

TABLE I.

Rat No.	Start		After 14 days	
	Symptoms	Weight	Symptoms	Weight
0.100 mg. level				
84-45	++++	51	0	77
86-19	++++	59	+	82
87-12	+++	39	0	59
87-31	+++	66	0	83
87-50	+++	57	0	80
89-25	+++	49	+	60
89-40	+++++	58	0	84
81-6	+++	54	0	68
81-20	+++	49	+	70
89-20	+++++	40	++	53
0.050 mg. level				
90-28	+++	38	+	43
84-11	+++	76	0	85
0.025 mg. level				
99-3	++	36	+++	36
99-47	++	52	dead in 12 days	
99-20	++	42	" " 11 "	

From these results it appears that a single curative dose of the crystalline preparation is no more than 0.100 mg.

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Reversed Iontophoresis of Histamine from Human Skin. Its Bearing on Histamine Theory of Allergic Wheal.

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By standardization of both metallic and absorbent electrode material, an iontophoretic method has been developed which permits the detection of histamine in dilutions as high as 1:5,000,000 by the formation of wheals in the human skin.¹ The method has been serviceable in the development of a procedure for assaying histamine in human, rabbit, and guinea pig blood. Thus, histamine can be assayed directly in the blood of rabbits killed by the intravenous administration of histamine. Only 0.1 cc. of blood is required.

When histamine is administered by the galvanic current so that a wheal forms in the human skin, the positive pole is applied to force

¹ Abramson, H. A., and Alley, A., *Arch. Phys. Ther., X-Ray, Radium*, 1937, 7, 327.

the positively charged histamine ions into the skin. It has now been found that if the negative pole be applied to the surface of the wheal formed by the scratch or by the iontophoretic method, sufficient histamine is transported out by this reversal of iontophoresis to form secondary wheals in new areas of the skin. In this way, histamine has been recovered from wheals which have been produced by iontophoresis from original dilutions as high as 1:100,000. Indeed, histamine may be recovered by diffusion alone, sufficient histamine being readily obtained for detection by means of the preceding methods within a diffusion period as short as 3 minutes. Histamine has been recovered from wheals produced by higher concentrations for as long as 40 minutes after wheal formation.

Using this method of reversed iontophoresis of histamine, attempts have been made to obtain histamine from (1) ragweed wheals, (2) timothy wheals, (3) wheals produced by ultraviolet light in a case of *urticaria solare*, (4) and wheals produced by stroking in a severe case of dermatographism. It should be noted that the size of the wheals in all of these instances corresponded as well as could be ascertained by present methods with the size of histamine wheal investigated by reversed iontophoresis. In no instances (in the 4 types of wheals just enumerated) was histamine obtainable by reversed iontophoresis. Since the size and character of the allergic wheals from which histamine was not obtained corresponded in general with the size and character of the histamine wheals from which histamine was readily obtained, it seems unlikely that histamine was present in sufficient quantity in the allergic wheals to produce the whealing observed. These experiments, then, do not support the point of view that histamine or a readily diffusible substance of low molecular weight (H-substance) like histamine is responsible for the production of the allergic wheal.

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Extra-Hormonal Factors in Maternal Behavior.

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In rats and mice the main manifestations of maternal behavior are retrieving, licking, and cuddling of the young. Along with these activities, but often independent of them, may occur nest-building,