Synthetic oxytocin was previously shown to afford protection against epinephrine induced arrhythmias under cyclopropane and trichlorethylene anesthesia in the dog[1]. PANISSET and BEAULNES[2] demonstrated an antiarrhythmic action on (1) atrial arrhythmias induced in isolated rabbit atria by electrical stimulation, administration of acetylcholine and lowering of potassium concentration, (2) ventricular arrhythmias produced by electrical stimulation of the isolated perfused rabbit heart, (3) chloroform-epinephrine induced cardia arrhythmias in the dog. BIRCHER, KANAI, and WANG[3] were able to convert ventricular arrhythmias induced by pentylenetetrazol administered intravenously in the dog, but not when pentylenetetrazol was injected into the fourth ventricale. The antiarrhythmic action has been attributed to a quinidine-like property of the molecule bringing about cell membrane permeability changes[2], or to an inhibition of oxidative metabolism[4,5].

Zusammenfassung. Synthetisches Oxytocin wurde für die Behandlung von ventrikulären Arrhythmien, welche bei Patienten im Lauf einer Allgemeinnarkose aufgetreten sind, verwendet. In 8 von 10 Fällen erfolgte eine prompte Wiederherstellung des normalen Sinusrhythmus. Es konnten keine unerwünschten kardiovaskulären Wirkungen beobachtet werden.

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The Effect of Bradykinin on Blood Flow and Heat Production in the Myocardium

The use of 'internal calorimetry' in the evaluation of blood flow in rabbit myocardium has already been described[1]. Its use in the evaluation of heat production changes in other tissues has also been described[2]. The technique uses a heated thermocouple which can be implanted in the myocardial muscle mass with little trauma. Measurements are of the difference between the apparent thermal conductivity of the living myocardium and the thermal conductivity of the dead myocardium (which has been shown to be an approximate linear function of blood flow in any likely biological range of flow) and of corrected temperature, i.e. myocardial temperature recorded with the 'cold junction' in the aorta and corrected for changes due solely to blood flow change. In so far as heat losses are constant and alterations in blood temperature are automatically compensated by the cold junction, the remaining changes are regarded as due to alterations in local heat production.

These methods were applied to a study of the action of bradykinin in various species.

Bradykinin was given by infusion and by single injection. The effect of infusion was investigated in 13 rabbits. Doses ranged from 0.05 μg/kg/min to 2.0 μg/kg/min continued for 10 min. In all animals blood pressure fell initially by amounts proportional to the concentration. In all perfusions, however, whatever the concentration, the blood pressure drop was transient, the pressure returning to resting levels or near resting levels within 5 to 10 min.

Blood flow responses were variable. When vascular resistance was calculated as pressure/flow, however, the results were consistent in every experiment. Vascular resistance always fell with bradykinin, the initial fall being a function of the dose. In every experiment and at all dose levels, however, vascular resistance recovered during the infusion *pari-passu* with the recovery in blood pressure, to resting or near resting levels.

Changes in heat production were not observed during infusions with bradykinin.

The effect of 40 single injections was investigated in 11 rabbits. Doses given ranged from 0.05 μg to 20 μg/kg.

The effect on blood pressure was consistent. Blood pressure fell by an amount proportional to the dose.

The effect on blood flow was variable and not directly related solely to the dose.

The effect on vascular resistance, however, was consistent in all experiments (Figure 1). Small doses of bradykinin produced small changes in resistance, large doses produced reductions of resistance of up to 50%, the magnitude of the change being a function of the dose.

The effect of bradykinin on corrected temperature was also recorded in the above experiments. A typical result is shown in Figure 1. Small doses of bradykinin had no effect. Doses of 5 μg/kg or more produced marked increments in corrected temperature.

In order to confirm that these effects were, in fact, due to change in myocardial heat production, experiments were performed in which absolute temperature was recorded by means of fine gauge thermocouples from the myocardium, the aorta and the thoracic cavity near the heart. In these experiments the temperature of the myocardium was the same as, or slightly hotter than, that of the aortic blood, the temperature of the thoracic cavity being lower than either. Injections of bradykinin in doses of 5.0 μg/kg increased the differential (i.e. myocardial temperature rose more than aortic) by values ranging from 0.06 to 0.38°C (Figure 2).

Since the heart was surrounded by a medium cooler than itself it could only attain a temperature higher than that of the afferent blood by virtue of considerable local heat production. A further increase of myocardial temperature relative to the afferent blood can only be interpreted as direct evidence of increased local heat production.

In the rabbit, therefore, we have concluded that bradykinin has a 'threshold' effect on heat production, small

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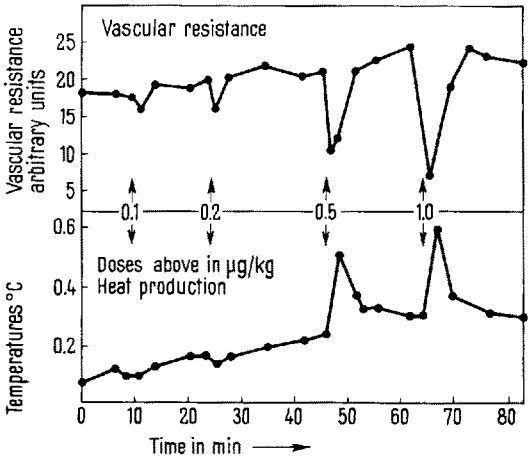

Fig. 1. The effect of bradykinin in varying doses on blood flow and heat production in the rabbit myocardium.

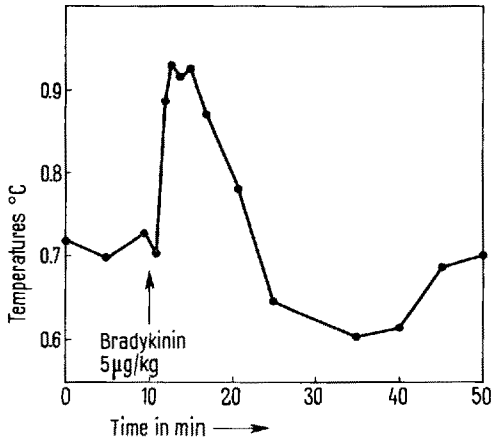

Fig. 2. Record of the difference in temperature between rabbit myocardium and aorta. The myocardium was hotter throughout than the aortic blood. Bradykinin raised its temperature still further with little effect on aorta blood temperature.

doses having no effect, large doses having a marked action in raising local heat production. This effect differs from the vascular action since bradykinin lowers vascular resistance in proportion to the dose. These effects may well be evidence of true vasodilatation in the coronary vessels but the present work does not exclude the possibility of extravascular factors.

Similar experiments have also been performed on the Patas monkey (*Erythrocebus patas*) and the cat. In all experiment the findings were the same as for the rabbit, bradykinin lowering vascular resistance in proportion to the dose and raising local heat production when the dose was large enough.

Résumé. En utilisant comme méthode la calorimétrie interne, nous avons montré que la bradykinine synthétique abaisse la résistance vasculaire dans le myocarde du lapin, du chat et du singe, même à doses aussi réduites que 0,05 µg/kg. Des doses plus fortes (5 µg/kg) augmentent aussi l'activité métabolique du myocarde[3].

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[3] The bradykinin was kindly donated by Dr. H. HOLGATE, Sandoz, Ltd. (England).

PRO EXPERIMENTIS

Avantages et inconvénients de la fixation par perfusion du tissu nerveux à la lumière d'une donnée de cytochimie

Un grand nombre de travaux de microscopie optique auront été nécessaires pour attirer l'attention sur les nombreux artefacts qui peuvent être liés au *mode* de fixation du tissu nerveux et particulièrement du système nerveux central (SCHARRER[1], COTTE[2], CAMMERMEYER[3]). Du point de vue *morphologique*, il est devenu évident que la fixation par perfusion, effectuée dans des conditions toujours plus précises[3] permet d'éviter ces artefacts. Dès lors ce procédé est d'une importance capitale en neurohistologie et surtout en neuropathologie expérimentale. Dans le domaine de la microscopie électronique, les inconvénients de la fixation du système nerveux central par immersion ont incité les chercheurs à surmonter un grand nombre de difficultés pour mettre au point des techniques de perfusion (PALAY et al.[4]).

Quelles que soient les modalités inhérentes à la microscopie optique ou électronique, la fixation par perfusion comporte très généralement, comme on le sait, l'utilisation de deux perfusats: le premier, destiné à «laver» les vaisseaux, peut aller du simple sérum physiologique à des solutions salines complexes[3,4]; le second, constitué par un fixateur approprié.

A l'heure actuelle, l'on peut admettre avec la plupart des auteurs, et nous l'avons nous-même vérifié, que du point de vue *morphologique* le procédé par perfusion est incontestablement le meilleur, au moins en matière de système nerveux central. La question se pose alors de savoir si ce procédé conserve cette supériorité du point de vue *cytochimique*.

Dans le but de répondre à cette question, nous avons pris en considération des phénomènes qui ont fait l'objet d'une série de travaux antérieurs[5–9]; dans les ganglions

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