

OBSERVATIONS on PURIN METABOLISM and on the ADMINISTRATION of a PURIN-FREE DIET in GOUT.

During the past year a study has been made at the Royal Mineral-Water Hospital at Bath as to the effect of a purin-free diet in persons suffering from Gout.

Gout is essentially a diathetic disease. There is some constitutional derangement, either derived by inheritance, or acquired by the individual in which Metabolism is altered in such a way as to produce an increased amount of urates in the form of quadri-urates in the blood (urataemia).

As a direct result of this there occurs a precipitation of the bi-urate of Sodium in the Synovial and other tissues (Uratosis). The chemical inter-relationships of the purin bases and uric acid are of great importance in connection with gout. Purin has the formula C₅ H₄ N₄, while uric acid is a tri-oxypurin with the formula C₅ H₄ N₄ O₃. Other oxy-purins found in the body and in the food stuffs are :

Xanthine (di-oxypurin)	C	H	N	O
	5	4	4	2
Hypo-Xanthine (mono-oxypurin)	C	H	N	O
	5	4	4	1
Adenine (amino-purin)	C	H	N	NH ₂
	5	3	4	2



	C	H	N	O	NH
Guanine (^m amino-oxypurin)	5	3	4		2

All these have their origin in the metabolism of the nucle^a of the cells of the body and from the nuclein in the food stuffs introduced into the body, moreover certain foods when introduced into the body have the power of producing leucocytosis with the ultimate breaking up of the nuclein contained in those cells. This latter is however an ^{un-}important factor as compared with the two former. The origin of the purin bodies as excreted in the urine has been studied in detail by Burian and Schur (1)

Their work goes to show that these bodies are created firstly as a product of the body metabolism, and secondly as a derivative of the purin containing foods assimilated. To the former category the term endogenous Purin Bodies has been given while the latter are termed the "exogenous purin bodies". It has also been established that in a normal healthy individual leading a regular life with daily regulation as to quantity and nature of food, and with a fixed daily amount of exercise that the daily output of endogenous purin bodies is more or less constant for each individual and that there are variations within certain limits as regards different individuals. It is calculated that the amount of purin substances excreted daily by a healthy individual is due in about equal proportions to endogenous and exogenous

causes. Burian and Schur in their experiments have shown that the out-put of ^{endo-}~~exo~~genous purins remain at a certain constant so long as the diet is kept purin-free. In normal healthy individuals this constancy in daily out-put is remarkable in its consistency.

It has further been shown (2) that the normal endogenous excretion of uric acid may fluctuate from day to day in the same individual to the extent of .11 gram of uric acid. The same observer has determined that the average daily endogenous uric acid excretion varies in different normal individuals from .25 to .55 grams of uric acid.

In gout, judging from the following figures, these various limitations in amount, both as regards the same individual, and as compared with other individuals, do not hold good.

As will be observed from a study of the following cases there is a marked variation both as regards the same individual and as between different individuals.

In Case 1. where the ordinary diet of the Hospital was given throughout, this irregularity is well marked. In this case both exogenous and endogenous factors were at work.

In Case 2. while on ordinary diet the patient was seized with an acute attack lasting four days.

During ~~three~~^{those} days, although placed on a purin-free diet, the out-put of uric acid still kept at a high level.

In Cases 3. and 4. while on a purin-free diet no symptoms of gout manifested themselves. Only the uric acid was estimated. As has been pointed out by Brugsch and Schittenhelm (3), that in cases of ~~great~~ gout uncomplicated by albuminuria, there is no need to determine the total Nitrogen or Purin.

The method of estimating the uric acid was according to that of Dr. Hopkins.

The urine was carefully collected for 24 hours. 100 ccs. of the urine was measured out and to this was added 25 grms. of solid chloride of Ammonium, then after the salt was dissolved sufficient Hydrate of Ammonium was added to make the mixture alkaline. The mixture was stirred thoroughly till the precipitate tended to settle. It was then allowed to stand till the supernat^{ant}~~ant~~ liquid became nearly clear.

It was then filtered through a small filter-paper, and then washed with a saturated solution of Ammonium Chloride. Two washings were found to be sufficient.

The precipitate of Ammonium Urate was washed off the filter with a jet of hot distilled water ~~was~~^{into} a small beaker.

To this was added 4 or 5 drops of strong hydrochloric acid - the whole being heated till the liquid just began to boil. After standing overnight the crystals of uric acid were filtered off through a small filter paper, while the amount of Mother Liquor was noted in CCS. The crystals were then washed off the filter paper ~~with~~^{into} a beaker. Finally to this was added a few crystals of Sodium carbonate and heated till the uric acid had dissolved. The solution was then made up to 100 CCs and cooled under the tap. ^{a burette fitted with twentieth} Meanwhile a normal permanganate solution (containing 1.581 grms. per litre of distilled water) is prepared.

To the "cooled solution" was added 20 ccs. of strong sulphuric acid and immediately titrated with the permanganate.

The end point was given by the first appearance of a momentary but diffuse flush of color throughout the liquid.

Each cubic centimetre of the permanganate is equal to 0.00375 gramme of uric acid. To the figure so obtained it is necessary to add 1 milligramme for each 15 cc; of the mother liquor (not reckoning washings) from which the uric acid separated.

The Purin free diet given consists of :

White bread, eggs, butter, cheese of white or yellow variety, but not strong cheeses, such as gorgonzola, stilton, roquefort; milk (two to three pints a day according to taste) sugar, cream, rice, tapioca, lettuce, cauliflour and cabbage.

The patient may be allowed as much of the above substances as he or she may desire, but these quantities are regulated for each day.

Tea, coffee or cocoa must on no account be allowed.

Breakfast: -

Hot toast, Scrambled, poached or boiled egg.

Hot roll.

Dinner:-

Macaroni cheese, cauliflour with cheese, omelette flavoured with cheese or parsley, lettuce, boiled cabbages chopped up with butter, salt and pepper served on toast. Hard-boiled egg with lettuce. Cream cheese. Poached egg served with macaroni. Stewed pears and cream. Boiled batter pudding. Apple pie (pastry made with butter) Treacle tart, Apple charlotte, Ground rice mould. Milk

puddings except cornflour. Pancakes, Egg custard, Bread and Butter pudding without fruit, Junket, Apple and tapioca, Boiled apple pudding made with butter instead of suet, Plain Soufflé.

Tea: -

Rice cake, plain scones and anything without currants, peel or flavouring.

Supper: -

Bread and milk.

The following are the results obtained : -

CASE I

J.H.W., a male, age 53, married, Farm Bailiff,

Onset two years ago when patient was seized suddenly one morning with excruciating pain in left great toe joint. ^{Tophi} ~~Tophi~~ in both ears. Teeth ground down. The body temperature was normal throughout. The urine was examined daily but there was no albuminuria, nor were there any casts. This patient was kept throughout on the ordinary diet of the Hospital with meat, tea and other purin containing foods in evenly regulated quantity -

Date	Total amount of urine passed in 24 hours in CC's.	Mother liquor in CC's	Potassium Permanganate solution used in Cc's	Total amount of uric acid in grams in the 24 hours.
Feb. 10	1218	34	17.	.789
11	1276	40	16.	.795
12	1160	23	10.	.452
13	1160	18	10.2	.457
14	1566	22	9.6	.574
15	1276	20	12.5	.611
16	1566	18	6.5	.400
17	1392	30	12.	.653
18	1740	22	9.2	.626
19	1160	25	14.4	.644
20	1160	16	16.	.707
21	1392	18	8.	.434
22	1972	22	5.8	.457
23	1247	19	8.	.390
24	2233	28	4.	.374
25	1276	22	9.	.450
26	1624	30	11.2	.696
27	1044	32	8.	.322
28	1624	28	6.4	.421

CASE 2.

J.T., a male, age 49, married, Cab-driver, weight 14 st. 11 lbs. Condition began 20 years previously in both ankle joints. Finger, toe, knee and wrist joints have at one time or another been affected with acute gout. Has large tophus ~~in~~ rim of each ear. Teeth ground down. While on the ordinary diet on Feb.17th the patient was seized with an attack of acute gout in the R. ~~ankle~~. The temperature rose to 101.6°F. Next day there was pain, swelling and redness in both ankle joints and the proximal interphalangeal joint of middle finger of right hand, patient was placed on a purin free diet. on Feb.17th (3 pints of milk daily). The symptoms of Acute Gout subsided on Feb.21st when the temperature regained the normal level. Coincident with this the output of uric acid fell very considerably and thereafter with one partial rebound maintained a much lower level. The purin free diet was given up to Feb.28th.

Date.	Total amount of urine passed in 24 hours in CC's.	Mother liquor in CC's.	Potassium Permanganate solution used in CC's.	Total amount of uric acid in grams in the 24 hours.
Feb 10	1788	31	7.2	.519
11	1392	29	13.	.700
12	1972	17	6.8	.534
13	1686	26	9.	.596
14	1044	20	15.6	.622
15	2668	18	5.5	.582
16	1914	24	11.	.793
17	754	34	21.6	.623
18	754	34	20.4	.570
19	870	34	18.6	.625
20	1334	21	13.8	.708
21	1276	18	12.5	.624
22	1218	39	10.5	.511
23	638	28	10.6	.262
24	1276	18	9.	.446
25	1160	18	6.	.275
26	1392	20	5.5	.306
27	1392	20	5.	.278
28	1334	8	5.2	.264

CASE 3.

W.P., a male, age 40, married, general labourer;

onset 8 years previously. Huge tophi present over all fingers, also both elbows, both great toe joints, along line of ~~phalanges~~^{tendo}, ~~metatarsals~~^{achilles} and patellae, also over rims of ears. Teeth markedly ground down. The body temperature throughout was normal. Daily examination of the urine showed that there was no albumin^{uria} and there were no casts in the urine.

Date	Total amount of urine passed in 24 hours in CC's.	Mother liquor in CC's	Potassium Permanganate solution used in CC's.	Total amount of uric acid in grams in the 24 hours.
Jan. 1	870	20	10.2	.343
2	1160	16	7.	.316
3	1508	23	4.6	.281
4	1450	13	3.5	.204
5	2030	15	3.4	.275
6	2494	18	3.6	.362
7	1980	30	3.4	.292
8	1160	22	4.4	.208
9	1450	32	3.2	.197
10	1740	25	2.8	.210
11	1856	27	3.4	.270
12	2030	17	2.8	.233
13	2262	21	2.8	.264
14	1624	20	3.4	.227
15	1276	19	3.3	.175
16	1276	20	2.4	.132
17	1740	22	3.6	.261
18	1914	15	3.5	.268
19	1914	14	3.4	.260
20	1624	24	3.6	.243
21	1856	13	2.	.158
22	1980	10	3.3	.257
23	1624	16	2.8	.186
24	1624	18	3.6	.238
25	1740	12	2.8	.196
26	1798	33	2.2	.184
27	1740	18	1.4	.112
28	1562	14	6.	.366
29	1624	19	3.4	.226
30	1392	17	2.8	.161
31	1392	15	3.	.157
Feb. 1	1276	17	3.	.158
2	1508	17	3.1	.192
3	1856	23	4.8	.362
4	1740	14	5.2	.356
5	1392	11	7.6	.306
6	1218	12	9	.412
7	1392	23	11.5	.638
8	1392	21	11.	.592
9	1218	25	10.	.475

The patient was placed on purin free diet on Jan. 8th 1911. Weight was 15st. 8lbs. on admission 15st. 7 lbs

← 15st. 10 lbs.

← 16 st.

← 15 st. 10 lbs

← Patient placed on "ordinary Diet".

CASE 4.

W.S., a male, age 52, married, pressman in Shoe Factory; weight 14 st. 7 lbs. The onset of the condition took place 8 years ago with pain in the left great toe joint, tophi present in rims of ears. The body temperature was normal throughout. The urine was examined daily, no albuminuria was present, and no casts were found. The patient was placed on purin free diet on Jan. 8th 1911 and put on "ordinary diet" on Feb. 2nd, after which a rise in the daily output in uric acid was evidenced. His weight was as follows:

January 7th 14 st. 5 lbs
 " 14th 14 st. 7 lbs
 " 21st 14 st. 11 lbs
 " 28th 14 st. 7 lbs

Date	Total amount of urine passed in 24 hours in CC's.	Mother liquor in CC's.	Potassium Permanganate solution used in CC's.	Total amount of uric acid in grams in the 24 hours.
Jan. 1	986	19	9.8	.373
2	986	16	9.6	.365
3	1392	23	8.	.434
4	1537	22	7.7	.466
5	1392	24	7.4	.406
6	1885	19	6.2	.461
7	1740	34	5.2	.377
8	1856	30	6.	.454
9	1972	32	7.4	.586
10	1044	35	6.8	.289
11	1972	36	3.8	.266
12	1972	22	5.	.394
13	1160	20	4.4	.206
14	1508	41	5.	.321
15	1392	23	5.5	.298
16	1624	35	4.5	.293
17	1740	33	4.6	.326
18	2146	40	4.5	.417
19	1740	24	5.5	.388
20	1566	34	5.5	.359
21	1856	17	5.	.371
22	1914	15	4.	.324
23	1566	18	4.3	.272
24	1508	43	5.	.315
25	1624	25	6.	.389
26	1160	30	3.	.153
27	1624	14	3.4	.238
28	1508	30	5.5	.339
29	1508	19	5.	.298
30	1624	27	4.	.272
31	1450	24	5.4	.327

CASE 4 Contd.

Date	Total amount of urine passed in 24 hours in CC's	Mother liquor in CC's.	Potassium Permanganate solution used in CC's.	Total amount of uric acid in grams in the 24 hours.
Feb. 1	1508	32	5.4	.334
2	1392	20	5.5	.305
3	1856	25	7.5	.552
4	1798	17	9.	.628
5	1508	12	12.2	.697
6	1122	16	15.5	.860
7	1218	21	14.	.656
8	1508	13	13.	.747
9	1450	31	12.	.681

← Patient placed
on "ordinary
diet".

Conclusions :

- I. In no case during the administration of a purin free-diet, in patients suffering from Gout, but who exhibited no albuminuria, did an acute attack supervene.
- II. The endogenous purin metabolism in gout is much more irregular than the endogenous purin metabolism in the normal individual.
- III. The normal excretion of uric acid fluctuates from day to day in a more exaggerated manner when the uric acid is derived from endogenous and exogenous sources.
- IV. In the above cases the greatest daily difference obtaining with a purin containing diet amounted to .374 grams of uric acid in the 24 hours, while with a purin free diet the greatest daily difference is .297 and taking the subject as a whole the daily difference is much less marked in the latter than in the former.
- V. Gouty patients on a purin free diet are not affected in any deleterious manner by this diet, but on the contrary thrive upon it, As will be observed from the weights noted on the table they tend rather to gain than to lose

weight, but only to a slight extent. They feel well and are physically more fit than when on a purin-containing diet.

VI. Based on the above work the purin free diet is now being given to patients suffering from gout in this Hospital. The results from this method of dieting are most satisfactory.

References :

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