

The potency of the histamine was tested in 3 guinea pigs weighing 700 g. Two of these animals died acutely following the injection of 0.4 mg while the third survived 0.3 mg.

Conclusions: The cotton rat was found relatively refractory to anaphylactic shock. In this respect it resembles the ordinary laboratory rat. Low titered precipitins occurred in 3 of the 9 serums tested after sensitization. The minimal lethal dose of histamine intravenously was approximately 0.8 mg per 100 g for the cotton rat. This is 15 times the quantity required to kill a guinea pig, but is 100 times less than that which has been reported lethal for the rat.

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Relation Between Volume of Vehicle and Chick Comb Response to Androsterone.*

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It was suggested previously (Frank, Klempner and Hollander¹) that, in the use of sesame oil as a vehicle in our bioassay method for androgens, a reduction in the volume of vehicle from 0.1 cc to 0.05 cc was one of the factors which contributed to the improvement in response. Subsequently, the possibility presented itself that a further reduction in this volume might effect further improvement, as manifested by increased comb growth for a given dose of androgen. Accordingly, we have investigated the response elicited by the application of various dosages of androsterone in 0.05 cc and in 0.02 cc† of oil, applied daily, in paired experiments run simultaneously. In all other respects, the experimental conditions were exactly the same as in our last report (*loc. cit.*).

The results of such paired experiments are summarized in Table

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¹ Frank, R. T., Klempner, E., and Hollander, F., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 853.

† In order to facilitate the application of these small volumes, as well as to control accuracy of delivery, a simple mechanical device was attached to the syringes used. This device, constructed by Mr. Vondrak, chief technician of laboratories, Mount Sinai Hospital, will be described elsewhere.

TABLE I.
Effect of Further Reduction in Volume of Vehicle (Sesame Oil) in the Bioassay
of Androgens by the Chick Comb Method.

Series No.	Androgen dosage (γ)	Vol. of oil (cc)	No. of chicks	Mean comb wt		Response to androgen application (comb wt corrected for controls)		Improvement in response (IR) ²
				Treated chicks	Control chicks	(W-W _c)	% of W _c ¹	
				W (mg)	W _c (mg)			
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
27	10	.05	25	34.0	18.5	15.5	84	+52
		.02	25	43.6	(28)*	25.1	136	
28	10	.05	30	31.1	17.5	13.6	78	+63
		.02	30	42.2	(26)	24.7	141	
29	10	.05	30	31.0	19.3	11.7	61	+89
		.02	30	48.3	(23)	29.0	150	
30	10	.05	29	35.6	17.7	17.9	101	+75
		.02	29	48.8	(31)	31.1	176	
26	12	.05	15	43.1	23.0	20.1	87	+56
		.02	15	55.9	(21)	32.9	143	
26	15	.05	14	45.7	23.0	22.7	99	+63
		.02	15	60.2	(21)	37.2	162	
28	15	.05	30	39.2	17.5	21.7	124	+66
		.02	30	50.8	(26)	33.3	190	
29	15	.05	30	38.1	19.3	18.8	97	+79
		.02	30	53.3	(23)	34.0	176	
25	30	.05	25	59.2	16.0	43.2	270	+53
		.02	25	67.6	(26)	51.6	323	
27	30	.05	24	49.1	18.5	30.6	165	+108
		.02	24	69.0	(28)	50.5	273	
25	50	.05	25	71.0	16.0	55.0	344	+43
		.02	25	77.9	(26)	61.9	387	
								Mean = 67.9%
								σ _M = ±5.4%

*Figures in parentheses No. of chicks.

$$^1 \text{ Response as \% of } W_c = \frac{W - W_c}{W_c} \times 100$$

$$^2 \text{ Improvement (IR) as \% of } W_c = \frac{W_{.02} - W_{.05}}{W_c} \times 100$$

I, using mean comb weight for each group of chicks, regardless of sex, which had been treated in the same way. The dosages ranged from 10 to 50 γ. The response to treatment in any one experiment was measured by the increase in comb growth for that experiment (W) over the comb growth for a control experiment (W_c) run simultaneously, in which the chicks were untreated (columns 5 and 6). This increase (W-W_c), the comb weight corrected for controls, is given in column 7. It is apparent from the data that the response obtained in any one experiment with the smaller volume of vehicle is in each case greater than the response in the corresponding experi-

ment with the larger volume. Each of these response values has likewise been calculated as per cent of the corresponding control value and is given in column 8. The improvement in response resulting from reduction in volume of sesame oil (IR, column 9) is therefore measured by the difference of these paired percentage values. These "improvement" values are uniformly positive, corresponding to the greater response with 0.02 cc of oil than with 0.05 cc. They vary in magnitude from 43% to 108% of the corresponding control comb weight. The mean improvement is 67.9%, with a standard deviation of 5.4, and is based on a total of 710 chicks: 277 treated with the larger volume of oil, 278 with the smaller volume, and 155 untreated controls. A second group of experiments, identical with the foregoing but restricted to the dosage range 1-9 γ inclusive, has also been performed. This series employed a total of 308 chicks, of which 238 were treated and 70 were controls. The results were similar to those in the foregoing series.

It may be concluded, therefore, that this further reduction in volume of vehicle effects a further increase in the comb growth response of baby chicks. The only explanation which we can offer at the present time for this improvement is that the smaller the volume, the greater is the proportion of androgen solution utilized on the comb surface instead of being diverted to adjacent, less-sensitive head areas.

We desire to express our thanks to Dr. Erwin Schwenk of the Schering Corporation of New Jersey for supplying us with the androsterone used in this investigation.

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Improvement in Chick Comb Response to Androsterone Obtained with Alcohol as Vehicle.*

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In our studies of the bioassay method for androgens, utilizing the comb of the baby chick, it has appeared that further improve-

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