ganglionic axotomy was performed to compare the results with those obtained after guanethidine.

Guanethidine monosulphate (20 mg/kg intraperitoneally) was administered daily from 3 to 14 days. Normal saline were used in controls. 1–30 days after discontinuation of the treatment the animals were killed and the superior cervical ganglia removed for titrimetric determination of cholinesterases (Jensen-Holm, 1965) or histochemical cholinesterase demonstration by means of the lead-ferrocyanide method modified from the technique described by Eränkö, Koelle & Räisänen (1967).

Fresh-frozen ganglia were sectioned at 5 and 10 μ in a cryostat and incubated for one hour at 22° C in a substrate mixture containing acetylthiocholine (2.5×10^{-3}M) for demonstration of both specific and non-specific cholinesterase activity, acetylthiocholine+mipafox (10^{-6}M) for demonstration of specific cholinesterase activity, and butyrylthiocholine (2.5×10^{-3}M) for demonstration of non-specific cholinesterase activity.

Biochemical analysis following guanethidine administration for 14 days shows an increase in protein content (approximately 50%) and a decrease per ganglion in specific cholinesterase activity (approximately 65%) and non-specific cholinesterase activity (approximately 50%), the changes being still more pronounced after preganglionic nerve division.

Histochemical localization shows that preganglionic nerve division leads to a decrease in cholinesterase activity of preganglionic fibres while the cholinesterase activity of the ganglion cells remains unchanged. Postganglionic axotomy leads to a decrease in the cholinesterase activity of the ganglion cells while the preganglionic fibres appear normal.

Following guanethidine, the decrease of the activity of both cholinesterases occurs in the ganglion cells as well as in the preganglionic nerve fibres. These changes were observed already after a few days of treatment with guanethidine and were still demonstrable 30 days after discontinuation of the drug.

After guanethidine and preganglionic nerve division, only traces of cholinesterases could be found. Furthermore, a pronounced increase of satellite cells was found, with increased distance between the nerve cells.

On the basis of these findings it is concluded that guanethidine has at least two probably independent actions: the depletion of catecholamines and of ganglionic cholinesterases, accompanied by increase of protein and by a satellite cell infiltration.

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The effect of drugs on the intracranial pressure of baboons

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Much of the carotid blood supply to the cat brain passes through the rete mirabilis from the external carotid artery. The internal carotid artery is rudimentary. In primates

there is no rete and the carotid supply to the brain is through the internal carotid artery. The cat experiments previously reported (Stephens & Corne, 1966) were repeated on baboons to determine whether these anatomical differences affected the response of intracranial pressure (ICP) to drugs and might invalidate correlations between responses in cats and responses in primates and man.

Nine baboons of either sex were anaesthetized with pentothal (10 mg/kg, I.V.) and chloralose (50 mg/kg, I.V.) after sedation with phencyclidine (1.0 mg/kg, I.M.). The ICP transducer (Corne & Stephens, 1966) was slightly modified, the sensing area being protected in a box covered with a thin rubber membrane. This was placed in contact with the dura through a trephine hole and cemented in place with acrylic cement. Blood pressure, end tidal CO_2 concentration and ICP were monitored continuously and arterial pCO_2 periodically. The animals were artifically ventilated so that the resting arterial pCO_2 was 35–45 mm Hg. Drugs were injected I.V. (saphenous) or I.A. (lingual).

The ICP response to noradrenaline (0.05–1.0 μg/kg) was similar in form and duration to the systemic arterial pressor response. Adrenaline (0.1–1.0 μg/kg) also induced simple ICP responses, but these were often associated with biphasic arterial responses. Both histamine (0.5–10 μg/kg) and bradykinin (0.1–4.0 μg/kg) induced an increase in ICP associated with arterial depressor responses at low doses and depressor/pressor responses at higher doses. Bradykinin I.A. was ten times more effective than I.V. upon ICP and was the only drug used that showed a marked route difference in effectiveness. An I.V. infusion of histamine caused a long progressive rise in ICP, whereas the blood pressure returned to control level rapidly. Addition of 3% CO_2 to the inspired gases induced a considerable increase in ICP and pulse amplitude. Blood pressure was unaffected.

As the skull forms a rigid, largely closed container it seems likely that rapid increases in ICP reflect increases in cerebral blood volume (vasodilatation?) and decreases reflect reductions of blood volume (vasoconstriction?). The increase in ICP after histamine, bradykinin and CO_2 probably indicated active vasodilatation, whereas the ICP response to noradrenaline may have been a passive following of the blood pressure response. The ICP and blood pressure responses to adrenaline were dissimilar in form, so a direct action upon the cerebral vasculature cannot be discounted.

Some minor differences were observed. The ICP responses of cats to catecholamines showed more variation than those of baboons, and the primates were relatively insensitive to histamine. Qualitatively, however, the activity of the cerebral vasculature that we measured in cats is comparable with that in baboons.

This work was carried out while S. J. C. and R. J. S. were members of the Department of Pharmacological Research, Parke, Davis & Co., Hounslow, Middlesex.

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Nitrazepam delays onset and shortens duration of visual after-images

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The effects of nitrazepam (5 and 10 mg), amylobarbitone sodium (100 and 200 mg) and placebo were compared in ten healthy male medical students. Dark-adapted subjects