The calculation is equally applicable to decreases in blood flow or to dual responses of vasodilatation and vasoconstriction.

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The importance of bradykinin in anaphylactic shock

SIR,—Brocklehurst & Lahiri (1962) showed that during anaphylaxis in the rat, detectable amounts of bradykinin were present in the blood and they suggested that it may contribute to the anaphylactic syndrome. As 5-hydroxytryptamine and histamine do not appear to be important mediators in anaphylactic shock in the rat (Sanyal & West, 1958), the toxicity of bradykinin was examined in male Wistar albino rats after various treatments.

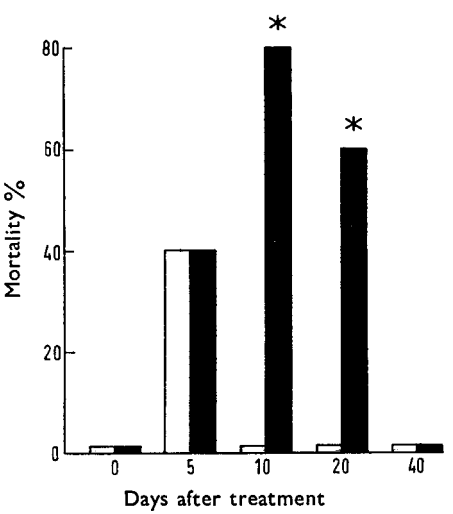

FIG. 1. Intravenous toxicity of bradykinin (2 mg/kg) in rats at varying times after treatment with *B. pertussis* vaccine and horse serum (solid columns) or *B. pertussis* vaccine (open columns). The asterisks denote the times when the specific antigen produces 100% mortality.

Groups of 5 rats weighing 200 g were used after sensitisation to horse serum. As an adjuvant (*Bordetella pertussis* vaccine) was necessary for full sensitisation, other groups were used after treatment with adjuvant only. The intravenous toxicity of bradykinin (2 mg/kg) was then measured, for which mortality rates are plotted in Fig. 1. Sensitivity to the polypeptide reached high values 10 and 20 days after sensitisation to antigen, the cause of death being characteristic haemorrhage in the jejunum and right ventricle. Similar lesions in anaphylactic shock have already been reported to be maximal at these times (Sanyal & West, 1958). In the group of rats injected previously with adjuvant only, bradykinin was not lethal at these times, although 5 days after treatment the

mortality rate was similar in both groups (see Fig. 1). Anaphylactic shock is not lethal 5 days after sensitisation so that the toxic effect of bradykinin in both groups at this time is probably due to an action of the adjuvant itself. Forty days after treatment (when anaphylactic shock is minimal), bradykinin was not toxic to either group. Konzett (1962) has already reported that the polypeptide was well tolerated by non-sensitised rats in doses of up to 10 mg/kg.

As the jejunum and heart are the tissues most damaged in both bradykinin shock and anaphylactic shock, the evidence suggests that bradykinin plays an important role in anaphylaxis in the rat.

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Modification of anaphylactic shock by mepyramine and ethanolamine

SIR,—It is evident that under different experimental circumstances the modification of anaphylactic shock by mepyramine and ethanolamine gives different answers. Herxheimer & Streseman (1965) found that ethanolamine did not improve the protection afforded by mepyramine to guinea-pigs exposed to an aerosol of antigen solution, whereas in this laboratory ethanolamine substantially improves the protective effect of mepyramine under these circumstances as originally reported by Smith (1961). It has recently been reported by Dawson, Hemsworth, & Stockham (1965) that the sensitivity of guinea-pig ileum to histamine can be influenced by dietary ascorbic acid. Since all guinea-pigs used in these laboratories receive approximately 50 mg of ascorbic acid per day in their drinking water, the discrepancy between my own findings and those of Herxheimer & Streseman might be due to this. Ascorbic acid is known to influence the metabolism and methyl donating capacity of folic acid, and the possibility that ethanolamine is dependent for its anti-anaphylactic activity upon *N*-methylation *in vivo* followed by incorporation into glycerophosphatide has been the subject of experimental investigation here for some time.

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