and in 6 hr to about fivefold. After 17 hr the HVA content was normal again. These increases are even larger than in the small rodents. The DOPAC concentration was about 1/5 of the HVA content. Probenecid treatment increased this metabolite also, but a dose of 200 mg/kg only doubled the DOPAC content in 4 hr.

We also studied the combined effect of probenecid and reserpine, because in contrast to the response in other species reserpine causes a fall in HVA concentration in pigeon brain (Juorio & Vogt, 1967). This effect was confirmed; 6 hr after reserpine the concentration of DOPAC was also slightly lowered. Four hours after probenecid (200 mg/kg) the HVA in the brain of a group of pigeons was $3{\cdot}47 \pm 0{\cdot}19$ μg/g, whereas if reserpine (2 mg/kg) had been injected 2 hr before the probenecid the value was $1{\cdot}77 \pm 0{\cdot}22$ μg/g. The combination of reserpine and probenecid also appeared to cause a small decrease in the DOPAC concentration.

The results indicate that there is an active transport mechanism for removal of HVA and possibly of DOPAC from pigeon brain. The effect of reserpine on the metabolism of dopamine seems to be different in pigeons and mammals, since in mammals there is an increase in the concentration of HVA after reserpine, and this increase is further enhanced by probenecid treatment.

L. A. is a Riker Fellow.

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The effects of two inhibitors of catecholamine synthesis on the content of noradrenaline and dopamine of the rat brain

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Two inhibitors of catecholamine synthesis have been used to investigate changes in the noradrenaline and dopamine content of the brains of male albino rats, estimated by the method of Brownlee & Spriggs (1965).

3-iodo-Tyrosine (3IT), a competitive inhibitor of tyrosine hydroxylase (Goldstein & Weiss, 1965; Ikeda, Levitt& Udenfriend, 1965) at a dose of 200 mg/kg subcutaneously reduces brain levels of noradrenaline and dopamine. Sodium diethyldithiocarbamate (DDC) inhibits dopamine-β-hydroxylase (Goldstein, Anagoste, Lauber & McKereghan, 1964) and DDC (500 mg/kg subcutaneously) decreases noradrenaline levels to a greater degree than 3IT, while increasing dopamine content. The doses chosen show maximal effects at the single dose level.

As was expected, simultaneous administration of DDC and 3IT at the above doses reduced dopamine levels, but at a slower rate than 3IT alone. Surprisingly, it was found that the combination of the two inhibitors reduced the noradrenaline content of the brain to a significantly lower degree ($P<0{\cdot}05$) than DDC alone. The possibility that DDC and 3IT when given together caused less depletion by mutual

interference was challenged by injecting either DDC or 3IT 1 hr before injection of the other inhibitor. In these conditions the rate of depletion of noradrenaline was not different from that observed after simultaneous administration.

Again the possibility was considered that combination of the two inhibitors modified catabolism or storage of noradrenaline but the available evidence makes this unlikely.

The possibility remains that the products of the two enzyme-controlled conversions, tyrosine to dopamine and dopamine to noradrenaline, themselves regulate the kinetics of the enzyme-catalysed reactions. Some evidence of this kind has been provided by Stjarne, Lishajko & Roth (1967), who showed that the intraneuronal level of noradrenaline activated the enzymes involved in biosynthesis.

This work was supported by a grant from the Medical Research Council.

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The removal of L-tryptophan from cerebrospinal fluid in the dog

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Endogenous levels of tryptophan, the amino-acid precursor of 5-hydroxytryptamine, in cerebrospinal fluid (CSF) obtained from lateral ventricle and cisterna magna were both found to be only 10% of tryptophan concentrations in plasma. The removal of L-tryptophan from CSF was studied in the conscious dog by means of the technique of Ashcroft, Dow & Moir (1968) for recirculatory perfusion of the cerebral ventricular system. The clearance from CSF of exogenous L-tryptophan or ^{14}C-L-tryptophan infused into the perfusion system over a wide range of infusion concentrations (0·18–1,800 μg/ml.) in different dogs, was found to be 270% of simultaneously determined clearance of inulin, a substance known to be removed from CSF almost solely through the arachnoid villi. Tryptophan and inulin clearances were not altered by thiopentone anaesthesia.

Levin, Nogueira & Garcia Argiz (1966) have studied the removal of the amino-acids, glutamic acid, glutamine, β-aminobutyric acid, leucine, β-alanine, glycine, phenylalanine, lysine, valine and tyrosine from a ventriculo-cisternal perfusion system in anaesthetized cats. They found that these amino-acids were cleared at similar rates to inulin.

In the dog, tryptophan obviously has mechanisms of removal from CSF additional to bulk filtration. As the clearance of tryptophan is apparently not dependent on