CREATIN AND CREATININ IN ANIMAL METABOLISM.

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(Preliminary Communication.)

OUR work on the nutritive effects of meat extracts has naturally led us into this field of inquiry, which is already occupied by many workers in this country and also abroad.

It is generally accepted that when creatin is taken a considerable amount is retained in the body without reappearing in the urine. Folin,¹ who first pointed this out, concluded that creatin is absorbed and retained by the muscles. In his first experiments he used a starch and cream diet, because it gave rise to little urea formation, and was therefore well adapted to decide whether any creatin was transformed into urea or not. He found no evidence of this, but concluded that the amount retained depended on the low content of protein in the diet. He did not connect the retention with the starch content of the food.

The next fact bearing on our position is one noted independently by Cathcart² and Benedict,³ namely, that creatin appears in the urine during starvation. Cathcart further showed that this output is stopped by taking starch, but not by fat.

Putting these facts together, it seemed to us, as no doubt it has to others, that Folin overlooked the significance of his results, and that the retention of creatin, whether given with food or formed in the body, is mainly connected with carbohydrate metabolism.

This provisional hypothesis we tested as follows. A dog was starved for two days and then fed on the following diets for periods of two days each. Throughout the series the daily diet contained, as a basis: Bread 20 grams, milk 20 c.cm.; lard 5 grams. To this was added other substances as shown below in the different periods:

Added to Diet.	Urine Nitrogen in Grams.	Creatin Output in Grams.	Creatinin Output in Grams.
(a) Starch 50 grams; creatin 1 gram	3.569	0.602	0.403
(b) Starch 75 grams; creatin 1 gram	2.747	0.426	0.376
(c) Starch 50 grams; crude casein (Merck) 25 grams; creatin 1 gram	4.459	0.676	0.388
(d) Starch 50 grams; meat (four times extracted) 25 grams; creatin 1 gram	3.024	0.710	0.327
(e) Diet same as (d) less creatin ...	2.702	0.095	0.329
(f) Diet same as (b) less creatin ...	2.625	0.026	0.387
(g) Diet same as (a) less creatin ...	—	—	—

Comparing (a) and (b), it will be seen that with the addition of 25 grams of starch the output of creatin fell in the two days from 602 to 426 mg. Again, comparing (a) with (c) and (d), it will further be seen that if the content of starch remains constant the output of creatin also remains practically the same, notwithstanding the introduction of protein. In the above there is, as a matter of fact, a slight increase in the output when casein was added to the diet, and a distinct increase when washed meat was added. We assume, however, that both these substances contained some creatin in themselves. The casein, as stated, was not pure, and the last wash-water of the extracted meat still gave a creatinin reaction on hydrolysis. We see also in the feeding period (e), where the same washed meat was added to the 50 grams of starch, but no creatin given as such,

that an excretion of 95 mg. took place in the two days, which, if deducted from the amount excreted in period (d), would bring it into very close harmony with that in period (a).

These facts strengthened our provisional working hypothesis. It has been confirmed also in another way.

We reasoned that if it were correct there ought to be a disturbance of creatin and probably of creatinin metabolism in diabetes. We found this to be so in three cases which we have examined. In all three there was an excretion of creatin in the urine, apparently increasing with the severity of the glycosuria. There was also a marked diminution in the output of creatinin. But on referring to the literature we learned that both these facts had already been established, the former by Cramer and Krause⁴ last year, the latter many years ago by K. B. Hoffman⁵ and others.

We continued the investigation, however, and have found in regard to one (the mildest) of the diabetic cases that the addition of creatin in 1 gram doses to the food had no pronounced effect on the output of sugar, whereas the administration of creatinin in doses of 0.15 to 0.18 gram, whether hypodermically or with the food, temporarily increased the output of sugar by nearly 50 per cent.

From this a practical point arises, namely, that soups, meats, and meat extracts liable to contain creatinin should not be given with the diet.

We may add that we are inclined to think that creatin is probably concerned with the liberation of energy from carbohydrate material in muscle, and that creatinin is an end product of this metabolism in mammals. In this we find ourselves more in agreement with Noël Paton⁶ than with E. Mellanby.⁷ We have to thank Dr. A. R. Parsons, Dr. H. T. Bewley, Dr. James Little, and Dr. Jocelyn Smyly for kindly enabling us to make the observations on the diabetic cases. Mr. W. Caldwell kindly did most of the sugar analyses in these latter observations, and also assisted us with the calculations.

REFERENCES.

¹ Hammarsten's *Festschrift*, Wiesbaden, 1906. ² *Biochem. Zeit.*, vi, p. 109 (1907); also *Journ. of Physiol.*, xxxix, p. 311 (1909). ³ Benedict and Myers, *Amer. Journ. of Physiol.*, xvii, p. 362 (1907). ⁴ *Journ. of Physiol.*, vol. xl, p. lxi of Proceedings of Physiol. Soc.; also *Quart. Journ. of Exper. Physiol.*, iii, 289 (1910). ⁵ *Virchow's Archiv.* xlviii, 358 (1869). ⁶ *Journ. of Physiol.*, xxxix, p. 485 (1910). ⁷ *Ibid.* xxvi, p. 458 (1908).

SEVENTY-NINTH ANNUAL MEETING

OF THE

British Medical Association.

Held in Birmingham on July 21st, 22nd, 24th, 25th, 26th, 27th, and 28th.

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Sir THOMAS CHAVASSE, M.D., F.R.C.S., President.

PRESIDENT'S INTRODUCTORY REMARKS.

THE PRESIDENT said: It is not customary for the President of the Section to inflict an address on the audience, and I intend to adhere to such an excellent rule. I think we cannot enter upon our deliberations here without a word on the great loss we have sustained so recently in the death of Mr. Furneaux Jordan. As an original investigator, clear thinker, lucid teacher, and skilful surgeon he has left an imprint on the surgery of our time which will ever remain and rebound to the credit of our school. Gentlemen, it gives me much pleasure to welcome you to Birmingham, and I hope that the scientific work will be profitable, and that you will enjoy also the opportunities afforded you of visiting places of interest in our neighbourhood. I now ask Mr. Rutherford Morison to read his paper introducing the discussion on the treatment of general septic peritonitis.