Elicitation of cutaneous anaphylactic reactions in guinea-pigs after passive sensitization with rabbit-anti-BPO-bovine γ-globulin-antiserum

Elicitor	Eliciting concentration μM BPO	mg/ml CMC	Application[a] of elicitor	Sensitization[b]	Cutaneous anaphylactic reactions in mm blue zone mean of 3 animals	1 animal
BPO-CMC	1	0.004	i.d.	i.v. 1:4	9.5	
	10	0.04	i.d.	i.v. 1:4	10	
	10	0.04	i.d.	none		4
BPO-poly-L-lysine	1	–	i.d.	i.v. 1:4	9.5	
	10	–	i.d.	i.v. 1:4	11.5	
BPO-CMC	2×10^3	8	i.v.	i.d. 1:100	20	
	2×10^3	8	i.v.	none	no reaction	
BPO-poly-L-lysine	2×10^3	–	i.v.	i.d. 1:100		24
CMC alone	–	8	i.v.	i.d. 1:100	no reaction	
CMC + benzylpenicillin[c]	–	8	i.v.	i.d. 1:100	no reaction	

[a] Intradermal (i.d.) injections of elicitors in 0.1 ml were given immediately after i.v. application of 0.5 ml 1% Evans blue. Intraveneous (i.v.) injections of elicitors were in 0.5 ml, together with 0.5 ml 1% Evans blue. [b] The i.v. and i.d. application of antiserum for passive sensitization in the indicated dilutions were performed 18–20 h before elicitation. [c] Benzylpenicillin was incubated for 20 h at 4 °C in 0.04 M barbital buffer pH 7.4 and ultrafiltered in the same way as BPO-CMC. The residual solution above the filter was mixed with CMC immediately before use in the test.

potassium salt and 20 mg CMC (Elmans) in 5 ml 0.04 M barbital buffer pH 7.4 against running tap water for 5 days. The cellulose derivatives contained 0.5 and 0.2 BPO-groups per 100 glucose units respectively and were still able to elicit cutaneous anaphylactic reactions whereas control solutions, which were dialyzed without CMC but mixed with the polysaccharide before application, were negative. It is to be expected therefore that anaphylactogenic BPO-CMC's could arise even in less than 1 h (see Figure).

Our conjugate has not been tried in skin tests on patients allergic to penicillins. It may be recalled however that a number of years ago SIEGEL[4] elicited positive skin reactions with incubated mixtures of benzylpenicillin and CMC while negative tests resulted with unincubated mixtures. From the data it appears that in fact, CMC additives are a potential source for anaphylactically active penicilloyl-CMC conjugates[5].

Zusammenfassung. Penicilloylierte Carboxymethylzellulose bildet sich schon in der Kälte beim Stehen von Penicillinlösungen mit Carboxymethylzellulose. Die entstehenden Konjugate sind befähigt, penicilloylspezifische, kutane anaphylaktische Reaktionen auszulösen.

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L-DOPA Administration to Neonate Chicks: Effects on Behavior and Levels of Brain Biogenic Amines

We have observed and subsequently reported an unusual behavioral effect of L-Dopa in neonate chicks. Animals administered this amino acid in relatively large doses (100 mg/kg) exhibited immediate signs of hyperactivity and excitement identical to those obtained with amphetamine. This was followed in several minutes by catatonia, fixed, staring, and akinesia indistinguishable from that obtained after i.v. injection of dopamine[1–3]. We were able to administer the amine parenterally in earlier experiments because of the permeable blood-brain barrier to biogenic amines that exists in the neonate[4–10]. Based on these behavioral observations, we investigated the effect of L-Dopa on concentrations of adrenaline (A), noradrenaline (NA), dopamine (DA), 5-hydroxytryptamine (5-HT), and histamine (H) in whole brain of neonate chicks.

One to 3-day-old sex-linked hybrid cockerels were administered i.v. L-Dopa (100 mg/kg) dissolved in 0.9% NaCl, whereas control animals received an equal volume of 0.9% NaCl per kg. Chicks were decapitated 10 min after injection, the peak of the catatonic response, and the brain removed and analyzed simultaneously for catecholamines, 5-HT, and H[11–13].

There was a significant decrease of 14% in brain 5-HT and a very large increase in brain DA of 12 fold. No significant changes were found in the levels of brain A, NA, or H (Table).

The results indicate that both DA and 5-HT alterations in the brain may be responsible for many of the behavioral and physiological effects of L-Dopa in chicks. Recently, EVERETT and BORCHERDING[14] have observed effects of L-Dopa in mice that are similar to those of our original

preliminary report[1]. Their chemical data are in very close agreement with ours.

Both the behavioral and neurochemical effects of L-Dopa seem to mimic what might occur if first amphetamine and then DA were administered to chicks with sufficient intervening time for recovery. Amphetamine which produces excitement and hyperactivity causes a significant decrease of brain 5-HT only (SEIFTER and HANIG, in preparation) whereas DA administration causes catatonia and akinesia with a significant elevation of DA only in the brain[1-3]. JOUVET and others[15-18] have suggested that diminution of brain 5-HT may play a primary role in arousal mechanisms, whereas HORNYKIEWICZ and others[19-22] have demonstrated the role of basal ganglia DA in control of muscle tonus. Our present report is consistent with these findings[23].

Changes in concentrations[a] of chick whole brain biogenic amines following administration of L-Dopa (100 mg/kg)

Amine estimated	Concentration (μg/g of brain)	Change (%)	N
Adrenaline	0.213 (0.195)	+ 9.2	16
Noradrenaline	0.543 (0.478)	+ 13.6	16
Dopamine	6.244 (0.529)[b]	+1177.0	16
5-Hydroxytryptamine	0.887 (1.012)[c]	— 14.1	16
Histamine	0.559 (0.498)	+ 12.2	16

[a] Control values in parenthesis. [b] $P < 0.001$. [c] $P < 0.01$ – Analysis of variance.

Zusammenfassung. Nachweis, dass bei Küken die i.v. Injektion von L-Dopa (100 mg/kg) eine sofortige Überaktivität herbeiführt. Nach 10 min wurde im Gehirn eine Verminderung des Serotoningehaltes (14%) und eine Erhöhung des Dopamingehaltes (12fach) festgestellt, während Adrenalin, Noradrenalin und Histamin unverändert blieben.

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Hyperlipidic Diet as a Factor Allowing α-Naphtyl-Isothiocyanate and Thioacetamide Toxicity on the Albino Rat Testis

Alpha-naphtyl-isothiocyanate (ANI)[1,2] and thioacetamide (TAA)[3-5] induce a proliferation of the small biliary ducts in rat liver. Similar changes have been observed in the liver of rats treated with DL-ethionine[6,7]. This substance has been reported to produce hepatic lesions as well as structural changes of the germinative epithelium of the testis[8,9]. Therefore the effect of ANI and TAA on the testis was studied in rats fed either a balanced or a hyperlipidic diet.

Material and method. Five groups of 10 male albino rats (body weight: 150–160 g) were used. Group 1 and 2 were fed a balanced diet containing ANI (0.5 g/kg of food) and TAA (0.6 g/kg of food) respectively. Group 3 and 4 were given a hyperlipid diet containing ANI or TAA at the same doses as above. Group 5 was fed the hyperlipidic diet without any addition. The overall experimental period was 26 days.

Results and discussion. No microscopical lesions were observed in the testis of rats fed both the balanced diet containing ANI or TAA and the hyperlipidic diet. On the contrary, remarkable changes occurred in the testis of the rats given the hyperlipidic diet containing ANI (Figure 1) or TAA (Figures 2 and 3). Such changes consisted in a marked decrease in the volume of several seminiferous tubules and in an almost complete disappearance of their germinative cells, which had progressively undergone vacuolar degeneration, nuclear pyknosis, caryolisis, caryorrhexis and necrosis.

At first these pathological changes affected spermatozoa, then spermatids and spermatocytes and finally spermatogonia. In the degenerate tubules several multinucleate cells containing from 2 to 6 large nuclei, closely resembling those of degenerating primary spermatocytes, were observed. After 26 days of treatment, the damaged