

surroundings. In 12 min flexor clonic convulsion appeared. The effect began to decrease in 25–30 min and excitement was over in 25–30 min.

(4) In anaesthetised cats and dogs differential action towards pressor amines was noticed. The pressor effect of 5 µg adrenaline and nor-adrenaline was increased, while the effect of 2–4 mg of amphetamine and ephedrine was reduced or blocked by 20 mg/kg intravenously in dogs and 30 mg/kg in cats.

Detailed studies of compounds in these series will be communicated in due course.

### The Infundibular Recess in the Brain of *Camelus dromedarius* with Particular Reference to its Neurosecretory Pathways into the Third Ventricle

It is thought that the neurosecretion plays a part in the control of the organism's fluid balance. Since ancient times, the camel is particularly renowned for its singular water economy. It is able to drink only once a week; on the other hand, it is able to drink water of such high salinity that man, for instance, would be poisoned by it<sup>1</sup>.

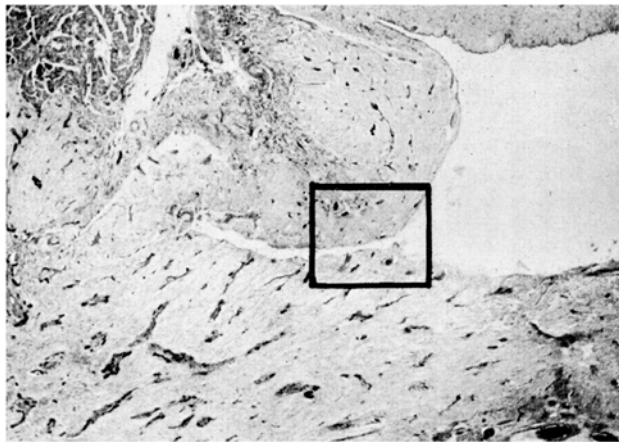


Fig. 1. Part of the floor of the infundibular recess and the bay extending caudally from it. – Haematoxylin-eosin;  $\times 16$ .

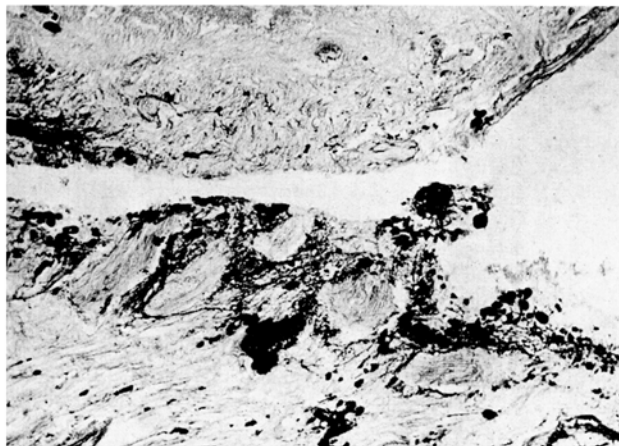


Fig. 2. The area of the rectangle in Figure 1. Neurosecretory material in great profusion in the ependymal barrier, subependymally and around the subependymal vessels. – Aldehyde-fuchsin;  $\times 100$ .

**Zusammenfassung.** Mit 2-Piperidyl(1)-3-phenylpropanol ( $CN_2$ ) wird an Mäusen, Ratten und Hunden eine deutliche zentralstimulierende Wirkung festgestellt. An anaesthetisierten Katzen und Hunden blockiert  $CN_2$  die vaso-pressorische Wirkung des Amphetamins und Ephedrins und verstärkt diejenige der Catecholamine.

R. S. KAPIL, NITYA ANAND,  
M. M. VOHRA, and J. D. KOHLI

Central Drug Research Institute, Lucknow (India), March 30, 1961.

The present work was undertaken in order to see if the peculiar water economy of the camel might be based on some morphological peculiarity in its hypothalamo-hypophysial system. Conditions distinct from those in other animals were found specially in the infundibular recess.

The material consisted of three brains, which were fixed in 10% formalin, embedded in paraffin, and sections were made sagittally at 5–7-micra. Staining was done with haematoxylin-eosin, Heidenhain's iron-haematoxylin, Gomori's chrome-haematoxylin and aldehyde-fuchsin.

The ventral part of the third ventricle formed a distinct infundibular recess. The posterior part of the recess was joined to a long, narrow bay running caudally, produced as a result of the forward pressure exerted on the caudal wall of the infundibulum by the pars tuberalis of the hypophysis.

The ependyma of the floor of the recess, and in the said bay, consisted of flat cells. The ependymal cell layer adjoined to a subependymal tissue with abundant quantities of hyaline mass visible in the haematoxylin-stained preparations, occurring in places in large drops. The mutual connection between the ependymal cells was broken in numerous places, where hyaline material was then seen also in the cell interstices. This made the margin of the ventricle hard to define. In certain places, hyaline material occurred also on the surface of the ependyma in the lumen of the ventricle. The hyaline material was particularly abundant around the subependymal vessels. Such

<sup>1</sup> Editorial, Modern Medicine 28, 14 (1960).

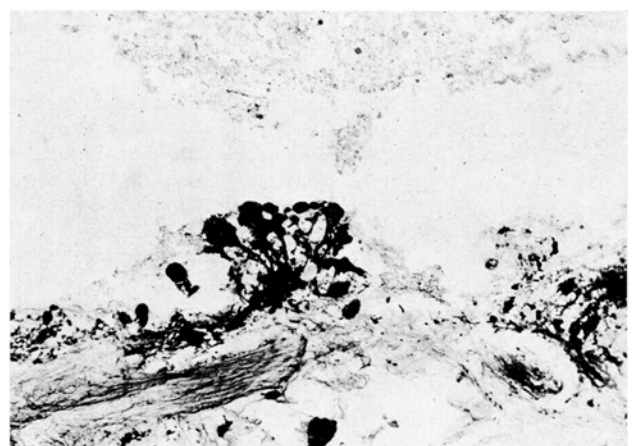


Fig. 3. Neurosecretory material around a subependymal vessel and extending as protuberances into the third ventricle. – Aldehyde-fuchsin;  $\times 200$ .

vessels were numerous, and they were separated from the ventricle only by a thin ependymal cover in some places.

The chrome-haematoxyphilous substance and the aldehyde-fuchsin-positive substance showed identical distribution in this region. Its abundance was extraordinarily high as compared with animals of other species. It occurred in profusion subependymally, in the ependymal cell interstices and also within the third ventricle. Its location was identical with that of the hyaline material demonstrated by haematoxylin. The material staining by the selective methods, i.e., by chrome-haematoxylin and aldehyde-fuchsin, partially occurred as a fine, granular mass, partially as typical Herring bodies. In the places where this selective material projected into the third ventricle through the interstices of ependymal cells, it formed club-shaped protuberances.

The location of the secretory material in the ependymal ridge of the recess seems to indicate that, in the camel, it is transferred into the third ventricle in great quantities in this area. According to some investigations, neurosecretory material could be released to a certain extent also into the third cerebral ventricle in some species<sup>2-6</sup>. The structure of the ependyma, which is here strikingly different from the usual ependyma in the camel, as well as in some other animals<sup>7</sup>, might also point to such transfer. Of course, the possibility has to be considered that the secretory material observed in the third ventricle might be an artifact; but such material was also encountered in sections with absolutely intact ependymal cover. The profuse occurrence of the material around the subependymal vessels is difficult to explain except by as-

suming that also release of the material into the circulation occurs here, as it obviously does also in the distal part of the neurosecretory system, in the neurohypophysis<sup>8</sup>.

*Zusammenfassung.* Es wird gezeigt, dass bei Kameliden das Ependym auf dem Boden des Recessus infundibularis aus platten Zellen besteht. Im Ependymbereich und in Zellinterstitien findet sich in reichlichem Masse hyaline Masse, die durch selektive, Neurosekretion anzeigende intensive Färbung dargestellt wird. Die Lokalisation des Materials deutet auf eine Ausschüttung des Neurosekrets in den dritten Gehirnventrikel hin.

S. TALANTI and E. KIVALO

*Department of Anatomy, Veterinary College Helsinki (Finland), The Research Department of Rinnekoti, Institute of Mental Deficiency, Helsinki (Finland), April 18, 1961.*

<sup>2</sup> W. BARGMANN and W. HILD, *Acta anat.* 8, 264 (1949).

<sup>3</sup> W. HILD, *Z. Zellforsch.* 35, 33 (1950).

<sup>4</sup> T. STUTINSKY, *Z. Zellforsch.* 39, 276 (1953).

<sup>5</sup> M. OKADA, T. BAN, and T. KUROTSU, *Med. J. Osaka Univ.* 6, 359 (1955).

<sup>6</sup> H. FUJITA, K. NAKAMURA and S. OKI, *Arch. hist. jap.* 8, 599 (1955).

<sup>7</sup> F. LÖFGREN, *Acta morph. neerl. scand.* 3, 55 (1960).

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## Antagonism Against the Arecoline Tremors of Oxyphenonium and its Tertiary Analogue after Intravenous and Intracerebral Administration in Mice

It is well known that the peripheral anticholinergic action of the quaternary ammonium compounds is much higher than that of their tertiary analogues. This is probably due to the great importance of the cationic 'head' in the interaction of drugs with cholinergic receptors<sup>1-3</sup>. Central effect of quaternary compounds is, however, much weaker than that of their tertiary analogues<sup>4-10</sup>.

Since the specific mediator for the cholinergic receptors in the periphery as well as in the central nervous system is the quaternary fully ionized substance, acetylcholine<sup>3,11-15</sup> it is likely that the cationic 'head' of the drug is important for the interaction with central as well as peripheral cholinergic receptors.

It is believed that the low central effect of quaternary compounds may be explained by the difficulty with which the fully ionized quaternary compounds<sup>13,16-23</sup> penetrate the blood-brain barrier.

Therefore it is possible to suppose that the quaternary compounds would be at least as active on the central as on the peripheral cholinergic receptors, if they could get into the central nervous system through the blood-brain barrier<sup>3</sup>.

It has been established in our preliminary experiments in rabbits that the quaternary analogue of nicotine, which was without convulsive effect intravenously, caused in suboccipital administration convulsions in doses even lower than those of nicotine<sup>10</sup>.

The aim of the present report is an investigation of the central anticholinergic effects of oxyphenonium and its tertiary analogue, compound VUFB-3100, after intra-

venous and intraventricular administration in mice, as evidenced by the ability to prevent tremors caused by intravenous injection of arecoline<sup>24</sup> (Formulae).

<sup>1</sup> H. R. INC, G. S. DAWES, and J. WAJDA, *J. Pharmacol.* 85, 85 (1945).

<sup>2</sup> R. B. BARLOW, *Introduction to Chemical Pharmacology* (London 1955).

<sup>3</sup> M. J. MICHELSON et al., *Physiological Role of Acetylcholine and Research of New Drugs* (in Russian), (Leningrad 1957).

<sup>4</sup> D. BOVET and V. G. LONGO, *J. Pharmacol.* 102, 22 (1957).

<sup>5</sup> F. R. LUDUENA and A. M. LANDS, *J. Pharmacol.* 110, 282 (1954).

<sup>6</sup> E. V. ZEJMAL, *Bjul. exp. Biol. Med.* 39, 42 (1955).

<sup>7</sup> M. J. MICHELSON, V. A. ARTEMJEV, I. V. DARDYMOV, E. V. ZEJMAL, F. V. PEVZNER, E. K. ROZKOVA, R. C. RYBOLOVLEV, N. V. SAVATEJEV, J. R. SAVINSKIJ, E. P. USPENSKAJA, N. V. CHROMOV-BORISOV, and K. G. CIRK, *Proc. of VIII All Union Soviet. Conf. Physiol., Biochem. and Pharmacol.* (Moscow 1955).

<sup>8</sup> R. C. URSILLO and B. B. CLARK, *J. Pharmacol.* 114, 54 (1955).

<sup>9</sup> M. VANĚČEK and Z. VOTAVA, *Čs. Fysiol.* 5, 362 (1956).

<sup>10</sup> E. V. ZEJMAL, *Dissert. I. Leningrad. Med. Inst.* (1958).

<sup>11</sup> E. BÜLBRING and J. H. BURN, *J. Physiol.* 100, 337 (1941).

<sup>12</sup> M. J. MICHELSON, E. K. ROZKOVA, and N. V. SAVATEJEV, *Bjul. exp. Biol. Med.* 37, 7 (1954).

<sup>13</sup> J. ECCLES, R. ECCLES, and P. FATT, *J. Physiol.* 131, 154 (1956).

<sup>14</sup> W. FELDBERG, *Acetylcholine, in Metabolism of Nervous System* (Ed. by RICHTER; Pergamon Press, London, N.J. 1957), p. 493.

<sup>15</sup> M. J. MICHELSON, *Activitas nerv. sup.* 3, in press (1961).

<sup>16</sup> A. S. V. BURGESS and L. M. CHIPMAN, *Quart. J. exp. Physiol.* 37, 61 (1951).

<sup>17</sup> J. ECCLES, P. FATT, and K. KOKETSU, *J. Physiol.* 126, 524 (1954).

<sup>18</sup> R. M. LEVIN and B. B. CLARK, *J. Pharmacol.* 114, 63 (1955).

<sup>19</sup> W. FELDBERG, J. L. MALCOLM, and S. L. SHERWOOD, *J. Physiol.* 132, 130 (1956).

<sup>20</sup> G. B. KOELLE and E. C. STEINER, *J. Pharmacol.* 118, 420 (1956).

<sup>21</sup> D. R. CURTIS, J. ECCLES, and R. ECCLES, *J. Physiol.* 136, 420 (1957).

<sup>22</sup> W. D. M. PATON, *Ann. Rev. Physiol.* 20, 431 (1958).

<sup>23</sup> E. V. ZEJMAL and M. J. MICHELSON, *Proc. of Conf. of Blood-Brain Barrier* (Moscow 1960).

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