AN INQUIRY

INTO

CERTAIN POINTS CONNECTED

WITH ALBUMINURIA.

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AN INQUIRY INTO CERTAIN POINTS CONNECTED WITH ALBUMINURIA.

RECENT observations* have established the frequency with which albumen appears in the urine apart from structural disease of the kidneys or any marked deterioration in the general health. It has been long known† that albumen is present in many grave diseases without structural renal disease or the other symptoms of Bright's disease accompanying it.

In an article published last year, on Albuminuria (*Birmingham Medical Review*, July 1879), I reviewed all these facts, and, having defined albuminuria as "the presence in the urine of a body coagulated by heat or precipitated by neutralisation", I showed that there were only two albuminous substances which are likely to be met with giving these reactions—viz., 1. Serum-albumen, and 2. Paraglobulin. I am not aware that any researches have been undertaken to show whether paraglobulin ever occurs by itself in the urine; but Edlefsen, J. C. Lehmann, and Senator found it constantly present, together with serum-albumen, in the urine of Bright's disease. The first part of my inquiry was therefore directed to settle this point.

Chemists tell us that paraglobulin is wholly precipitated from its sodium-chloride solutions by saturation with the latter salt or by carbonic acid. On my applying for information on this point to Professor Crum-Brown of Edinburgh, he wrote to Professor Hoppe-Seyler, who referred me to a paper by Hammarsten (Pflüger's *Archiv*, Band xviii, s. 38), in which magnesium-sulphate is recommended; and this method Professor Hoppe-Seyler informed Professor Crum-Brown he had found trustworthy in his own investigations on milk. In the following experiments, all these methods were used, but in many they were combined.

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* Dr. Moxon, *Guy's Hospital Reports*, third series, vol. xxiii; Dr. Dukes, BRITISH MEDICAL JOURNAL, November 30th, 1878; Dr. Morley Rooke, *ibid.*, October 19th, 1878; Dr. Lauder Brunton, *The Practitioner*, June 1877; Professor Leube, Virchow's *Archiv*, Band lxxii, Heft 2; Dr. Saundby, *Birmingham Medical Review*, October 1879; Dr. Mahomed, *Guy's Hospital Reports*, vol. xxiv; Dr. Geo. Johnson, BRITISH MEDICAL JOURNAL, December 13th, 1879.

† Dr. Parkes, *On the Composition of the Urine*, page 186; Dr. W. Roberts, *On Urinary and Renal Diseases*, p. 173; Dr. Quain, *The Lancet*, January 18th, 1879; Dr. Paul Fürbringer, Virchow's *Archiv*, Band lxxi, Heft 3.

The method of proceeding was to test an urine for albumen by boiling and adding acetic acid, then taking a fresh portion to precipitate it, filter, and test the filtrate as before; the two test-tubes were then compared. The cases were taken as they appeared in the out-patient room, without any kind of selection, and present most of the conditions under which albuminuria occurs apart from acute disease. In all, forty-two examinations were made; two of these being of the same person in one instance only. They comprised cases which may be thus classified: Chronic Bright's disease, 5; albuminuria of adolescents, 16; epilepsy, 7; morbus cordis, 3; amenorrhœa, 3; phthisis, 3; bronchitis, 3; gastric catarrh, 1; scabies, 1. The albuminous cloud diminished after precipitation as above in a large number of these cases, and entirely disappeared in two. One of these was a case of phthisis; the other presented symptoms of dyspepsia, and has been included among the cases of albuminuria of adolescents. On subsequently examining the urine of the same case, the albuminous cloud disappeared partially only. Hence the existence of paraglobulinuria as an independent condition is certainly rare, and cannot be held to explain the frequency with which the reaction of albumen is given by the urines of adolescents and others supposed to be suffering from merely functional derangements of the renal organs.

The next point alluded to in my article already quoted is the doctrine of "food-albuminuria", originated in modern times by Parkes (*Medical Times and Gazette*, 1852, p. 357, and 1854, p. 395). He found that the albumen was increased after food in two cases of chronic Bright's disease, although it was diminished after food in a case of heart-disease. He inclined to the view that the increase after food was due to the passage of imperfectly digested albumen, analogous to that which occurs when albumen is injected into the veins, or to the albumen undergoing some modification in the digestive process, such as its conversion into an acid albuminate, by which its diffusibility would be increased.

Parkes's facts do not seem to warrant this conclusion; for, while the albumen was increased after food in the two cases of Bright's disease, it was diminished under similar circumstances in the case of heart-disease, so that it is necessary to postulate a peculiar inability to digest albumen in the former cases which did not exist in the latter. On the other hand, if we regard albuminuria as a mechanical process, resulting from increase of the lateral pressure within the vessels to such a degree as to permit transudation, we can easily understand why, in the cases of chronic Bright's disease, the stimulus to the circulation increased the albuminuria in already inflamed organs, while it diminished it in the case of heart-disease, where the transudation was due to passive engorgement of the renal capillaries and veins. But Parkes's views have been adopted by many writers. Dr. Pavy (Gulstonian Lectures, *Lancet*, 1863, p. 573) supports Parkes by giving a table of the amounts of albumen excreted before and after breakfast in six experiments, all showing a marked increase. Dr. Pavy further adopted Parkes's view that this might be due to the increased diffusibility of the urine, and supported it by showing that the albumen in some urines is highly diffusible, but did not attempt to prove that the albumen passed after food was more diffusible than that passed before food, or to indicate to what circumstances this increased diffusibility might be due.

Most physiologists deny that unchanged albumen is absorbed into the blood, and the only piece of direct evidence I know to the contrary is

the statement of Brücke, that he has found coagulable albumen in the lacteals. My attention was first directed to the question whether the albumen is increased after food.

The following experiments were undertaken to decide this point.

CASE.—T. B. Chronic Bright's disease with anasarca. Diet: Milk, bread and butter; fish for dinner; and one boiled egg for tea.

Experiment I.—*Before breakfast:* In bed. Urine faintly acid; 1013; contained one-third of a column of albumen.—*After breakfast;* In bed. Urine acid; 1018; two-thirds of a column of albumen.—*Before dinner:* Up. Urine acid; 1018; half a column of albumen.—*After dinner:* Up. Urine strongly acid; 1024; a whole column of albumen.

Experiment II.—*Before breakfast:* In bed. Urine 1012, faintly acid; one-third of a column of albumen.—*After breakfast:* In bed. Urine 1020, acid; two-thirds of a column of albumen.—*Before dinner:* In bed. Urine acid; 1015; half a column of albumen.—*After dinner:* In bed. Urine faintly acid; 1016; one-third of a column of albumen.

Experiment III.—*Before breakfast:* In bed. Urine 1014, faintly acid; contained half a column of albumen.—*After breakfast:* In bed. Urine acid; 1022; two-thirds of a column of albumen.—*Before dinner:* Up. Urine acid; 1020; three-fifths of a column of albumen.—*After dinner:* Up. Urine faintly acid; 1019; two-fifths of a column of albumen.

Experiment IV.—*Before breakfast:* In bed. Urine faintly acid; 1013; two-fifths of a column of albumen.—*After breakfast:* In bed. Urine 1018, acid; four-fifths of a column of albumen.—*Before dinner:* Up. Urine acid; 1021; nearly a whole column of albumen.—*After dinner:* Up. Urine faintly acid; 1022; contained nine-tenths of a column of albumen.

In all these experiments, the urine was collected for one hour before and one hour after the meals in question. If we add up these quantities, we find that the totals are:

Before breakfast	... ...	1.56 column
After ,,	... ...	2.8 ,,
Before dinner	... ...	2.6 ,,
After ,,	... ...	2.6 ,,

Thus, in spite of the assistance of exercise (except on one occasion) in augmenting the excretion of albumen at dinner-time, and in spite, too, of the more albuminous diet at that period, the after-breakfast urine is not only relatively more albuminous than that passed when fasting, but is also more albuminous than that passed after dinner.

At my request, Dr. A. H. Carter made the following valuable observation on a case of Bright's disease, under his care, in the Queen's Hospital, Birmingham. The quantitative analyses were made by Dr. C. A. MacMunn of Wolverhampton, whose competence and care are a guarantee for their accuracy. The observations were made on the 10th, 11th, 12th, and 13th of March, 1880; but, as one of the bottles was broken in transit, only three days are recorded.

Diet.—Breakfast, 5 A.M., two slices bread and butter, with tea.
Lunch, 10 A.M., ,, ,, ,, milk, 1 pt.
Dinner, 1 P.M., cooked meat 4 ozs., potatoes 8 ozs., bread and water.
Tea, 6 P.M., same as breakfast.
Supper, 7 P.M., milk half-pint.

Exercise.—Walking exercise twice daily for half-an-hour, at 12.30 and 2.30 P.M.

Date.	Period.	Quantity of Urine.	Albumen in 40 ccms.	Total Albumen.
March 10.....	7 P.M. to 5 A.M.	1620 cc.	.008 grms.	.1296 grm.
,, ...	5 A.M. to 1 P.M.	150 cc.	.016 ,,	.06 ,,
,, ...	1 P.M. to 5 P.M.	180 cc.	.01 ,,	.045 ,,
,, ...	5 P.M. to 7 P.M.	120 cc.	.008 ,,	.024 ,,
,, 12.....	7 P.M. to 5 A.M.	870 cc.	.0069 ,,	.1479 ,,
,, ...	5 A.M. to 1 P.M.	180 cc.	.017 ,,	.0756 ,,
,, ...	1 P.M. to 5 P.M.	180 cc.	.0141 ,,	.0630 ,,
,, ...	5 P.M. to 7 P.M.	150 cc.	.009 ,,	.0330 ,,
,, 13.....	7 P.M. to 5 A.M.	1410 cc.	.0155 ,,	.5358 ,,
,, ...	5 A.M. to 1 P.M.	180 cc.	.020 ,,	.090 ,,
,, ...	1 P.M. to 5 P.M.	180 cc.	.0166 ,,	.0738 ,,
,, ...	5 P.M. to 7 P.M.	120 cc.	.015 ,,	.0444 ,,

On each day, the relatively greatest quantity of albumen was excreted between breakfast and dinner. The quantity each day fell as the day advanced, in spite of the meat eaten at dinner and the exercise taken in the afternoon. The total quantity of albumen excreted rose steadily under the influence of meat diet, being three times greater on the fourth day than on the first.

This supports the opinion expressed by Dr. Moxon, that in cases of intermittent albuminuria the after-breakfast urine is most likely to contain albumen. It corroborates Dr. Pavy's facts, but weakens his inference, as it shows that the amount of albumen does not depend upon the quality of the food so much as on the period of the day. In illustration of the last observation, it is worth while calling to mind the well known researches of Dr. Edward Smith* on the diurnal variations of the vital processes. He showed that the pulse, respiration, and urea excretion were each influenced to a much greater degree by breakfast than by any other meal, and that the maximum of all these vital processes occurred at this period of the day, although the food taken at dinner was much more nitrogenous.

These facts are opposed to the view that nitrogenous food increases albuminuria, by passing with the urine as unassimilated albumen. They prove that the maximum albuminuria occurs in that period of the twenty-four hours in which the whole of the excretory functional activities are also at their maximum; and the inference is permissible, that the increased albuminuria depends immediately upon the increased functional activity of the kidney during that period.

This relation of albuminuria to a particular period of the day has never before been carefully investigated; and the want of acquaintance with it explains the incorrect conclusions of Parkes and Pavy.

These observations are not opposed to the conclusions of Drs. Sparks and Mitchell Bruce (*Medico-Chirurgical Transactions*, vol. lxii); there can be no doubt of the general influence of nitrogenous food in increasing albuminuria, but they suggest the probability that this relation depends upon the increase of urea, that is, the increase of the physiological stimulus to the kidney, and they show that this effect is greatest at that period of the day in which the renal functions are most easily excited.

* *Health and Disease.* By Edward Smith, M.D., etc. London: 1861. Pp. 27-48.

The next point was to determine whether the albumen passed after food diffused more readily than that passed before food. In considering this question, it must be borne in mind that acid albumen diffuses readily, and, as is well known, the urine passed during digestion is usually of higher specific gravity and more acid than that passed at other times. The septum used was vegetable parchment ; and the time allowed was twenty-four hours in each case.

The following experiments were made on the urine of the same case.

Experiment I.—*Before breakfast:* In bed. Urine faintly acid ; one-third of a column of albumen ; no albumen in diffusate.—*After breakfast:* In bed. Urine acid ; four-fifths of a column of albumen ; a trace of albumen in diffusate.

Experiment II.—*Before breakfast:* In bed. Urine neutral ; a trace of albumen in diffusate.—*After breakfast:* In bed. Urine acid ; a trace in diffusate.

Experiment III.—*Before breakfast:* In bed. Urine faintly acid ; one-third of a column of albumen ; a faint trace in diffusate.—*After breakfast:* In bed. Urine acid ; two-thirds of a column ; a trace in diffusate.

Experiment IV.—*Before breakfast:* In bed. Urine faintly acid; one-third of a column of albumen ; a trace in diffusate.—*After breakfast:* In bed. Urine acid ; two-thirds of a column of albumen ; a trace in diffusate.

Experiment V.—*Before dinner:* Up. Urine neutral; a distinct cloud in diffusate.—*After dinner:* Up. Urine acid ; a distinct cloud in diffusate, but less than before dinner.

Experiment VI.—*Before dinner:* Up. Urine acid ; half a column of albumen; a cloud in diffusate.—*After dinner:* Up. Urine strongly acid ; a whole column of albumen ; a dense cloud in diffusate.

Experiment VII.—*Before dinner:* Up. Urine acid ; half a column of albumen; a faint trace in diffusate.—*After dinner:* Up. Urine faintly acid ; one-third of a column of albumen ; a faint trace in diffusate.

In two urines, marked neutral, albumen is stated to have diffused; this may possibly be accounted for by an acid fermentation having taken place. As a rule, the albumen appeared to diffuse in proportion to the acidity of the urine. The diffusate bore no relation to the quantity of albumen present in the urine.

Finally, as it might be presumed that the albumen met with frequently in dyspepsia and other functional derangements might be a modified form of albuminuria, I submitted the albuminous urines of twenty-one out-patients to diffusion, and found albumen in the diffusates of nineteen. There was no special frequency in any particular class of case, but diffusion to a moderate extent was plainly the rule. In one case, the diffused albumen disappeared after precipitation by magnesium sulphate. The twenty-one cases comprised six cases of chronic Bright's disease, in all of which diffusion occurred ; one of subacute nephritis, diffused ; eight of albuminuria of adolescents, of which only one did not diffuse ; phthisis, one; morbus cordis, one ; epilepsy, one; rheumatism, one; scabies, one; eczema, one, no diffusate.

These observations appear to me to be opposed to the doctrine, that albuminuria is ever due to the transudation of a modified or more easily diffusible form of albumen.

I have shown that the coagulation temperature, as determined by [illegible] *Hospital Reports*, vol. xiii)

and Mr. D'Arcy Power, cannot be relied upon to afford any distinction between different forms of albumen, if such there be, as it depends upon the quantity of albumen and salts present. "The urine of a case of subacute nephritis, pale, faintly acid, specific gravity 1008, showed signs of coagulation when the thermometer, with its bulb immersed below the surface of the urine, marked 112° Fahr. Coagulation was looked for by the side of the bulb. The urine contained three-fourths of a column of albumen. Diluted five times, the coagulation point rose to 120° Fahr.; diluted ten times, to 130° Fahr.; twenty times, to 145° Fahr.; forty times, to 170° Fahr.; eighty times, to 180° Fahr. The same quantity of fluid and the same apparatus were used on each occasion."*

These facts appear to warrant the following conclusions.

1. The body present in urine which is coagulated by heat or precipitated by neutralisation is almost invariably serum-albumen, rarely paraglobulin.

2. The presence of paraglobulin alone in the urine is still somewhat obscure, and has not been correlated with any clinical group of cases.

3. The maximum amount of albumen excreted by the kidneys is during the after-breakfast period, and this relation is maintained in spite of the more albuminous character of the midday meal.

4. While there can be no doubt that nitrogenous diet increases albuminuria, this is not due to the absorption of undigested albumen, but to the increase of nitrogenous excreta, and the consequent stimulus to the renal functions.

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* *Birmingham Medical Review*, 1879, p. 227.