

A CASE OF ALBUMOSURIA  
IN WHICH THE  
ALBUMOSE WAS SPONTANEOUSLY PRECIPITATED

BY

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THE case which I wish to bring to your notice is that of H—, a man 70 years of age, a small shopkeeper in Liverpool. He has enjoyed fairly good health for the greater part of his life, having never had any serious illness. He states that some years ago his urine was occasionally turbid, and that he had it examined by a medical man; but as he believes it became clear on heating, and the practitioner assured him that it was healthy, I conclude the turbidity was of a different nature from that observed now. His present complaint seems to

date from about the end of last year (1896), when he experienced a severe domestic affliction. He states that about Christmas he noticed something wrong with the urine—that it looked like coffee on one occasion, but the exact condition I am unable to ascertain. After this he noticed from time to time that it was turbid when voided, resembling the specimen I now show. This turbidity has been noticed at intervals ever since, but has gradually increased in frequency, so that at the time of writing (December, 1897) it is often present on several days in succession.

*Present condition.*—He is a spare, rather pale man, below the average height. He easily gets tired, and often suffers from pain and a feeling of weakness in the lumbar region, but he can hardly be considered an invalid, as he is able to follow his occupation as a shopkeeper with as much activity as could be expected of a man of his age and naturally feeble physique. His appetite is capricious, and his bowels are rather confined. The arterial tension is rather high, but not abnormally so; the vessels feel healthy, and there is no evidence of cardiac affection and no dropsy. There is marked anæmia; the red corpuscles number 1,750,000 per cubic millimetre; there is no poikilocytosis nor leucocytosis. Inoculations of the blood on agar, by my friend Dr. Warrington, show that it is sterile.

For some years he has had a small wart on the side of the nose near the inner canthus of the left eye. This was removed by my colleague Mr. W. Thelwall Thomas on November 16th, and proved to be a rodent cancer, which had not yet ulcerated. The patient made a rapid and complete recovery both from the chloroform and the operation.

The chief interest of the case lies in the remarkable condition of the urine. It is generally passed clear, when on inspection it presents nothing abnormal except that it is remarkably viscid and forms a very persistent froth. The quantity excreted in the twenty-four hours is not

much below normal. On three days when careful measurements were made it was 1660 c.c., 1000 c.c., and 1100 c.c. respectively, giving an average of 1220 c.c. (40 ounces).

The urine passed about the middle of the day between 11 a.m. and 5 p.m. is, however, as a rule turbid when voided, and looks at first not unlike milk, or a mixture of milk and urine, being white or nearly so. On standing it deposits an abundant white sediment, which may occupy as much as one sixth of the containing vessel. This sediment cannot be identified with any of the ordinary urinary deposits. Under the microscope it is seen to be amorphous, or more strictly to consist of minute structureless spherical particles. Collected on a filter, washed and dried, it forms a glue-like mass which gives the xanthoproteic and other colour reactions of a proteid, and is digested by an artificial gastric juice. It is almost insoluble in cold distilled water, and in dilute solutions of common salt, but is quickly dissolved in a cold weak solution of caustic soda (2 parts per 1000), in strong acetic acid, and to some extent in boiling water. When the deposit has been removed by filtration or decantation the remaining urine is for the most part identical with the clear urine which is passed at other times, and which I will now describe.

It generally contains a slight amount of mucus, and has the natural colour and odour of urine; it is generally acid, and its specific gravity is between 1015 and 1022. It is free from sugar and casts; the proportion of urea is about normal. It is remarkably viscid, almost syrupy in consistence, and forms a very persistent froth when shaken up with the air.

When carefully heated on a water-bath it begins to get turbid at about 50° C., sometimes at a lower temperature, and it becomes absolutely opaque between 56° and 60°, and a dense white precipitate begins to settle down. When this is removed by filtration, the filtrate gives no further coagulum when heated to the boiling-point, or at

most a faint cloud appears, showing that it is practically free from albumin.

The precipitate which forms at 60° is in all essential characters identical with the white sediment which is found in the turbid urine voided from time to time, and is manifestly the same body.

It is not properly a heat coagulum, as it is readily soluble in cold weak caustic soda (2 per 1000), and is partially redissolved if the urine is heated to boiling-point. It has, however, undergone some change during the process of heating to 60° C., in virtue of which it has lost the property of dissolving in urine at ordinary temperatures.

If a drop or two of dilute acetic acid be added to the urine before heating, the precipitation comes on at a much lower temperature, sometimes at 31° C. A very slight addition of acid will cause some precipitation to take place at the temperature of the body (37° C.).

A portion of the urine was placed in a dialyser for some weeks. When it was heated without any addition a turbidity came on about 60° C., which could not be removed by filtering. Heated with a trace of acetic acid it remained almost clear, but if neutral salt was also present coagulation occurred.

The proteid body is also thrown down by mineral acids, sulphuric and hydrochloric as well as nitric, and is not to any notable degree soluble in excess of these reagents, unless by the aid of heat. The reaction with strong hydrochloric acid is distinct, even when the urine has been diluted with nineteen volumes of water, so that I look on it as a very delicate as well as convenient test for the body in question. It is best applied by the contact method, as in Heller's test for albumin. On the other hand, a large excess of acetic acid prevents its precipitation by heat, but it may in this case be precipitated by neutralisation, in a manner analogous to an albuminate.

When the urine is treated with concentrated nitric acid a precipitate takes place, which is partially dissolved by

heat and comes back on cooling, in the manner characteristic of an albumose. This reaction is not equally distinct in all the specimens of the urine, but is particularly well marked in the urine from which the salts have been removed by dialysis.

The body is also precipitated by saturation with ammonium sulphate and by absolute alcohol. The precipitate when fresh is dissolved by the simple addition of water, but after standing a few hours it is no longer soluble in neutral solutions, and so comes to resemble the precipitate formed by heat.

As regards the quantity of this body present in the urine, I find as the result of forty estimations made with Esbach's albuminometer, that the proportion varies from 6 to 16 per 1000. In one half the specimens it was over 10 parts per 1000. One specimen contained as much as 22 per 1000, which was confirmed by the gravimetric method.

The absolute amount on three days when the whole of the excretion was collected was 12·0, 10·5, and 12·9 grammes respectively. The largest proportion is generally found in the scanty urine passed in the middle of the day, but the absolute amount excreted seems pretty constant throughout the twenty-four hours.

The turbid specimens generally contain the largest proportion of proteid, but there are many exceptions to this. [See tables.]

The body which I have described as occurring in H—'s urine corresponds in most of its characters with a body which has been recognised as a constituent of the urine in about six cases during the last fifty years, and has been regarded for the most part as an albumose. It must not be confounded with the albumose which has been detected in minute quantities as a temporary constituent of the urine during the course of specific fevers and other diseases, and which presents very different characters from those which I have described. In the rare cases to which I refer it has occurred in large quantities and for prolonged

periods. The earliest known case of this kind is that investigated by Bence Jones, which will be found recorded in the 'Philosophical Transactions' of the Royal Society for 1848 (1). Since then no other case has been published in this country, with the possible exception of one to which I will presently refer, and which was not recognised as belonging to this class (5). The condition remained practically unknown until Kühne published a case in 1883, and since then five more cases have been investigated, which, with the present case, bring up the total to eight.

My case, however, appears to be unique in this respect, that a large quantity of the albumose is passed in the solid state, and in a form which could not fail to attract the notice of the most casual observer.

Bence Jones spoke of the body he found as a new substance occurring in the urine, and added some theoretical speculations as to its chemical constitution which are of no interest at the present time. It was precipitated from the urine by alcohol, and formed a coagulum with nitric acid, which dissolved on heating and returned on cooling. It was also precipitated by hydrochloric acid. Sometimes the urine yielded a coagulum on heating, but at other times it did not, although the reaction was acid. As it is not stated at what temperature coagulation took place it seems not unlikely that albumin may have been present at times, especially as casts were detected. In Kühne's case the urine behaved for the most part like H—'s, the chief difference being that the coagulum with heat and that with nitric acid were much more readily soluble on boiling in Kühne's case than in mine (2). Kühne concluded that the body was hetero-albumose, one of the products of the gastric digestion of albumin. The next case was reported by Huppert of Prague in 1889 (3). The reactions were identical with those in Kühne's case, and Huppert likewise looked on the body as hetero-albumose. A fourth case was recorded by Stokvis of Amsterdam in 1891, but I have not been able to ascer-

tain any particulars as to the behaviour of the urine (4). A remarkable case recorded by Dr. Byrom Bramwell and Dr. Noel Paton in 1892 is considered by Professor Huppert as belonging to the same category. The case was unique in this respect, that the proteid was easily obtained in the form of crystals (5). Dr. Bramwell described it as a crystalline globulin, and does not seem to have had any suspicion that it was in any way related to albumose, and I think we must hesitate before accepting Professor Huppert's conclusions as to its nature, in spite of the fact that its coagulation point corresponded to that of the body we are now considering.

A sixth case has been recently investigated by Matthes of Jena, under the direction of Professor Neumeister (6). Matthes's results in general correspond with those obtained by previous observers and by me, but he appears to have succeeded in obtaining the body in a state of greater purity than any of his predecessors have done. As the result of experiments with the purified substance he concludes that it is not hetero-albumose, and further, that it is not identical with any other known compound. Elementary analysis in his hands shows that it consists of carbon, hydrogen, nitrogen, sulphur, and oxygen only. Earlier observers found a considerable proportion of phosphorus, but Matthes believes this was derived from the nucleo-albumin which was also present. The process employed by Matthes to obtain the body in a state of purity has not yielded satisfactory results in my hands; and although by various methods I have obtained it in a solution practically free from salts, I am not satisfied that it is of sufficient purity to be submitted to elementary analysis.

A seventh case was under the care of Prof. Senator of Berlin in 1897, and has been recorded by Rosin (7).

As I have already pointed out, my case seems to be unique in this respect, that the albumose is often precipitated in the urinary passages, causing the urine to be turbid when it is passed, and I have tried to ascertain

the conditions which lead to this precipitation. I believe it is really of the same nature as the precipitation which takes place by heat, and that it is chiefly determined by an increase in the acidity of the urine. As I have shown, the addition of acetic acid to the urine causes coagulation to come on much below  $50^{\circ}$ , and even at a temperature below that of the body. The acidity of the turbid specimens is on the average considerably higher than that of the clear specimens (the exact figures are shown in the table), and the administration of an alkali to the patient causes the urine to remain clear for days together, although Esbach's test shows that the amount of the albumose present is as great as at other times. In Matthes's case the presence of salt was as necessary as an acid reaction to insure precipitation of the pure substance by heat; and, as I have stated, the dialysed urine in my own case did not coagulate when heated unless neutral salt was added. I therefore think the fact that the amount of turbidity is not always in proportion to the acidity may be accounted for by the modifying influence of the other constituents of the urine. The solubility at the boiling point of the precipitate formed with nitric acid also seems to be influenced by the amount of salts present, as it is most nearly complete when they have been removed by dialysis.

As regards the nature of the body my observations lead me to agree with Neumeister and Matthes that it is not hetero-albumose, but a peculiar body which is not identical with any other known compound. It differs from hetero-albumose in being soluble in distilled water and from the other digestion albumoses in being coagulated by heat.

As I pointed out in the beginning, there is nothing in the state of my patient to indicate the pathology of the condition, but I think the history of the other cases I have alluded to may lead us to a provisional diagnosis.

In Bence Jones's, Kühne's, and Huppert's cases there was some form of softening of bone; and in Stokvis's.



although there was no sign of bone affection during life, the autopsy showed that the bone marrow was replaced by a red gelatinous mass, the exact structure of which was unfortunately not ascertained microscopically.

In Byrom Bramwell's case the bones were not examined, but the kidneys were but slightly diseased.

In a private communication which I have received from Dr. Matthes he tells me that his case has come to an autopsy, and that the condition was that which has been described as multiple myeloid sarcoma; and in Prof. Senator's case the autopsy showed that several ribs were affected with a new formation, which was described as myelogenous round-celled sarcoma, but which had given rise to no objective symptoms during life.

I shall anxiously watch for any signs of affections of the bones in my patient, and I hope that the further progress of the case will form the subject of a future communication.

I have to express my best thanks to my friend Dr. O'Flaherty of Liverpool, who first sent me a specimen of the urine for analysis, and afterwards kindly placed the case at my disposal for purposes of investigation. I also wish to thank Dr. Lauder Brunton for the kindly interest he has shown in the case, and Professor Huppert and Professor Matthes for sending me copies of their various writings, to which I was unable to obtain access.

*Postscript*, April 9th, 1898.—Towards the end of December the patient became confined to bed in consequence of increasing weakness and distressing pains in the back and loins, which were much aggravated by movement. There was also marked tenderness over the ribs and sternum, especially at one spot on the latter at the level of the fourth intercostal space. In the beginning of February there was a good deal of bronchitis with viscid expectoration, which gave the nitric acid reaction for albumose. On the 5th, when sitting up in bed, a spontaneous separation of the second right rib from

the cartilage apparently occurred, followed by a localised painful swelling. Distressing dyspnoea and cough with rust-coloured sputum came on, and signs of pneumonia appeared at the left base. Latterly he has quite got rid of his lung troubles, has less pain, and is able to get up. There is, however, marked kyphosis in the dorsal region, with prominence of the dorsal spines from the sixth to the twelfth, and lordosis in the lumbar region, together with complete immobility of the vertebral column below the sixth dorsal vertebra. His friends think that he is shorter than he was before his illness, and his height is two inches less than he thinks it used to be. There are tender spots over the ribs and sternum. The main characters of the urine have not altered, but it is now seldom turbid. After it had been clear for a month a little benzoate of ammonia was administered, whereupon the acidity increased, and a dense turbidity appeared, which ceased when the drug was discontinued. On one or two occasions a few ill-defined granular casts were seen. The symptoms lead me to believe that the patient is suffering from some affection of the bones, probably the same as has been found in other cases of albumosuria.

### *Bibliography.*

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*Huppert*.—"Analyse des Harns," 1890, 1te Theil, S. 287.
3. *Kahler*.—"Zur Symptomatologie des multiplen Myeloms, &c.," 'Prager med. Woch.,' 1889, 4.  
*Huppert*. Ein Fall von Albumosurie, *ibid.*, 1889, 4.
4. See *Huppert*, "Ueber ein Fall von Albumosurie," 'Hoppe-Seyler's Zeitschr. f. phys. Chemie,' Bd. xxii, Heft 6, S. 500.

5. *Byrom Bramwell and Noel Paton*.—"On a Crystalline Globulin occurring in Human Urine," 'Reports from the Laboratory of the Roy. Coll. of Phys. of Ed.,' 1892.

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*Neumeister*.—"Lehrbuch der phys. Chem.," Aufl. ii, 1897, S. 804.

7. *Rosin*.—"Über einen eigenartigen Eiweisskörper im Harne, &c.," 'Berliner klin. Woch.,' 1897, No. 48.

TABLE.

Time.	Amount in c.c.	Condition.	Sp. gr.	Acidity per mill. as oxalic acid.	Proteids Per 1000.	Amount in grammes.	Remarks.
Nov. 7th.							
A.m. 12.15	128	Clear	1019	1.449	12.0	1.536	Patient took about 2 grammes of Potass. Acetas during the day and on the three previous days. Clear during the four days.
" 4.50	312	"	1011	0.756	7.0	2.184	
" 8.30	313	"	1011	0.567	5.6	1.752	
P.m. 12.0	152	"	1014	0.504	5.8	0.881	
" 2.10	265	"	1018	1.008	9.0	2.385	
" 5.0	246	"	1017	0.630	6.0	1.476	
" 9.50	243	"	1017	1.134	8.0	1.944	
	1659					12.153	
Nov. 8th.—Potass. Acetas stopped. About noon a turbid specimen passed. Acidity 3.465 per mill., proteid 14.5 per mill.							
Nov. 10th							
A.m. 4.30	310	Clear	1011	1.134	6.0	1.860	Patient took .5 c.c. Acid. Hydro- chloric, dil. three times a day. after meals.
" 7.0	260	"	1013	0.964	6.0	1.560	
P.m. 12.30	80	Turbid	1023	3.276	16.0	1.280	
" 4.30	140	"	1023	2.502	12.0	1.680	
" 9.30	200	Clear	1020	2.835	12.0	2.400	
	990					8.740	

Nov. 13th	90	Moderately turbid	—	2·016	16·0	1·440	Patient took ·5 gramme Ammon. Benzoas three times a day. The early morning's urine was probably lost.
A.m. 10.0	85	Densely turbid	—	3·150	15·0	1·275	
P.m. 2.0	65	"	1020	2·772	13·0	0·845	
" 4.0	84	"	—	2·502	12·0	1·008	
" 5.30	80	Moderately turbid	—	2·142	12·0	0·960	
" 7.30	385	Clear	1019	1·134	8·0	2·684	
" 11.30	200	Turbid	1022	1·953	14·0	2·800	
	939					11·012	
Dec. 2nd.							Patient was taking about 2 gms. Pot. Acet. in twenty-four hours. The clear specimen of 9.30 p.m. the richest in proteid of any examined and tabulated.
A.m. 1.40	310	Clear	1014	0·630	8·0	2·480	
" 5.0	210	"	1013	0·567	6·0	1·260	
" 9.0	150	"	1013	0·441	9·0	1·350	
P.m. 1.0	130	Clear when passed, but found turbid soon afterwards	1021	2·583	18·0	2·340	
" 4.0	130	Clear	1018	1·449	16·0	2·080	
" 9.30	180	"	1021	1·890	19·0	3·420	
	1110					12·930	

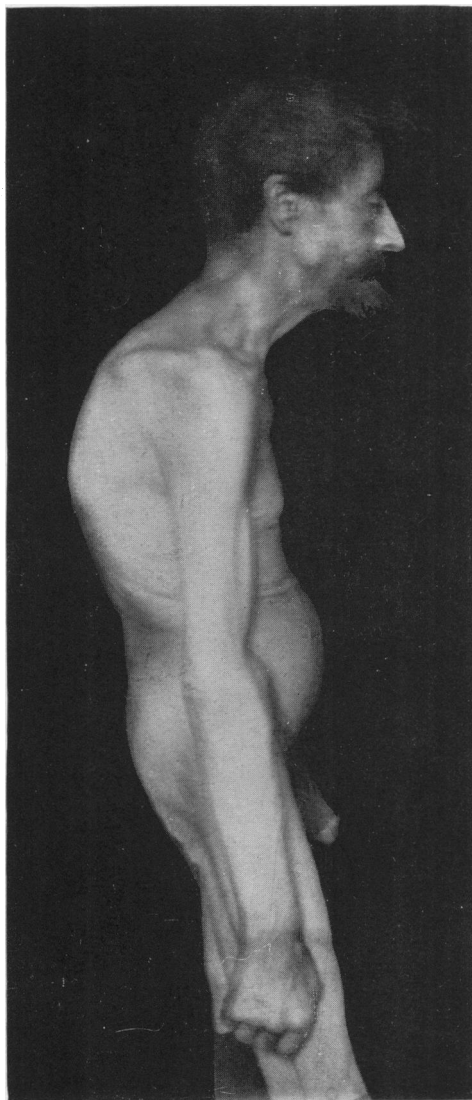
On an average the acidity of the turbid urine is greater than of that which is clear. Seven clear specimens which contain 10 parts per 1000 and upwards of proteid have an average acidity of 2.039 per 1000. Seven turbid specimens taken at random, but all containing not less than 10 parts per 1000, have an average acidity of 2.530 per 1000.

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. x, p. 119.)

## DESCRIPTION OF PLATE VII.

### A Case of Albumosuria (T. R. BEADSHAW).

The plate is reproduced from a photograph kindly taken for me in April, 1898, by Mr. Prosper H. Marsden, Dispenser to the Liverpool Royal Infirmary. The prominence in the dorsal region and the forward projection of the neck due to the kyphosis are obvious. It will be noticed that the integuments over the front of the thorax are thrown into transverse wrinkles. The lordosis in the lumbar region is indicated by the prominence of the abdomen.



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