

# U r e i n e <sup>1)</sup>.

By **W. Ovid Moor**,

of New-York City, U. S. A.

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About one year ago I began studies regarding substances, which could be easily oxydized and which gave as a proof of their easy oxydability the characteristic blue reaction which we observe, when we bring in contact morphine with a solution of Ferrid-Kalium-Cyanat and Ferrum-Sesquichloratum. To my great astonishment I found that the human urine contained a large quantity of some organic substance, which gave this blue reaction in a very intense manner. Numerous and exact investigations forced me to the conclusion, that none of the known organic or inorganic substances of the urine could account for this blue reaction, and that therefore some until the present unknown chemical body must be the cause of this strange phenomenon. For the last three months I labored in vain to isolate this mysterious body, until at last, on July 5 th, 1900, I discovered, that the human urine contained a liquid organic body, in a quantity superior to urea (Harnstoff). It is not surprising that the existence of a metabolism-product of such paramount importance should have escaped the observation of all investigators, for every urinary analyses until the present moment has been made with the firmly rooted idea, that urine is a liquid composed of water and inorganic and organic solid ingredients.

For obvious reasons it must be evident, that the principal scope of this communication will be a description of the method to be employed for the isolation of this new constituent of urine; an accurate knowledge of its physical and chemical characteristics and of its clinical importance in relation to the pathological conditions of the body can be only the result of careful and assiduous investigations by serious workers all over the world.

In isolating this organic liquid, two principal rules should be followed:

- 1) Avoidance of high temperatures.
- 2) Avoidance, as far as possible, of chemicals.

The urine to be examined for its organic liquid should be put in a large, shallow, flat recipient and should be evaporated at a temperature of not over 50° Celsius. If the quantity of the urine should be considerable, it would be advisable to evaporate simultaneously in several recipients. As soon as we observe that there is no more vapor ascending from the recipient for about ten

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<sup>1)</sup> Nous faisons paraître ce travail uniquement parce que notre jeune savant Kouljabko a jugé nécessaire de contrôler les déductions plus qu'étonnantes de Mr. Moor. Le travail de Mr. Kouljabko suivra immédiatement celui de Mr. Moor. Note de la Rédaction,

or fifteen minutes, the remainder of the liquid is poured into an appropriately small cup and heated to 65° Celsius. New aqueous vapor will be forming and the temperature must be kept at 65° C., as long as this is the case. As soon as the formation of vapor ceases, we may assume that very little water has remained. To determine, however, accurately whether or not the rest of the liquid contains water, the following delicate test will be indispensable: By placing an ordinary thermometer with a long and narrow mercury bulb into the liquid and rapidly withdrawing it just at 65° C., we will probably see a puff of vapor ascending from the mercury bulb, which is an indication that some water is still present in the remainder of the urine. This procedure is repeated at short intervals and finally we will arrive to a point, when there is no more vapor ascending from the mercury-bulb. Now we can feel certain that most, or rather nearly all of the remaining liquid is nothing less than the heretofore unknown component of the urine. We now measure in a small measure glass the amount of organic liquid obtained and add to it the same amount of absolute alcohol together with 0,5 (five decigramm) of pure, powdered oxalic acid for each 100 Cubic centimeter of urine evaporated. The newly formed Urea-Oxalate being practically insoluble in such a small quantity of alcohol, can be easily separated together with most of the solid ingredients of the urine by filtrating the alcoholic liquid through a very small filter, provided, however, that the same (the liquid) has been allowed to cool off sufficiently. Should a new precipitate form in the filtrate, an additional small quantity of alcohol should be added to it and the whole should be filtered again through the old filter in order not to lose unnecessarily any however small portion of the new organic substance; for the same reason it is advisable to wash out carefully the first and second recipient with a little alcohol, which is to be added to the referred to.

We now evaporate carefully the alcoholic solution of our organic body, until every trace of alcohol has disappeared. When the presence of alcohol is no more noticeable either through smell or through a slight vapor, we let stand the remaining reddish-brown liquid until cooled off and turn around and around the latter for some length of time in its recipient, until all solid particles of urea and salts have separated and have stuck to the sides of the cup. There is finally nothing left in the recipient but the organic body in question together with the coloring matters of the urine, principally the «Urochrom». To separate the coloring matters from our organic body, the latter must be treated with a saturated solution of Mercury Nitrate (**Mercuric**,  $\text{Hg}(\text{NO}_3)_2$ ) until no further precipitate is forming. Filter again and evaporate carefully, resorting at short intervals to the test above referred to (heating to 65° C. and examining with longmercury-bulb thermometer as to the formation of vapor). The liquid thus obtained resembles in aspect olive-oil, is of a pale yellow color, of a slightly bitter taste, gives to the touch the impression of a fatty substance, produces on paper spots resembling fat spots, though not so markedly as spots produced by fat. Its specific gravity is about 1,065. Its quantity is about **double** that of urea.

I have found as much as 75 (seventy-five) gramms in 24 hours, and as

little as 30 grammes in 24 hours, but always twice as much as urea. It is freely miscible in all proportions with water and alcohol, whether neutral, acid or alkaline in reaction; its own reaction is very slightly alkaline, almost neutral. My preliminary investigations have led me to the conclusion that this body belongs to the group of alcohols of the aromatic series; at a temperature of about 80° Celsius it begins to split into several bodies belonging to the class of aromatic oxyacids, and if heated to above 120° Celsius, it leaves behind pure Carbon. This organic liquid has a characteristic odor; in fact, it is **this** constituent of urine, which is the cause of its specific odor. It is able to take up a large quantity of Oxygen with great facility: fifty cubic centimeter of the average human urine are able to deoxydize two grammes (2,0) of Potassium Permanganate. When subjected for some length of time to the influence of 70°—80° Celsius, it loses in a great measure its capacity of taking up Oxygen. It does not take up all at once all the Oxygen which it is able to absorb, but does so with great avidity in the beginning, and gradually takes up less and less during equal periods of time; its capacity of absorbing Oxygen is not wholly extinguished before a lapse of about 20 days! This organic liquid is of the very greatest importance in the economy of nature, as the urea cannot be decomposed without its presence into  $\text{NH}_3$  (Ammonia) and  $\text{CO}_2$  (Carbon-Dioxide), and thus within a limited period all organic matter would be changed into urea, which would remain in nature without any use, and consequently all vegetation and animal—as well as human life would cease sooner or later, for it is evident that the amount of organic matter existing upon this globe remains the same no matter how the physical form and chemical constitution of this organic matter may become changed. Our newly found organic liquid being of a sticky nature adheres to the smallest particles of urea, takes up Oxygen in large quantities, which in turn acts upon urea, and thus is the principal cause of the amoniacal fermentation of urine. I have oxydized different urines with permanganates, leaving the latter in contact with the urine for one week, and found that such urine whose liquid organic component had been completely oxydized, does not undergo amoniacal fermentation. Furthermore, I have dissolved pure urea in ordinary, not sterilized water, and have found that the urea was not decomposed after five days, so that I could through addition of Nitric Acid convert this urea into Urea-Nitrat, just like any other fresh urea. It will undoubtedly be gratifying to all investigators to learn, that this wonderful product of animal body-metabolism is the **long sought cause of those complex toxic symptoms**, which have been designated by the collective name of **Uraemia**, and to which have been attributed the awful toxic phenomena, so frequently incidental with the puerperium. Rabbits weighing over one Kilogramm, have succumbed after about 8—10 hours to 4 or 5 Cubic Centimeter of this poison, showing symptoms resembling somewhat those of morphine poisoning; the animals remained quietly for hours on the same spot, turning now and then in a circle around the same point, being evidently extremely nauseated, lacking muscular power, being motionless, when held up by their ears, refusing food, though not having eaten for several hours, and dying amid

convulsions. Their respiration, however, was very fast, about 140 per minute, and very irregular. Vomiting and diarrhea were absent; there was neither salivation nor perspiration.

Considering the fact, that this liquid organic constituent of urine is practically the most characteristic component of urine, giving to it its characteristic odor, being indispensable for its amoniacal fermentation, occuring in quantities superior to urea, and being the principal cause of the uraemic phenomena, I consider the most appropriate name for this wonderful chemical body: «Ureine» <sup>1)</sup>.

Rome, Italy, July 15, 1900.

## Ueber Dr. Moor's «Urein» und dessen physiologische Wirkung <sup>2)</sup>).

Von Dr. A. Kuljabko,

Pr.-Docenten an der Universität und Laboranten der physiologischen Abteilung der Akademie der Wissenschaften zu St.-Petersburg.

Dr. W. O. Moor in New-York übersandte im September 1900 des Kais. Akademie der Wissenschaften einen Bericht über die von ihm im normalen menschlichen Urin entdeckte neue Substanz «Urein», welche die Menge des Harnstoffs um das Doppelte übertreffen und sich durch stark reducirende und giftige Eigenschaften auszeichnen soll. Auf Grund der Untersuchungen des Referenten ist die nach Dr. Moor's Angaben erhaltene Substanz keine selbständige chemische Verbindung und die Herstellung derselben unsicher, wobei die Reinheit des Präparats durch nichts garantirt ist. Das Urein enthält viel Wasser, Harnstoff und mehrere andre Bestandteile des Urins und stellt ein von Alkohol und zum Teil von Harnstoff befreites weingeistig-wässriges Extrakt des Urins vor. Die giftige Wirkung desselben auf die Tiere erinnert in allgemeinen Zügen an diejenige der Extraktivstoffe des Urins und unterscheidet sich davon nur durch gewisse Einzelheiten. Bei der Vergiftung mit dieser Substanz werden ebenfalls die Nervencentra, namentlich das Atmungscentrum getroffen, was eben die Ursache des Todes ist. Sogleich nach der Einführung der

<sup>1)</sup> Pronounce: U-re-in.

<sup>2)</sup> Kurzes Referat über den am 13 Oktober 1900 der phys.-math. Abteilung der Akademie der Wissensch. zugestellten Bericht und die am 18 December stattgehabte Mitteilung in d. Gesellschaft für Volkshygiene.