Potentiation of the noradrenaline-releasing action of tyramine by monoamine oxidase inhibitors

SIR,—Severe hypertension has been reported in patients treated with monoamine oxidase inhibitors after eating cheese, beans, or certain yeast extracts (Blackwell, 1963; Blackwell, Marley & Mabbitt, 1965). The tyramine content of these foods is considered to be the principal pressor substance (Blackwell & Mabbit, 1965; Horwitz, Lovenberg, Engelman & Sjoerdsma, 1964). I now report the influence of monoamine oxidase inhibition on the noradrenaline-releasing effect of tyramine in rats.

Adult Wistar male albino rats, 200 to 300 g, were given intraperitoneally pargyline 80 mg/kg. Twelve hr after this treatment the rats were deprived of food and 24 hr after the drug they were given different doses of tyramine by mouth. Four hr after the last treatment the rats were killed and their hearts were analysed for noradrenaline fluorometrically (Brodie, Dablac & Costa, 1966). Control animals fasting for 12 hr received tyramine only. The results (Table 1) demonstrate that the monoamine oxidase inhibitor potentiated the effect of tyramine in depleting noradrenaline and indicate that the enhancement of the pressor effects of tyramine by mouth (Tedeschi & Fellows, 1964) is caused by an increased release of peripheral noradrenaline.

TABLE 1. AUGMENTATION BY PARGYLINE OF THE EFFECT OF TYRAMINE IN DEPLETING NORADRENALINE IN RATS

Treatment (drugs in mg/kg)	Heart noradrenaline, μg/g (mean and range), 4 hr after the depleting agent
Controls	0·83 (0·80–0·85)
*Tyramine 12·5	0·77 (0·75–0·78)
" 25·0	0·65 (0·61–0·67)
" 50·0	0·48 (0·46–0·50)
Pargyline (80 mg)	0·94 (0·93–0·95)
Pargyline (80 mg) + tyramine (12·5)	0·92 (0·86–0·95)
" + " (25·0)	0·50 (0·40–0·52)
" + " (50·0)	0·21 (0·18–0·25)
" + " (25·0) + **(desipramine (10)	0·80 (0·75–0·87)

* Tyramine hydrochloride diluted in saline was given by mouth, 1 ml/100 g, 24 hr after pargyline.
** Desipramine was given intraperitoneally 20 min before the tyramine.

Both the hypertensive and noradrenaline-depleting actions of tyramine are known to be blocked by desipramine (Gessa, Vargiu & Crabai, 1966) and it is interesting that the experiments show an analogous effect in monoamine oxidase inhibited animals.

Acknowledgement. Abbott Laboratories, North Chicago, Ill., kindly supplied the pargyline.

Institutes of Pharmacology and
Nutritional Physiology,
University of Cagliari,
Cagliari, Italy.

P. F. SPANO

May 25, 1966

References

Blackwell, B. (1963). *Lancet*, **1**, 849–851.
Blackwell, B. & Mabbit, L. A. (1965). *Ibid.*, **1**, 938–940.
Blackwell, B., Marley, E. & Mabbit, L. A. (1965). *Ibid.*, **1**, 940–945.
Brodie, B. B., Dablac, A. & Costa, E. (1966). *J. Pharmac. exp. Ther.*, in the press.

Gessa, G. L., Vargiu, L. & Crabai, F. (1966). *Life Sci.*, **5**, 501–507.
Horwitz, D., Lovenberg, W., Engelman, K. & Sjoerdsma, A. (1964). *J. Am. med. Ass.*, **188**, 1108–1110.
Tedeschi, D. H. & Fellows, E. J. (1964). *Science, N.Y.*, **144**, 1225–1226.

Differences in the response to insulin of pathogen-free mice and mice bred conventionally

SIR,—In 1961 comparisons were made of the responses to insulin of mice from a number of strains at room temperature (21°). Since 1961 these strains have been transferred into pathogen-free buildings by caesarian derivation and one or two of the strains were re-tested. Alterations in response cannot be attributed solely to the lack of pathogen burden, since in the five intervening years a number of generations have been produced; and also considerable genetic drift may have ensued particularly in the random bred LAC grey mice.

TABLE 1. THE REACTION TO INSULIN OF STARVED CONVENTIONALLY BRED MICE COMPARED WITH THAT OF STARVED PATHOGEN-FREE MICE

Strain	No. of tests	Approx. ED50 milliunits/kg mouse	Mean slopes of regression
	Conventionally bred mice at 21° (1961)		
LAC grey	2	1,845	1·28
DBA/1	2	875	2·84
	Pathogen-free mice at 21° (1966)		
LAC grey	2	12,050	1·87
DBA/1fCFWLac ..	2	3,250	4·10
	Pathogen-free mice at 33°		
LAC grey	2	2,450	4·54
DBA/1fCFWLac ..	2	1,700	3·31

Table 1 gives the relevant comparisons of the ED50 values and of the mean slopes of the regression lines. Both strains of mice are now much less sensitive to insulin at 21° (six and three times less sensitive). At 33° the mice are still not as sensitive as the original mice at 21°. With both strains of mice the precision of the reaction is increased but the difference is less than significant ($P = 0{\cdot}7$ $P = 0{\cdot}2$). These results are in agreement with the statement made by Davey (1962) that pathogen-free mice are less sensitive than conventionally bred mice to toxic substances.

M.R.C. Laboratory Animals Centre,
Carshalton, Surrey.

ANNIE M. BROWN

May 25, 1966

References

Brown, A. M. (1961). *J. Pharm. Pharmac.*, **13**, 670–678.
Davey, D. G. (1962). *Proc. R. Soc. Med.*, **55**, 256.