. The region at the tip of the cannula was irrigated with Locke's solution modified by the omission of bicarbonate. Fluid was forced through the cannula by a motor-driven syringe at a rate of 0.1–0.15 ml/min, and the outflows collected in cooled tubes each containing a drop of 0.5N acetic acid. Samples were collected over 15 min periods, and 5–10 min were allowed between successive samples.

¹ Å. BERTLER, *Acta physiol. scand.* 51, 97 (1961).

² O. HORNYKIEWICZ, *Arch. exp. Path. Pharmacol.* 247, 304 (1964).

³ P. HOLTZ, *Psychiat. Neurol., Basel* 140, 175 (1960).

⁴ N.-E. ANDÉN, A. CARLSSON, A. DAHLSTRÖM, K. FUXE, N.-Å. HILLARP, and K. LARSSON, *Life Sci.* 3, 523 (1964).

⁵ Å. BERTLER, B. FALCK, C. G. GOTTFRIES, L. LJUNGGREN, and E. ROSENGREN, *Acta pharmacol. toxicol.* 27, 283 (1964).

⁶ H. McLENNAN, *J. Physiol.* 174, 152 (1964).

⁷ J. H. GADDUM, *J. Physiol.* 155, 1P (1961).