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EGG WHITE EDEMA IN RATS AND ADRENAL ACTIVITY

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INTRAPERITONEAL injection of egg white in rats induces edema of the paws, nose, and tongue, hemoconcentration and hypotension. The mechanism of this reaction is not yet well known. It could conceivably be caused by a local release of histamine or histamine-like substance. Adrenalectomy sensitizes to this edema and leads to death in a certain percentage of animals.^{1, 2, 4} In similar conditions, adrenocortical extract prevents death but does not inhibit edema. Many workers have tried to inhibit the egg white edema syndrome by various pharmacologic substances or by stress such as exercise, cold, and formalin injection.^{2, 7, 8, 9} Since epinephrine protects against egg white edema in the normal rat, Clark and Mackay think that "alarming stimuli" may act by releasing endogenous epinephrine.³

We have, in this article, studied the effect of intraperitoneal egg white injection on adrenal cholesterol and ascorbic acid as well as upon the circulating eosinophils.

METHODS

Our experiments were carried out on 69 adult male rats weighing from 125 to 200 grams fed on a standard diet and kept at constant temperature. These animals from two different rearings were divided into two groups corresponding to each rearing.

In the first group, 15 acted as controls and were not injected, 30 rats received an intraperitoneal injection of 1 ml. of egg white associated with 0.5 ml. of a chlorazol blue sky solution.

In the second group, 12 animals acted as controls and 12 others received an injection of fresh egg white and blue.

All the animals were sacrificed three or four hours after the injection. The degree of edema was estimates

- + Scrotum colored in blue.
- ++ Edema of the paws.
- +++ Important edema of the paws and nose colored in blue.
- ++++ Important edema of the paws and important blue coloration.
- 0 No edema.

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The amounts of ascorbic acid and of cholesterol in the adrenals, the number of circulating eosinophils were studied in each rat.

Ascorbic acid was extracted from the adrenals with metaphosphoric acid and titrated against a solution of 2 to 6 dichlorophenol-indophenol.

TABLE I

EDEMA			ASCORBIC ACID 100% = 356 μg./100 MG. OF GLAND	CHOLESTEROL 100% = 2.934 μg./100 MG. OF GLAND	EOSINOPHILS 100% = 93/ CU. MM.
			Per Cent	Per Cent	Per Cent
Controls intact animals	1	-	96	76	76
	2	-	108	104	108
	3	-	100	108	72
	4	-	82	112	86
	5	-	112	124	130
	6	-	117	76	140
	7	-	98	72	65
	8	-	80	98	80
	9	-	89	96	100
	10	-	120	104	104
	11	-	100	126	122
	12	-	92	84	72
	13	-	102	102	120
	14	-	97	112	100
	15	-	107	106	125
Animals in- jected with egg white and blue	1	+++	69	130	80
	2	+++±	70	146	120
	3	+++	79	149	93
	4	-	79	165	93
	5	++++	83	116	83
	6	+++	125	141	70
	7	+++±	63	116	65
	8	+++	85	80	72
	9	++++	81	70	77
	10	+++	53	153	76
	11	+++	68	144	89
	12	++	67	78	55
	13	+++	50	109	95
	14	+++	69	93	106
	15	++++	74	77	92
	16	++++	67	75	64
	17	++++	67	84	68
	18	+++	60	93	72
	19	+++	71	100	50
	20	++++	68	87	75
	21	+++	80	93	88
	22	++++	54	79	77
	23	++	59	77	94
	24	+++	59	87	61
	25	+++	71	83	94
	26	++++	79	100	72
	27	++	50	112	77
	28	++++	79	72	77
	29	++	53	122	83
	30	++++	73	95	77

Total cholesterol was estimated by photometry after its extraction from crushed adrenal tissue with ethyl alcohol followed by Liebermann's reaction.

The circulating eosinophils were counted on blood drawn from the rat's heart when it was killed. The counts were made by the direct eosin method using Dunger's fluid. The blood was withdrawn in three white-cell pipettes and

six counts were made on each specimen of blood in four double-celled Fuchs-Rosenthal counting chambers.

RESULTS

Our results are summarized in Tables I and II.

After the intraperitoneal injection of egg white and blue, a significant fall of adrenal ascorbic acid is observed in the two groups of animals we studied. No change occurs in the adrenal cholesterol or in the circulating eosinophils.

There is no relation between the degree of edema and the value of the fall of adrenal ascorbic acid.

TABLE II

EDEMA			ASCORBIC ACID 100% = 413 $\mu\text{G.}/100 \text{ MG.}$ OF GLAND	CHOLESTEROL 100% = 2.66 $\mu\text{G.}/100 \text{ MG.}$ OF GLAND	EOSINOPHILS 100% = 112 CU. MM.
			<i>Per Cent</i>	<i>Per Cent</i>	<i>Per Cent</i>
Controls intact animals	1	-	107	89	75
	2	-	104	72	110
	3	-	88	94	122
	4	-	79	108	125
	5	-	121	122	76
	6	-	88 $\sigma = 12\%$	102 $\sigma = 17\%$	79 $\sigma = 19\%$
	7	-	97	79	94
	8	-	108	86	122
	9	-	96	120	126
	10	-	109	92	89
	11	-	92	122	85
	12	-	111	114	97
Animal	1	++	58	106	74
	2	++	72	118	74
	3	++++	67	94	79
	4	++	70	95	80
	5	+++	42	145	65
	6	++	- M = 68%	67 M = 94%	83 M = 82%
	7	++	86	120	74
	8	+++	50	63	108
	9	++	75	85	91
	10	++++	84	77	98
	11	+++	78	83	79
	12	++	62	74	79

DISCUSSION

A fall of adrenal ascorbic acid occurs after the intraperitoneal injection of egg white but no significant modification of adrenal cholesterol or of circulating eosinophils is observed. How is this to be explained?

A similar fact has already been reported by us in a previous article.¹⁰ We have indeed observed in rats after intraperitoneal injection of mercapto-ethylamine (or cysteinamine or 1573 L. Labaz), 10 mg. per 100 grams of body weight, a fall of more than 50 per cent of adrenal ascorbic acid. No changes occur in adrenal cholesterol nor in circulating eosinophils.

Nelson has already shown that the modifications of the circulating eosinophils after administration of cortisone or compound F are directly correlated with changes in the plasmatic levels of 17-hydroxycorticosteroids. Compound S or its acetate does not produce these hematologic modifications.⁶ On the basis of this experimentation it may be thought that neither egg white asso-

ciated with blue sky solution nor cysteinamine liberates 17-hydroxycorticosteroids. In these conditions is another group of adrenal hormones liberated by the adrenals?

A fall of circulating eosinophils, of adrenal ascorbic acid and cholesterol is regularly to be observed with sufficient doses of ACTH or salicylates. If the amount of corticotropic hormone (unpublished) or sodium salicylates¹¹ injected is progressively reduced, the initial significant fall of circulating eosinophils disappears but the significant ascorbic acid and cholesterol decrease remains; when smaller doses of the drugs are injected, the latter also disappear. In that experimentation with ACTH or salicylate a decrease of more than 30 per cent of ascorbic acid is regularly accompanied by a significant change in the circulating eosinophils. That is not observed in our study here reported. Thus we are led to conclude that no corticotropic hormone is liberated by cysteinamine or egg white injection.

Only hypophysectomy would enable us to eliminate the intervention of a pituitary-adrenal stimulation and to relate the observed fall of ascorbic acid to a metabolic process independent of adrenal hyperactivity.

SUMMARY AND CONCLUSIONS

Edema occurs in rats after egg white intraperitoneal injection and is accompanied by an important decrease of adrenal ascorbic acid. No significant change of adrenal cholesterol nor circulating eosinophils is observed. The modifications of ascorbic acid do not seem related to a liberation of 17-hydroxycorticosteroids by the adrenals or of ACTH by the pituitary gland. However, an adrenocorticotrophic stimulation cannot be eliminated.

This phenomenon has an important bearing upon the use of adrenal ascorbic acid depletion in the researches on the activity of the pituitary-adrenal cortex axis.

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