ON THE ESTIMATION OF URIC ACID IN THE URINE: A REPLY TO CRITICISMS UPON THE SILVER METHOD.

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I PUBLISHED in the BRITISH MEDICAL JOURNAL of December 12th, 1885, a method invented by me for the easy and yet accurate estimation of uric acid. The method consists in precipitating the uric acid as a silver salt, estimating the silver, and calculating the uric acid from the silver (168 uric acid to 108 silver). As no process was then invented which had itself been tested, except as Salkowski's, by the side of others acknowledged to be inexact, I did all my work with weighed quantities of uric acid, and tested my process—the only straightforward way of working—by adding known quantities of uric acid to one of two samples of a urine, finding, as a result of my estimations of the uric acid in the two samples, practically the same difference as the weight of acid added. Hermann confirms my work,¹ and Czapek, working with Professor Huppert, proposes a modification of my method, while Camerer's results² run on parallel lines. My results have been adversely criticised by Salkowski, who still maintains that uric acid and silver do not combine in a definite ratio. This observer published in 1872 twelve analyses which show, as he believes, that there is no constancy in the proportion between the silver and uric acid, and again in 1889 he reaffirms the same thing, bringing forward in proof of his assertion some dozen analyses made by his colleague, Professor Jolin, and himself. I was for some time unwilling to take up the controversy where Professor Salkowski had left it; being conscious of the care with which my own work had been done, I was quite willing to let the matter be settled by others and less prejudiced workers, especially as such seemed willing enough to undertake the task. As, however, my method had been widely used, especially for clinical purposes, and as I had frequently to answer queries concerning its accuracy, I felt it my duty carefully to examine once more the whole question, and, if there was any doubt about it, at once to set that doubt at rest. I was, I confess, agreeably surprised to find that Professor Salkowski had made a slight mistake, which, when rectified, places his own results and mine in complete accord. In order to make this point quite clear, I will venture to reproduce Professor Salkowski's results, arranging his analyses in order, beginning with the one having the least uric acid.

Salkowski's First Table (1892).

No.	1 Silver obtained.	2 Uric Acid reckoned from 1.	3 Uric Acid obtained.	4 Difference in Milli-gramme.	5 Ratio between Uric Acid.
1	0.029	0.045	0.033	-12	4.1 : 3
2	0.035	0.051	0.040	-11	1.09 : 3
3	0.037	0.057	0.042	-15	4.2 : 3
4	0.045	0.070	0.056	-14	3.71 : 3
5	0.046	0.071	0.051	-20	4.03 : 3
6	0.043	0.077	0.056	-21	4.02 : 3
7	0.050	0.078	0.067	-11	3.43 : 3
8	0.051	0.079	0.100	+21	2.24 : 3
9	0.051	0.084	0.070	-14	3.36 : 3
10	0.060	0.091	0.083	-11	3.63 : 3
11	0.061	0.100	0.088	-12	3.41 : 3
12	0.073	0.114	0.086	-28	3.96 : 3

I think No. 8 is evidently a spoilt analysis, for no similar result is ever again to be found in the tables of Salkowski, Jolin, Hermann, or Czapek, and the last urine, No. 12, must be considered under the head of "urine saturated with uric acid." Such urines, and Czapek estimated some of these, stand by themselves and probably require dilution before the analysis is made. Omitting these two cases, and arranging the results as I have done, it is evident that there is in each case an excess of the uric acid estimated from the silver over

that actually found by Salkowski's own process of about 14 milligrammes. (See Col. 4.) This difference is as constant as one can expect, for Jolin and Salkowski, in performing two check-analyses of the uric acid in one and the same urine by one and the same process, fail to make them coincide by 3 or 4 milligrammes. What Salkowski proves, therefore, is that by his method about 14 milligrammes less uric are found than by the silver calculation.

The mistake he falls into in interpreting his results will be obvious on referring to column 5 of the table. He here calculates the ratio between the silver and uric acid found by his method, and does not find it constant. The reason is very obvious, for in the weaker urines the loss of 14 milligrammes will be comparatively a heavy loss, making the ratio of the uric acid to the silver low, while in the stronger urines the loss will be less felt. A glance at the table will show this, for the silver in the upper part of the table is say 4.1 to 3, while in the lower part it sinks to say 3.4 to 3. The loss of a pound is much to a poor man, but will not inconvenience a rich one, because it bears a small ratio to the sum that he possesses.

In Jolin and Salkowski's recent paper the same error is repeated without discovery, the table of estimation they give showing a "constant difference" as a result of their estimations. In the last two pages of his article this is shown very forcibly in the case of two final experiments Salkowski makes, estimating both the silver and the uric acid (by his method) in one and the same urine.

No.	Uric acid reckoned from the silver.	Uric acid directly estimated (Salkowski).	Difference.	Ratio between silver and uric acid.
1	0.0756	0.0556	19.1	3.99 : 3
2	0.0938	0.0757	18.1	3.66 : 3

He says: "Das Äquivalentverhältniss zwischen Harnsäure und Silber berechnet sich aus Versuch 1 = 3 : 3.90 aus Versuch 2 = 3 : 3.66. Auch diese Bestimmungen bestätigen also lediglich meine früheren Angaben." It is obvious that a constant difference of about 19 milligrammes (more urine was used in this case, hence the greater deficit) was all he really proves, and this constant deficit tells most in the case of the weaker urine.

Salkowski would not have misinterpreted his results had he arranged them with sufficient care or put in a column of differences, which I have taken the liberty of adding. His results are therefore valuable evidence in favour of the silver process, for a constant difference, such as he obtains, would not be possible were the compound (we will call it urate of silver) of unfixed and varying composition, and therefore his own results prove the proposition he intended to destroy.

The constant difference of 14 milligrammes is due at any rate in part to the imperfections of his own method, which he had never taken the trouble to test, merely comparing his results with those obtained by the inexact method of Heintz. This difference has been reduced to within the limits of manipulative error by Hermann and Czapek, when comparing the silver method with the method introduced by Ludwig.

Mr. Gossage has also criticised my method on the same grounds as Salkowski, but I am afraid that his results must suffer a totally different explanation. He gives five estimations in which he obtains the uric acid by the silver method and by Salkowski's method. His results may therefore strictly be compared with the exactly similar ones of Salkowski and Jolin. His average difference is 32 milligrammes, which is more than the extreme difference obtained by the other chemists (28 milligrammes). If we accept the results of Salkowski and Jolin as trustworthy we are forced to look upon Mr. Gossage's analyses as untrustworthy, and indeed his least manipulative error is greater than the greatest ever quoted by them. (I have discussed this subject in detail in the last number of Hoppe-Seyler's *Zeitschrift für physiol. Chemie.*)

THE GUY MEDAL.—At the fifty-seventh annual general meeting of the Royal Statistical Society, held last week, it was resolved to found a gold medal, to be called the Guy Medal, to commemorate the services of the late Dr. Guy, the eminent authority on forensic medicine. The medal will be awarded from time to time as a recognition of original statistical work.

¹ *Zeitsch. f. physiol. Chemie*, Bd. 12, S. 496.

² *Zeitsch. f. Biologie*, Bd. 27, S. 115.