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REFERENCES.

¹ *Münchener med. Woch.*, August 24th, 1897. ² *Münchener med. Woch.*, November 2nd, 1897. ³ Abstract of papers by Einhorn and Heinz, also Neumeyer, by Leech in *Manchester Med. Chron.*, December, 1897. ⁴ *Pharm. Journ.*, (3) xvi, 1897. ⁵ *Berl. klin. Woch.*, 1887, p. 107. ⁶ *Deut. med. Woch.*, 1890, No. 32. ⁷ *Archiv. für exper. Path. und Pharm.*, 1891, p. 301. ⁸ Ehrlich and Leppmann, *Deut. med. Woch.*, 1890, p. 23. See also *Pharmaceutical Journal*, September 25th, 1897; *EPITOME OF THE BRITISH MEDICAL JOURNAL*, ii, 1897, pars. 279 and 533.

A NEW VOLUMETRIC METHOD OF ESTIMATING URIC ACID IN URINE.

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In a preliminary communication in the *BRITISH MEDICAL JOURNAL*,¹ one of us (Tunncliffe) drew attention to the solubility in water of urate of piperidine, the salt formed by the action of piperidine on uric acid. This property of piperidine to combine in molecular proportion with uric acid and the solubility of the resulting salt form the fundamental principles of our method.²

If the uric acid is separated from the urine by any of the known methods, and the resulting acid be suspended in water to which a few drops of an alcoholic solution of phenolphthalein have been added, there will be no colour reaction upon the addition of piperidine solution until all the acid is dissolved. If after this point has been reached any further piperidine be added it will remain as such, and by virtue of its alkaline reaction will cause the development of a red colour. Until all the uric acid is dissolved, any piperidine falling into the liquid will be at once converted into piperidine urate, which latter produces no colour reaction with phenolphthalein. By using a solution of piperidine of known strength, the amount which must be added to produce the clearing of the liquid and the development of the purple colour, gives by a simple calculation the amount of uric acid present.³

The method resolves itself into three distinct procedures:

1. The preparation of the standard piperidine solution.
2. The obtaining of the uric acid in a pure state from the urine.

3. The titration of the same with the standard solution.

1. We found a $\frac{1}{10}$ normal piperidine solution most suitable. This may be standardised by estimating the amount of it which is required to neutralise a certain amount of a $\frac{1}{10}$ normal acid solution. We do not purpose here giving any fuller directions with regard to the preparation of the $\frac{1}{10}$ normal piperidine solution. To those possessed of a chemical training this would be superfluous, those unpractised in the preparation of standard solutions are advised to purchase the solution from a firm of manufacturing chemists.⁴

2. The uric acid may be obtained from the urine in several ways. The one which we have used, and consider the best, is the method described by Hopkins,⁵ which consists in precipitating the uric acid from the urine with ammonium chloride, that is as ammonium salt, and subsequently decomposing with hydrochloric acid. The uric acid obtained from 100 c.cm. of urine by this method is carefully filtered and freed from hydrochloric acid by washing with water until the washing shows no reaction with Congo paper. For this purpose we have found 15 to 20 c.cm. of water suffice, if an unreasonable excess of hydrochloric acid has not been taken.

3. The pure acid is rinsed with 20 to 30 c.cm. of hot water off the filter paper into a small vessel. Although the urate of piperidine, as we have shown elsewhere, is soluble at 15° C. to the extent of 5.3 per cent., we regard it as advisable in order to obtain a sharp end reaction to bring the fluid which is to be titrated up to the boiling point. A few drops of an alco-

holic phenolphthalein solution are then added, and the piperidine solution allowed to run in from a burette, the liquid being the while kept hot. The complete saturation of the uric acid present is shown by the appearance of a red colour which remains on shaking, and also by the fact that no uric acid remains undissolved.

Since 1 c.cm. of a $\frac{1}{10}$ normal piperidine solution corresponds to 0.00425 g. piperidine, and this is equal to 0.0084 g. of uric acid, the number of c.cm. required to produce the end reaction described above multiplied by 0.0084 will give the amount of uric acid present. In those cases in which 100 c.cm. of urine was the amount originally taken, it is obvious that the number thus obtained will give the percentage of uric acid in the urine.

It may be of interest here to subjoin the following comparative table, which gives the amounts of uric acid present in several urines, as estimated by weighing and by titration with piperidine. The method was to take two portions, of 100 c.cm. each, of each urine, and to estimate the uric acid by titration in one case, and by weighing in the other.

	Uric Acid by Weighing (Hopkins).	Uric Acid by Titration.	Difference.
			Mg.
Urine with an abnormally large percentage of uric acid	0.1056	0.1042	- 1.4
Normal urine	0.0809	0.0809	± 0
"	0.0818	0.0827	+ 0.9
"	0.0849	0.0846	- 0.3
"	0.0640	0.0647	+ 0.7
"	0.0799	0.0786	- 1.3
"	0.0550	0.0559	+ 0.9
"	0.0424	0.0422	- 0.2
"	0.0716	0.0728	+ 1.2
"	0.0809	0.0809	± 0
"	0.0923	0.0909	- 1.4
"	0.0799	0.0777	- 2.2
"	0.0674	0.0674	± 0
"	0.0426	0.0423	- 0.3

From these experiments it will be seen that the average difference between these two methods amounts to $-\frac{1}{10}$ mg. The difference is so small as to be practically negligible. The probable explanation of it is that the urinary pigments thrown down with the uric acid are, in the case of the weighing estimations, weighed with it; in the case, however, of the titration, they remain unattacked by the piperidine solution, and thus do not vitiate the result.

NOTES AND REFERENCES.

¹ February 27th, 1897. ² For the proof that piperidine and uric acid combine in molecular proportions readers are referred to the authors' article in *Centralblatt für Physiol.*, xi, No. 14. ³ *BRITISH MEDICAL JOURNAL*, February 27th, 1897. ⁴ At the request of the authors Messrs. Baird and Tatlock, of Cross Street, Hatton Garden, have undertaken to supply the piperidine solution ready for use. ⁵ *Jour. of Path. and Bact.*, 1893, p. 458. See also G. v. Ritter, *Zeitsch. für phys. Chemie*, xxi, 288.

MITRAL STENOSIS: A STATISTICAL INQUIRY.

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In [the *BRITISH MEDICAL JOURNAL* of November 28th, 1896, I communicated a paper on the above subject, and endeavoured to show, from the *post-mortem* statistics of cases of mitral stenosis during four years at Guy's Hospital, that "the characteristic alteration in the left auricle in mitral stenosis is not dilatation but hypertrophy," and that the necropsy excessively exaggerates the importance of dilatation, which probably is introduced only with the auricular breakdown, and is thus an "old age phenomenon in the history of mitral stenosis."

I have lately analysed the *post-mortem* reports of all the cases of death at Guy's Hospital in the ten years 1886 to 1895 inclusive, in which stenosis of the mitral orifice was found present. The results appear to me sufficiently interesting to be worth recording.

In 4,791 necropsies during this period, there was a total of 196 cases (about 4 per cent. therefore of all examined) in which