group than in the suckled, respectively. The figure shows the relationship between body weight and cerebellar bilirubin content. Statistically significant negative correlations were obtained both in the suckled and the starved groups.

Discussion. The marked increase of plasma unbound-bilirubin concentration by suckling is shown in the table. The cerebellar bilirubin content of the suckled group was, however, lower than that of the starved, in spite of the increase of plasma unbound-bilirubin concentration. Our earlier study showed that plasma free fatty acid concentration of the suckled group was 4 times higher than that of the starved, and the molar ratio of free fatty acids/albumin of the suckled rats reached 7[10]. Since plasma unbound-bilirubin concentration increases when the free fatty acids/albumin molar ratio exceeds 3–5[13–15], the increased concentration of plasma unbound-bilirubin (table) may be accounted for by the elevated level of plasma fatty acids. However, the present findings are not necessarily in agreement with the generally accepted concept that in newborns an increased concentration of plasma unbound-bilirubin, which is easily transferred across the blood-brain-barrier[6], may result in accumulation of the pigment in the brain tissue with an enhanced risk of kernicterus[15,16]. The reason why cerebellar bilirubin content and plasma unbound-bilirubin concentration did not show parallel changes remains a problem for further investigation.

There were significant negative correlations both in the suckled ($r = -0.462$, $n = 21$, $p < 0.05$) and starved ($r = -0.626$, $n = 21$, $p < 0.01$) groups between body weight and cerebellar bilirubin content (figure). The results are consistent with the finding that in humans kernicterus is rife among small-for-date babies[9,17].

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Cataract induced by administration of a single dose of sodium selenite to suckling rats

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Summary. A single dose of sodium selenite to male suckling rats causes permanent or intermittent cataracts. The resistance to the lethal effect of selenite in suckling rats is significantly higher in comparison with adult animals.

In previous papers from our laboratory, effects of selenium compounds in rats of different age were reported[1]. In the experiments, in which selenite was administered to suckling rats, a new, till unknown and unexpected effect of selenite upon the eyes was investigated.

Materials and methods. For the experiments male Wistar rats (substrain Konárovice) were used. On the 2nd day of life, the sucklings were divided in such a way that 8 males were kept with one mother. On the 10th day of life (i.e. when they are in absolute nutritive dependence on the mother[2]) a single dose of 0.02 M solution of Na_2SeO_3 was administered s.c. to 5 experimental groups receiving 5, 10, 20, 40 and 60 μmoles/kg b.wt, respectively. The first control group received s.c. 0.02 M solution of a sulphur compound (Na_2SO_3, i.e. an element homologous with selenium), in a dose of 60 μmoles/kg b.wt. The second control group was without any treatment. As reference group the 2-month-old male rats were used to which 0.02 M solution of Na_2SeO_3 was administered s.c. in amount of 20 μmoles/kg b.wt. Mothers of the sucklings, as well as the group of adult males, were fed on a standard laboratory diet with water ad libitum. All animals were checked daily and the experiment was terminated 20 days after the treatment.

Results and discussion. The survival of experimental animals and the occurrence of cataracts are summarized in the table. Except for the cataracts, all surviving animals had no other signs of disease. Cataracts in the sucklings were visible by the naked eye after the opening of their eyes, i.e. on the 14–16th day of life. The opacity

The lethal and cataractogenic effect of sodium selenite on adult and suckling male rats (20 days after treatment)

Age	Group of rats	Dose (μmoles/kg b.wt)	No. of rats	Mortality 24 h	Mortality 7th day	Cataract Permanent	Cataract Intermittent	Without evident damage
Sucklings (10-day-old)	Na_2SeO_3	60	24	24	0	0	0	0
		40	36	0	8	22	6	0
		20	31	0	1	20	5	5
		10	28	0	0	5	6	17
		5	40	0	0	0	0	40
	Without treatment	0	16	0	0	0	0	16
	Na_2SO_3	60	16	0	0	0	0	16
Adults (2-month-old)	Na_2SeO_3	20	15	11	0	0	0	4

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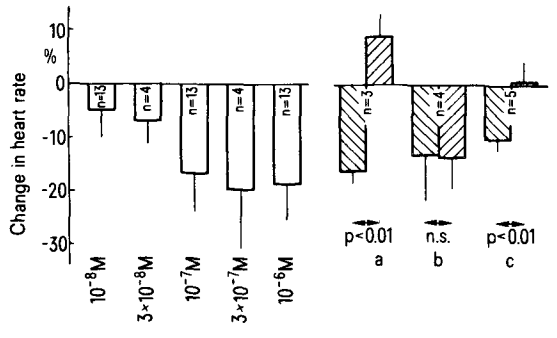
Summary. Bradykinin slows the heart rate of the rabbit isolated heart. It appears to act as a non-nicotine-like stimulant on the cardiac parasympathetic ganglia.

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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