was yellowish white, localized in the centre of the lens (nuclear cataract). We have observed 2 forms: permanent cataracts, persisting throughout the whole experimental period, and intermittent cataracts, which disappeared after some time and reappeared after a certain delay.

Statistical evaluation of the above results reveals undoubtedly that the extent of damage in the sucklings depends significantly on the amount of selenite used (chi-square, $\alpha = 0.001$). The largest dose used was associated with death, while the lowest dose did not cause any damage. Evaluating 40 animals in this latter group we can say, with 97.5% confidence, that the probability of absence of ocular damage is greater than 0.91. Doses of 40 and 20 μmoles/kg are mostly associated with permanent cataract, the dose of 10 μmoles/kg causes uneven distribution of both types of cataracts.

The above results demonstrated that sodium selenite administered in a single dose on the 10th day of postnatal life to male rats causes permanent or intermittent cataracts. A number of different agents (e.g. p-chlorophenylalanine[3], virus[4], radiation[5]) induce cataracts in the young during the first weeks of life. However, each cataractogenic agent has a special type of mechanism of action. From this point of view it is difficult to compare the cataractogenic effect of selenite and above-mentioned agents. Some of the cataracts have intermittent character, which could be explained by changing water contents in the lens. It cannot be excluded that in the experimental group where the smallest dose was used some cataracts will develop after the end of our experimental period. Sodium selenite-induced mortality of adult rats, under our experimental conditions, was significantly higher in comparison with sucklings (Fisher's test, $p = 0.001$). The cataractogenic effect of sodium selenite was not found in surviving adult animals. It seems that the sensitivity of sucklings and adult males to the toxic action of selenite markedly differs, and that the cataractogenic effect of selenite can be attributed only to the early postnatal period of the rat. This finding is in a good agreement with the opinion that the susceptibility of lens to many types of experimental cataracts decreases with age[6].

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Bradykinin-induced stimulation of cardiac parasympathetic ganglia

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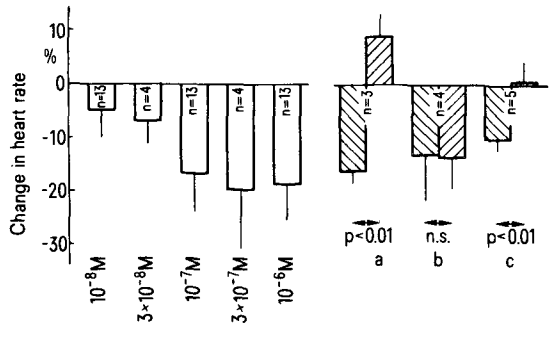
Summary. Bradykinin slows the heart rate of the rabbit isolated heart. It appears to act as a non-nicotine-like stimulant on the cardiac parasympathetic ganglia.

Bradykinin stimulates the adrenal medulla[2], as well as the superior cervical ganglion[3] and the noradrenergic cell population of the stellate ganglion of the cat[4]. The receptors involved differ from those with which nicotine and acetylcholine interact, since hexamethonium fails to antagonize the effect of bradykinin. Therefore, the mode of action has been classified as non-nicotine-like[3,5]. Unlike noradrenergic ganglion cells, cholinergic ones are supposed to be refractory to bradykinin. Thus, the peptide failed to stimulate the postganglionic cholinergic neurones originating from the feline stellate ganglion[4] and those of the guinea-pig ileum[6]. We have recently shown that bradykinin lowers the heart rate of the rabbit isolated heart[7]. Hence, it appeared of interest to study whether bradykinin possesses the ability to excite the parasympathetic ganglia of this tissue.

Methods. The study was performed on isolated rabbit hearts perfused according to the Langendorff technique with a modified Tyrode solution; experimental details have been described previously[7]. Drugs were either dissolved in the perfusion fluid reservoir or infused into the aortic cannula to give the required final concentrations. Infusions of nicotine were made in the presence of propanolol (5×10^{-7} M). Data are given as means ± SD.

Results. As can be seen in the left-hand columns of the figure, bradykinin evoked a dose-related negative



Effect of bradykinin on the rate of beat of the rabbit isolated heart. Left-hand columns (□): dose-response relationship. Right-hand pairs of columns: interaction experiments; 3×10^{-7} M bradykinin was administered twice at a 35 min interval before (▨) and 15 min after (▨) the addition of a) 10^{-7} M atropine, b) 10^{-5} M hexamethonium, c) 10^{-8} M tetrodotoxin. Means ± SD. n, number of experiments.

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chronotropic effect. However, the sensitivity to bradykinin varied considerably since 15 out of 45 hearts remained unaffected up to a concentration of 10^{-6} M; these hearts are not included in the statistical evaluation of the figure. In 'sensitive' hearts, the maximum decrease in rate obtained upon the infusion of bradykinin (3×10^{-7} M) was reached within about 3 min and amounted to 21 $\pm$ 6% (N = 4); any further increase of the dose did not result in a stronger response. Moreover, pronounced tachyphylaxis was observed; soon after the maximum decrease, heart rate returned to normal. When the infusion was discontinued, this refractory state was reversible; about 15 min later, the negative chronotropic effect could be reproduced by a second infusion of the same dose.

The right-hand columns of the figure show that pretreatment with atropine completely antagonized the retardation induced by bradykinin and frequently even reversed it into a slight but significant acceleration; the latter was also subject to a distinct tachyphylaxis, but was not further analysed. The negative chronotropic effect of bradykinin was equally suppressed by 10^{-9} M (not shown) or 10^{-8} M tetrodotoxin. On the other hand, it remained unchanged in the presence of hexamethonium (10^{-5} M); this concentration of hexamethonium reduced the bradycardic effect of 10^{-4} M nicotine by about 90% (N = 3; not shown).

10^{-4} M nicotine transiently decreased the heart rate by 25 $\pm$ 3% (N = 4). In some experiments, 3×10^{-7} M bradykinin was added during continuous infusion of nicotine (10^{-4} M) both immediately after complete development of nicotine tachyphylaxis and 30 min later. In either case, the effect of bradykinin was abolished (N = 4; not shown).

Discussion. It has previously been shown that 10^{-7} M bradykinin lowers the heart rate of the isolated rabbit heart[7]. The present results show that the effect is concentration-dependent. Moreover, several findings suggest that it is mediated through the parasympathetic innervation of the heart. 1. The bradykinin-induced decrease was prevented by atropine, thus demonstrating an involvement of muscarine receptors. 2. It was also abolished by tetrodotoxin, which blocks the propagation of nerve action potentials by interfering with the rapid sodium inward current[8]. This makes excitation by bradykinin of a proximal (ganglionic or preganglionic) site most likely, from whence impulses are carried down to the postganglionic parasympathetic nerve endings. On the other hand, a tetrodotoxin-sensitive direct depolarization of the postganglionic nerve endings cannot be entirely ruled out (cf. the interaction of tetrodotoxin and nicotine on postganglionic sympathetic axon terminals[9]). 3. The effect of bradykinin was not changed by hexamethonium. This observation excludes the possibility that the decrease in heart rate was due to stimulation of preganglionic vagal fibres, and confines possible sites of action to the ganglion cells. Moreover, the lack of antagonism by hexamethonium indicates that the ganglionic receptors are distinct from nicotine receptors. 4. In sympathetic ganglia, the effect of non-nicotinic stimulants such as angiotensin is abolished during the early, depolarizing phase of the block produced by nicotine; during the late, non-depolarizing phase, the effect is facilitated[5]. Only block, but no subsequent facilitation was observed in the present experiments. It should be noted, however, that even in sympathetic ganglia the effect of bradykinin differs from that of other non-nicotinic stimulants in that it recovers only to a very small extent after prolonged exposure to nicotine[5].

In conclusion, our results are consistent with the view that bradykinin excites not only sympathetic, but also some parasympathetic ganglion cells. In the rabbit isolated heart, only $^2/_3$ of all preparations tested were found to be responsive. As in sympathetic ganglia, the effect can be classified as non-nicotine-like.

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Efficacy of ethanol as a discriminative stimulus in ethanol-preferring and ethanol-nonpreferring rats

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Summary. Rats which exhibited a preference for drinking a 6% w/v solution of ethanol in a free choice situation did not differ in their sensitivity to ethanol from animals exhibiting an aversion for ethanol, as measured by learning rates in a T-maze task in which ethanol served as a discriminative stimulus.

Under some circumstances, the consumption of alcoholic beverages in man may be partially determined by inherited characteristics[2–5]. Alcohol drinking behavior in some strains of laboratory mice and rats has also been reported to be an inherited characteristic[6–9]. Studies on such strains may yield valuable information concerning the inherited characteristics which predispose some individuals to the excessive consumption of beverages containing ethyl alcohol. It has been reported, for example, that animals that prefer ethanol are less sensitive to the hypnotic and depressant effects of ethanol than are ethanol-nonpreferring animals[10–14]. Whether such differences in sensitivity to the effects of ethanol play a role in the self-selection of solutions of ethanol remains a major, unanswered question. However, implicit in such an inquiry, is the premise that conscious animals n a free choice situation are capable of gaining information concerning the effects of injested ethanol and may titrate drinking behavior accordingly. Drug discrimination procedures have proved to be useful for determining the extent to which animals are aware of the effects produced by specific drugs[15]. The present study employed a drug discrimination task to determine if ethanol-preferring rats differ from ethanol-nonpreferring rats with respect to the magnitude of the internal stimulus produced by a moderate dose of ethanol.

Subjects and methods. 105 female, Wistar rats (Woodlyn Laboratories, Guelph, Ontario, Canada) about 4 months of age and approximately the same weight were housed individually in transparent plastic cages (18″ l × 8″ w × 9″