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THE RELATION OF PURIN BODIES TO CERTAIN METABOLIC DISORDERS.

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PART I.—THE ESTIMATION OF PURIN BODIES IN FOODSTUFFS.

UNDER the term "purin" all the substances that contain the nucleus C_5N_4 may be included. Those that specially relate to the human organism are hypoxanthin $C_5H_4N_4O$, xanthin $C_5H_4N_4O_2$, uric acid $C_5H_4N_4O_3$, guanin $C_5H_5N_5O$, adenin $C_5H_5N_5$, and the methyl-xanthins. Hypoxanthin, xanthin, and uric acid are respectively known as mono- di- and tri-oxypurin. They exist as "free" substances in partial solution, or are "bound" together with the other constituents of nuclein, from which they may be obtained as cleavage products. Together with creatin and other nitrogenous bodies they are generally known as the "extractives." Existing textbooks and handbooks regard them as possessing little value as food, and class them as "waste products," in that while they yield no energy to the body they require considerable metabolic efforts for their excretion. Precise information concerning their quantity and properties is difficult of access¹. Many clinicians, however, consider them harmful in certain metabolic disorders, and a theory exists which indicates these bodies as the exciting cause of some nephritic inflammations.

The quantitative relation which obtains between the purins contained in the food and those excreted in the urine has been recently worked out by Burian and Schur², Loewi³, and others. By the use of purin-free foods they ascertained the average amounts of urinary purin in various individuals, and attributed such quantity to an "endogenous" origin. The addition of certain foods of a known purin holding (per cent.) to the previous diet led to an increased egestion of urinary purins, and permitted the ascription of the difference in the two values to an exogenous or food-purin origin. But this difference was not equal to the amount of purin present in the food, and it thus appeared that only a definite percentage of the food purin passed through the body unaltered—at all events as regards its nitrogen holding—and the remainder was probably excreted as allantoin, oxaluric acid, or urea. This quantity varied within about 10 per cent. in different individuals. In Part II. I hope to confirm some of these results, also to indicate some additional factors and to treat in detail of the rôle of the faeces in regard to the metabolism of purins.

A knowledge of the quantities of the exogenous purins, must, therefore, be of clinical use, for were such determinations made, the physician could regulate at will the nuclein metabolism of his patients. In addition, the existent records of uric-acid excretion in health and disease are merely those from a uric acid of mixed origin (endogenous plus exogenous). Such figures state neither the quantity of uric acid directly due to the cleavage of cell-nucleins, nor indicate the percentage decomposition of the ingested purin by the metabolic organs. Hence, until new determinations have been made of the urinary uric acid which individually accompanies a purin-free diet, and there exist exact estimations of the purin-contents of purin-rich foods, we are much in the dark as to the meaning of increases or decreases in uric acid excretion and of their definite relations with disease. But uric acid is only one of the purin bodies present in the urine, and it is incorrect to regard it as the alone end-product of nuclein metabolism. The associated mono- and di-oxypurins hypoxanthin and xanthin should be equally included and the total urinary purins always determined.

Further to their importance in metabolism the question of the toxicity of the purin bodies is of interest. They exert no immediate action, but in long continued small doses are not entirely harmless. Other workers are now engaged upon this subject, and their results may shed further light upon a difficult question, but already Kolisch⁴ and Croftan⁵ have produced lesions of the renal cells and arterioles by the injection of certain purin bodies in animals, and my own experiments of daily injection of hypoxanthin into rabbits for two months resulted in the appearance of distinct degenerative changes in the liver and alterations in the constituents of the bone marrow.⁶

Some old estimations of hypoxanthin and xanthin in muscles exist, but the methods by which they were obtained could scarcely be expected to yield accurate results. Offer and Rosenqvist⁷, at von Noorden's suggestion, extracted and estimated the purins of white and red meats, but they examined only a few varieties, and their methods, although simple and expeditious, would only extract and precipitate the "unbound" purins.⁸ Burian and Schur⁹ give the results of their analyses of a few foods, but their object was primarily to find purin-free foods, and later to employ the foods which were richest in purin bodies.

The following estimations were therefore made with the view to their practical use in regard to dietaries (particularly those in relation to metabolic disorders), and also to provide extended data for experiments in normal and abnormal metabolism. The conclusions of these later observations will be stated in another paper.

The considerations and investigations which led to the selection of the method employed are given elsewhere.¹⁰ It will be sufficient to indicate that the extraction and estimation of the purins gave an error of only + 1 to - 1 per cent. The details were mainly those used by Burian and Schur,⁹ but several important modifications were introduced. In each case 100 to 250 grams of the raw substance were taken, boiled for 12 to 24 hours in acid solution in a special apparatus, and the albumins and acid removed. The purins were then precipitated by ammoniacal silver nitrate solution, and after certain precautions their nitrogen estimated by Kjeldahl's method. From the original filtrate the soluble proteids, albumoses and peptones (which hinder the purin precipitation or form weak compounds with them) were removed, and the remaining purins were precipitated and their nitrogen holding added to that of the first precipitate. With the vegetables and beverages the same method was not applicable. These were boiled in acid solution for twelve hours, and after removal of the albumins the filtrate was precipitated by excess of copper sulphate and sodium bisulphite. The precipitate, after well washing, was decomposed by SH_2 , the copper sulphide removed and the resultant filtrate freed from SH_2 , precipitated by ammoniacal silver nitrate, and its nitrogen estimated. (See Tables on p. 1642.)

Milk, butter, eggs and cheese should be placed under the heading of animal foods, but they are best estimated by the method which was employed for vegetables, and so may be considered as a separate class. Eggs contain neither free purin nor purin-yielding substance. Butter and cheese are derivatives from milk, and so may hold "traces" of nuclein bodies. The percentages of casein and water vary in different samples of butter, and the same remark may be applied to cheese. When the curd is present, any xanthin present in the milk will pass into the slightly acid whey, just as the process of churning or separation assists their removal from the butter. Hence only minute traces can remain in these two substances. In milk, Petren¹¹ was unable to find any purin bodies, but Burian and Schur¹² by complete removal of all the albuminous bodies found 0.0014 gram purin N. per litre. An estimation of my own yielded 0.0020 gram purin N. per litre. These four articles of diet form together our most valuable means of withholding purin substances from the body, and yet allow the provision of a diet at once digestible, easily absorbed, and capable of maintaining nitrogenous equilibrium.

It may appear that owing to the different varieties of cattle and their altered foods during the several seasons, the above estimations are only valid for the particular samples examined. They may, however, be taken as representing a general working average, as the figures stated are from meats purchased at

different times of the year, and from such widely different sources as Manchester, Leipzig, and Stockholm. Senator¹³ considers that cooking alters the proportions of the purin bodies, but the observations of Rosenqvist, which I have repeated, show that little effect is produced. If it were customary to eat meat minus the gravy produced during the process, the objection would deserve further discussion, but as not only the gravy obtained from the meat, but also an

The Quantities of Purins in Meats, Vegetables, and Beverages.

	Percentage of Purin Nitrogen.	Average Per Cent. Purin Nitrogen.	Calculated as Purin Bodies.	Undried Purins	
				As Grams per Kilo.	As Grains per Lb.
Fish—					
Cod	0.0219 0.0247	0.0233	0.0582	0.582	4.074
Plaice	0.0334 0.0302	0.0318	0.0795	0.795	5.565
Halibut	0.0405 0.0412	0.0408	0.1020	1.020	7.140
Salmon	0.0482 0.0450	0.0466	0.1165	1.165	8.155
Meats—					
Tripe... ..	0.0235 0.0224	0.0229	0.0572	0.572	4.007
Mutton:					
Australian	0.0365	0.0386	0.0965	0.965	6.755
English	0.0411				
Veal:					
Loin	0.0484 0.0481	0.0465	0.1162	1.162	8.137
Neck	0.0300				
Pork:					
Loin	0.0485 0.0257	0.0485	0.1212	1.212	8.487
Neck	0.0168	0.0227	0.0567	0.567	3.969
Ham (fat)	0.0505 0.0419	0.0462	0.1155	1.155	8.085
Beef:					
Ribs	0.0455	0.0455	0.1137	1.137	7.959
Sirloin	0.0506 0.0538	0.0522	0.1305	1.305	9.135
Steak	0.0826	0.0826	0.2065	2.065	14.455
Liver	0.1125 0.1078	0.1101	0.2752	2.752	19.264
Sweetbread (thymus)	0.4025	0.4025	1.0063	10.063	70.431
Chicken	0.0495 0.0546	0.0518	0.1295	1.295	9.065
Turkey	0.0512 0.0504				
Rabbit	0.0385 0.0456	0.0504	0.1260	1.260	8.820
		0.0380	0.0970	0.970	6.314

Vegetables and Beverages.

	Quantity Used for Estimations.	Purin Nitrogen Per Cent.	Calculated as Purin Bodies.	Grams Per Kilo.	Grains Per Lb.
Cereals—					
Bread (white)	500 grams	No trace	—	—	—
Oatmeal	250 grams	0.0212 0.0210	0.0530	0.530	3.4563
Rice	500 grams	No trace	—	—	—
Pulses—					
Peameal	250 grams	0.0156	0.0390	0.390	2.5413
Beans (haricot)	500 grams	0.0278 0.0247 0.0250 0.0252 0.0250	0.0637	0.637	4.1661
Roots and Tubers—					
Potatoes	1,000 grams	0.0008 0.0006 0.0031 0.0040	0.0020	0.020	0.1400
Onions	250 grams		0.0090	0.090	0.0630
Tapioca	250 grams	No trace	—	—	—
Green Vegetables—					
Cabbage	Large head	"	—	—	—
Lettuce	"	"	—	—	—
Cauliflower	"	"	—	—	—
Asparagus (cooked)	700 grams	0.0086	0.0215	0.2150	1.5050

	Quantity Used for Estimations.	Purin Nitrogen per Cent.	Calculated as Purin Bodies.	Purin, Grams Per Litre.	Purin, Grains Per Pint.
Beers—					
Lager beer... ..	1,000 C.C.M.	0.0050 0.0053 0.0020 0.0021	0.0125	0.1250	1.0955
Lager drink	"	0.0050	0.0050	0.0500	0.1533
Pale ale	"	0.0050 0.0056	0.0155	0.1450	1.2708
Porter	"	0.0060 0.0062	0.0145	0.1550	1.3578
Wines—					
Claret	500 C.C.M.	No trace	—	—	—
Voulay	"	"	—	—	—
Sherry	"	"	—	—	—
Port (Commenda- dor)	"	"	—	—	—

additional purin contribution from some fashionable meat extract is served, it is probable that much more purin is taken with the cooked meat than exists in the freshly killed muscles.

Although certain differences occur in the percentage contents of fish and meats, little variations exist between those known as the red and white meats. The glandular organs yield large amounts of purins.¹⁴

Amongst vegetables the somewhat high percentages of beans, peas, and oatmeal will be noticed. Their significance will be dealt with in the second part under "metabolism." The alloxur bodies of asparagus had been previously pointed out by Jerome,¹⁵ who observed an increased uric acid excretion after the addition of asparagus to his diet. By the Krüger-Wulff method he found 0.0854 gram of alloxur bodies in 500 grams of asparagus (0.0068 per cent. purin-N.).

The presence of purin bodies in beers is probably due to the yeasting and processes of manufacture. At room or body temperature guanine and hypoxanthine readily split off from yeast when in slightly acid solution, and the precaution of "fining" does not entirely remove the "yeast" itself. The avoidance of fermented liquors in gout, etc., is generally prescribed, and perhaps to their purin contents may be attributed some of the harmful effects in such diseases, for it is not impossible that the purins play a part in the production of the lesions usually met with in beer drinkers.

REFERENCES.

¹ A full summary may now be found in the *Thesis Purin Bodies*, Walker Hall, 1902. ² *Arch. f. d. ges. Phys.*, 8, 239, 1901, and 8, 309, 1900. ³ *Arch. f. exp. Path. und Pharm.*, 8, 159, 1901. ⁴ *Wien. klin. Woch.*, 1895. ⁵ *Journal of Amer. Med. Soc.*, p. 502, 1900. ⁶ Walker Hall, *Arch. f. exp. Path. und Pharm.*, 1902. ⁷ *Berl. klin. Woch.*, 44, 45, 49, 1899. ⁸ *Vide Thesis Purin Bodies*, p. 25, 1902. ⁹ *Arch. f. d. ges. Phys.*, 1901. ¹⁰ *Zett. f. phys. Chemie.*, 1902. ¹¹ *Skand. Arch. f. Phys.*, 8, 412, 1899; and *Arch. f. exp. Path.*, 8, 269, 1900. ¹² *Arch. f. d. ges. Phys.*, 1900. ¹³ *Berl. klin. Woch.*, No. 45, 1899. ¹⁴ *Estimations of "free" and "bound" purins will be published later.* ¹⁵ *Journ. of Phys.*, 1898-99.

PART II.—THE EXOGENOUS PURIN IN NORMAL METABOLISM.

(From the Carolinska Institutet, Stockholm.)

A STUDY of the normal metabolism of purin bodies must precede any observations under abnormal conditions. The work of Burian and Schur¹ requires confirmation by as many workers as possible, and may with advantage be extended to include the other foodstuffs whose purin contents have now been estimated.² In addition, the faeces might be examined as to their relations with the ingested and the urinary purins. Weintraud,³ Umber,⁴ Petren,⁵ and Parker⁶ have already investigated the faecal purins from the standpoint of their origin, and Parker has shown how they vary with different diets, but as their source is not precisely defined, the results obtained are inapplicable to the subject here in view. Since this portion of the work was concluded, Krüger⁷ has published observations upon a case in which a mixed diet was alone taken. His figures will be considered at a later stage, when I hope to make a detailed communication on the relation of the faecal purins to the following results. (As they do not materially affect the present issue they are here omitted.)

TABLE I.

1901.	Urine. c.cm.	Total Nitrogen.	Total Purin Nitrogen.	Uric Acid Nitrogen.	Xanthin Bases Nitrogen.	P ₂ O ₅	Remarks.
Oct. 9	1,260	21.8232	0.3769	—	—	—	Usual mixed food, with tea and coffee.
" 10	995	16.2486	0.2739	—	—	—	
" 11	1,215	18.4294	0.3472	—	—	—	
" 12	1,010	17.5210	0.2208	—	—	—	
" 13	1,170	20.2132	0.1611	0.1454	0.0157	2.6208	Purin-free fixed diet.
" 14	1,125	20.4975	0.1608	0.1380	0.0228	2.4712	
" 15	1,255	23.5683	0.2650*	0.2190*	0.0460	3.7650	Purin-free fixed diet, plus 450 grams chicken.
" 16	1,110	20.4680	0.1798	0.1435	0.0353	3.3858	Purin-free diet.
" 17	1,085	19.4215	0.1500	0.1280	0.0280	3.3743	Purin-free diet.
" 18	1,415	23.7294	0.2489*	0.1995*	0.0494	3.8771	Purin-free diet, plus 530 grams plaice.
" 19	1,140	19.6506	0.1755	0.1644	0.0111	2.9153	Purin-free diet.
" 20	1,010	18.2966	0.1646	0.1250	0.0386	2.6260	Purin-free diet.
" 21	1,860	22.4680	0.2480*	0.2108*	0.0372	5.9520	Purin-free diet, plus 400 grams beef.
" 22	1,450	18.2990	0.1898	0.1565	0.0333	2.4460	Purin-free diet.
" 23	900	16.8940	0.1660	0.1270	0.0390	2.5475	Purin-free diet.
" 24	1,150	17.2368	0.1857*	0.1391*	0.0466	2.8980	Purin-free diet, plus 408 grams beans.
" 25	1,260	17.4630	0.1563	0.1261	0.0302	2.7468	Purin-free diet.
" 26	1,150	17.8542	0.1654	0.1220	0.0434	2.6532	Purin-free diet.
" 27	2,080	21.8025	0.2218*	0.1761*	0.0457	3.0784	Purin-free diet, plus 1,700 c.cm. lager beer.
" 28	1,100	19.7281	—	0.1224	—	2.7546	Purin-free diet.
" 29	1,030	17.8625	0.1645	0.1200	0.0395	2.6150	Purin-free diet.
" 30	1,120	21.5621	0.2475*	0.2038*	0.0437	3.5430	Usual mixed food.

Neither tea nor coffee was taken during the experiment.

* = Uricate deposit in urine.

The subject of experiment: W. H., 33 years old; weight, 70 kilos (155 lb.). Urine free from albumen and sugar. The twenty-four hours' collection was taken to and from 8 a.m. During the experiment ten hours' laboratory work was performed and a walk of four English miles taken each day. The total nitrogen was estimated by Kjeldahl's method, the total purin bodies by Arnstein's modification of Camerer's process, the uric acid by Hopkins's ammonium chloride method, and the xanthin bases calculated by difference. The phosphates were determined by titration against uranium nitrate with cochineal as indicator.

To obtain an average endogenous purin excretion an eight-days' experiment was made upon a fixed purin-free diet, consisting of milk, butter, bread, eggs, and cheese—no coffee or tea. The individual quantities were varied so as to gradually decrease the nitrogen from 22 to 17 grams and inversely increase the carbohydrates from 2,631 to 3,053 calories. The total urinary purin ranged from 0.1560 to 0.1655 purin-nitrogen, an average of 0.1625 purin-N.

Table I shows the results of the main experiment. Except when mentioned, only a fixed purin-free diet was taken. That the effect of the purin-rich food might be at once evident, the principal meal was taken at 7.45 a.m., when the larger portion of the food was eaten. A light lunch preceded the next meal at 4 p.m., when the remaining purin-rich food was consumed. Bed, 10 p.m. The meats were weighed raw, then steaked with fat sufficient for the purpose, and every particle of gravy, etc., preserved.

In reviewing the results obtained, the large purin excretion (with mixed diet) at the commencement and close of the experiment will be observed, and also that on those days upon which the purin-free diet was taken, the total urinary purin excretion approached the average of 0.1625 N. But when the chicken, plaice, beef, etc., were added, the urinary purin was at once increased. During the whole period the "bases" remained practically stationary, and the increase in the total purin excretion was entirely due to an increase in the uric acid.

The total urinary purin-N. during the forty-eight hours following the ingestion of 450 grams of chicken was 0.4448. The endogenous purin for two days (namely, the purin excreted on purin-free food) was $0.1625 \times 2 = 0.3250$. Hence the difference of 0.1198 was derived from the purin bodies contained in the chicken. These would equal (*vide* Part I) 0.2200 purin-N., so that 54.4 per cent. of the food purin appeared in the urine as increased or exogenous purin within forty-eight hours. Similarly, 537 grams of plaice contain 0.707 purin-N. (*vide* Part I), and the total urinary purin during the succeeding forty-eight hours was 0.4244 N. This minus 0.3250 endogenous purin (0.1625×2) leaves 0.0994, or 58.7 per cent. of exogenous origin. Again, 400 grams of beef contain 0.2400 purin-N.; the total urinary purin was 0.4378; this, less 0.3250 endogenous purin, equals 0.1128 purin-N., or 47.4 per cent. of the beef purin appeared in the urine as exogenous purin.

It thus appears probable, that allowing for the variations which occur in different animals, as well as in separate species, the system excretes in the urine (within 48 hours) about one-half of the fish, fowl, or beef purins contained in the food. These figures confirm the results of Burian and Schur⁸ as regards the metabolism of beef purins, and indicate

that the purins or alloxur bodies of fish and fowl flesh undergo similar chemical or vito-chemical changes during their passage through the human body.

TABLE II.—W. H.; 70 Kilos; Health Normal; Urine Free from Albumen and Sugar.

—	Urine.	Total Purin Nitrogen.	Uric Acid Nitrogen	Remarks.
1901.	c.cm.			
Oct. 23	900	0.1660	0.1270	—
" 24	1,150	0.1857	0.1391	408 grams dried beans.
" 25	1,260	0.1563	0.1261	—

TABLE III.—N.; 49 Kilos; Healthy; Urine Normal.

—	Urine.	Total Purin Nitrogen.	Uric Acid Nitrogen	Remarks.
1901.	c.cm.			
Oct. 22	960	0.1478	0.1180	Purin-free diet.
" 23	760	0.1504	0.1290	" "
" 24	670	0.1589	0.1348	75 to 50 grams of beans.
" 25	560	0.1095	0.0979	Purin-free diet.
" 26	1,310	0.2315	0.1985	Usual mixed diet, with tea and coffee.

TABLE IV.—M.; 22 Kilos; aged 7 Years; Healthy; Urine Normal.

—	Urine.	Total Purin Nitrogen.	Uric Acid Nitrogen	Remarks.
1901.	c.cm.			
Oct. 22	535	0.1224	0.1013	Purin-free diet.
" 23	560	0.1170	0.0927	" "
" 24	570	0.1355	0.1177	120 grams of beans.
" 25	650	0.1072	0.0900	Purin-free diet.
" 26	510	0.1570	0.1463	Usual mixed diet.

Although it is customary to regard vegetables as comparatively harmless in gout and nephritis, it is noteworthy that Camerer⁹ found increased urinary alloxuric (purin) nitrogen after a vegetable diet. Von Noorden¹⁰ states that patients on a diet of beans, asparagus, and sauerkraut excrete almost the

same quantity of uric acid as with a meat diet, and Douglas¹¹ found that with a diet rich in peas, beans, and lentils, the output of uric acid was 0.702 gram, as compared with 0.675 on ordinary diet. Haig¹² has recently called attention to the effect of asparagus in increasing his uric acid output. This he strangely enough ascribes to the large amount of asparagin it contains.

It will be evident from a reference to the estimations of the vegetable purins contained in Part I, and a glance at the results of the preceding experiment that certain vegetables contain considerable quantities of purin bodies, and so provide "exogenous" purin. That such an inference might be supported by experimental evidence, additional observations were made.

Dry haricot beans, after weighing, were allowed to soak in water for twelve hours, then boiled and reweighed. All three subjects of experiment ate from the same lot of beans and at the same time; otherwise, during the experiment, the food consisted solely of eggs, milk, cheese, bread, butter, sugar, and rice. Tables II, III, and IV (p. 1463) give the results obtained.

In each case there was a distinct increase in the urinary purin on the day when the beans were eaten. As Rubner and others have pointed out the small absorption of the proteids of the pulses it was in this case absolutely necessary to estimate the faecal purins. On the day in question the faeces from W. H. yielded 0.0407 N. as exogenous purin-N. Now 408 grams of haricot beans contain 0.0920 purin-N (*vide* Part I), therefore, 0.0513 purin-N. was absorbed. The increase of the urinary purin over the normal endogenous factor (0.1625 N.) was 0.0232, and thus represented 45.5 per cent. of the food purin-N. It was impossible to obtain the faeces from M and N., so that a precise calculation cannot be made. But if the absorption was at all approximate to that of W. H. there would be an absorbed amount of bean-purin 0.0162 N., an increase of 0.0090 N. above the average normal endogenous quantity of 0.1250 N., and thus an exogenous urinary purin of 56.2 per cent. With M. there was an increase of 0.0180 N. absorbed, giving an exogenous urinary purin of 55 per cent.

Thus these observations demonstrate both the presence of purin bodies in the pulses and their relation with the functional excretions. It is, therefore, apparent that in the formation of dietaries, particularly in regard to metabolic disorders, the purin contents of foodstuffs should be considered equally with their proteid percentage.

As I have elsewhere given a summary of the action of alcohol on the formation and excretion of uric acid,¹³ it is here only necessary to state that in the human body the elimination of uric acid is generally diminished after taking alcohol. Rosenfeld,¹⁴ however, had a patient whose uric acid rose considerably after a single bottle of beer, and it is common knowledge that gout is more frequent in countries where fermented drinks are taken than in those in which distilled spirits are consumed.

On a day when no laboratory work was undertaken and purin-free food was eaten I drank 1½ litre of lager beer. The urine for the following twenty-four hours amounted to 2,080 c.cm. It contained 18.2640 total N., 0.2218 total purin-N., and 0.1761 uric acid N. In the 1,700 c.cm. of beer there would be 0.090 purin-N. (*vide* Part I), and my endogenous purin quotient was 0.1625. The difference of 0.0593 might thus be attributed to substances present in the beer. The experiment, however, was not entirely free from objections. The quantity of fluid was greater than the daily average of 1,000 cc.m. of milk, and Laquer¹⁵ has shown that after 1½ to 1½ litre of water the alloxur-N. may be increased. In addition, it is contrary to my usual custom to take alcoholic beverages, and so any effects would be more pronounced; thus, although the general depression of nervous and metabolic functions might diminish the purin excretion the dilatation of the smaller arterioles might assist the removal of an abnormal amount of undecomposed tri-oxypurin. The experiment was therefore repeated in the following manner: To one litre of lager beer 1 c.cm. H₂SO₄ was added, the alcohol distilled off, the remainder evaporated to 500 c.cm., and then neutralized. The whole was drunk at 9 a.m. on the day of the experiment, and a purin-free diet observed during the several preceding and following days. An increase of 0.0175 purin-N. was obtained. As each litre of beer contains 0.05 purin-N. this quantity would represent 35 per cent. of the beer purins

appearing as urinary purins. The results of the second experiment show that the first yielded, through adverse conditions, too high an amount. The low percentage obtained in the second experiment led to an inquiry as to the form in which the purin bodies exist in beer, and further estimations were made, from which it was ascertained that each litre contained 0.0327 free purin-N.

As the addition of foods containing known quantities of purin bodies to a purin-free diet results in an increased egestion of urinary purin, varying with the nature of the food, and perhaps also with the individual, the question naturally occurs, what becomes of the balance which is not excreted as urinary purin? As the work which attempts to solve this problem is fully cited in another place,¹⁶ it may be shortly answered by the statement that the present condition of our knowledge appears to warrant the assumption that the "purin" first oxidized to tri-oxypurin is later decomposed by the liver (perhaps to a slight extent also by the general tissues) and finally excreted as urea, or the intermediate substances, allantoin and oxaluric acid.

From the action of the body in regard to the exogenous purin it has been argued that of the purin of endogenous formation only a certain percentage is excreted as such in the urine, the remainder undergoing decomposition into urea or bodies intermediate. If from the experimental data obtained these inferences are correct, then it is obvious that the balance normally maintained between the amount of purin destroyed and the quantity excreted in an unaltered condition will depend upon the integrity of the metabolic and excretory organs. Any alteration in their functional capacity will be at once reflected in a changed purin elimination. Whether retention of purin bodies is sufficient to account for any lesions with which their non-oxidation or non-excretion may be associated is another question? When the results of similar experiments under abnormal metabolic conditions are available the relation of cause and effect may be more evident than it is at the present moment.

The precise quantities of exogenous purin taken with the food and excreted in the urine may now be somewhat easily ascertained. A knowledge of the normal and abnormal individual reactions towards purin substances permits to a certain degree the measurement of the personal metabolism of purin bodies, and thus the clinician may increase or decrease the purin-rich foods according to the activity manifested by his patient during the several stages of disease or convalescence. Another point in relation to this activity is the rate of purin elimination. Some of my experiments indicate that a fairly constant period obtains for the excretion of "free" purins, and that this is much extended before the "bound" purins appear. The subject will be more fully dealt with in a later communication.

The exogenous "purin" can thus be easily controlled, but of the endogenous purin as yet little is definitely known. That it bears a somewhat close relation to the body weight I have elsewhere shown.¹⁶ Leucocytic destruction probably only slightly affects its quantity. There is a certain amount of evidence which points to its variation with nitrogenous excretion, and it may perhaps be taken as an index of the functional activities of the body. The last word, however, has not been said upon this subject.

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REPORT LXIX.

THE OEDEMA OF ANAEMIA.

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IN the BRITISH MEDICAL JOURNAL of June 15th, 1901, I endeavoured to show that, by taking into consideration the dilution of the blood that may occur in typhoid fever, a satis-