YOUNG

Original Communications.

A STUDY OF THE NITROGENOUS METABOLISM IN CHYLURIA.

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The condition of the urine in chyluria has hitherto been studied from the point of view of the fatty material which it contains, and very little work has been done on the albuminous matter and other nitrogenous constituents. In 1913 and 1914 two cases of chyluria were admitted to the tropical ward of the Townsville General Hospital, and the opportunity was taken to examine the urines with regard to the distribution of nitrogen in them. The cases were in the charge of Dr. Breinl, who has contributed the clinical notes.

Case 1.—Mrs. D., aged 42, was admitted to the hospital on March 12, 1913. She had lived all her life in North Queensland, mostly in the north-western portion. According to her own statement she noticed about twenty years ago that her urine suddenly became milky in appearance, and clotted into jelly-like masses if left standing for any length of time. She did not notice any blood in the urine at the time. This condition was not accompanied by any discomfort and she suffered no pains whatsoever. Within the last ten years, however, she had experienced dull aching pains in the small of the back and had observed at times that the urine was stained with blood. At no time was any difficulty experienced in passing the urine.

On examination no physical signs could be detected. The patient was a tall well-nourished woman and seemed hardly affected in her well-being by her condition. The urine had a milky appearance and when allowed to stand for some time gelatinous clots formed. The blood of the patient had never been previously examined for filaria. Samples of the blood were taken on admission and at varying intervals both in the day and night time, but it was never found to contain any filaria larvæ.

The patient remained in the hospital for nearly seven weeks, being treated at first with increasing doses of oleum terebinthini. As this treatment did not seem to give any relief it was changed to ichthyol in capsules.

The bladder was washed out with a solution of silver nitrate, which was increased from 4 to 8 gr. per 16 oz. Her diet was carefully regulated and all fats in the shape of milk, butter, &c., were banished from it.

During the whole time in the hospital her temperature only rose on two days to 99° F. with a corresponding rise in the pulse-rate, but was always normal otherwise.

On the whole neither the turpentine nor the ichthyol affected the condition. The urine was always milky. The washing out of the bladder with silver nitrate, however, seemed to give the patient some relief.

The patient left the hospital on April 28, without showing any improvement as regards the condition of her urine.

Case 2.—Matthew F., aged 23, a miner, was admitted to the hospital on December 13. This patient had spent all his life in North Queensland, north of Cairns. He noticed first about eight years ago that he had difficulty in passing his urine as it contained small jelly-like, blood-stained clots. He noticed further that his urine became milky and clotted when left standing for some time. At the same time he had dull aching pains in his back. His urine then remained milky for about two weeks. Ever since he had the same kind of attacks periodically, which lasted only for a short time, the urine being quite normal in the interval.

Within the last three months, however, his urine had remained milky continuously, being often very much blood-stained, and was always more cloudy in the morning than during the rest of the day. With the exception of his trouble in passing the urine, and slight pains in the back, the patient felt quite well.

On admission, no physical signs could be detected; there was no swelling in the groin, nor any other sign of filariasis. His blood was examined repeatedly at different hours of the day and night, but filaria larvæ could never be found. His urine was slightly increased in amount, varying between 48 and 104 oz., the increased quantity being due to the administration of diuretics. The urine was milky and generally of a pinkish colour.

The treatment consisted first in the administration of oleum terebinthini in increasing doses, starting with 21 minims daily and increasing to 84 minims. This medication was kept up for nearly three weeks, but did not seem to effect any improvement. Ichthyol in pill form was substituted later, beginning with 7·5 gr. daily and increasing to 30 gr. As this did not affect the condition to any appreciable extent, methylene blue was administered in gelatine capsules up to 20 gr. daily.

The urine improved slightly, the morning urine became quite clear for a time, but the daily urine was still of the same condition as before. The improvement, however, only lasted for a few days.

Diuretics seemed to be the only effective remedy, as during the time of their administration no retention took place. The patient was kept in bed on a fat-free diet.

The temperature remained normal all the time he was in the hospital.

He was discharged on March 16, 1914, without showing any improvement in the condition of his urine.

Both these cases were true chyluria. The urines always contained fat, which could be extracted with ether, but the milky appearance could not be entirely removed in this way.

An estimation of the quantity of fat in the urine was only made on one twenty-four-hour sample in each case. This was done by a modification of Meig's method for determining the fat in milk. 100 c.c. of urine were shaken in a stoppered cylinder with a mixture of ether (20 c.c.) and alcohol (20 c.c.). The fluid was allowed to stand for a few minutes and the ethereal layer removed into a tarred flask, by replacing the cylinder by a rubber stopper containing the well-known wash-bottle arrangement of tubes, dipping down just above the junction of the two layers. This extraction process was repeated three or four times, the ether was then evaporated off, and the flask and contents dried at 100° and weighed. The twenty-four-hour sample in Case 1 contained 1·8 per cent. and that in Case 2, 2·6 per cent. of fat.

A quantity of protein was present which showed the properties of the proteins of the lymph. It coagulated when the urines were heated to 70 to 75° C. and contained a globulin precipitated by half saturation with ammonium sulphate, and an albumin precipitated when the liquid was completely saturated with this salt.

On standing, large jelly-like masses formed in the urines, due to the action of the clotting enzymes of the lymph on the proteins. This could be prevented by collecting the urines in a vessel containing potassium oxalate, when the urines remained quite liquid and free from all clots, and in the analyses tabulated later this procedure was always followed.

In Case 1 the sediment on centrifugalization contained some leucocytes, a varying but always small number of red blood corpuscles, epithelial cells and crystals. After prolonged centrifugalization, or after standing in the presence of antiseptics for some days, the fluid became somewhat clearer, but no distinct separation into two layers could be observed

In Case 2, a separation into two layers was often observed, a pinkish blood-stained, slimy bottom layer, containing the sediment, and a second milky layer. The sediment when examined microscopically consisted of red and white corpuscles and granules.

In neither case was any sugar found in the urine.

In Case 1, a fairly complete analysis of the nitrogenous constituents of the urine was made daily for a period of fourteen days. The results are given in Table I, all the constituents being expressed in terms of the nitrogen they contain.

The protein nitrogen was determined by adding 20 c.c. of a saturated solution of sodium chloride to 100 c.c. of the urine contained in a 200 c.c. measuring flask, making faintly acid with acetic acid, and coagulating the protein by immersing the flask in a bath of boiling water for thirty minutes. The mixture was then cooled, made up to the mark with distilled water, filtered, and the unpreciptated nitrogen determined in an aliquot part of the clear filtrate by Kjeldahl. The difference between this non-protein nitrogen, calculated up to the original volume of the twenty-four-hour urine, and the total nitrogen of the urine determined by Kjeldahl, corresponded to the nitrogen present as protein. The absolute quantity of protein may be obtained by multiplying this figure by the usual protein-nitrogen factor 6·25. This method is much simpler than the usual one of weighing the coagulate, since it avoids the laborious process of washing and drying to a constant weight. Moreover, in these urines, fat is carried down with the coagulate, and this would have to be removed before the protein could be weighed.

The result by this shorter method is substantially the same as is seen in the following experiment in which the protein was determined by both methods in samples of the same urine. The figures are calculated for the total volume of urine for twenty-four hours.

Total nitrogen of urine	..	7·310 grm.	
Uncoagulated nitrogen	..	6·350 ,,	
Protein nitrogen ..	..	0·960	.. 6·00 grm. protein.

By weighing the coagulate after washing, drying, extracting the fat with ether and drying to constancy, 6·06 grm. were obtained. In every case the clear filtrate from the protein precipitation was tested to see that it was quite free from protein, and if any was found a fresh determination was made.

The other nitrogenous constituents were determined in the urine after removal of the protein, urea by Folin's potassium acetate method, ammonia (Folin), uric acid (Folin-Schäfer), creatinine and creatine (Folin).

The patient was maintained on a diet consisting of lean meat, bread and potatoes, the nitrogen content of which was approximately 15 grm. However, the quantity of food represented by the amount of nitrogen invariably proved more than that dictated by the patient's appetite, and some food was always left untouched.

The weight of the patient was unfortunately not taken, but she was above medium height and showed no signs of wasting.

The quantity of protein-nitrogen excreted per day varied considerably, from 0·49 grm. to as much as 1·94 grm., the average for the fourteen days being 0·95 grm. per diem, corresponding approximately to 6 grm. of protein.

Table I shows a low grade of nitrogenous metabolism. The non-protein nitrogen representing protein actually utilized in metabolism was very small in quantity, the average twenty-four hourly excretion being 6·39 grm. This represents approximately only 40 grm. of protein catabolized.

If the protein nitrogen be left out of account the other constituents of the urine show a normally balanced nitrogenous metabolism. When considered in percentages of the total non-protein nitrogen they are of the same order as those given by Folin (*American Journal Physiology*, xiii, p. 70) for similar levels of catabolized protein. Thus the urea rises and falls with the total non-protein nitrogen representing on the average 69·4 per cent. of this nitrogen, whilst the ammonia corresponded to 6·6 per cent. and the uric acid to 2·2 per cent. The quantity of creatinine nitrogen excreted is rather low, the average being only 0·34 grm. per diem, or 5·5 per cent. of the non-protein nitrogen. The creatinine in the urine of normal individuals represents the tissue or endogenous metabolism, and is independent of the quantity of nitrogen in the diet. The percentage of the total nitrogen which is excreted as creatinine or $\frac{\text{Creatinine} \times 100}{\text{Total nitrogen}}$ therefore increases as the total

TABLE I.

Date	Volume in cubic centimetres	Gravity	Total nitrogen	Protein as nitrogen	Non-protein nitrogen	Nitrogen as				Per cent. of non-protein nitrogen				
						Urea	Ammonia	Creatinine	Uric acid	Urea	Ammonia	Creatinine	Uric acid	Undetermined
1913														
April 8 ..	975	1014	7·31	0·96	6·35	4·70	0·45	0·34	0·13	74·0	7·1	5·4	2·0	11·4
,, 9 ..	1,112	1012	7·21	0·94	6·27	4·75	0·51	0·40	0·17	75·7	8·1	6·4	2·7	5·4
,, 10 ..	1,113	1014	6·98	1·00	5·98	4·34	0·38	0·34	0·12	72·7	6·3	5·7	2·0	13·2
,, 11 ..	1,220	1013	8·25	1·13	7·12	4·98	0·60	0·39	0·16	69·9	8·4	5·5	2·2	13·9
,, 12 ..	1,070	1016	7·52	0·60	6·92	4·87	0·44	0·34	0·15	70·4	6·3	4·9	2·2	16·2
,, 13 ..	990	1016	7·12	1·44	5·68	3·97	0·36	0·38	0·08	69·9	6·3	6·7	1·4	14·2
,, 14 ..	760	1017	6·79	0·83	5·96	3·87	0·32	0·34	0·16	64·9	5·4	5·7	2·7	21·3
,, 15 ..	730	1017	6·01	0·82	5·19	3·42	0·25	0·34	0·13	66·0	4·8	6·5	2·5	20·2
,, 16 ..	666	1016	6·68	1·94	4·74	3·00	0·35	0·33	0·14	63·3	7·4	7·0	2·9	19·4
,, 17 ..	890	1018	8·16	0·49	7·67	5·13	0·46	0·34	0·18	66·8	6·0	4·4	2·3	20·8
,, 18 ..	785	1018	8·68	0·62	8·06	6·01	0·50	0·38	0·19	74·4	6·2	4·7	2·4	12·3
,, 19 ..	935	1012	7·22	1·27	5·95	3·71	0·36	0·27	0·13	62·4	6·0	4·5	2·2	24·9
,, 20 ..	640	1018	6·08	0·82	5·26	3·10	0·40	0·28	0·11	58·9	7·6	5·3	2·1	26·1
,, 21 ..	930	1020	8·79	0·53	8·26	6·11	0·56	0·27	0·15	74·0	6·8	3·3	1·8	14·2
Average ..	..	..	7·34	0·95	6·39	4·42	0·42	0·34	0·14	69·4	6·6	5·4	2·2	16·9

protein catabolized decreases, and at a protein level corresponding to that of the patient this ratio is normally somewhat higher than was observed in this case.

Case 2.—In this experiment the patient was kept on two different diets. During the first eight days the diet consisted of lean meat, eggs, and bread carefully weighed out and equal in quantity to 15·4 grm. of nitrogen per diem, whilst in the succeeding six days a diet of eggs, milk, bread and butter was partaken of which was uncontrolled as regards quantity.

TABLE II.

Date	Volume in cubic centimetres	Total nitrogen	Protein nitrogen	Non-protein nitrogen	Creatinine nitrogen	Creatine nitrogen	Creatinine and creatine per cent. of non-protein nitrogen
1914							
Dec. 20 ..	1,865	14·56	1·90	12·66	0·48	0·21	5·4
,, 21 ..	1,120	15·25	1·81	13·44	0·47	0·20	5·0
,, 22 ..	1,765	13·72	2·18	11·54	0·46	0·0	4·0
,, 23 ..	1,984	15·29	3·00	12·29	0·54	0·11	5·3
,, 24 ..	2,195	14·18	2·96	11·22	0·42	..	3·8
,, 25 ..	1,525	14·21	3·12	11·09	0·43	..	3·9
,, 26 ..	1,880	16·18	3·39	12·79	0·52	..	4·1
,, 27 ..	2,110	11·68	1·57	10·08	0·37	0·20	5·6
Average ..	..	14·38	2·49	11·89	0·46	0·18	4·6
Dec. 28 ..	1,640	12·21	2·80	9· 1	0·52	..	5·5
,, 29 ..	2,155	11·76	2·42	9·34	0·51	..	5·5
,, 30 ..	2,820	10·58	2·48	8·10	0·47	..	5·8
,, 31 ..	2,040	9·76	2·06	7·70	0·48	..	6·2
Jan. 1 ..	3,195	8·66	1·93	6·73	0·44	..	6·6
,, 2 ..	1,500	8·06	1·96	6·10	0·43	..	7·0
Average ..	..	10·17	2·27	7·90	0·47	..	6·1

The analyses of the urine are given in Table II. It will be noticed that the volume of urine passed varied very considerably, the two extremes being 1,120 c.c. and 3,195 c.c. in twenty-four hours.

The daily loss of lymph proteins as determined by the albumin passed in the urine was much greater than in the previous case, the daily average for the fourteen days being 2·40 grm. of nitrogen, equivalent to 15 grm. of protein. It varied from 10 grm. to as much as 21·5 grm. per diem.

TABLE III.

Nitrogen consumed in food, 15·4 grm.

Nitrogen excreted						
Urine		Fæces		Total		Balance
14·56	..	0·95	..	15·51	..	− 0·1
15·25	..	0·76	..	16·01	..	− 0·6
13·72	..	1·20	..	14·92	..	+ 0·5
15·29	..	..	..	15·29	..	+ 0·1
14·18	..	1·11	..	15·29	..	+ 0·1
14·21	..	0·99	..	15·20	..	+ 0·2
16·18	..	..	..	16·18	..	− 1·8
11·65	..	1·45	..	13·10	..	+ 2·3
						+ 0·7

During the first eight days the protein catabolized daily, as represented by the non-protein nitrogen, averaged 11·89 grm., approximately 74 grm. of protein, which is quite a normal figure. The patient consumed the whole of the food given, and did not find the amount excessive. In the second period, however, when the diet was controlled only by his appetite, the quantity of nitrogen excreted decreased gradually and steadily the non-protein nitrogen falling as low as 6·1 grm. per diem, corresponding to only 38 grm. of protein catabolized, a figure below normal. Moreover, it had not reached a minimum, but was still decreasing when the experiment ceased.

The only other constituents of the urine which were estimated were the creatinine and creatine, the former being quite normal in amount, the percentage ratio to the total nitrogen normally increasing as the protein catabolized decreased. The second diet had the advantage of being practically free from creatinine and creatine, so that the creatinine present in the urine during this time should give a fair picture of the tissue metabolism. Creatine was occasionally present in the urine when the patient was on a meat diet, but was always absent when the food was creatine-free.

It seemed of interest to ascertain whether a patient losing so much protein was maintaining nitrogen equilibrium, and during the first period when a definite amount of protein was eaten a balance-sheet was made out between the nitrogen intake and that excreted. The total nitrogen in the urine and fæces was determined in the usual manner, and a sample of each food was analysed as regards its nitrogen content. During this experiment the food was carefully weighed and the whole quantity was eaten.

Table III embodies the results of this experiment and shows that the patient was practically in nitrogen equilibrium, the result of the whole eight days being a nitrogen retention of 0·7 grm. or about 5 grm. of protein.

An examination of the figures representing the quantity of protein passed in the urine in this case shows that it was not materially affected by the nature of the diet. In the first eight days the diet was chosen in accordance with the usual treatment and was almost free from fat, whereas in the second period the diet was rich in fat. The quantity of protein excreted remained on the average practically the same, and the urine was not altered in appearance by the change.

Both cases were true chyluria, the urines containing fat and lymph proteins. It has been pointed out that in both cases filaria larvæ could not be found in the peripheral blood, neither during the day nor during the night. This absence, however, does not prove that the chyluria was not of filaria origin as it is well known that definite symptoms of filariasis may be observed in patients, even when repeated and careful examination does not reveal the presence of the parasites. Moreover, filaria larvæ may have been previously present in the blood and may have since disappeared.

The general protein metabolism was not affected by the continued loss of lymph. In the first case the level of protein catabolized was very low, but the relative quantities of ammonia, uric acid and creatinine were of the same order as those in normal urines with similar protein levels of metabolism.

In the second case, when the diet was constant in amount and of normal protein content, nitrogenous equilibrium was more than maintained.

The quantity of chyle in the urine as measured by the proteins excreted was, on the average, the same whether the diet was free from fat or rich in fat. The usual practice of reducing the fats to a minimum does not appear to be justified by this experiment.

The quantity of proteins present in the urines is the best guide to the condition of the patient in chyluria, since these are the substances which clot to jelly-like masses, to which is due the difficulty of passing urine often experienced.

FURTHER NOTES ON ENTAMŒBIASIS.

By Dr. Lim Boon Keng.

Since writing my last paper I have had many opportunities of examining patients suffering from various diseases, which clinically we have been in the habit of associating with one another, such as rheumatism with sciatica, pleurisy, asthma and sundry skin affections of the urticarious and erythematous type. The relation of rheumatic pains, erythema and prurigo with dysentery and hepatic abscess, has been noted since the days of Graves and Murchison. The result of my observations is that all rheumatic inflammations and rheumatism as seen in Singapore, are associated with a protozoon organism, whose characteristics and life-cycles I propose to summarize briefly, leaving to a later occasion to bring forward clinical and other data to substantitate my conclusions.

The organism is found in the intestinal canal in many persons, but mainly in those suffering from lithæmia, rheumatism, bronchitis, asthma, an irregular remittent fever, various inflammations, sciatica, lumbago, urticaria, erythema marginatum, erythema nodosum, prurigo, impetigo herpetiformis, lichen rubra acuminata, and chronic gastrodynia. One patient had painful micturition as if passing gravel, the urine being red and having a brick-dust deposit. In many of these patients, the organism is also found in the sputum, the urine, in the blood and in the skin eruptions.

As the life-cycles are somewhat complicated, we may begin with the small free trophozoite amœba, which has small granules and moves by means of hyaline pseudopodia. Probably these are similar to the amœba described by Noc. They form a plasmodium, and are embedded in a large mass of mucin-like substance into which the cells discharge numerous rounded oval or spindle-shaped granules. This stage corresponds with the myxamœba state of the mycetozoa. From this plasmodium is developed a fungus-like thallus with cellulose walls with central venation, which sends off branches. The veins are filled with a mucin-like mass of fibrils, many of which are twisted round. The substance of the thallus is divided into many cylindrical cells. The walls are perforated so that the chambers communicate with one another. In the substance of the thallus in proximity to the vein, a crystalline core is developed, there being two kinds of crystalline bodies, colourless phosphatic and brownish-red urates. Around these the cells of the plasmodium grow and build up the crystals, and the bodies called sori, which develop in the chambers of the thallus, between the soral masses, which appear like pieces of indian corn thrown together in a systematic way. These are oval or round cysts. From these grow amœbulæ and flagellæ, which undergo

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