DETERMINATION OF THE THRESHOLD OF STIMULATION OF THE SKIN RECEPTORS BY DYSENTERY AND TYPHOID ANTIGENS

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Our previous investigations showed that the injection of vaccine into the skin of the ear causes stimulation of receptors and this, when transformed into a specific process of excitation, spreads along the great auricular nerve. We studied the action potentials in the auricular nerve in response to the injection of dysentery, typhoid, coliform, paratyphoid A and B and whooping cough bacilli and streptococci. Each of these vaccines showed certain special features in the action potentials of the nerve. Analysis of the action of the vaccine showed, moreover, that the bioelectrical phenomena in the electrogram are observed not only in the intact nerve, but also in its peripheral cut end. Similar changes in the waves of action potentials in the nerve are also observed when the antigen is injected during immobilization of the animal by means of the administration of curare-like drugs and anaesthetics.

These findings suggest that antigen has the power, like many other stimuli, to cause excitation of the receptors of the skin. If this is so, then antigens, like other stimuli (chemical, thermal, mechanical, and electrical), must also have a definite threshold of stimulation.

In the present investigation our aim was to determine the threshold of stimulation of the receptors of the skin by antigen from dysentery and typhoid bacilli.

METHOD

Experiments were carried out on dogs under hexobarbital anaesthesia. The great auricular nerve was dissected out at the base of the ear, where it partially split up into branches, and its fibers were placed on electrodes. In certain cases another part of the fibers was divided and placed on a second pair of electrodes. The potentials were fed into a four-channel amplifier with symmetrical input. The action currents were recorded by means of a loop oscillograph (Siemens and Halske) on photographic paper.

The vaccines were injected into each animal strictly intradermally, at intervals of 30 min, in the upper third of the ear. Such intervals of time prevented summation of stimulation. The vaccines were injected in a dose of 0.25 ml, at room temperature (22-25°).

As the previous investigations showed, the injection of an isotonic solution of sodium chloride in the same volume and at the same temperature into the tip of the ear caused no essential changes. Different dilutions of the vaccines were used. At first, vaccine was injected containing 10,000 bacterial cells in 1 ml, and then, successively, 100,000 and 1,000,000 in 1 ml. After each injection of vaccine, the potentials were recorded for 10-15 sec at intervals of 3-5 min.

RESULTS

In the first series of experiments on 20 dogs (20 experiments), the effect of different dilutions of typhoid vaccine was studied.

After the injection of this vaccine (containing 10,000 bacterial cells in 1 ml) into the ear, no changes in the potentials in the auricular nerve were observed (Fig. 1,I).

The intradermal injection of a typhoid vaccine containing 100,000 bacterial cells caused a very slight reaction in the form of an increase in the amplitude of the oscillations.

Grouped oscillations of biphasic potentials appeared, having sharp peaks (Fig. 1, II). The reaction described usually developed soon after injection of the vaccine and lasted for 3-5 minutes.

The intradermal injection of typhoid vaccine containing 1,000,000 bacterial cells in 1 ml at once caused a considerable reaction, lasting on the average about 7 minutes. At first this was shown by single waves with an amplitude of 8-10 μv and a frequency of 5-10 per sec. After 3 minutes there appeared groups of successive oscillations with a frequency of 15-18 per second and an amplitude of 12-30 μv. After a further five minutes a continuous stream of impulses appeared, with a frequency of 18-25 per second and an amplitude of 10-20 μv (Fig. 1, III).

In a second series of experiments on 18 dogs (18 experiments) the action of dysentery vaccine was studied.

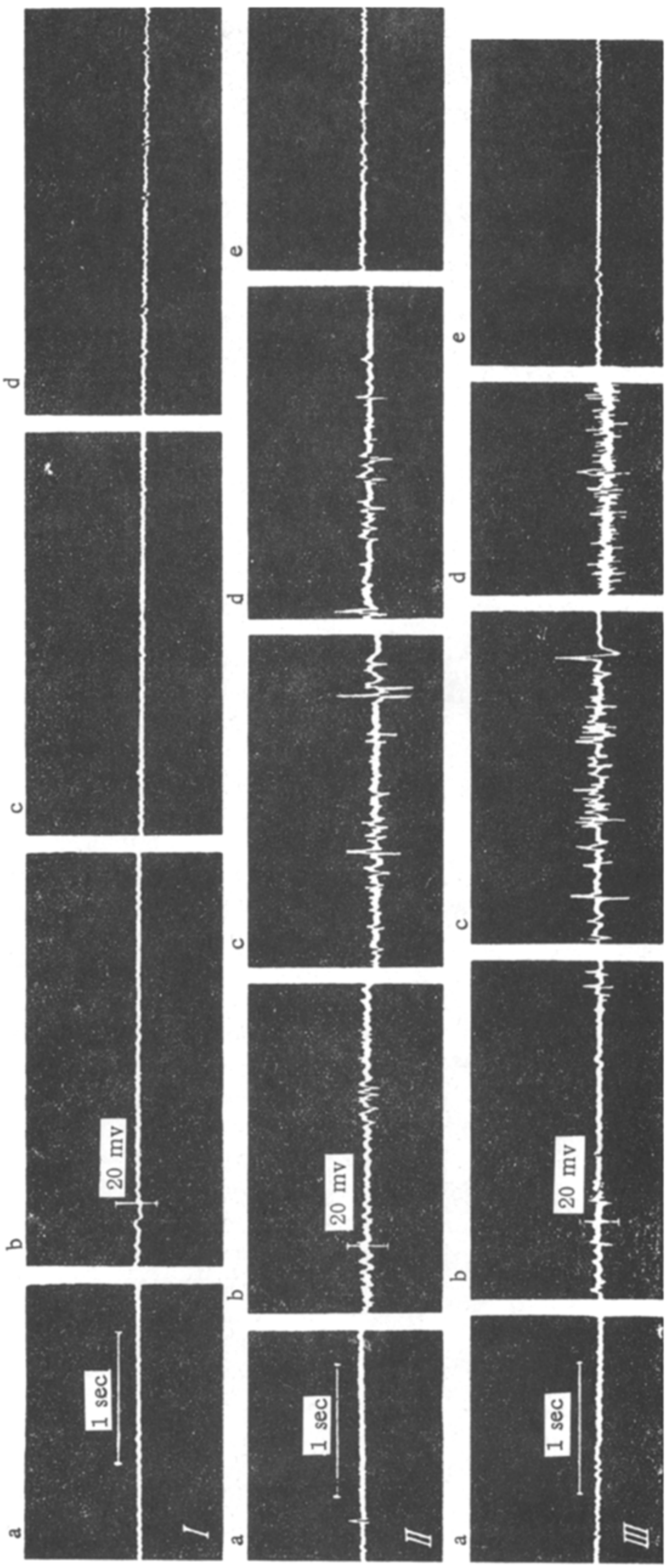

Fig. 1. Changes in the electrogram of the auricular nerve after the intradermal injection of different dilutions of typhoid antigen. Legend: a) Initial background, b) immediately after injection of antigen, c, d, e) 3, 5 and 7 minutes after injection of antigen. I) Injection of vaccine containing 10,000, II) containing 100,000 and III) containing 1,000,000 bacterial cells in 1 ml.

The experiments showed that the intradermal injection of a vaccine containing 10,000 bacterial cells in 1 ml caused no changes in the action currents in either the intact or the divided fibers of the auricular nerve (Fig. 2,I).

The intradermal injection of a vaccine containing 100,000 bacterial cells caused changes in the action

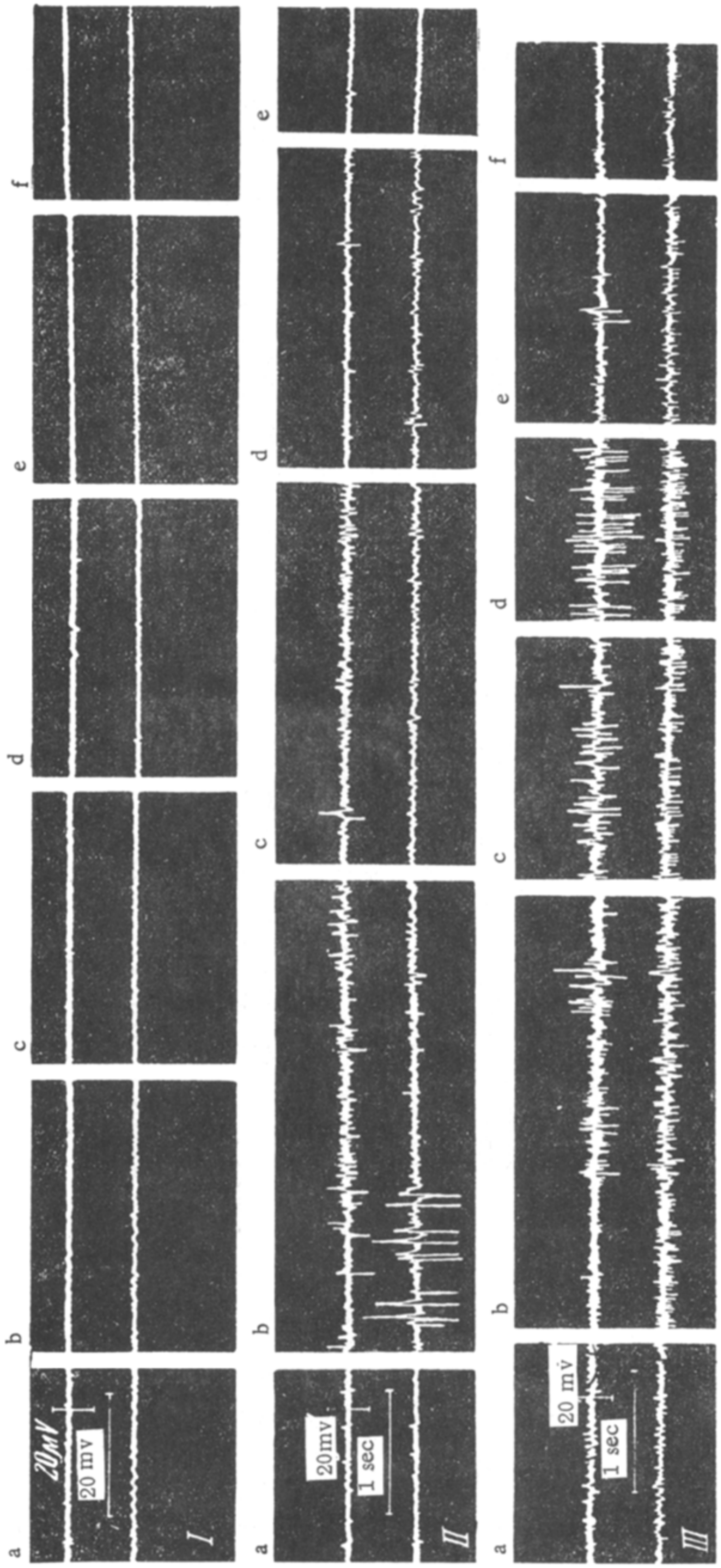

Fig. 2. Changes in the electrogram of the intact and divided auricular nerve after injection of different dilutions of dysentery antigen. Significance of the curves (from above down): electrogram of the divided nerve, electrogram of the intact nerve, time marker (50 cps): a) initial background; b) immediately after injection of antigen; c, d, e, f) 3, 5, 7 and 10 minutes after injection of antigen. Legend as in Fig. 1.

currents in the nerve as shown by the appearance of solitary and grouped waves with an amplitude of 10-15 μv and a frequency of 8-12 per second (Fig. 2, II).

The injection of a vaccine containing 1,000,000 bacterial cells caused the appearance of single and grouped waves with an amplitude of 10-15 μv, and in individual groups up to 60-70 μv, and a frequency of 8-12 per second (Fig. 2, III). In contrast to the reaction observed after the injection of vaccine containing 100,000 bacterial cells in 1 ml, in this case a more intensive and prolonged reaction was observed, which was dependent on the strength and duration of the antigenic stimulus. The character of the changes in the potentials depended only slightly on the density of the vaccine. In the peripheral cut end of the auricular nerve, the same potentials appeared as in the intact nerve.

Antigens, like many other stimuli, thus caused stimulation of the receptors of the skin when a definite concentration was attained. Dysentery and typhoid vaccines were inactive at a concentration of 10,000 bacterial cells in 1 ml. In the presence of 100,000 bacterial cells in 1 ml, these vaccines caused excitation of the receptors and the appearance of action currents in the nerve. An increase in the concentration of the vaccine to 1,000,000 bacterial cells in 1 ml was accompanied by a more pronounced increase in the amplitude of the variations of the potentials in the nerve and a more prolonged reaction.

It is difficult at present to explain why dysentery and typhoid vaccines should have the same threshold.

More detailed investigations are necessary for this purpose. For example, by the use of more fractional dilutions than those which we used, it might be possible to obtain more accurate data regarding the true threshold of stimulation, and this might reveal different threshold values for typhoid and dysentery vaccines, which probably might vary between limits of 20-30 to 100,000 bacterial cells in 1 ml.

The negative results obtained in the experiments with injection of vaccine in a concentration of 10,000 bacterial cells in 1 ml leave no doubt about the appearance of potentials in the auricular nerve in response to the intradermal injection of the vaccine being not a side effect of the prick of the needle the stretching of the skin by the volume of fluid injected, the pain reaction, the movements of the muscles of the ear, temperature changes at the site of injection and other factors, but an expression of the stimulation of the receptors by the vaccine. This is also confirmed by the fact that the injection of physiological saline, as our previous investigations showed, does not affect the character of the background bioelectrical activity.

The appearance of impulses in the peripheral cut end of the divided afferent nerve, just as in the intact nerve, in response to the action of threshold values of antigenic stimulation, is evidence of the afferent origin of the recorded waves of bioelectrical potentials.

The ability of a vaccine to cause stimulation of receptors is evidently one of the important factors determining the development of infectious and immunological processes.

SUMMARY

Dysentery and typhoid vaccine with a definite concentration of bacterial cells may cause excitation of cutaneous receptors. Intra-dermal administration of 0.25 ml of dysentery and typhoid vaccine containing 10,000 bacterial cells per ml does not cause any excitation of receptors detectable by recording the bioelectric activity of the sensory nerve. Intra-dermal injection of typhoid or dysentery vaccine containing 100,000 bacterial cells per ml in a dose of 0.25 ml causes excitation of cutaneous receptors and biocurrents of short duration in the nerve. Intra-dermal administration of the same vaccines containing 1,000,000 bacterial cells per ml gives rise to excitation of the receptors and to the appearance of biocurrents of considerable duration and strength.

LITERATURE CITED

[1] A. N. Gordienko, V. I. Kiseleva, B. A. Saakov, and A. V. Let'en, Byull. Eksptl. Biol. i Med. (Supplement) 1, 147 (1957).*

[2] A. N. Gordienko, V. I. Kiseleva, B. A. Saakov, R. B. Tsynkalovskii, Ya. I. Azhipa, and A. V. Let'en, Byull. Eksptl. Biol. i Med. 45, 4, 96 (1958).*

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