THE PURINE METABOLISM OF THE DALMATIAN COACH HOUND.

By H. GIDEON WELLS.

(From the Department of Pathology of the University of Chicago, and the Otho S. A. Sprague Memorial Institute, Chicago.)

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Recently Benedict\(^1\) reported the observation that the Dalmatian breed of coach hound exhibits a marked peculiarity in its purine metabolism, to the extent that it excretes large amounts of uric acid, even when on a purine-free diet. This peculiarity was exhibited by four Dalmatians examined, but a fifth, "obviously not of very pure breed," did not eliminate much uric acid. That a single species of dog should exhibit this characteristic is remarkable, especially in view of the fact that the only other mammals that excrete uric acid in any considerable amounts are man and the anthropoid apes. The Dalmatian coach hound, however, differs also from man and the anthropoids, in that it excretes allantoin in considerable amounts; i.e., from one-half to two-thirds as much allantoin as uric acid. Hence the Dalmatian is unique in respect to purine metabolism.

This fact is of more than academic interest, for it gives us for the first time a laboratory mammal that excretes considerable amounts of uric acid, and hence serves as a possible medium for experimentation under conditions somewhat resembling those obtaining in the human subject. Benedict has already employed the Dalmatian for such investigations. Since other species of dogs differ so radically from the Dalmatian in respect to purine metabolism, there is also opened a most interesting field of investigation in the inheritance of a metabolic process, as exhibited by the products of mating of Dalmatians with other species.

Having found an apparently pure blooded Dalmatian in one of our laboratories it seemed desirable to determine whether it was

equipped with the same outfit of purine enzymes as other dogs, or not. We first made several observations at different times on the uric acid excretion, and corroborated Benedict's findings completely. Uric acid was determined by direct isolation and weighing of the crystalline product, in order to avoid the possibility of any unknown substance being responsible for the results obtained. The animal was a female, the weight being about 13.5 kilos, and it was given a liberal diet, chiefly meat. On this diet the excretion of uric acid was found to be as follows:

<table>
<thead>
<tr>
<th>Date</th>
<th>Uric Acid</th>
<th>Uric Acid (gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apr. 25</td>
<td>573</td>
<td>0.3673</td>
</tr>
<tr>
<td>May 10</td>
<td>610</td>
<td>0.5132</td>
</tr>
<tr>
<td>&quot; 13</td>
<td>351</td>
<td>0.4409</td>
</tr>
<tr>
<td>June 15</td>
<td>910</td>
<td>0.5425</td>
</tr>
<tr>
<td>July 5</td>
<td></td>
<td>0.499</td>
</tr>
</tbody>
</table>

Average daily excretion

This rate of excretion, 0.037 gm. per kilo, corresponds to a daily excretion of 2.59 gm. of uric acid by a 70 kilo man.

Benedict found about 0.360 gm. of uric acid excretion daily by his 10 kilo dog, or 0.036 gm. per kilo, even on a purine-free diet. When thymus was fed the uric acid rose to as high as 0.600 gm. of uric acid per day, but at the same time the allantoin nitrogen rose from 0.050 to 0.210 gm. Evidently this dog was able to destroy a large part of the exogenous purines, but not all. When uric acid was injected subcutaneously it was recovered quantitatively in the urine, yet there was also a marked increase in the allantoin excretion. These findings are difficult to explain on the basis of our present knowledge of purine metabolism, and Benedict is obliged to suggest that, "It seems probable that uric acid and allantoin are interrelated in metabolism in other ways than have been heretofore assumed."

*This article was written in June, 1917, but its publication was delayed during the author's absence in foreign service. In October, 1917, C. K. Watanabe published a paper (J. Urol., 1917, i, 485) on experimental uranium nephritis in two Dalmatian coach hounds, in which animals he observed excretion of uric acid, but in much smaller amounts than found by Benedict or with my dog. Dr. M. H. Givens at Yale has analyzed the urine of two fasting Dalmatians, obtaining figures more...
In studying the purine enzymes of this dog the same methods were used as described in previous papers from this laboratory. The dog was killed with chloroform, and the tissues, ground to a pulp, were allowed to act upon uric acid and purines both aerobically and anaerobically, with the following results.

Experiment 1.—80 gm. of liver pulp were added to 0.240 gm. of uric acid dissolved with a minimum amount of NaOH in boiling water. The mixture was digested with toluene at 38–40°C. for 24 hours, with a constant stream of warm moist air bubbling through it. At the end of this time the proteins were removed by coagulation and filtration. The filtrate contained only a very small amount of purine material, in which not a trace of uric acid could be detected. There was recovered from the scanty purine precipitate about 0.045 gm. of xanthine. The liver of this dog contains uricase.

Experiment 2.—80 gm. of liver pulp were digested with 0.229 gm. of xanthine under the same aerobic conditions as described above. After the digestion there could be detected no uric acid in the mixture, but a considerable amount of xanthine, 0.150 gm. being recovered. This experiment indicates that the liver of this dog exhibits less xanthine-oxidase activity than is seen in other species of dogs, for ordinary dog liver tissue would have converted the xanthine into uric acid and destroyed it quantitatively under these conditions. The rather low recovery suggests that possibly there has been some xanthine-oxidase activity, but does not establish it, since there are sources of quantitative error in this work.

closely resembling those of Benedict and myself. He has authorized me to publish these results, which were as follows:

<table>
<thead>
<tr>
<th>Weight of dog (kg)</th>
<th>Volume (cc)</th>
<th>Uric Acid (N. mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>455</td>
<td>214</td>
</tr>
<tr>
<td></td>
<td>190</td>
<td>208</td>
</tr>
<tr>
<td></td>
<td>240</td>
<td>208</td>
</tr>
<tr>
<td>10.5</td>
<td>330</td>
<td>232</td>
</tr>
<tr>
<td></td>
<td>335</td>
<td>233</td>
</tr>
<tr>
<td></td>
<td>350</td>
<td>213</td>
</tr>
</tbody>
</table>

These figures show a daily excretion of 0.640 gm. and 0.678 gm. of uric acid for these dogs, or respectively 0.040 gm. and 0.064 gm. per kilo.

The recovery of a small amount of xanthine in Experiment 1, furthermore, implies an almost or quite complete lack of xanthine oxidase.

**Experiment 3.—** Control to Experiment 1. 80 gm. of liver pulp were added to 0.240 gm. of uric acid, in solution, and the mixture was immediately brought to 100°C., and held at this temperature for 30 minutes. 0.205 gm. of uric acid was recovered, after incubating with an air current as in Experiment 1.

**Experiment 4.—** 62 gm. of kidney pulp were added to 0.240 gm. of uric acid and digested aerobically. 0.150 gm. of uric acid was recovered. Possibly there was a slight uricolytic activity by the kidney, but repetition of this result would be necessary to prove it.

**Experiment 5.—** 31 gm. of spleen pulp were added to 0.229 gm. of xanthine and digested aerobically. No uric acid could be recovered or detected but 0.155 gm. of xanthine was found. Evidently the spleen lacks xanthine oxidase.

**Experiment 6.—** 80 gm. of liver pulp were placed in 400 cc. of water containing 0.120 gm. of guanine and 0.154 gm. of adenine. The mixture was digested under toluene, without aeration, for 7 days at 37°. Analysis yielded no guanine, 0.208 gm. of xanthine, no adenine, and 0.172 gm. of hypoxanthine. Evidently the liver possesses guanase, and converts added guanine into xanthine; also apparently it converts some of its own purines into xanthine. It also contains adenase which converts adenine into hypoxanthine.

From these experiments on a single specimen of Dalmatian coach hound, it seems that this animal had uricase in its liver, but probably not in the kidney. This observation indicates that the constant excretion of large amounts of uric acid does not depend upon the absence of uricase from the tissues of this breed of dog, although possibly there is a quantitative deficiency in uricase activity that is not disclosed by our experiments. Further studies are necessary to determine this, but as yet no more Dalmatians have become available. A surprising result is the apparent absence of xanthine oxidase in both the liver and spleen. It is unfortunate that we were unable to examine all the tissues of this dog to learn where it forms its uric acid. The absence of uricase from the kidney is to be expected in view of the free passage
of uric acid through this organ. The presence of adenase and guanase in the liver indicates that in respect to the possession of these two enzymes the Dalmatian does not differ from other dogs, although we do not know whether these enzymes have the same wider distribution as in other species of dogs.

SUMMARY.

In corroboration of Benedict’s observation, a Dalmatian coach hound was found to excrete large quantities of uric acid. The liver of this same dog possessed the power of destroying uric acid in vitro, indicating that the presence of uric acid in the urine of the Dalmatian does not depend on the absence of uricase in its tissues. The kidney did not exhibit uricolytic activity. Neither the liver nor spleen converted xanthine into uric acid, but the liver deaminized both guanine and adenine.
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