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**Physical Allergy and "Auto-Antigens."**

EDWARD H. RICHARDSON, JR. (Introduced by Arnold R. Rich.)

*From the Department of Pathology, The Johns Hopkins Medical School,  
Baltimore, Md.*

In an attempt to determine whether physical allergies could be explained on an immunological basis Karady,<sup>1</sup> in recent experiments, subjected a number of guinea pigs to heat and another group to cold in the manner described below. He found that a re-exposure to the same stimulus at the end of 2 weeks produced anaphylactic shock in the animals so treated, and in some of the guinea pigs the shock was severe enough to cause death. He also injected guinea pigs with guinea pig serum that had been subjected to heat and others with serum that had been subjected to cold. After 2 weeks the reinjection of heated or chilled serum into the animals that had previously been injected with heated or chilled serum respectively produced signs of anaphylaxis, and at autopsy the animals showed the pulmonary emphysema characteristic of anaphylactic shock. On the basis of these results Karady suggested that a physical stimulus, such as heat or cold, might so alter the protein of the blood plasma as to form an "auto-antigen" within the animal's own body, so that a re-exposure to the same stimulus would cause anaphylactic shock as in the above experiments. It was thought desirable to repeat these experiments and, if they could be confirmed, to study the mechanism of the sensitization. To this end we used the methods described by Karady, as follows:

Serum was obtained from normal guinea pigs, and half was heated at 56°C for 1.5 minutes and the other half cooled to -5°C for 1.5 minutes. Three cc of the heated serum was then injected into each of 7 guinea pigs by the intraabdominal route and 7 guinea pigs were injected with the same amount of cold-treated serum. When these injections were repeated at the end of 2 weeks the animals were observed closely for an hour following the injection and during that period no signs of anaphylaxis were seen in any of them. On the contrary their behavior seemed perfectly normal, and all survived.

In our next experiment, following the procedure of Karady, we subjected 12 male guinea pigs (which were somewhat larger than those used by Karady) to cold by immersing their hind limbs in an

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<sup>1</sup> Karady, S., *J. Immunol.*, 1939, **37**, 457.

ice-salt mixture at  $-5^{\circ}\text{C}$  for 2 minutes. At the end of 2 weeks the immersion was repeated without any apparent effect on the animals which were carefully observed for an hour following the second exposure. All of them survived.

In order to be certain that the size of the animals had nothing to do with their lack of response to this treatment we repeated this portion of the experiment using 10 male guinea pigs all of which weighed between 200 and 250 g (the size of those used by Karady). Again the second exposure was entirely without effect in producing any signs of shock. After another lapse of 2 weeks their hind limbs were again immersed in the ice-salt mixture. Following this third exposure they were carefully observed for a period of one hour and once more failed to show any anaphylactic response. All animals survived.

Finally, another group of 7 male guinea pigs (weighing 200 to 250 g) were subjected to heat by immersing their hind limbs in water at  $56^{\circ}\text{C}$  for 2 minutes. Three weeks later they were again subjected to the same treatment, but no signs of anaphylaxis were observed in any of them during the hour following the re-exposure, and all survived.

*Summary.* We have been unable to confirm the report of Karady that guinea pigs can be sensitized anaphylactically to heat or cold by heating or chilling their limbs. We were also unable to confirm Karady's report that guinea pigs can be sensitized to heated or chilled guinea pig serum.

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### **Uterine and Extrauterine Localizations of Experimental Fibroids Induced in Guinea Pig by Prolonged Administration of Estrogens.\***

ALEXANDER LIPSCHÜTZ, RIGOBERTO IGLESIAS AND LUIS VARGAS JUN. (Introduced by Emil Witschi.)

*From the Department of Experimental Medicine, National Health Service of the Republic of Chile, Santiago.*

The occurrence of uterine fibroids was reported in a number of guinea pigs treated for several months with estrogens.<sup>1</sup> *Extrauterine*

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