1839

On

Urea and Uric Acid

by

William Douglas.
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 14th June; otherwise they cannot graduate" took me very much by surprise. Originally intended to discuss this subject in its relation to foot Rheumatism,Albumenuria, 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 Schwanau's Physiological Chemistry, which I could not procure, either from the University Library, or the Library of the College of Physicians.

June 18th, 1859
Urea—The ultimate chemical composition of this important substance is as follows: 2 atoms of Carbon, 2 of Nitrogen, 4 of Hydrogen, 1 of Oxygen. As usually met with, it is prepared from dimethylamide 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, salic, and 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 constancy 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
The analysis by Becquerel is the one ushally adopted. That chemist states the quantity of urea existing in 1000 parts of urine to be 18.238 grains. Assuming 35 oz. of urine to be the usual quantity passed in 24 hours, we should thus have 239 grains or about half an ounce as the daily amount of the secretion of urea.

Urie 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 made by the Boar constrictor, and when well prepared consists of a shining powder made up of distinct but minute crystals. The quantity usually stated to be exerted by a healthy man in 24 hours, is a little more than 8 grains. According to Prout's first unit 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 urine of ammonia, while Siedig 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 containing 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 acid urine depositing uric acid is generally of high specific gravity, often containing a small excess of its always acid. The crystalline form 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, combined with alkalies to form urate. Lehmann states that this deposit principally consists of urate of soda, mixed with very small quantities of urate of lime, urate of ammonia. The deposit of urates vary in color, and the character of the urine containing these
are also various. The most common form of the deposit of
waste is of a slightly higher
colour than the white wine in which
it is contained, and this latter
is characterised by being of an
amber color, acid reaction, high
specific gravity. They quickly
dissolve in water and are
acted on by diuretic agents. When
examined under the microscope, they
are generally seen to be amorphous

The amount of urea thrown off
from the system varies, as regards the
early period of life, because it is
the result of several analyses, the
mean proportion excreted in 24 hours
by - in old mead 125.22 grains, in
ordinary adults, 455.13 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, whose average calculation
is as stated above, gives 287.99 grains as the average amount excreted by
children 8 years of age, in 24 hours.
And Scherer states, that whilst, 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. Scherer states, that
in the urine passed after two
hours violent exercise, the propor-
ton of urea was double that
contained in the morning urine.
And Schenck found that by
the substitution of violent for
moderate exercise the quantity
of urea was raised from 32" to
25½ parts.
A difference in the amount
of the secretion of urea is also
Reserved, according as the food is rich in azote or otherwise. The amount of this variation is shown by Lehmann, who examined the excretion of ura by his own kidneys, while living at separate times on a purely vegetable, purely animal, mixed, and nonvegetables diet. He found the amount of ura in the urine of 24 hours, while living on an animal diet to be 819.2 grains, on vegetable diet 346.5 grains, on mixed diet 510.5 grains, on nonvegetables diet 237.1 grains.

Certain drugs exert a remarkable influence on the amount of ura in the urine. Dr. Segg has shown that the use of tea, as an article of diet, causes a manifest decrease in the amount of ura; 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 1/2 oz of coffee was only 21.888 grammes.

Alcohol also causes a decrease in the amount of urea. Dr. Becker states that 13 1/2 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. There are as far as is at present known, the alkalies, their carbonates, other salts, especially those of the vegetable acids, which are capable of being converted into carbonates in the system. Dr. Golding Bird shows the result
In this respect of the administration of 300 of acetate of potash in 24 hours. The patient laboured under a condition of the orifice of the urethe, 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 262.46 grains.

Drinking large quantities of water, especially of aerated water also caused 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 urine, yet the nitrogenuous material.
which rna 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
dall other remedies have failed.
In these diseases, in which there
is reason to believe there is a
want of sufficient elimination of
excreted matter, it is easy
to see how cures may be accom-
plished, by the vast increase of
the eliminative function of
the skin & kidneys, brought on
by means of drinking large quan-
tities of water, & the use of the
wet sheet, causing abundant
perspiration.

That rna & 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 Pront 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 Pront has brought forward any grounds for his 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 dielebig may be shortly stated as follows:

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 lead the body in the form of urea.

Uric acid is stated by Liebig to be the most highly oxidised form, which the effete nitrogenous material can assume, that, creatine, creatinuric, and 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 reptiles, 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 urea acid produced by the quickly respiring tiger,
whose food is much the same as that of the serpents.
Highly carbonaceous food by appropriating much of the oxygen to
form carbolic acid is said to
prevent the transformation of
urea 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 it was found that the
excrement of birds contains little or no urea, a large quantity of
urea 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
for the disease, also, instead of giving
any support to this theory, are in many cases directly opposed to it. We should expect to find ureic acid, relatively in small quantity, in cases of acute inflammation, and in large quantity in Dyspnoea. So far from this being the case, we find that Pasquerel states the ratio of ureic acid to urea, in Pulmonary Emphysema, with Dyspnoea, to be 1 to 3.5, and in Miliary Fever 15 to 47, and in Hepatitis 1 to 10.1; the ratio in healthy urine, 1 to 31.4.

Although a very near relationship certainly exists between the chemical composition of urea and ureic acid, and although the former is convertible into the latter, out of the body, by means of boiling with permanganate of lead; yet, when we take it to 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 is
gradually exposed to oxygen, and liable to con-
derible change in chemical
composition. Never, so far as I know,
changes into urea.

The statement, that carbo-oro-
ous food, by appropriating the
oxygen, prevents the transformation
of uric acid into urea, is proved
to be incorrect, by the expeiments
of Magendie. He fed animals for
several months for
brushous animals, for three
weeks, on carbo-hydrates food, and found
that uric acid disappeared
from the urine. The experi-
cuts of Lehmann, also, prove the
incoherence of Liebig's theory.

While living on an exclusively
animal diet, that philosopher
found, that the amount of
uric acid, in proportion to the
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, and 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, for instance, 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 general theory of chemistry is applied to the explanation of too many phenomena, and there is every likelihood that in the subject of this essay
as well as by other departments of physiology and pathology, that it will be replaced by others more near to the truth. If that time arrive, 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 purulent digestion, when too much food is taken to supply the place of the worn tissues. But the reason why the excreta 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 operation 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 Wound

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. Nor 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 dependent 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 extravasated 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. Landolff in his book "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.

<table>
<thead>
<tr>
<th>Vomit</th>
<th>Stool</th>
<th>Ear</th>
<th>Eyes</th>
<th>Saliva</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>20</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nose</th>
<th>Mammary</th>
<th>Navel</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>4</td>
<td>34</td>
<td>14</td>
</tr>
</tbody>
</table>
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 caecal, contained a brownish liquid, having the odor of urine; the tears expelled 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." Chirae 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 Nesperus in which the no urine was passed by the urinaria for 33 years, and during that time, a fluid of a urinous odor, and vomiting of
Wine 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 disorganized that they could not have furnished the secretion. In cases of Bright's disease, urine frequently exists in large quantities in the watery evacuations of the intestines, produced by the action of chloridium and other cathartics. Meat also in cases of this disease often passes off in large quantities from the skin, and it is frequently found in the pleura, peritonem, and ventricles of the brain. In cases in which the urinary secretion from the kidneys was deficient, a purulent 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—