Duplicate 0.1 ml aliquots of plasma and urine were assayed for ^{3}H-activity in a Packard Model 3375 liquid scintillation spectrometer and quenching corrected by means of the automatic external standard.

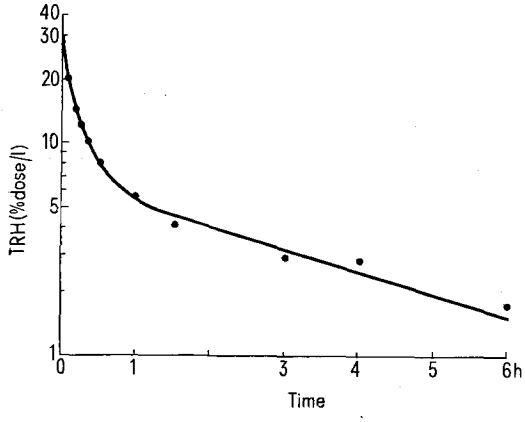
Results. The plasma concentrations (C_p) of ^{3}H-activity, expressed as % dose/L plasma, apparently declined biexponentially and were fitted, by means of an iterative non-linear digital computer programme, to the equation: $C_p = Ae^{-\alpha t} + Be^{-\beta t}$, where A and B are the zero ordinate axis intercepts and α and β are both hybrid rate constants reflecting all the individual rate processes. A typical disappearance curve is shown in the Figure. In each subject, the initial fast disposition phase had a half-life ($0.693/\alpha$) of about 10 min followed by a slower disappearance with a half-life ($0.693/\beta$) of around 3 h.

Of the total radioactive dose, 70–78% was excreted in the urine within 24 h after administration.

Discussion. It should be stressed, that the data reported in this communication concerns the disappearance of total plasma ^{3}H-activity following administration of 2,5-^{3}H-histidyl TRH to man and does not necessarily reflect the overall disappearance of intact TRH. Since TRH undergoes rapid inactivation in both tissue and blood[9] our data represents the disappearance and excretion of TRH and its biotransformation products which contain the 2,5-^{3}H-histidyl moiety.

Recently LEPPALUOTO et al.[10] have reported that, after injection of 200 µg of unlabelled TRH to man, plasma TRH had a halflife of 5 min within the first 5 min after administration. This observation is in close agreement with the data reported here.

It is interesting to note that the mean maximum TSH response in normal individuals receiving 200 µg of TRH intravenously[11,12] occurs during the initial fast distribution phase (0–60 min) observed in the present study. It would not appear unreasonable to suggest that the TSH response is the result of TRH stimulation of the pituitary during this period following administration.



Total ^{3}H-activity in plasma (C_p) following i.v. administration of 200 µg (120 µC) of tritium labelled TRH to man. (●), observed data; (—), computer calculated curve; $C_p = 18.9e^{-4.8t} + 6.6e^{-0.24t}$.

Zusammenfassung. Nach i.v. Verabreichung von Thyrotrophin-releasing Hormonen an Versuchspersonen ergibt sich eine biphasische Kurve für den Abfall der Tritiumaktivität im Plasma mit einer Exkretions-Halbwertszeit von 3 h.

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Effect of 2-Br-α-Ergokryptine (CB 154) on Lactation in the Bitch

Lactation and other prolactin-dependent mechanisms in the reproduction of the rat are inhibited by 2-Br-α-ergokryptine (CB 154 Sandoz, Basel)[1,2]. This action is based on inhibiting prolactin secretion at the pituitary level[3]. Suppression of serum prolactin levels by CB 154 have been shown by radio-immuno-assay methods in humans[4], cows[5] and in sheep[6]. Inhibition of lactation by CB 154 has been demonstrated, apart from the rat[1], in humans[7,8], in pigs[2], and in rabbits[2]. In contrast, even after repeated applications of CB 154, lactation could not be inhibited in cows[5] and sheep[6]. This means that prolactin is not essential in all mammalian species for the maintenance of lactation. Therefore it is of interest to test different mammalian species for the sensitivity of established lactation towards the action of CB 154.

It was the objective of the following experiments to find whether lactation in the bitch can be influenced by CB 154.

Material and method. Female beagles (6 groups, consisting of 5 animals each), aged 2–6 years, weighing between 9–18 kg were used. After parturition the animals were housed in single boxes at a temperature of 20–23 °C Only litters of 5 or 6 pups were used. In cases of more than 6 pups per litter, the supernumerary animals were removed on the 2nd day of life. From the 2nd–21st day

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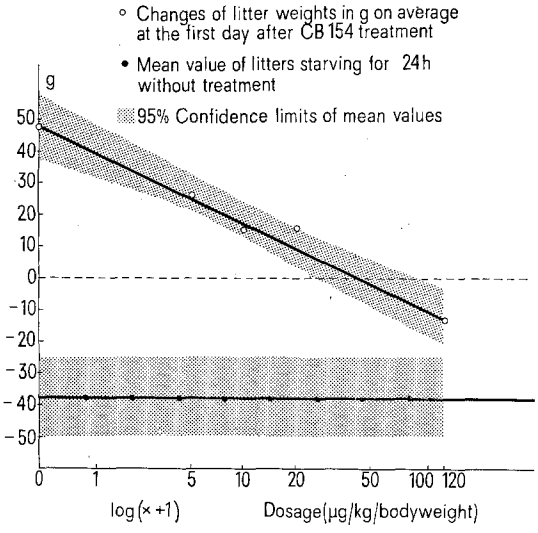
of life the pups were weighed daily at 08.00 and 17.00 h. The gain of weight of the pups within 24 h served as a direct measure for the amount of lactation of a bitch. A solution of CB 154 was administered i.m. to the bitches after weighing the pups in the evening of the 12th day post partum. The dosages used were 5, 10, 20 and 120 µg per kg bodyweight. For controls 1 group of bitches remained untreated. In another group the pups were removed at the same time for 24 h in order to show the effect of starvation.



Dose response curve for lactation inhibition by CB 154 i.m.

Results and discussion. The dose-response relation of CB 154 on the change of weight of pups is presented in the Figure and shows an inhibition of lactation in bitches. The statistical evaluation of the results was carried out by variance analysis. The regression of the curve is highly significant with $p < 0.001$. The ED_{50} (50% reduction of weight in comparison with untreated controls) of the inhibition of lactation in bitches was calculated to be 6 µg/kg bodyweight (95% confidence limit = 4–12 µg/kg).

These experiments show that CB 154 suppresses the lactation in the bitch and allow the assumption that prolactin is necessary to maintain lactation in bitches.

Zusammenfassung. Es wurde gezeigt, dass bei Hündinnen die Lactation durch den Prolactin-Sekretionshemmer 2-Br-α-Ergokryptin-methanesulfonat (CB 154, Sandoz) gehemmt wird. Gemessen über 24 Stunden beträgt die ED_{50} i.m. 6 µg/kg.

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Distribution of Potassium in Rat Adrenal Zones studied by Electron Probe X-Ray Microanalysis

Several factors are well known to be involved in the regulation of aldosterone production[1,2], still the mechanism of the regulation is far from being clarified. Experimental data from the literature[3] and from our previous work[4] yielded indirect arguments for the assumption that changes of the potassium and sodium content of the Zona glomerulosa might be the final stimuli for the regulation of aldosterone production.

The main obstacle to demonstrating potassium within tissues and cells lies in its excellent solubility in water and other solvents. At present no histochemical method providing reliable localization of potassium is available. Attempts have recently been made to use the electron probe X-ray microanalyzer to measure potassium content in tissue sections[5,6]. Kriz et al.[7–9] succeeded in determining relative potassium concentrations in different portions of the nephron.

We have made an effort to use the electron probe X-ray microanalyzer to study the distribution of potassium in the adrenal Zona glomerulosa and in the outermost cells of the Zona fasciculata.

26 male CFE rats weighing 150 g were decapitated. The adrenal glands were frozen to the specimen holders of a cryostat by means of isopentane chilled with liquid nitrogen, cut at 6 µm, and lyophilized. Quarz slides were coated with aluminium (ca. 100 Å), the frozen-dried cryostat sections were pressed on it, and coated again with aluminium.

The potassium K_α radiation was analyzed in a JXA-5 microanalyzer. The diameter of the electron beam was

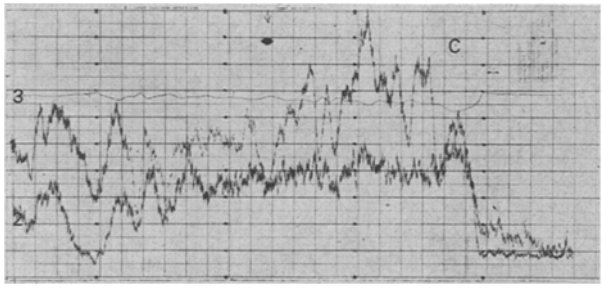

Fig. 1. Strip chart record of the potassium K_α radiation registered along a straight line perpendicular to the adrenal surface in a 6 µm section (line 1). Arrow indicates the borderline between Zona glomerulosa (right) and Zona fasciculata (left). C, capsule. Further right aluminium-coated quarz slide only. Line 2 is the graph for sodium, not considered here. Line 3, specimen current.

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