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On

Urea and Uric Acid

by

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A few words of apology, or rather explanation, are necessary, to prevent this Thesis from being misunderstood. When I determined to write on this subject, I was not aware that the time for receiving Theses, was more limited this year than in former years; and I was not prepared to give in my Thesis before July. Consequently the announcement made on wednesday last, that,—"Candidates for the degree must give in their Theses on or before saturday first the 18th June; otherwise they cannot graduate"—took me very much by surprise. Originally I intended to discuss this subject, in its relation to Goat, Phacuatism, & Albuminuria; but the limited time at my disposal rendered a fuller discussion impossible.

I may also mention, that I could not get access to several books, the perusal of which would have given me considerable assistance in the preparation of this Thesis. I may refer more particularly to Lehmann's Physiological Chemistry, which I could not procure, either from the University Library, or the Library of the College of Physicians—

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Urea - The ultimate chemical composition of this important substance is as follows - 2 atoms of Carbon, 2 of Nitrogen, 4 of Hydrogen & 2 of oxygen. As usually met with, it is prepared from Ferrocyanide of potassium, and exists in the form of delicate acicular crystals, which, by the aid of the microscope, are seen to be four-sided prisms. It is soluble in water and alcohol. Urea is an organic base, forming crystallizable compounds with nitric, oxalic & other acids. It exists in the urine in a state of solution, and may be demonstrated there, by adding to a small quantity of urine, evaporated to the consistence of syrup, an equal quantity of nitric acid, when a crystallization of nitrate of urea will take place.

The amount of urea excreted in a given time by a healthy individual is liable to considerable variation, and is stated differently by the various chemists who have analysed

it. The analysis by Becquerel is the one usually adopted. That chemist states the quantity of urea existing in 1000 parts of urine to be 14.238 grains. Assuming 35 oz. of urine to be the usual quantity of passed in 24 hours, we should thus have 239 grains or about half an ounce as the daily amount of the excretion of urea!

Uric acid - This is composed of 10 atoms of Carbon, 4 of Nitrogen, 4 of Hydrogen and 6 of Oxygen. It is best prepared from the excrement of the Boa constrictor, and when well ^{made} ~~prepared~~ consists of a shining powder, made up of distinct but minute crystals. The quantity usually stated to be excreted by a healthy man in 24 hours, is a little more than 8 grains, according to Prout pure uric acid requires 10,000 parts its weight of water to dissolve it.

The state in which it exists in the urine has given rise to much discussion! Dr Prout says that it exists principally in the form of urate of ammonia, while Liebig holds that it is combined with soda, to form urate of soda, Dr Golding Bird adheres to the view of Prout, and gives the following explanation as to the way in which it occurs.

"Uric acid, at the moment of separation from the blood, comes in contact with the double phosphate of soda and ammonia, derived from the food, forming urate of ammonia evolving phosphoric acid which thus produces the natural acid reaction of the urine".

In normal urine, uric acid may be demonstrated by adding to a quantity of urine, evaporated to half its bulk some Hydrochloric acid when a crystallization of free uric acid will

take place - When free uric acid exists as a deposit in the urine, it always possesses a crystalline form - These crystals are never colorless, but exhibit a variety of tints; being generally known as yellow or red sand - Urine depositing uric acid is generally of high specific gravity, often contains urea in excess, & is always acid. The crystalline forms which uric acid presents are various; but they may all be referred to some modification of the rhombic prism. Uric acid may occur in the urine, ^{as a deposit,} combined with alkalis to form urates.

Lehmann states that this deposit principally consists of urate of soda, mixed with very small quantities of urate of lime & urate of ammonia - The deposits of urates vary in color, and the characters of the urine containing them

are also various. The most common form of the deposit of urates is of a slightly higher colour than the urine, in which it is contained, and this latter is characterised by being of an amber color, acid reaction, & high specific gravity. They quickly disappear when heated and when acted on by liquor Potassae. When examined by the microscope, they are generally seen to be amorphous

The amount of uric acid thrown off from the system ~~varies~~ in a given time, varies, as regards the sex & period of life. DeCanu states as the result in 120 analyses, the mean proportion excreted in 24 hours to be - in old men 125.22 grains, in ordinary adults, 433.13 grains, & in women 295.15 grains. It is also much higher in children than in adults as compared with the

weight of their bodies. Thus
Lecanu, whose average calculation
is as stated above, gives 287.99 grains
as the average amount excreted by
children of 8 years of age, in 24 hours.
And Scherer states, that whilst, ^{in a man} ex-
cretes 2.94 grains for every pound
weight of his body, a child excretes
nearly double that amount.
A variation in the amount of
urea in the urine of a healthy
individual, is caused by mus-
cular exercise. Simon states that
in the urine passed after two
hours violent exercise, the prop-
ortion of urea was double that
contained in the morning urine.
And Schumann found that by
the substitution of violent for
moderate exercise the quantity
of urea was raised from $32\frac{1}{2}$ to
 $45\frac{1}{2}$ parts.

A difference in the amount
of the secretion of urea is also

observed, according as the food is rich in azote, or otherwise.

The amount of this variation is shown by Lehmann, who examined the excretion of urea by his own kidneys, while living at separate times, on a purely vegetable, purely animal, mixed, and nonnitrogenous diet. He found the amount of urea in the urine of 24 hours, while living on animal diet to be 819.2 grains, on vegetable diet 346.5 grains, on mixed diet 500.5 grains, on nonazotised diet 237.1 grains.

Certain drugs exert a remarkable influence on the amount of urea in the urine. Bocher has shown that the use of tea, as an article of diet, causes a manifest decrease in the amount of urea; while Lehmann has shown that the same result is attained through the use

of coffee, Lehmann found, that while the quantity of urea voided in 24 hours without the use of coffee, was 31.298 grammes, the amount under the use of $1\frac{1}{2}$ oz of coffee was only 21.888 grammes

Alcohol also causes a decrease in the amount of urea. Dr Pocker states that $13\frac{1}{3}$ grammes less urea is excreted when a spoonful of proof spirit is taken, than when ordinary water is drunk.

Tobacco has also a like influence.

There is a class of drugs which in this respect exert a diametrically opposite influence to the above, viz - an increase in the amount of urea. These are so far as is at present known, the alkalis, their carbonates & other salts especially those of the vegetable acids which are capable of being converted into carbonates in the system. Dr Golding Bird shews the result

in this respect of the administration of Zij of acetate of potash in 24 hours. The patient laboured under a condition of the orifice of the urethra, which required the use of the catheter; so that perfect accuracy, as to quantity, may be relied on.

Without medicine, there was 130.5 grains of urea, while with medicine there was 202.46 grains.

Drinking large quantities of water, especially of aerated water also causes an increase in the amount of urea excreted, although the solids are much decreased, relatively to the amount of urea passed, yet the absolute increase of the amount of urea, in 24 hours is considerable.

although normally only a very small quantity of urea leaves the system by the skin, yet the nitrogenous material into

which urea is convertible, is exhaled from it in considerable quantity.

In the above facts we have a ready explanation of the cures of chronic gout & rheumatism, which frequently take place at Hydropathic establishments, after all other remedies have failed. In those diseases, in which there is reason to believe there is a want of sufficient elimination of acrid matter, it is easy to see how cures may be accomplished, by the vast increase of the eliminative function of the skin & kidneys, brought on by means of drinking large quantities of water, & the use of the wet sheet, causing abundant perspiration.

That urea and uric acid are the main forms in which

the effete nitrogenised material is removed from the system, and that they may be likewise derived directly from animal food, when too much is taken to supply the wants of the system, are facts admitted by all. The processes by which urea and uric acid are formed, and the relations which they bear to each other, are not well understood.

Dr Prout believed that urea resulted from the transformation of the gelatinous tissues and that uric acid was produced from the albuminous. I do not know that Dr Prout has brought forward any grounds for this belief, and the statement is not worth much when we find, that in some animals little or no uric is secreted at all.

The theory of Liebig may be shortly stated as follows -
When the vital force of the

tissues is no longer able to withstand the influence, of the oxygen, carried to them by the capillaries, these textures combine with oxygen, pass through various forms, & ultimately leave the body in the form of urea & uric acid - ~~uric acid~~ ^{uric acid} is stated by Liebig, to be the most highly oxidised form, which the effete nitrogenous material can assume, & that, ^{uric acid} creatine, with creatinine & some other substances are merely different links in the stages of oxidation. According to this theory, therefore, the more freely the circulation of the blood takes place, the greater will be the transformation of uric acid into urea. By this is explained the large quantity of uric acid in the excrement of serpents, which being cold blooded, slowly respiring animals, bring little oxygen in

contact with their tissues. This theory also serves to explain the small quantity of uric acid produced by the quickly respiring tiger, whose food is much the same as that of the serpent.

Highly carbonaceous food by appropriating ^{much of} ~~the~~ the oxygen to form carbonic acid is said to prevent the transformation of uric acid into urea.

However plausible this theory of Liebig may at first sight seem, it will be found on enquiry that there are many facts opposed to it. Thus we find that the excrement of birds contains little or no urea, & large quantity of uric acid, yet if Professor Liebig's theory be true these animals live under the most favorable conditions for the development of urea. The phenomena observed in disease, also, instead of giving

any support to this theory, are in many cases directly opposed to it. We would expect to find uric acid, relatively in small quantity, in cases of acute inflammation, and in large quantity in Dyspnea.

So far from this being the case, we find that Picquet states the ratio of uric acid to urea, in Pulmonary Emphysema, with Dyspnea, to be 1 to 35, and in Milk Fever 1 to 7.47 and in Hepatitis 1 to 16.1; the ratio in healthy urine, ^{being} 1 to 31.48

although a very near relationship certainly exists between the chemical composition of urea and uric acid, and although the former is convertible into the latter, out of the body, by means of boiling with peroxide of lead; yet, when we take into account the facts stated above, I do not think, we are justified in the belief, that such a process

takes place in the living body. and further, the uric acid in guano although freely exposed to oxygen, and liable to considerable change in chemical composition, never, so far as I know, changes into urea.

The statement, that carbonaceous food, by appropriating the oxygen, prevents the transformation of uric acid into urea, is proved to be incorrect, by the experiments of Maguadie. He fed ~~animals~~ for carnivorous animals, for three weeks, on carbonaceous food, & found that uric acid disappeared from the urine. The experiments of Lehmann, also, prove the incorrectness of Liebig's theory. While living on an exclusively animal diet, that philosopher found, that the amount of uric acid, ~~in proportion to the~~ ~~was~~ excreted from his kidneys, was,

22.64 grains, on a mixed animal and vegetable diet. 18.17 grains, on an exclusively vegetable diet, 15.17 grains, and while living on a diet free from nitrogen the quantity was reduced to 11.24 grains -

However pleasing and beautiful the theories of Liebig and his followers, on these and other subjects, may be, yet in this case at least they do not correspond with facts. In their following the changes, which take place in the processes of living bodies, and representing them in numbers, it seems to me that they adhere too closely to the phenomena observed in ordinary chemistry, and do not sufficiently take into account, the modifying influence of the vital force.

That such influences are at work and that as far as our investigations are concerned they vary in different cases may be seen from the fact, of certain diseases, as Gout, occurring in persons, whose mode of life and every other circumstance are exactly opposed to the ordinary causes of that disease - as an example of how the ordinary results of chemistry may be modified, we may refer to the influence which platinum exerts on a mixture of oxygen and hydrogen, causing them to combine with explosion.

~~This oxygen theory of diseases is applied to the explanation of too many phenomena, and there is every likelihood, that in the subject of this essay~~

as well as in other Departments of Physiology and Pathology, that it will be perceived by others more near to the truth. Till that time arrives, let us hope that our minds as well as our bodies will be less subject than hitherto to the influence of this all-devouring element

Urea and uric acid are products of the metamorphosis of the tissues, and they may likewise be derived from primary digestion, when too much food is taken to supply the place of the worn tissues, but the reason why the effete nitrogenised material should in one organism, take the form of urea, and in another the form of uric acid, and the vital chemical relations, which these substances bear to each other,

are not known. I believe that the form of the excretion, is not much influenced by external & physical causes, but that it is determined in each case, by the influence of the vital forces peculiar to the constitution of the animal—

Metastasis of urea

In the lowest forms of plants and animals, we find that the same surface which serves to appropriate the new matter is adapted also for the removal of the old. The higher we ascend in the scale of organisation, however, we find that the provision for this function is rendered gradually more and more complex, until in man and the higher animals, we meet with a set of organs, each having its own peculiar function; these

organs are, the Skin, Lungs, Liver, Kidneys, and Intestines. Now as the elementary structure of these different parts is essentially the same, and as the duty of each is merely the modification of a general function, they are all to a certain extent dependant on each other. Although under ordinary circumstances, each of these parts of the excretory apparatus is limited to its own special duty, yet we can easily understand, that, when the function of any one is interfered with, by disease or otherwise, the others may to a certain extent act in its place. And we find that these complementary relations do exist between the different organs. Such a relation seems to exist between the Lungs and Liver, but it is much better observed in the case of the Kidneys and Skin. Not only may these

organs act thus vicariously for one another, but in certain diseased and other pathological states complete metastasis of excretion may take place. Thus it has been established, by observations in disease, and experiments on living animals, that urine may pass off from nearly any surface of the body. Such cases of metastasis are very frequent in hysteria - Dr Laycock in his "Lectures on nervous diseases of women" gives the following table of 125 cases of metastasis of urine, which occurred in hysterical patients. The numbers represent the relative frequency of each form -

Vomit	Stool	Ears	Eyes	Saliva
34	20	4	4	5
Nose	Mammæ	Navel	Skin	
3	4	34	14	

Mayer found that "when the two kidneys were extirpated in the Guinea-pig, the cavities of the peritoneum, and the pleura, the ventricles of the brain, the stomach, and the intestinal canal, contained a brownish liquid, having the odor of urine; the tears exhaled the same odor; the gall bladder contained a brownish liquid, not resembling bile; the testes, the epididymis, the vasa deferentia, and the vesiculae seminales were gorged with a liquid perfectly similar to urine." Chirac and Helvetius tied the renal arteries in dogs, and remarked that a urinous fluid was passed off from the stomach by vomiting. A case is quoted by Nysten in which, ~~the~~ no urine was passed by the urethra for 33 years, and during that time, sweats of a urinous odor, and vomiting of ~~a~~

Urine continued daily. There are cases in which, the mucous membrane of the bladder, must have secreted the urine, as the usual discharge took place to the end of life, and the kidneys were found, on dissection after death, to be so completely disorganised, that they could not have furnished the secretion. In cases of Bright's disease, Urea frequently exists in large quantity, in the watery evacuations of the intestines, produced by the action of elaterium and other cathartics. Urea also in cases of this disease often passes off in large quantities from the skin, and it is frequently found in the pleura, peritoneum, and ventricles of the brain. In cases in which the ~~urinary~~ secretion from the kidneys was deficient, a urinous fluid has been frequently observed to pass

from the skin. The critical
sweats, in which Gout sometimes
terminates, often contain Urates in
such abundance, as to cause a
powdery deposit on the skin —