In the visceral arteries, prazosin (40 and 80 nmol/l) produced a dose-dependent parallel shift in the noradrenaline dose-response curves, thus acting as a competitive alpha-adrenoceptor antagonist. In the peripheral arteries, however, the same concentrations did not significantly shift the curves, and the maximum response to noradrenaline was only slightly reduced. This appeared to be the maximum effect of prazosin in the digital arteries as a higher concentration (320 nmol/l) caused no further shift of the curves or reduction in the maximum response to noradrenaline.

This lack of effect of prazosin was not due to an inability of the peripheral arteries to respond to competitive antagonists, since plasma-ammonia produced typical dose-dependent shifts of the noradrenaline response curves.

These results suggest that in concentrations resembling therapeutic plasma levels, prazosin acts as a competitive alpha-adrenoceptor antagonist, rather than a direct arterial smooth-muscle relaxant. Secondly, prazosin has a selective effect on different vascular beds, the visceral vascular bed being sensitive and the peripheral vascular bed resistant to its sympatholytic activity.

We suggest that cardiovascular collapse caused by prazosin is due to selective blockade of visceral sympathetic activity. The consequent pooling of blood in the viscera then leads to a redistribution of blood in some patients who are insufficiently severe to cause an acute hypovolemic state and cardiovascular collapse.

To investigate further the mechanisms involved, blood-ammonia levels in healthy cats were raised to values similar to intracranial pressure. The cause of such increases in intracranial pressure has been thought to be cerebral oedema. To determine the variables involved, blood-ammonia levels in healthy cats were raised to values similar to intracranial pressure. The cause of such increases in intracranial pressure has been thought to be cerebral oedema.

Ammonia infusion led to increases in intracranial pressure in all animals, and caused death in most of them. In no animal did we observe extravasation of Evans blue except at sites where brain tissue herniation had taken place (e.g., foramen of Monro). The consequent pooling of blood in the viscera then leads to a redistribution of blood in some patients who are insufficiently severe to cause an acute hypovolemic state and cardiovascular collapse.

Our observations suggest that the massive rises in intracranial pressure seen in ammonia intoxication may be due to an increased intracranial blood volume caused by impairment of autoregulation leading to vasodilatation. We do not know whether this impairment of autoregulation is due to a direct toxic action of ammonia on autoregulatory mechanisms of the vessel wall or on metabolic processes within the brain tissue.

**BLOOD/BRAIN BARRIER AND BRAIN OEDEMA IN AMMONIA INTOXICATION**

Sir,—Episodes of very high intracranial pressure have been recorded in patients with hepatic encephalopathy, Reye's syndrome, and mushroom poisoning. 1—4 Ammonia intoxication has often been considered the cause of increased intracranial pressure. Studies in the monkey 5 showed that increased blood-ammonia levels are accompanied by massive increases in intracranial pressure. The cause of such increases in intracranial pressure has been thought to be cerebral oedema.

To determine the variables involved, blood-ammonia levels in healthy cats were raised to values similar to intracranial pressure. The cause of such increases in intracranial pressure has been thought to be cerebral oedema. To determine the variables involved, blood-ammonia levels in healthy cats were raised to values similar to intracranial pressure. The cause of such increases in intracranial pressure has been thought to be cerebral oedema.

Ammonia infusion led to increases in intracranial pressure in all animals, and caused death in most of them. In no animal did we observe extravasation of Evans blue except at sites where brain tissue herniation had taken place (e.g., foramen magnum). In no animal did we observe brain oedema defined by an increase in tissue water content.


6 Anderson et al. 1977, 45, 697.