INHIBITION OF ANAPHYLACTIC SHOCK IN GUINEA PIGS BY IMURAN

V. A. Ado and A. A. Podkolzin

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When given in a dose of 70-75 mg/kg to guinea pigs simultaneously sensitized with normal horse serum, imuran effectively inhibits the development of anaphylactic shock when a second injection of the same antigen is given to the animals.

Imuran (azathioprin, compound BW-57-322) is used to inhibit immune reactions of various types [1-8].

The object of this investigation was to test the effect of imuran on the development of anaphylactic shock in guinea pigs when administered simultaneously with the antigen sensitizing the animals.

EXPERIMENTAL METHOD

Experiments were carried out on guinea pigs (white-haired males) weighing 350-450 g by the usual method.

The experimental animals were divided into three groups: group 1 (20) received imuran intraperitoneally, in warm physiological saline, in a dose of 300 mg/kg, on alternate days; group 2 (23 animals) received 150 mg/kg on alternate days, and group 3 (18 animals) received 70-75 mg/kg* on alternate days. The total dose of the compound received by the animals was 600 mg in group 1, 300 mg in group 2, and 195 mg in group 3. Imuran was dissolved when required. On the 14th day after the beginning of sensitization, 13 control animals and all the experimental guinea pigs received the reacting dose of antigen by injection into a vein of the hind limb. The reactions which developed (anaphylactic shock) were recorded by the formula of Weigle, Cochrane, and Dixon (WCD) [7].

TABLE 1. Effect of Imuran (70-75 mg/kg) on Anaphylactic Reaction in Guinea Pigs

Assessment of reaction	Number of animals		Anaphylactic index (WCD)
	abs.	%	
++++	0	0	4,0
+++	1	5,5	3,0
++	2	11	2,0
+	3	16,5	1,0
—	12	67	0

Note. Anaphylactic index = $\frac{(0\times4)+(1\times3)+(2\times2)+(3\times1)+(12\times0)}{18}=0.55$.

EXPERIMENTAL RESULTS

The guinea pigs of group 1, which received imuran in a dose of 300 mg/kg body weight, died in 80% of cases on the 7th-9th day after administration of the immunodepressant began (this agrees with preliminary reports of the toxicity of the compound in this dose range).

The surviving guinea pigs (20%) did not die from anaphylactic shock after injection of the reacting dose of antigen on the 14th day (reaction 0 by the WCD index).

*The compound is extremely difficult to give in accurate doses because of its sparing solubility (as a suspension), and this is especially true of small doses.

Department of Pathological Physiology, Medical Faculty, P. Lumumba "Peoples' Friendship" University. Department of Pathological Physiology, N. I. Pirogov Second Moscow Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 69, No. 1, pp. 37-38, January, 1970. Original article submitted January 2, 1969.

Injection of the reacting dose of antigen into the guinea pigs of group 2 gave the following results: anaphylactic shock with a WCD index of 3 developed in only three guinea pigs (13%).

A reacting injection of antigen into the guinea pigs of group 3 gave anaphylactic shock with an index of 0.55 (Table 1). After injection of the reacting dose of antigen into the guinea pigs of the control group, they all died from anaphylactic shock, with the fully developed, vivid, classical picture ending in death (WCD index 4).

Administration of imuran to guinea pigs simultaneously with the sensitizing dose of normal horse serum thus considerably inhibits the development of anaphylactic shock in 90-95% of animals. The optimal dose of imuran for guinea pigs is 70-75 mg/kg body weight. A dose of 300 mg/kg gave a mortality of 100%.

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