LXXI. URIC ACID AND ALLANTOIN EXCRETION AMONG OFFSPRING OF DALMATIAN HYBRIDS.

BY THE LATE HERBERT ONSLOW.

From the Biochemical Laboratory, Cambridge.

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IN a previous communication [Onslow, 1923] evidence was given for the fact that hybrids, from a cross between the Dalmatian hound and a terrier, excrete uric acid and allantoin in relatively the same proportion as in the normal dog. The appearance of the two hybrids, a dog and a bitch, was there described, the former being without spots, the latter only very slightly spotted.

In the late autumn of 1922, the hybrid dog and bitch were mated. Six puppies were born on December 26th, 1922. With the purine metabolism of these, the present communication is concerned. Photographs of five of the puppies, *A*, *B*, *C*, *D* and *E*, at the age of about 5 months, are shown in Plate VIII. Two of the puppies were reared only with great difficulty¹, and one, a male, died at the age of 8 weeks. Three of the puppies developed spots, namely, *D*, *E* and the one that died. The spots did not begin to appear until some 3 or 4 weeks after birth.

The bitch *A* (Plate VIII, Fig. 1) resembles a terrier; the ears are yellow and she has a yellow patch round one eye with a slight development of black pigment. The bitch *B* (Plate VIII, Fig. 2) also resembles a terrier; she has brindled ears and patches round the eyes. The bitch *C* (Plate VIII, Fig. 3) is without pigment except for a small black spot or two on the nose and a small yellow patch on the ear. The bitch *D* (Plate VIII, Fig. 4) resembles a true Dalmatian, being spotted more or less regularly over the body and more heavily on the ears. The bitch *E* (Plate VIII, Fig. 5) is a good deal spotted, but not so regularly as *D* and has also black ears, black eye patches, a black patch on the right fore flank and one on the tail.

The puppies were trained for the dog cage early, and the method of procedure was as described in the previous paper, except that the duration of time in the cage did not exceed 12 hours. In the case of all the animals, two preliminary estimations of uric acid were performed before the estimations of both uric acid and allantoin were made simultaneously. The diet was chiefly puppy biscuit and was much less varied than in the case of the parents previously described.

¹ The estimations in the present (as in the previous) paper were carried out by Mr John Lowndes, assistant to the late Mr Onslow. The success of the research is entirely due to Mr Lowndes' skilful and unfailing care for the puppies. (M.W.O.)

Fig. 1. Bitch *A*.

Fig. 2. Bitch *B*.

Fig. 3. Bitch *C*.

Fig. 4. Bitch *D*.

Fig. 5. Bitch *E*.

The results are recorded in Table I. *Bitch A* was 12 weeks and 6 days old at the date of the first experiment, and 17 weeks and 1 day at the date of the last experiment. At the beginning of the experiments she weighed 3.2 kilos. (7 lbs.), and at the end, 4.5 kilos. (10 lbs.). The duration of time in the cage for Exps. 1 and 2 was 8 hours, and for Exps. 3 and 4, 12 hours.

Table I.

Bitch A.

Date of experiment 1923	Vol. of urine cc.	Sp. gr. of urine	In whole volume of urine			Uricolytic index	Percentage of total N as	
			Total N g.	Uric acid N g.	Allantoin N g.		Uric acid N	Allantoin N
1. March 26	83 (100)*	—	0.7477 ⁴ _†	0.0016 ⁵ _†	— [†]	—	0.22	—
2. April 6	53 (100)	—	0.766 ⁰⁰	0.000 ⁹⁴	—	—	0.12	—
3. „ 20	132 (200)	1.020	1.474 ⁶⁴	0.004 ²⁴	0.311 ⁵²	99	0.29	21.13
4. „ 25	120 (200)	1.025	1.533 ¹⁴	0.002 ⁵²	0.329 ¹⁰	99	0.16	21.46
Average for Exps. 3 and 4 only:						99	0.22	21.29

Bitch B.

1. March 27	64 (100)	—	0.581 ³⁶	0.001 ⁷³	—	—	0.30	—
2. April 9	92 (100)	—	0.780 ²⁰	0.001 ⁸⁹	—	—	0.24	—
3. „ 16	142 (200)	1.020	1.392 ⁴⁰	0.004 ⁷²	0.288 ⁰⁸	98	0.34	20.69
4. May 2	172 (200)	1.021	2.166 ⁰⁶	0.006 ⁹²	0.457 ²³	98	0.32	21.11
Average for Exps. 3 and 4 only:						98	0.33	20.90

Bitch C.

1. March 20	30 (50)	—	0.332 ²⁷	0.002 ³³	—	—	0.70	—
2. „ 28	64 (100)	—	0.729 ⁴⁸	0.002 ⁵²	—	—	0.34	—
3. April 11	75 (150)	—	1.158 ⁵⁶	0.005 ⁴⁰	0.220 ⁴⁶	98	0.47	19.03
4. „ 30	206 (250)	1.016	1.418 ²⁹	0.006 ⁰⁹	0.294 ¹⁷	98	0.43	20.74
5. May 11	210 (250)	1.012	1.506 ²⁰	0.002 ³⁶	0.264 ⁸⁷	99	0.16	17.58
Average for Exps. 3 and 4 only:						98	0.45	19.88

Bitch D.

1. March 21	32 (50)	—	0.464 ¹⁶	0.002 ⁶⁴	—	—	0.57	—
2. April 4	43 (50)	—	0.617 ³⁴	0.002 ²⁷	—	—	0.37	—
3. „ 23	170 (200)	1.015	1.204 ⁹⁶	0.003 ⁷⁷	0.258 ⁷⁸	99	0.31	21.48
4. May 9	145 (200)	1.021	1.919 ⁹²	0.005 ⁰³	0.386 ⁹⁰	99	0.26	20.15
5. „ 15	65 (200)	1.066	0.773 ⁶⁹	0.000 ⁹⁴	0.088 ⁸³	99	0.12	11.48
Average for Exps. 3 and 4 only:						99	0.28	20.81

Bitch E.

1. March 23	72 (100)	—	0.291 ²²	0.012 ²¹	—	—	4.19	—
2. April 5	85 (85)	—	0.561 ⁴²	0.013 ³⁷	—	—	2.38	—
3. „ 18	120 (200)	1.021	1.386 ⁶³	0.042 ⁴⁶	0.235 ³⁴	85	3.06	16.97
4. May 7	160 (200)	1.020	1.580 ⁰²	0.039 ³¹	0.270 ⁵⁰	87	2.49	17.12
5. „ 14	185 (200)	1.020	1.908 ²¹	0.049 ³⁸	0.288 ⁰⁸	85	2.59	15.10
6. „ 16	160 (200)	1.025	3.076 ²⁸	0.051 ⁸⁹	0.258 ⁷⁸	83	1.69	8.41
Average for Exps. 3 and 4 only:						86	2.77	17.04

* Figures in brackets denote volume of first dilution.

† Unfortunately four figures only were given in these columns in the previous paper [Onslow, 1923]. The percentages, however, were calculated on six figures and are therefore correct and strictly comparable with those given in the present paper.

Bitch B was 13 weeks old at the date of the first experiment, and 18 weeks and 1 day at the date of the last experiment. At the beginning she weighed 2.7 kilos. (6 lbs.) and at the end 4.5 kilos. (10 lbs.). The duration of time in the cage for Exps. 1 and 2 was 8 hours, and for Exps. 3 and 4, 12 hours.

Scheme showing the inheritance of the Dalmatian characters in the first and second generations.
The numbers denote percentages of uric acid nitrogen of total nitrogen.

Bitch C was 12 weeks old at the date of the first experiment, and 19 weeks and 3 days at the date of the last experiment. At the beginning of the experiments she weighed 4.1 kilos. (9 lbs.); at the end 6.6 kilos. (14½ lbs.). The time in the cage for Exps. 1 and 2 was 8 hours, and for Exps. 3, 4 and 5, 12 hours.

During Exp. 5 the animal refused to eat; hence the results are not strictly comparable with the previous experiments and will be considered later.

Bitch D was 12 weeks and 1 day old at the date of the first experiment, and 20 weeks at the date of the last experiment. At the beginning of the experiments she weighed 2.7 kilos. (6 lbs.), and at the end 4.5 kilos. (10 lbs.). The time in the cage for Exp. 1 was 8 hours; for Exp. 2, 7 hours; for Exps. 3 and 4, 12 hours and for Exp. 5, 13½ hours.

Again, Exp. 5 was not comparable to the others, as the animal refused to eat while in the cage.

Bitch E was 12 weeks and 3 days old at the beginning of the experiments, 20 weeks and 1 day at the end. She weighed 3.6 kilos. (8 lbs.) at the beginning of the experiments and 6.3 kilos. (14 lbs.) at the end. The time in the cage for Exps. 1 and 2 was 8 hours and for Exps. 3, 4, 5 and 6, 12 hours. Exp. 6 took place after a diet of water biscuit for 24 hours.

A practice was made of feeding the animals while in the cage. Towards the end of the experimental period, three, namely *C*, *D* and *E* refused to eat. It will be seen, from Exps. *C* 5, *D* 5 and *E* 5 that starvation reduced the percentage of allantoin. Further, for Exps. 1 and 2 in each case the animals were very young. Hence the average of Exps. 3 and 4 is considered the most representative for the normal animal in each case. They are recapitulated as follows:

	Percentage of total N as	
	Uric acid N	Allantoin N
<i>A</i>	0.22	21.29
<i>B</i>	0.33	20.90
<i>C</i>	0.45	19.88
<i>D</i>	0.28	20.81
<i>E</i>	2.77	17.04

In regard to the allantoin excretion, the amounts excreted (except in the starvation experiments) were much more constant than in the case of the parents [Onslow, 1923]. This is probably due to the fact that the diet was more constant, the animals being fed almost entirely on biscuit. Starvation, either self-imposed or designed, as in Exp. *E* 6; reduces the allantoin percentage. At the same time it also reduces the uric acid percentage but does not appear to reach the condition, described by Benedict [1916], in which the animal may excrete a higher percentage of uric acid than of allantoin.

From the urine of the bitch *E*, uric acid crystals separated on adding 10 % hydrochloric acid and allowing to stand.

In regard to the uric acid excretion, it is clear, from the results in the second generation, that there has been a segregation of the character involving the power to destroy this substance from the character involving lack of this

power. Apart from this outstanding fact, it is difficult to postulate the exact course of inheritance from the data given by this one family alone. The results, however, suggest that, in main outline, the grandfather terrier (probably of mixed breed) carried a dominant factor for destruction of uric acid; also a factor for the inhibition of spotting which is not always entirely dominant in the hybrid. If it is assumed that these two factors segregate independently, then it is a simple two-factor Mendelian case (though there are, without doubt, subsidiary complications). Sixteen individuals would then, theoretically, be of the following kinds:

Four unspotted dogs; of these one only (*i.e.* 1 in a total of 16) should produce uric acid.

Twelve more or less spotted dogs; of these four are pure bred and eight are hybrid. Of the four pure bred, one only (*i.e.* 1 in the total 16) should produce uric acid. Of the hybrid spotted, two (*i.e.* 2 in the total 16) should produce uric acid.

Only a certain number, of course, of the above animals of different composition would appear in a small litter and the proportions, moreover, would not necessarily be in close agreement with expectation.

It is suggested that the bitches *A*, *B* and *C* belong to the unspotted class; the bitch *D*, which closely resembles a pure Dalmatian, to the pure spotted class which does not produce uric acid; and, finally, the bitch *E* to the hybrid spotted class which does produce uric acid.

The accompanying scheme (p. 566) sets forth the inheritance of the two characters in the first and second generations. The criticism may be made that the animals in the scheme are represented as more heavily spotted than is justified by the photographs. Observation, however, demonstrates the fact that the spots, though slight in the young animal, increase in size and intensity, month by month, until the animal is 18 months or even two years old. The scheme is therefore designed to show, as correctly as possible, the markings of the mature animals.

In regard to the question as to whether the purine metabolism might not alter further with age, it may be pointed out that, at the completion of their experiments, the dogs of the second generation were approximately the same age as the dogs of the first generation at the beginning of their experiments. The metabolism of the latter did not change during the subsequent three months of experimental work.

Further matings and experiments no doubt would yield interesting results, but the main object of the research as formulated by the late author, namely, the mode of inheritance of the uric acid-producing character through two generations, has been determined.

REFERENCES.

- Benedict (1916). *J. Lab. Clin. Med.* 2, 1.
Onslow (1923). *Biochem. J.* 17, 334.