a blood relationship nor an overlap of family surnames can be established (Conley, C. L., personal communication).

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BIOCHEMISTRY

Activity of Phenethanolamine *N*-Methyl Transferase in the Adrenal Glands of Foetal and Neonatal Rats

THE proportions of adrenaline and noradrenaline in the adrenal glands differ from one species to another and within a species during development. Comline and Silver[1] have compiled a list of reports showing the percentage of noradrenaline in the adrenal gland catecholamines of foetal, newly born and adult animals of seven species. In general, a higher proportion of noradrenaline is associated with the foetal state and a higher proportion of adrenaline with the adult animal, which suggests that the ability of the adrenal glands to form adrenaline develops late in the foetal life or in the early life of the animal.

Adrenaline is formed from noradrenaline in the adrenal medulla[2]. The conversion involves a single enzyme step, with *S*-adenosylmethionine acting as the methyl donor[3,4]. Kirshner and Goodall[3] first demonstrated the activity of this enzyme; Axelrod[4] investigated its properties and named it phenethanolamine *N*-methyl transferase (PNMT). We have recently devised a microassay technique for PNMT (ref. 5). The method involves the measurement of radioactive adrenaline formed by incubation of a tissue homogenate with noradrenaline and *S*-adenosylmethionine-methyl-^{14}C. Using this method it has been possible to determine the activity of PNMT in single adrenal pairs from rat foetuses and from newly born rats. In these experiments, whole adrenal glands were removed from newly born rats or foetuses taken from pregnant Carworth *CFE* female rats under ether anaesthesia. The results of PNMT determinations are shown in Fig. 1.

Enzyme activity was detected at 17·5 days, the earliest time studied. In Fig. 1 the enzyme activity is expressed as units per adrenal pair, because PNMT is localized in the adrenal medulla[4] rather than in the cortex which comprises most of the total adrenal weight[6]. Josimovich *et al.*[6] found that there was a rapid increase in volume of the adrenal medulla between 19·5 and 20·5 days of gestation in the rat foetus. The increase in enzyme activity shown in Fig. 1 corresponds exactly to this. Such an increase may thus be a reflexion of the increase in volume of the adrenal medulla. Likewise, Kamoun *et al.*[7] found that the ratio of adrenaline to noradrenaline in the adrenal glands of foetal rats first became greater than one at 20·5 days—the time when a marked increase in the activity of PNMT occurred (Cheoux and Roffi[8] have reported that the change in the ratio of adrenaline : noradrenaline occurs at 19·5 days). Thus, the volume of the adrenal medulla, the ability to form adrenaline and the preponderance of adrenaline appear to develop simultaneously in the rat in the late stage of foetal life.

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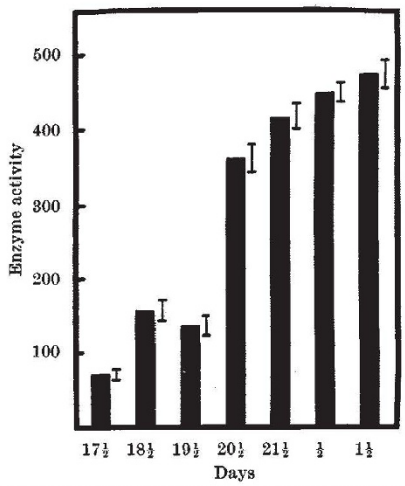

Fig. 1. The activity of PNMT in adrenal glands of foetal and neonatal rats. *Abscissa*, Age of foetus or of newborn rat in days. *Ordinate*, enzyme activity expressed as $\mu\mu$moles of adrenaline formed per 30 min of *in vitro* incubation per pair of adrenals. Mean determinations for between twenty and forty-nine rats in each age group are shown with standard errors.

Note added in proof. These data were first presented at the Ohio Valley Section, Society of Experimental Biology and Medicine, West Lafayette, Indiana, October 9, 1965. While this paper was in the press, a report by Margolis, Roffi and Jost appeared in *Science*, **154**, 275 (1966), showing an increase in PNMT activity during late foetal life in rats.

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Metronidazole and Human Alcohol Dehydrogenase

RECENTLY, metronidazole ('Flagyl') has been used in the treatment of alcoholism[1] and it has been suggested that it might inhibit alcohol dehydrogenase[2]. We wish to present evidence to shed light on this suggestion.

Macroscopically normal human liver obtained during operation on a patient with a chronic duodenal ulcer, free from liver disease, was homogenized by hand in nine volumes of sodium phosphate buffer (*p*H 7·0, 0·05 molar) using a Griffiths tube. The homogenate was centrifuged at 1,000*g* for 15 min and the supernatant used as the enzyme solution. The enzyme was subjected to the screening procedure described by J. P. von Wartburg *et al.*[3], and found to be the "typical" form of human alcohol dehydrogenase.

The catalytic activity of the enzyme was measured with a spectrophotometer at 25° C. The rate of formation of $NADH_2$ according to the equation

$$C_2H_5OH + NAD \rightleftarrows CH_3CHO + NADH_2$$

was followed at either 376 mμ or 385 mμ using a double beam optical recording spectrophotometer.