

C: black pigment in the gingival 2/3 and partial depigmentation in the incisal 1/3 in a rat from group 2. D: black pigment in the gingival 1/2 and normal yellow-brown pigment in the rest of the enamel in a rat from group 2A. E: black pigment in the gingival 2/3 and normal yellow-brown pigment in the incisal 1/3 in a rat from group 4. F: black pigment in the gingival 1/2 and normal yellow-brown pigment in the rest of the enamel in a rat from group 5.

In both experiments each of the animals fed the purified diets received daily, through the cod liver oil, about 152 units of vitamin A, which should cover amply the requirement of the rat for this vitamin. Therefore it appears doubtful that, as stated by PAUL and PAUL, the black pigment is due to vitamin A deficiency. Experiments are being carried out in order to study this problem.

The following preliminary observations on the characteristics of the black pigment have been made: it disappears rapidly by incineration in the gas flame, slowly in contact with hydrogen peroxide, and very slowly when the teeth are kept in 5% neutral formalin. On the other hand, the black pigment remains the same when the teeth are kept for a long time in 70% ethanol, ether, chloroform, acetone or xylol. Keeping the teeth in boiling water for one hour neither affects the black pigmentation.

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Physiological Institute, University of Basel, January 25, 1952.

Zusammenfassung

Junge Albinoratten beiderlei Geschlechtes, normale und adrenaletomierte Tiere, wurden auf synthetischen Diäten gehalten, in welchen entweder eine Anzahl von Vitaminen fehlte oder welche die Vitamine A, D, E sowie alle chemisch identifizierten B-Vitamine in genügenden Mengen enthielten.

Bei diesen Tieren entstand ein abnormes schwarzes Pigment an den Inzisoren, besonders oben. Kontrolltiere aus der Zuchtdiät zeigten dieses Pigment niemals. Die Häufigkeit in den einzelnen Gruppen ist in der Tabelle wiedergegeben. Die Abbildung zeigt Beispiele.

Are Ba-Ions a Pure Muscular Stimulant on the Rat's Ileum but not on the Guinea Pig's? The Species Difference in Spasmolytic Potency of Some Ganglionic Blocking Agents

FELDBERG¹ recently reported that barium-induced contractions of the guinea pig's and rabbit's ileum were mainly of ganglionic origin, since the induced muscular contractions were partly inhibited by hexamethonium. The concentrations of C_6 which reduced the responses to barium ions had little or no influence on the contractions caused by histamine or acetylcholine. He furthermore suggested that the use of barium salts as a smooth muscle stimulant when testing spasmolytic compounds needed a reinvestigation. FELDBERG's findings that C_6 reduces Ba-induced contractions of guinea pig's and rabbit's ileum, as well as the negligible effect of C_6 on the action of acetylcholine and histamine, have been verified by us. The results are the same if the bath fluid has the composition given by FELDBERG or the composition given below with a $MgCl_2$ content between 5 mg/l and 100 mg/l.

In our experiments we have used ileal preparations from animals killed just before the experiment. The bath fluid was kept at a temperature of 35°C and contained per litre: NaCl 9.2 g, KCl 0.42 g, $CaCl_2$ 0.24 g, NaH_2PO_4 0.1 g, $NaHCO_3$ 0.1 g, $MgCl_2$ 0.005–0.1 g, dextrose 1 g. The pH of this fluid at 35°C is 7.4 when oxygen has been bubbling through the bath for some minutes.

In experiments on rat ileum, however, it was found that hexamethonium had no influence on the contractions caused by $BaCl_2$ (30–80 μ g/ml in the bath) or acetylcholine HCl (0.005–0.05 μ g/ml in the bath). The concentration of hexamethonium bromide used was 40 μ g/ml bath fluid. C_6 was allowed to remain in the bath 2–20 min before the gut was stimulated with Ba or acetylcholine. When hexamethonium in the same concentration was kept in the bath for 2 min, it always completely abolished the contraction otherwise caused by 10 μ g nicotine-bitartrate/ml bath fluid.

On the rat ileum this concentration of nicotine caused a contraction of about the same magnitude as the Ba concentrations mentioned above.

Variations of the $MgCl_2$ concentration of the bath fluid from 5–100 mg/l had no influence on the effects of C_6 on rat ileum.

Thus it may be expected that spasmolytics which have slight or no inhibitory effect on the transmission in auto-

¹ W. FELDBERG, J. Physiol. 113, 483 (1951).

nomic ganglia ought to have about the same potency against Ba-induced spasm on the rat's and guinea pig's ileum. Spasmolytic compounds with ganglionic blocking properties, on the other hand, ought to have a higher inhibitory potency on guinea pig's ileum when BaCl_2 is used as stimulant.

In order to test this hypothesis the following compounds were assayed against ileal spasm due to BaCl_2 : Papaverine-HCl, (I); trasentin-6H, (II); 10-(α -diethylaminopropionyl)-phenothiazine, (III); Banthine, (IV), and another quarternary ammonium compound, 10-(triethyl-ammoniumacetyl)-phenothiazinebromide, (V). III has the ability to inhibit nicotine-induced convulsions in animals^{1,2}.

In all tests the inhibitor preceded the stimulant, BaCl_2 , by 2 min. The concentrations of BaCl_2 used in the trials were the same as mentioned above.

The averaged results are given in the Table.

Compound	ED ₅₀ $\mu\text{g/ml}$ bath fluid. Ba-stimulated guinea pig's ileum. 100 mg MgCl_2 per litre bath fluid	ED ₅₀ $\mu\text{g/ml}$ bath fluid. Ba-stimulated rat's ileum. 100 mg MgCl_2 per litre bath fluid
I	2	1.2
II	0.6	0.4
III	2	2
IV	0.4	50
V	0.1	30

Using guinea pig's ileum it has been found that an addition of 5 mg/l of C_6 to the Tyrode solution used by us results in ED₅₀ values for (IV) and (V) which are the same as those given for rat's ileum. This concentration of C_6 has a weak influence on the contraction of guinea pig's ileum caused by 10 $\mu\text{g/ml}$ nicotine but practically abolishes the response to 1 $\mu\text{g/ml}$.

It may thus be concluded that Ba-ions are a pure muscular stimulant on the rat's ileum, as far as the specificity of C_6 can be trusted.

A more detailed report including studies on the effect of Mg-ions on the potency of spasmolytics will be published later.

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Zusammenfassung

FELDBERGS Befund, dass Bariumionen nicht nur die Längsmuskulatur des Dünndarms, sondern auch die Ganglien stimulieren, konnte am Ileum des Meerschweinchens bestätigt werden. Dagegen haben Bariumionen wahrscheinlich eine rein myogene Wirkung auf das Ileum der Ratte.

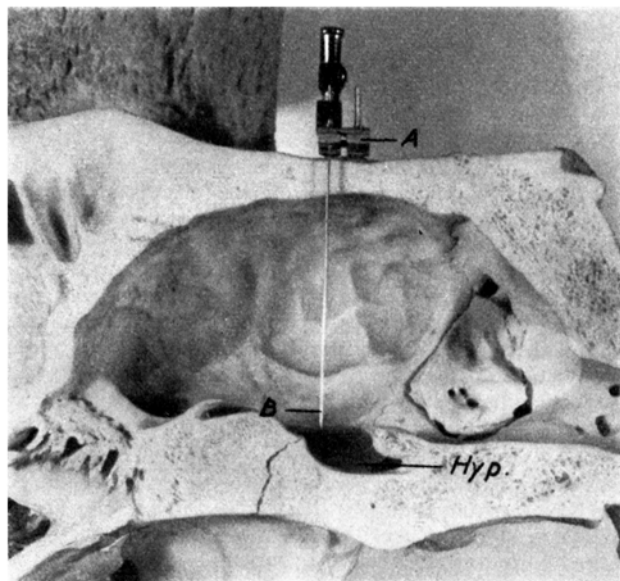
¹ R. DAHLBOM and T. EKSTRAND, Acta chem. Scand. 5, 102 (1951).

² R. DAHLBOM *et al.*, Arch. int. Pharmacodyn. (1952) (in press).

Polydipsia Caused by Intrahypothalamic Injections of Hypertonic NaCl-Solutions

According to a common theory ordinary thirst is closely correlated with cellular dehydration. Thus the sensation of thirst should be of "general origin". But the generation of primary polydipsia by injuries in the hypothalamus suggests that the sensation of thirst could be induced from this part of the brain stem. WOLF¹ in a paper on osmometric analysis of thirst in man and dog also states that the consequences of such a cellular dehydration hypothesis would remain substantially intact if it were postulated that osmoreceptors of the VERNEY² type, rather than general body tissues, were the receptors in a thirst reflex.

In order to study the effect of an increased osmotic pressure in the hypothalamus, injections of hypertonic NaCl-solutions were performed directly into this part of the brain stem of unanaesthetized goats. Further work on this subject is going on.



Paramedian sagittal section through the cranium of a goat with the cannula fixed on the skull. A — Socle fixed on the skull. B — Point of injection. Hyp. — Position of the pituitary gland.

Methods: For the injections 0.5 mm thick cannulae were used. HESS³ technique was applied for fixation and guidance of the cannulae, the length of which varied after the size of the heads and the points of stimulation desired. X-ray pictures of the skull were taken before and after each experiment in order to secure and control the position of the cannulae. The injections were performed through small holes in the cannulae 3–6 mm from their tips and orally directed. The Figure shows a paramedian sagittal section through a cranium of a goat with a cannula placed in the manner used when injecting into the anterior hypothalamus. Body warm 1.5–2.0 °C. NaCl-solutions were used, and the amount injected was 0.1 cm³. After having finished an experiment a small amount of Indian ink or Evans blue was injected through the

¹ A. V. WOLF, Amer. J. Physiol. 161, 75 (1950).

² E. B. VERNEY, Proc. Roy. Soc. [B] 135, 25 (1947).

³ W. R. HESS, Beiträge zur Physiologie des Hirnstammes, I. (Georg Thieme, Leipzig 1932); Das Zwischenhirn (Benno Schwabe & Co., Basel 1949).