THE ROLE OF CALCIUM, POTASSIUM AND SODIUM IONS ON THE NORADRENALINE INDUCED CONTRACTION IN THE VAS DEFERENS ISOLATED FROM GUINEA-PIGS

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The vas deferens, innervated by the hypogastric nerve (1, 2), contains a large amount of noradrenaline (3, 4), the presence of which suggests a role in the physiological function of the tissue. Inorganic ions such as calcium, potassium, and sodium would necessarily influence the noradrenaline action of this smooth muscle, therefore a clarification of physiology of same was attempted in the early summer season.

Excision of the vas deferens of male adult guinea-pigs weighing 350-450 g was carried out following cranial clubbing. The excised tissue was then suspended in a Magnus' apparatus in Locke's solution at 30-31°C, which had been saturated with pure oxygen. The tissue was next loaded with approx. 0.1 gw of tension and changes in the tension level induced by the dosage of noradrenaline (2 x 10^{-5} g/ml, the supramaximal dose) were recorded on a smoked drum via a lever. The contraction of the preparation induced by the noradrenaline was influenced by the four series of modified media, the constituents of which are summarized in Table 1. Fig. 1 illustrates these influences on the response to the noradrenaline. 1) In the first series of media containing CaCl_2 at 2.2 mM and NaCl at various concentrations between 154 and 0 mM (100 and 0% that of Locke's solution), the resultant contraction was linearly proportional to the concentration of NaCl in the medium (Fig. 1).

| Media                        | KCl | CaCl_2 | NaCl | NaHCO_3 | Glucose |
|------------------------------|-----|--------|------|---------|---------|
| Locke's solution             | 5.6 | 2.2    | 154  | 8.3     | 5.5     |
| First series (modified K-free Locke's s.) | —    | 2.2    | changed | 8.3 | 5.5 |
| Second series (modified Locke's s.) | 5.6 | 2.2    | changed | 8.3 | 5.5 |
| Third series (modified K- and Ca-free Locke's s.) | —    | —      | changed | 8.3 | 5.5 |
| Fourth series (modified Ca-free Locke's s.) | 5.6 | —      | changed | 8.3 | 5.5 |

NaCl concentration was changed from 154 to 0 mM and the osmotic pressure of medium was adjusted by sucrose.
The contraction was very slight when NaCl had not been added to the medium, yet when the concentration of NaCl was equal in moles to that in the Locke's solution, the contraction almost equaled that observed in the control even though the medium contained no KCl. 2) When the media contained CaCl₂ at 2.2 mM, KCl at 5.6 mM and NaCl at various concentrations of 154-0 mM, the contraction was greater than that observed in the first series of media when the concentration of NaCl was the same. Almost the same contraction was induced by noradrenaline, when NaCl was present in concentrations between 154 and 62 mM (100 and 40% that of Locke's solution). With a reduction of less than 62 mM of NaCl, the contraction began to reduce and decreased to 63% that of the control, when NaCl had not been added to the medium (Fig. 1). 3) When NaCl only at concentrations of 154-0 mM was contained in the third series of media, the contraction induced by noradrenaline was always very slight (Fig. 1). 4) In the fourth series of media containing KCl at 5.6 mM and NaCl at various concentrations of 154-62 mM the contraction was very slight, however with a concentration of less than 62 mM, the contraction due to noradrenaline gradually increased. When the concentration had been reduced to 15 mM, the contraction increased to approx. 53% of that seen in the control (Fig. 1). When pretreated with a Ca-free Locke's solution for 1 hr before the fourth series, the increase in contraction was hardly visible as tested after noradrenaline addition to the low NaCl medium. When there was a concentration of less than 15 mM of NaCl in the media, the response of the pre-
paration was difficult to measure, as the basic tension had already been increased by the applied medium before the addition of noradrenaline.

These results demonstrate the following: (a) the contraction of the vas deferens preparation induced by noradrenaline $2 \times 10^{-5}$ is dependent on CaCl$_2$ not on KCl in a medium containing NaCl at 154 mM, (b) the contraction induced by the noradrenaline is dependent on NaCl concentration in the medium when the medium contains CaCl$_2$ but not KCl, and (c) the presence of KCl in the medium promotes the noradrenaline induced contraction when NaCl concentration is less than 154 mM and those of NaCl and CaCl$_2$ are comparably the same.

Increase of the noradrenaline induced contraction due to a decrease in the concentration of NaCl in the fourth series was rarely observed, when the preparation had been pretreated with a Ca-free Locke's solution for 1 hr, or when the preparation was maintained in the third series. These facts suggest that calcium ions bound to the tissue would be released and play a part in the contraction, at which time potassium ions would be essential. This mode of action of potassium ions would thus account for the contraction, which was produced by a small amount of potassium ions in the vas deferens preparation kept in an isotonic sucrose medium containing 0.07% NaHCO$_3$ and 0.1% glucose, as reported by the author (5).

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EFFECT OF BRETYLIUM ON ADRENERGIC NEURONS AND ITS RELATION TO SODIUM

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Guanethidine and bretylium are believed to interfere in some way with the release of noradrenaline from adrenergic endings (1, 2). Kubo and Misu (3) have done studies on the adrenergic neuron blockade induced by guanethidine which is restored by washing out the drug with solution containing low sodium and accentuated with solution containing high sodium in the perfused heart of rabbits. The hypothesis has been presented that guanethidi-