

EFFECT OF CHORIONIC GONADOTROPIN ON GENERAL
IMMUNOLOGICAL REACTIVITY, ANTIBODY FORMATION,
AND HYPERSENSITIVITY OF IMMEDIATE AND DELAYED
TYPES IN GUINEA-PIGS

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Chorionic gonadotropin from the urine of pregnant women increased general immunological reactivity (V. I. Ioffe's test) in guinea pigs, did not affect the formation of precipitins against horse γ globulin in male guinea-pigs, but suppressed their synthesis in females and protected animals of both sexes against active anaphylactic shock. The protective action of the hormone against passive systemic anaphylaxis was exhibited only in females. In the animals of this species the hormone had no significant effect on the intensity of the cutaneous test for hypersensitivity of delayed type to foreign protein when assessed visually.

The antianaphylactic properties of chorionic gonadotropin, described by several other workers [6, 8] and confirmed by the present writer [2-4], require more precise definition, detailed analysis, and further study.

The object of this investigation was to make a differential study of the effect of the hormone on general immunological reactivity, antibody formation, and the formation of hypersensitivity of immediate and delayed types in guinea pigs (male and female).

EXPERIMENTAL METHOD

Experiments were carried out on 459 noninbred guinea pigs of both sexes weighing 350-400 g. The Hungarian preparation "Choriogonin" with an activity of 1500 i.u. per ampule was used. The antigen for immunization (sensitization) of the animals was horse γ -globulin.

The general immunological reactivity (GIR) of the guinea-pigs was assessed by Ioffe's method [1] by calculating the index of intensity of the skin reaction by the formula:

$$\frac{D_1 + D_2}{2} \cdot K,$$

where $D_1 + D_2 / 2$ represents half the sum of the two mutually perpendicular diameters of the area of hyperemia and K the intensity of the hyperemia in points (pale pink 1 point, pink 2 points, red 3 points, and hyperemia of any degree accompanied by edema or necrosis 4 points). The guinea pigs of the experimental groups received chorionic gonadotropin parenterally in a dose of 10 i.u./kg body weight 24 h after the antigen. The hormone was injected for 15 days, so that the total dose was about 24 i.u. per animal.

The immune response was judged from the percentage of animals responding by the formation of precipitins to this antigen. These antibodies were determined in the blood serum 2-2.5 weeks after immunization. Their titers (antigen dilution) were expressed in milligrams antigen protein per ml serum. The serum globulin content in the experimental and control animals was determined by electrophoresis on paper [5].

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TABLE 1. Changes in Immunological Reactivity of Guinea Pigs under the Influence of Chorionic Gonadotropin

Index	Total No. of animals in experiment	Males				Females			
		control		n	val. ind. imm. react.	control		n	val. ind. imm. react.
		val.	ind. imm. react.			val.	ind. imm. react.		
GIR	150	33	23.4±5.2	37	45.8±7.0 <i>P</i> <0.05	40	21.0±4.80	40	62.8±6.20 <i>P</i> <0.001
Immune response: number of animals immunized	107 (100%)	23	100%	23	100%	31	100%	30	100%
number of immune animals	72 (67%)	14	61%	15	65%	29	93.5%	14	40.6%
titers of precipitins			1.34±0.45		1.02±0.31 <i>P</i> >0.05		0.45±0.04		1.04±0.06 <i>P</i> <0.05
γ-globulin level (in percent of total protein)			13.2±1.1		15.5±0.61 <i>P</i> <0.05		15.9±0.72		15.17±0.78 <i>P</i> <0.05
Index of active anaphylactic shock	128	30	2.36	31	1.84 <i>P</i> <0.05	37	2.78	30	2.26 <i>P</i> <0.05
Index of passive anaphylactic shock	41	10	2.5	11	2.6 <i>P</i> >0.05	10	2.1	10	1.2 <i>P</i> <0.05
Intensity of skin reaction (HDT)	33	7	9.8±3.73	7	12.7±3.94 0.1> <i>P</i> >0.05	9	16.4±4.30	10	16.2±3.80 <i>P</i> >0.05

Active anaphylactic shock was induced in the guinea pigs 2 weeks after sensitization. The severity of the shock was estimated and expressed in anaphylactic indices [11]. Throughout the 2-week period of sensitization, the animals of the experiment groups received subcutaneous injections of 10 i.u. choriogonin per kg body weight on alternate days. The control guinea pigs were injected with the solvent of the hormone.

Systemic passive anaphylaxis was induced in the guinea pigs by sensitization with homologous anti-serum. This was injected intravenously in a dose of 0.4 ml/100 g body weight. The experimental guinea pigs were injected subcutaneously with 30 i.u. choriogonin and the controls with the solvent the night before and on the day of the experiment. The reacting dose of an antigen was injected intravenously. The severity of the manifestations of passive anaphylactic shock was also expressed in anaphylactic indices [11].

Hypersensitivity of delayed type (HDT) was reproduced in the guinea pigs by the method of Raffel and Newell [9] and assessed on the 6th day of sensitization by the method of Voisin and Toillet [10], with calculation of the index of intensity of the reaction by the formula given above.

The numerical results were subjected to statistical analysis by the Fisher-Student method. The level of significance of the difference between the experimental and control series was $P \leq 0.05$.

EXPERIMENTAL RESULTS

The results of the study of the effect of chorionic gonadotropin on the indices of immunological reactivity in the guinea pigs are given in Table 1.

A statistically significant increase in the GIR indices was found in the experimental group of animals of both sexes. In the opinion of Ioffe and many other workers, this is a favorable prognostic sign, reflecting to some extent resistance to infections, the action of toxins, and allergy.

The hormone did not affect the immune response in male guinea pigs but exhibited immunodepressant properties in experiments on females. This immunodepressant effect of chorionic gonadotropin was shown by the fact that two-thirds of the immunized female guinea pigs gave no reaction to the antigen used for immunization, while in animals responding by antibody production their titer in the blood serum was lower than in the corresponding control. The hormone had no significant effect on the serum γ globulin concentration.

In the series of experiments to study generalized active and passive anaphylaxis, the significant de-

crease (compared with the control) in the values of the anaphylactic indices in the groups of animals receiving chorionic gonadotropin is evidence of the protective action of the hormone, alleviating the symptoms of shock and reducing the number of deaths from it.

HDT to horse γ globulin in the guinea pigs (male and female) developed roughly identically whether the hormone was given or not, and no statistically significant difference was found between the HDT indices (with visual assessment of the reaction) in the experimental and control series.

Chorionic gonadotropin thus increased the general immunological reactivity in guinea pigs of both sexes but had no significant effect in males on the serum levels of normal and immune γ globulins. Injection of the hormone into female guinea pigs was accompanied by suppression of the synthesis of precipitins.

The hormone manifested its anaphylactic properties about equally in the experiments with active and passive anaphylaxis in guinea pigs of both sexes. The antianaphylactic properties of chorionic gonadotropin in the experiments upon male guinea pigs, unlike in the experiments on the females, were evidently not connected with the immunodepressant action of the hormone.

It can be assumed that the antiallergic and immunodepressant effects obtained by administration of chorionic gonadotropin to guinea pigs are due partly to activation of the endocrine function of the gonads, the hormones of which also possess antiallergic properties [7].

The results of these experiments widen our knowledge of chorionic gonadotropin and may prove useful when the role of the hormone is assessed in the immunobiological relationships between mother and fetus, its pharmacodynamics, and its therapeutic possibilities. This information may assist in securing a correct interpretation of the antiallergic properties of preparations of placental γ globulin, protein, and albumin containing this hormone.

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