Histamine and rat blood pressure

SIR,—In 1962, Beleslin reported that intravenous doses of histamine (10–50 μg/kg) produced in 75% of rats a fall of blood pressure which was followed by a pronounced rise. We have found that Wistar albino rats obtained from one colony showed this biphasic response to histamine when tested in the autumn but were unresponsive to histamine in the summer, whilst animals from another colony showed only a depressor response in the autumn and were also unresponsive in the summer. Thus, there is a colony difference, as well as a seasonal variation, in the response of Wistar rats to intravenous histamine.

Rats weighing 180–200 g were obtained from the Agricultural Research Council's Field Station, Compton (hereinafter called A.R.C. rats) and from the Wellcome Research Laboratories, Beckenham (hereinafter called BW rats). They were anaesthetised with urethane (1·5 g/kg) intraperitoneally and their tracheae were cannulated to reduce interference from excessive mucous secretion. Records of blood pressure were taken from the carotid artery with a Condon manometer; animals from both colonies had similar resting levels (95–100 mm Hg). Heparin (1,000 units/kg) was given intravenously and subsequent injections were made into the exposed femoral vein. During the months of September to January, the A.R.C. rats responded to histamine (10–50 μg/kg) with a fall of blood pressure of about 40 mm Hg which was always followed by a pronounced rise of about 20 mm Hg. At the same time of the year, the BW rats responded with a fall of blood pressure of about the same intensity, but no secondary rise followed. The secondary rise obtained in A.R.C. rats diminished with repeated doses of histamine and was restored when a single intravenous dose of noradrenaline (1–2 μg) was given 2–5 min before the next histamine dose. In fact, noradrenaline often markedly increased the secondary rise of blood pressure produced in A.R.C. rats by histamine early in some experiments, although it did not modify the initial fall of pressure. The secondary rise was greatly reduced by adrenalectomy, suggesting that in these rats histamine released relatively large amounts of noradrenaline and adrenaline from the adrenal medulla.

TABLE 1. BLOOD PRESSURE RESPONSES OF WISTAR RATS FROM TWO COLONIES TO INTRAVENOUS DOSES OF HISTAMINE AT DIFFERENT TIMES OF THE YEAR

Time of year	No. of rats	Threshold dose of histamine (μg/kg)	Response	
			A.R.C. rats	BW rats
Sept.–Jan.	51	10–50	Depressor followed by a secondary rise	Depressor only
Feb.–April	25	100–500	Slight depressor followed by a a secondary rise	Slight depressor only
May–Aug.	47	1000—5000	None	None

During February and March, the sensitivity of rats from both colonies to intravenous histamine decreased about ten-fold and only reduced depressor and secondary pressor responses were obtained in A.R.C. rats.

By April, all animals from both colonies were completely insensitive to histamine, doses as high as 5 mg/kg having no effect on the blood pressure. This insensitivity remained for the next 4 months and then reactivity suddenly returned (usually in late August), the difference in response of the rats from the two colonies again becoming prominent.

The present results showing that rats are relatively insensitive to histamine during the summer months may be linked with the seasonal variation in the response of rats to anaphylactic shock, experimental traumatic shock, and tourniquet shock, some colonies being resistant during the period from May to August each year (Ankier, Dawson, Karady & West, 1965). Furthermore, the secondary rise of blood pressure produced in A.R.C. rats by the injection of histamine and probably resulting from the release of catecholamines helps to explain why A.R.C. rats are more resistant to histamine liberators such as dextran than are BW rats (Ankier, Harris, Luscombe & West, 1965; Fearn & West, 1965). The importance of stating the time of year when experimental results are obtained is again stressed.

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meso-OO'-Succinylbis(β-methylcholine)

SIR,—Attention has been drawn (Lesser, 1961) to an apparently specific effect of *meso*-succinylbis(β-methylcholine), in that it produced a contracture in the innervated chick biventer cervicis preparation, whereas the optical enantiomorphs showed a reduction of twitch height without contracture. The material used was believed to be a mixture of the racemic and *meso-OO'*-succinylbis-(β-methylcholine iodides) (Clitherow, 1961).

Since the publication of that note, a sample of the *meso*-compound prepared by a specific synthesis has come to hand (Clitherow, personal communication) and has been tested. The results did not bear out the original observation. This compound not only had qualitatively the same action as the optical isomers but also had quantitatively an activity lying intermediate between theirs.

There are some indications that the effect previously observed may have been due to contamination of the commercially obtained 1-dimethylaminopropan-2-ol by 2-dimethylaminopropan-1-ol, which as a result, yielded some *OO'*-succinylbis(α-methylcholine). This is being further investigated.

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