A quantitative measure of qualitative changes in blood flow

SIR,—I have been attempting to make quantitative measurements of changes in the blood flow of the cat through the hind limb caused by intravenously and intra-arterial administered vasoactive substances. The design of the experiments required answers which represented the absolute changes in flow, but it was found that qualitative differences in the responses, and the different resting flow rates observed from animal to animal, invalidated the calculations of changes in flow by the usual method. This problem may be overlooked when making measurements from actual blood flow records. Thus, Fig. 1 illustrates the records obtained of venous outflow from the hind limbs of three different cats measured with a Thorp impulse counter, in response to the same dose of vasodilator drug X.

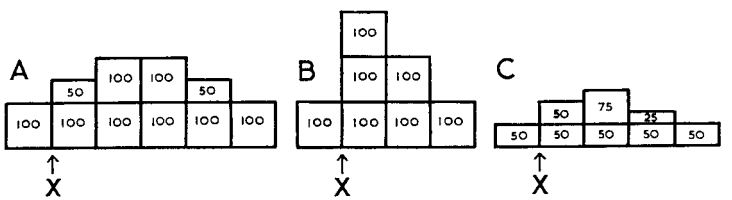

FIG. 1. Diagram of the femoral venous blood flow records obtained from three cats in response to the same dose of vasodilator drug X. The distance between consecutive vertical lines represent time intervals of 1 min and the figures indicate the number of drops flowing through the recorder. In cat A, for example, the resting flow rate is 100 drops/min and a total of 700 drops are recorded during the 4 min response to X.

In cats A and B the resting flow rate is 100 drops/min compared with a rate of 50 drops/min in cat C. An examination of the responses shows that the increased volume of blood which flowed through the drop recorder in response to X was the same in cats A and B, and that this volume was twice that measured in cat C. But, if the increase in blood flow is calculated by a usual equation in which the original flow is subtracted from the new flow and divided by the original flow, and this figure is multiplied by 100, the figures obtained for cats A, B and C are 75%, 150% and 100% respectively. The same answers are obtained by making the same calculations but using flow per unit of time; they therefore express the increases in flow as rates of flow.

It seems valid to express the vasodilation produced as the volume of blood flowing through the drop recorder in excess of the resting volume per unit of time.

$$\text{Thus, change in flow} = \frac{\text{new flow} - \text{old flow}}{\text{old flow/unit time}}$$

It might be thought that the unit of time should be that of the longest response obtained in any one series of experiments, but this has the disadvantages that all experiments must be completed before results can be calculated and that atypically long responses introduce complications. In practice, a unit of 1 min works well. Applying this equation to Fig. 1 the change in blood flow in each case is 3. This means that the extra volume of blood returning from the limb during each response is three times the amount of blood returning from the limb during 1 min before the response.

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.

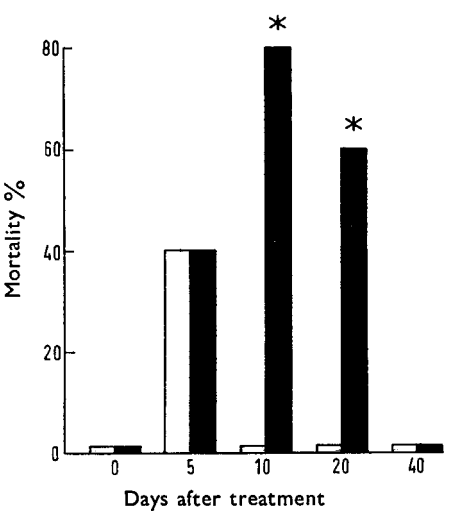

FIG. 1. Intravenous toxicity of bradykinin (2 mg/kg) in rats at varying times after treatment with *B. pertussis* vaccine and horse serum (solid columns) or *B. pertussis* vaccine (open columns). The asterisks denote the times when the specific antigen produces 100% mortality.

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