

ROLE OF THE ADENYL CYCLASE SYSTEM IN STIMULATION OF IMMUNOGENESIS BY BACTERIAL LIPOPOLYSACCHARIDE AND BY ENDOGENOUS SERUM PYROGEN

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Experiments on rabbits immunized intraperitoneally with corpuscular typhoid vaccine showed that after injection of the bacterial lipopolysaccharide pyrogenal (LPS) and endogenous serum pyrogen (ESP), together with theophylline, the number of antibody-forming cells in the spleen was increased. The results point to a role of the adenylyl cyclase system in the mechanism of the stimulating action of LPS and ESP.

KEY WORDS: immune response; lipopolysaccharide (pyrogenal); endogenous serum pyrogen; adenylyl cyclase system.

In the writers' previous investigations the stimulating action of the bacterial lipopolysaccharide pyrogenal (LPS) and of endogenous serum pyrogen (ESP) on the antibody-forming cells (AFC) of the spleen was studied in rabbits immunized with corpuscular typhoid vaccine [1, 2]. An important role in the development of immunological responses and in the stimulation of antibody formation by certain chemicals has been ascribed by some workers [3-5, 7] to the adenylyl cyclase system, including its main component, cyclic AMP.

In the present investigation the role of the adenylyl cyclase system in the mechanism of the adjuvant effect of LPS and ESP was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 60 chinchilla rabbits, mainly males, weighing 2.5-3.5 kg. Methods of determination of AFC and of obtaining ESP, the characteristics of the vaccine used, and the method of statistical analysis were described previously [1, 2]. Theophylline was chosen as the chemical compound acting on the adenylyl cyclase system. This substance blocks the action of phosphodiesterase, the enzyme breaking down cyclic AMP [5]. Theophylline, like all the other preparations, was injected intraperitoneally. The doses were chosen so that each substance separately had no effect on AFC of the rabbit spleen, which was determined 72 h after the beginning of the experiment.

EXPERIMENTAL RESULTS

The results are given in Tables 1 and 2. It follows from Table 1 that after injection of LPS together with theophylline the number of AFC, both relative (per 10^6 nucleated spleen cells) and absolute, was increased by 2.7-5 and 4.1-9.1 times, respectively. Similar results were obtained by Braun [6] who immunized mice with sheep's red cells.

After combined injection of ESP and theophylline the relative number of AFC was increased by 10.4-15.5 times and the total number of AFC by 14-17 times (Table 2). Since the experiments were carried out on noninbred animals, the doses of the substances producing an adjuvant action were different from those when pyrogenal was given. It should be noted that when the doses for combined administration of ESP and theo-

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TABLE 1. Effect of LPS and Theophylline on AFC and Weight of Spleens of Rabbits Immunized Intraperitoneally with Corpuscular Typhoid Vaccine ($M \pm m$)

Group	Treatment of animals	Weight of spleens (in g)	No. of AFC per 10^6 nucleated spleen cells (log)	No. of AFC per whole spleen (log)
1.	Vaccine (10 billion bacterial cells/kg)	$1,6 \pm 0,1$	$1,05 \pm 0,11$ (11,2) $P < 0,001$	$4,46 \pm 0,14$ (28 800) $P < 0,001$
2.	The same + theophylline (150 μ g/kg)	$1,6 \pm 0,2$	$1,07 \pm 0,21$ (11,8) $P < 0,05$	$4,63 \pm 0,14$ (42 600) $P < 0,01$
3.	The same + pyrogenal (75 μ g/kg)	$1,6 \pm 0,1$	$1,3 \pm 0,1$ (20,0) $P < 0,02$	$4,8 \pm 0,16$ (63 100) $P < 0,02$
4.	The same + theophylline (150 μ g/kg) + pyrogenal (75 μ g/kg)	$1,8 \pm 0,3$	$1,73 \pm 0,12$ (53,7)	$5,42 \pm 0,14$ (263 000)

Legend. Here and in Table 2 geometric mean values given in parentheses. P calculated relative to group 4.

TABLE 2. Effect of ESP and Theophylline on AFC and Weight of Spleens of Rabbits Immunized Intraperitoneally with Corpuscular Typhoid Vaccine ($M \pm m$)

Group	Treatment of animals	Weight of spleens (in g)	No. of AFC per 10^6 nucleated spleen cells (log)	No. of AFC per whole spleen (log)
1.	Vaccine (15 billion bacterial cells/kg) + normal serum (7 ml/kg)	$1,4 \pm 0,1$	$0 \pm 0,2$ (1,0) $P < 0,002$	$3,48 \pm 0,23$ (3 020) $P < 0,001$
2.	The same + theophylline (15 μ g/kg) + normal serum (7 ml/kg)	$1,6 \pm 0,2$	$0,17 \pm 0,24$ (1,5) $P < 0,02$	$3,52 \pm 0,37$ (3 310) $P < 0,02$
3.	The same + ESP (7 ml/kg)	$1,8 \pm 0,3$	$0 \pm 0,2$ (1,0) $P < 0,002$	$3,58 \pm 0,2$ (3 800) $P < 0,001$
4.	The same + theophylline (15 μ g/kg) + ESP (7 ml/kg)	$1,7 \pm 0,2$	$1,19 \pm 0,17$ (15,5)	$4,73 \pm 0,06$ (53 700)

phylline were chosen, in some cases a reduction in the number of AFC was observed.

The results thus indicate that bacterial LPS (pyrogenal) and its secondary product ESP, formed as a result of the action of LPS on the body of the recipient, probably exert their stimulating action on AFC through the adenyl cyclase system.

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