**Endotoxin shock in dogs pretreated with cellulose sulphate, an agent causing partial plasma kininogen depletion**

SIR,—Cellulose sulphate, a polyanionic macromolecule previously described by Astrup, Galsmar & Volkert (1944) as a semi-synthetic anticoagulant, has been recently shown (Rothschild & Gascon, 1966; Rothschild, 1967) to be a potent activator of the kinin generating system of rat, guinea-pig and human plasma. On intravenous administration to the pentobarbitone-anaesthetized dog, cellulose sulphate causes intense, transient hypotension probably mediated by released bardykinin since a rapid fall of kinin precursor (kininogen) in plasma accompanies the hypotensive response. After return to the normotensive condition, the animal becomes refractory towards the effects of a second injection of cellulose sulphate both in so far as plasma kininogen disappearance and fall of blood pressure are concerned.

Recent results (Scharnagel, Greeff & others, 1965; Diniz, Carvalho & others, 1967) have indicated that endotoxin shock in the dog is accompanied by a pronounced fall of plasma bradykininogen levels; for these reasons we have investigated the effect of *Escherichia coli* endotoxin in dogs partly depleted of plasma kininogen by previous cellulose sulphate treatment.

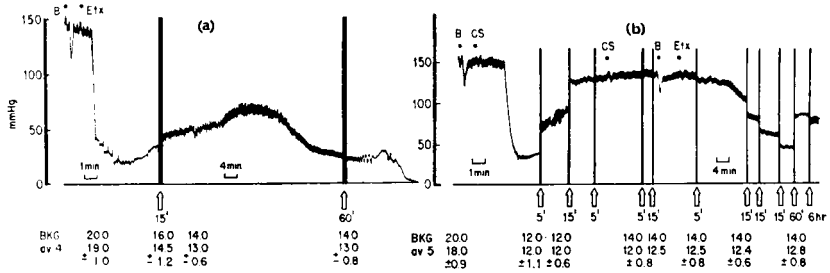


FIG. 1 (a). Effect of intravenous injection of *E. coli* endotoxin on arterial blood pressure and plasma kininogen (BKG) levels of the dog. At B, bradykinin (Sandoz), 1 $\mu$g; Etx, 5 mg/kg endotoxin. BKG = kininogen units/ml of plasma of samples withdrawn from femoral artery at times indicated: values shown in the upper line correspond to the experiment depicted; those in the lower line, to averages of four identical experiments. One unit of BKG yields 0·44 $\mu$g of synthetic bradykinin.

(b) Effect of intravenous injection of cellulose sulphate and subsequently of endotoxin, on dog arterial blood pressure and plasma kininogen content. At B, bradykinin, 1 $\mu$g; CS, cellulose sulphate, 20 mg/kg; Etx, endotoxin, 5 mg/kg. Other details as in Fig. 1 (a). Note partial recovery of blood pressure 2 hr after injection of endotoxin and increased survival time of the animal.

Fig. 1 (a) shows the typical, rapid hypotension leading to irreversible shock which is observed in dogs receiving a lethal dose of endotoxin (*E. coli* lipopolysaccharide, B26 : O26, Difco). This effect is no longer observed in dogs pretreated with cellulose sulphate; as shown in Fig. 1 (b), such animals respond to the toxin with a delayed, slowly progressing hypotension, starting approximately 15 min after the injection and reaching its lowest level 60 min afterwards. Partial recovery and a tendency towards longer survival times are noted in this group of animals. Kininogen levels, determined by the method of Diniz & others (1961), were reduced to about the same extent by either endotoxin or by cellulose sulphate; the bacterial polysaccharide, however, was unable to cause a further reduction of kinin precursor in the plasma of dogs which had first received an injection of cellulose sulphate.

These results, while lending further weight to the hypothesis of a participation of kinins in the early hypotensive response of the dog to endotoxin suggest that in addition, the toxin can induce a delayed hypotensive response appearing after a latency period of at least 15 min, and apparently not involving plasma kininogen breakdown. This response may be due to the direct impairing effect of *E. coli* endotoxin on ventricular performance (Solis & Downing, 1966), which has a similar latency period.

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### A new tracheal strip preparation for the evaluation of β-adrenergic activity

SIR,—The preparation we have used in our laboratory for the evaluation of β-adrenergic activity has been the tracheal muscle of the calf, described by Ariëns & Simonis (1960). However, dependence on an abattoir supply is a disadvantage as is the lack of the animal's history, while the tracheal muscles of the usual laboratory animals are too small to be used in the same way.

The preparations described in the literature are either too tedious to prepare, such as the guinea-pig tracheal chain* according to Castillo & De Beer (1947) and its modifications by Akcasu (1952) and Foster (1960), or otherwise inconvenient, like the spirally cut guinea-pig trachea of Constantine (1965) which has a torsion strength of its own.

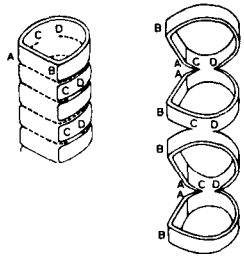


FIG. 1. Diagram of a new way of cutting the guinea-pig trachea. A-B: tracheal muscle; C-D: part which is cut open (along the dotted line).

We now wish to report that a satisfactory preparation can be obtained by cutting—with scissors—the trachea of a guinea-pig (400–600 g), after having removed all extraneous tissue, as indicated in Fig. 1. Between the cuts we left one cartilage ring and the total number of cuts was 10–15, depending on the size of the trachea.