ON THE PRODUCTION AND EXCRETION OF URIC ACID.

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IN studying the composition of any excretion, the animal body may be viewed in the light of a manufactory, in which the substances administered are the raw material, the sum of the excretions the finished product, and the substances remaining in the body undergoing change may be regarded as the stock in process of manufacture. If this view be taken, we can easily see that, although we may measure in the raw material, and strive to regulate the physical conditions with mathematical accuracy, yet, inasmuch as our power over physical conditions is deficient, and our power of regulating mental emotions nearly nil, we cannot determine with mathematical accuracy what will be the precise outcome of a given ingestion of material. Causes of change are at work beyond our control, and beyond our powers of measurement, and therefore a mathematically exact result following a given ingestion, would rather prove error than accuracy. Since, then, we cannot hope to determine exactly the varying causes of change in the body, we must admit that results of observation of excretions are bound to vary within limits; and that the utmost we can expect from observations of the effects of drugs on any given excretion is, that such results shall be approximate, or in the same direction in several experiments, and when a slight variation is noticed, even in several experiments, it is not enough to warrant us in attributing it to the drug administered.

The experiments, of which the subjoined are a portion, were undertaken with a process for the estimation of uric acid, in which the usual sources of error in the estimation were believed to be eliminated, which was published in this JOURNAL, April 15th, 1882. A set of conditions under which an accuracy up to 1 or 2 grains of uric acid production were not to be obtained, and therefore in the experiments themselves such variations of result were not deemed important, although, in most estimations, agreeing duplicate results were obtained before the estimation was considered satisfactory.

A preliminary series of estimations led to the determination to consider an elimination of 400 grains of urea, and 11 grains of uric acid as normal under the conditions. The urea was subject to much greater variations, without apparent cause, than was the uric acid.

The diet taken during the experiments was: breakfast, bread or toast, 6 ozs.; butter, not noted, but not varying; tea, 12 ozs. Mid-day dinner, bread, 2 ozs.; meat, 8 ozs.; potatoes, 4 ozs.; green vegetables, 4 ozs.; pudding, 8 ozs., with variations; water, 10 ozs. Tea, as breakfast. Supper, bread 4 ozs.; butter, not noted, but not varying; water, 10 ozs.

The exercise taken daily amounted to four miles of walking. When any variations occurred, they are mentioned in the experiments. No alcohol or tobacco was used in any form.

The above diet was found to be that which best suited the individual, and had practically been in use for some period prior to the experiments being commenced; a moderate variation in the direction of increase being followed by lassitude and languor, while a diminution soon made itself felt as hunger. The weight varied one pound above or below 140 lbs. The experiments were regularly commenced in October 1881. The twenty-four hours was made to commence at 8 A.M., after emptying the bladder and before breakfast; and the date always refers to the day on which the collection of the quantity ended. The first variation experiment was commenced unwittingly.

	Amount of urine.	Colour to litmus.	Sp. gr.	Urea.	Uric acid.
Oct. 20	40 oz.	acid	1020	349 grs.	9.9 grs.
" 21	36 "	"	1023	498 "	14 "
" 22	50 "	"	1023	654 "	10 "
" 23	40 "	"	1020	458 "	10.8 "
" 24	41 "	"	1025	382 "	8.5 "

So great an increase in the amount of uric acid and urea on the 21st and 22nd was certainly surprising; and, as there was no consciousness of any marked change of diet from the scale given, it seemed, at first, unaccountable; and it was only after carefully thinking over every item, that it was remembered that on the 20th the green vegetables of the dinner had been changed to tomatoes, and it was learned they had an influence on the secretion. The tomatoes were only taken once, on the 20th, at 2 P.M., and therefore their influence, if any, would be felt on the urine collection of the 21st; but whatever caused the increase, affected also, in larger degree, the urine of the 22nd. The weather had been dry all the time. The

first portion of the urine of the 22nd was cloudy on cooling; but the whole collection was clear.

On the 24th, when the urea and uric acid had returned to the normal, a small quantity of tomato was added to the diet, and no other change was made. The effect was seen on the 26th, and on the following day it had passed off.

	Urine.	To litmus.	Sp. gr.	Urea.	Uric acid.
Oct. 25	38 oz.	acid	1023	482	11.5
" 26	41 "	"	1018	447	9.9

The tomatoes were abandoned until November 13th. The urine collection was as follows:—

	Urine.	To litmus.	Sp. gr.	Urea.	Uric acid.
Nov. 12	32 oz.	acid	1030	478	12.4
" 13	31 "	"	1026	403	10.7
" 14	50 "	"	1020	508	19.3
" 15	43 "	"	1023	432	18.4
" 16	56 "	"	1013	400	15.3

On November 13th, half a pound of tomatoes was taken in place of green vegetables, the whole of the other conditions remaining the same. The weather was bright and clear; the health perfect. On the 14th, another half a pound of tomatoes was taken; and six ounces extra water. The urine of the 15th was cloudy when cold, but cleared on slight warming.

It is to be noted particularly that the liquids taken during these experiments amounted to forty-four ounces, and any variation is mentioned; but although this was the case, the urine passed varied in amount, and did not follow the weather, *ie.*, it was not regularly greater in quantity on wet days and smaller on bright days. Dr. T. L. Brunton suggested to me that this might have been due to variations of blood-pressure.

The acids to be found in tomatoes are malic and oxalic. In the experiments of Mesner and Kock, it is stated that malate of lime increases the uric acid, but in some experiments of my own it was found that a practically unlimited quantity of apples might be eaten without increasing the uric acid excreted. Malic acid cannot, therefore, be credited with the large increase in the tomato experiments, and we are forced to consider whether it be not due to the oxalic acid, especially as the presence of this substance would cause a deficient oxidation of the blood. There is one other article of diet which contains oxalic acid, *viz.*, rhubarb, and this was found to largely increase the excretion of uric acid when added to the fixed diet. The fact has since been noted in various patients liable to gout, that both tomatoes and rhubarb will cause discomfort and disorder of the urine. One gentleman who complained of what he called "poor man's gout," admitted he had been eating largely of stewed rhubarb, and stated that the pain in the toe disappeared when he, under advice, abstained from it.

I can find no chronicle of the effect of oxalic acid or oxalates on the excretion of uric acid; but the following experiment confirms the view taken that it was the oxalic acid of the tomatoes which caused the increased excretion.

	Urine.	To litmus.	Sp. gr.	Urea.	Uric acid.
1882 Sept. 8	49	acid	1017	339 grs.	11 grs.
" 9	46	"	1020	284 "	12.3 "
" 10	60	"	1014	416 "	18.6 "
" 11	46	"	1020	340 "	12.4 "

The fixed diet had been resumed for some days prior to September 8th, 1882, and the collection of that date is seen to be normal as to uric acid, as, also, is that of the 9th. On the 9th, after breakfast, two grains and a half of oxalic acid neutralised with sodic carbonate were taken in one ounce of water, and after dinner three grains and a half in a similar manner—making in all, six grains of oxalic acid. After the first dose, there was headache, which continued through the morning. After the second dose there was renewed headache and considerable eructations, with sleepiness. At 3 P.M., went to sleep; slept for about an hour, and awoke with flushed face and headache, with chilliness and general dazed feeling. This passed off after tea, and the headache diminished towards evening. The following day, all effects of oxalic acid seemed to have passed off. There was no pain in the lumbar region, nor pain in passing urine during the experiment. Nevertheless, the urine collection of 10th contained about twelve or eighteen tube casts, a circumstance which had never been noticed before and has not occurred since.

It is well known that urea and uric acid always accompany each other in human urine. Wurtz has shown this blood to be a store-house of urea; and as there is no satisfactory reason for supposing the healthy blood to be entirely freed from uric acid as that sub-

stance is formed, or, in other words, that its formation occurs in the kidney, it is legitimate, considering the evidence, to decide that it is probable, if not certain, that the blood is also a storehouse of uric acid, and that only the excess is daily eliminated. Garrod states the blood in gout to contain at least 0.25 to .175 parts per 1,000 of uric acid, "whereas" he says, "in health and many other diseases (than gout) it has been shown to contain mere traces." But Garrod also states that his test will not detect less than 0.25 per 1,000, and Gairdner found in the blood of a boy aged 4, with bronchitis, evidence of uric acid, and he states his belief that this acid is a constant ingredient of pure and healthy blood. This is confirmed by Strahl and Luberkühn.

There appears to be nothing in either tomatoes, rhubarb stalks, or oxalic acid, which by process of digestion can be transformed bodily into uric acid, or so increase the daily production; therefore, when we find that the ingestion of these articles is followed by a largely increased excretion of the acid, we are driven to the conclusion that this increased excretion arises from one of two causes. 1, it is either an increased output from the store in the blood; or, 2, more than normal is formed from the blood materials, or from the blood or tissues, and this excess is excreted, the blood remaining, as before, in a condition of saturation under the conditions present. If the increased output was caused by a diminished store in the body, the cessation of the administration of the vegetable or oxalate would be followed by an excretion below the normal amount, until the deficiency had been made up. This was never the case, and hence the conclusion seems irresistible that the excess excreted was due to an increased production.

We know that the oxalic acid and soluble oxalates are poisonous, whether administered in a state of concentration or dilution; that digestive disturbance is a marked symptom of their action; and this poisonous action has been ascribed to the power which oxalic acid possesses of absorbing oxygen and becoming carbonic acid, thus robbing the blood of its vital oxygen. The presence of excess of uric acid in the system has again and again been ascribed to deficient oxidation. Todd, it is true, disbelieves in the theory of deficient oxidation, and points out that digestive disturbance, such as gastric catarrh with formation of acid, are commonly attended by a sediment of urates in the urine. This occurrence of sediment used formerly, and even now, to be frequently taken as proof of an increased formation and elimination of uric acid. Todd states this inference to be quite erroneous, and says "that there is not the slightest evidence of any real increase in the amount of uric acid produced in the system; and even if there were, the increase could only be transient and of short duration, since the digestive disorder would tend to limit the supply of nourishment; and therefore of the material from which uric acid is formed, and would thus interfere with any continued accession of acid in the system, and with the production of uric acid dyscrasia." This inference may be correct, always supposing that the uric acid is always found from the food ingested and is never found in a fasting animal, or from the decomposition of the tissues of the body—which may be doubted. Todd further quotes the experiments of Wochler and Frerichs against the deficient oxidation theory, these observers having introduced uric acid into the blood and found it eliminated as urea, and decides: "We are thus forced to conclude that, in gout, there is either so great a disproportion between the rate at which uric acid is formed and that at which it is eliminated, as to cause it to accumulate in the blood to an extent beyond the solvent capacity of that fluid, or else that the solvent power of the blood itself is diminished." Garrod takes the view that, "Conditions similar to those which cause a premature deposit of uric acid and its salts in urine without the quantity being augmented, may also occur in the interior of the body. Among these conditions is an increase in the proportion of acids, or acid salts." Both these observers thus seem to favour the idea that the production of uric acid is nearly, if not always, a constant quantity, and variations in its elimination are due to variations in the power of the blood to hold it in solution, a deficient elimination meaning an increased accumulation; an excess of elimination meaning a decreased accumulation.

If this view be correct, we have but to note the normal elimination from day to day, and then any excess when it occurs, and predict that this excess of the normal, will be surely followed by a corresponding deficit. During more than three months of experiments I have noted a good many instances of excess, and but one diminution from the normal of upwards of two grains. I believe a more careful consideration of this matter will lead to the conclusion that the production of uric acid is increased in the body under certain circumstances, and that either this increased production, or a deficient elimination may produce gouty symptoms.

GUMMATA OF THE SCLEROTIC.

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THE following cases, which have been under my treatment at Guy's Hospital, are well marked examples of that rare affection, gummata of the sclerotic.

CASE I has been already published (BRITISH MEDICAL JOURNAL, October 23rd, 1880), but at the time of publication I did not recognise the true nature of the disease, and called it an "Unusual Case of Episcleritis." I am indebted to Mr. Nettleship—under whose treatment the patient had previously been—for a correct diagnosis.

The disease is extremely chronic, and for a long time resists all remedies.

The first case was constantly under treatment, taking either iodide of potassium, or mercury, from the second week of June till the last week in August, 1880. At the beginning of July there was marked improvement, which, however, was only temporary. On one occasion I punctured one of the swellings, only blood escaped. A small circular ulcer formed, which took a long time to heal.

Towards the end of August I decided to cut into the swellings, and, if possible, ascertain their true nature; the patient, however, made some objection, and disappeared till the middle of September, when she returned, the swellings being larger than ever, and extremely painful.

She was again ordered iodide of potassium, in ten-grain doses, and a mercurial purge. The eye rapidly improved, and by the middle of October had entirely recovered, with normal vision. Subsequently, in January, 1881, the patient again came under treatment with severe interstitial keratitis of both eyes, from which she eventually recovered with rather thick corneal nebulae.

The second case was different from the first, in that the gummata was single, and affected the internal, as well as the external, surface of the sclerotic, projecting into the eyeball and displacing the retina to a considerable extent; and although the swelling eventually subsided, the eye was left blind from the total retinal detachment; and when the patient was discharged, the globe appeared to be shrinking.

In this, as in the other case, I was uncertain as to the nature of the tumour. On two occasions I fixed a day for excision of the globe, but was deterred from performing the operation by noticing some slight improvement. In this case excision would probably have been the best treatment, and may yet have to be performed.

In another case, that of a woman, the notes of which I have lost, the patient left another hospital because removal of the eyeball had been recommended; I certainly thought that no other treatment would be of much avail, but determined to try, with the result that, after some months of antisyphilitic treatment, and once or twice deciding to excise the eyeball, perfect recovery took place.

The diagnosis of gummata of the sclerotic is not easy. They appear as more or less prominent, well defined bosses, the conjunctiva over them is greatly congested, giving them a red appearance. They may be single, or there may be two or three swellings. They are likely to be confounded with sarcomata and episcleritis. From the former they can be distinguished more by their progress, which is, though slow, towards recovery, than by any distinctive physical signs. A syphilitic history, or other evidence of syphilis, should also put the surgeon on his guard. From the latter, by the more severe symptoms, larger size of the swelling, and its resistance to treatment. Further, they do not recur or shift their position, as is the case with patches of episcleritis. They may also be confounded with cystitis, or scleral staphyloma.

CASE I.—Mary Ann L., aged 27, case previously reported (BRITISH MEDICAL JOURNAL, October 23rd, 1882, p. 660), was under treatment from June 11th, 1880, till the middle of October, up to the fifth of which month the previous report extends. When first the patient came under my care the disease had existed nine months; she had been under treatment for some time. She was married, and brought with her a syphilitic infant suffering from purulent ophthalmia. The baby, however, was not her own, as stated in the report referred to. The conjunctiva of the right eye was congested throughout, but intensely so over the outer two-thirds of its ocular portion. Beneath it were three large bosses, the largest of which was situated about the insertion of the external rectus muscle; the other two were placed one above the other below the largest one. The appearance was that of staphylomata near the equator of