calcium precipitants, (2) those which act on the gray matter only, as creatin and strychnin. In order to determine possible similarities and differences between mammalian nervous tissue and that of one of the annelids, experiments were carried out on the nerve cord of the earthworm, *Lumbricus terrestris*. In these experiments the worm was decapitated, the anterior end of the preparation pinned down and the nerve cord laid bare. The cord was then dissected free for a distance of about 20 segments and the stimulating substances applied directly to it. Stimulation was indicated by squirming movements of the posterior segments.

Excitants of the first class, KCl, $BaCl_2$, and Na_3 citrate, each in $M/8$ concentration, gave marked excitation. Of the excitants of the second class, camphor and strychnin, each in saturated solution, and picrotoxin crystals, all yielded positive results within a minute after application, but phenol, nicotin and creatin had no effect, used either as crystals or in solution. $M/64$ tetra-ethylammonium chloride gave strong stimulation.

The fact that excitants of the first class act on the annelid nerve cord shows that the nerve processes reacting do not differ in this respect from the axons of the myelinated fibers of mammals. The action of the excitants of the second class exhibits two peculiarities; the action is almost immediate, there is no latent period of several minutes as in mammals and in squid[1]; the fact that the nerve cells of the earthworm are unaffected by phenol, nicotin and creatin indicates a chemical organization different from that obtaining in the neurones of higher forms in which stimulation by these substances does take place.

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Observations on the specific exhaustion of cutaneous reactions.

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Cutaneous reactions in hypersensitive individuals are of two quite distinct types. The reactions observed in patients with hay fever or asthma and after sensitization by foreign serum

[1] Moore, A. R., *J. Gen. Physiol.*, 1919, i, 505.

develop in a few minutes, consist essentially of a wheal and erythema, and fade out completely in one to two hours. The skin then appears normal. There is no visible evidence of cell destruction. Such reactions may be obtained with extracts of pollen, animal dandruff and feathers, with food proteins, with foreign serum, and occasionally with bacterial or other proteins.

This type of cutaneous reaction has little in common with the local cutaneous reactions to tuberculin, typhoidin, luetin, and mallein. Here the reaction does not usually develop for 12 to 24 hours; it is characterized by induration and persistent signs of inflammation, requires many days to fade out entirely and c early involves cell destruction. Zinsser[1] has recently shown that the local tuberculin reaction in the guinea-pig is independent of the development of a state of anaphylaxis and it is highly probable that the same holds true for the reactions of this type produced by other substances of bacterial origin.

Although it has commonly been assumed that the immediate skin reactions with urticaria-like lesions are manifestations of anaphylaxis, it has not been demonstrated that the mechanism consists of an antigen-antibody reaction. Similar reactions may sometimes be obtained with non-antigenic substances such as aspirin, salicylates and quinine, and there are a few substances, notably histamine, morphine and pituitrin, which produce this type of reaction in normal individuals. It appears to be essentially a vascular phenomenon with localized edema.

In an effort to determine the nature of these urticaria-like skin reactions we have studied their exhaustibility by a simple procedure in five hypersensitive patients, the subjects of hay fever or bronchial asthma. Our results indicate that the reactivity of the skin may readily be abolished in the area involved in the reaction. This exhaustion has been accomplished with such biologically different substances as egg white, extracts of ragweed and chicken feathers, the proteins of almond, pea, oat and wheat. In the experiments in which the cutaneous method of eliciting the reaction was employed, the exhaustion was usually not complete until the reaction had been repeated five or six times on the same site, at intervals of one or two hours. When the intracutaneous

[1] Zinsser, H., PROC. SOC. EXP. BIOL. AND MED., 1921, xviii, 123.

method was employed and the protein solution injected into the skin, the rapidity with which the local exhaustion can be accomplished was found to vary with the concentration of the protein solution. With a 1–10 dilution of egg white, a single test done on a child of six with bronchial asthma and hypersensitiveness to egg, completely abolished the skin reactivity at the site of the reaction.

The duration of the exhaustion has likewise been found to be dependent to some extent upon the concentration of the protein solution and the method employed for producing the reaction. With the 1–10 egg white solution and the intracutaneous method, the reactivity of the child's skin was completely abolished for three days and partially abolished at the site of the test for five days. In other instances with weaker solutions, the exhaustion did not persist more than twenty-four hours.

The extent of the area in which the reactivity is abolished is strictly limited to the site of the reaction. The area actually occupied by the wheal becomes completely exhausted, the area of the erythema partially so and beyond this the skin reacts as strongly as at a fresh site.

When two substances to which the individual gives positive reactions are simultaneously applied to the same site, the reaction is no stronger than that produced by the substances applied singly. There does not appear, therefore, to be any summation of effect.

Observations on the specificity of the exhaustion are not yet complete, but they suggest that there is a strict specificity for substances biologically unrelated and something similar to group reactions for substances closely related biologically. A patient reacting to ragweed and chicken feather showed a specific exhaustion, the exhausted ragweed site reacting as strongly to chicken feather as a fresh site and vice versa. With another patient, the specificity of the exhaustion was found to hold true for the proteins of almond and pea, while in a third patient giving positive reactions to wheat and oat, it was found that the exhausted wheat site reacted less strongly to oat than a fresh site.

As a control series of observations, we have attempted in six patients to abolish the cutaneous reactions to histamine. It is, of course, well known that the application of histamine in

solution to a small cut or scarification in the skin produces an urticarial lesion quite similar in appearance to the reactions of individuals hypersensitive to pollen, dandruff and feather extracts. Sollman[1] has reported observations on the effect upon the skin reactivity of repeatedly applying histamine to the same site. In agreement with his results, we have found that the histamine skin reaction is not exhaustible—on the contrary, it progressively increases with each subsequent application on the same area. Since histamine is non-antigenic, the non-specific skin reaction produced by it can not be dependent upon an antigen-antibody reaction. To us, it seems significant that this non-antigenic substance produces a local reaction which is not exhaustible, while the antigenic substances which we have used in the skin reactions on hypersensitive patients produce a reaction which may easily be completely exhausted.

Since our observations demonstrate that it is possible to abolish locally the reactivity of the skin, it seemed possible that by local application of pollen or dandruff extracts to the mucous membrane of the nose and throat of patients with allergic rhinitis, the reactivity might here also be abolished. We have not as yet carried far enough this therapeutic application of our observations to draw conclusions, but the results, so far as they go, are very satisfactory.

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Preliminary report on a staphylococcus bacteriophage.

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In 1915, two years before the discovery of d'Hérelle, Twort described the following phenomenon.[2] If glycerinated calf vaccinia is streaked on agar slants, a certain number of the micrococcus colonies which grow become glassy and transparent, and degenerate into a granular material which cannot be subcultured and which, even when diluted 1,000,000 times and filtered, gives rise to the same degeneration when added to a normal culture of micrococci, and so on indefinitely.

[1] Sollmann, T., and Pilcher, J. D., *Jour. Pharm. and Exp. Ther.*, 1919, ix, 309.

[2] *The Lancet*, 1915, ii, 1241.