Medical Memoranda

Simplification of the Ferric Chloride Test for P.A.S. in Urine

It has been shown (Venkataraman *et al.*, 1948) that most of an ingested dose of *para*-aminosalicylic acid (P.A.S.) is excreted in the urine within a few hours. Several tests for its detection have been used (Penman and Wraith, 1956; Simpson, 1956; Ruiz, 1957). Because of their greater sensitivity and distinctive violet colour, the tests based on the reaction of salicylates with ferric chloride are those most favoured.

The disadvantage of the ferric chloride test on undiluted urine as used by Simpson (1956) is that heavy precipitates frequently form, making interpretation very difficult. Dixon *et al.* (1957) have described a modification consisting of considerably diluting the urine used. It certainly overcomes the difficulties caused by precipitation, but it is more complicated to carry out, necessitating measuring 5 ml. of water and adding 0.1 ml. or 6 drops of urine and 1 drop of 3% ferric chloride solution.

The test described was developed as a simple method for field work in a primitive country, but has applications other than this. It can be used in any clinic, and is much more simple to perform than either of the tests mentioned above.

METHOD

The patient is given a piece of white blotting-paper measuring approximately 1 by 4 in. (2.5 by 10 cm.) and told to wet one end with his urine. The blotting-paper has previously been marked with a number or other identification on the end he is given to hold. On its return a single drop of 3% ferric chloride solution is dropped on to the wetted blotting-paper. The presence of P.A.S. is shown by an immediate reaction, which may vary from an intense violet-black colour to a violet ring around the spreading yellow spot of ferric chloride solution. In more civilized places the strip of blotting-paper would simply be dipped into the urine, which had been collected in a container, and then the test carried out as described.

This test has the advantage of using undiluted urine, so that positive results are less likely to be missed, without the disadvantage of precipitation to interfere with the interpretation of the result.

In some instances a brown ring forms around the yellow spot of ferric chloride solution, but this is easily distinguished from the violet colour of a positive reaction.

By adding known quantities of P.A.S. to urine it was shown that concentrations as low as 25 mg./100 ml. could easily be detected. The test on undiluted urine (Simpson, 1956) will detect even lower concentrations, such as 5 mg./100 ml., provided the urine is not dark in colour and that precipitation does not occur. However, this greater sensitivity is of no practical significance. The test on diluted urine (Dixon *et al.*, 1957) will detect 100 mg./100 ml., provided the urine is not very dark in colour, but at a level of 50 mg./100 ml. it is negative.

In some of the ferric chloride tests previously described it has been the practice to add hydrochloric

acid. Many tests have been done in the present series with and without this addition, without any apparent effect on the results.

RESULTS

Tests were made of the urine of 319 out-patients, who were all on 3 g. of P.A.S. three times a day. Little significance should be accorded to the low percentage of positive results, since the patients were seen at the end of the period (one month) for which their chemotherapy had been prescribed, and often finished their P.A.S. a day or two before. Unlike experience with European patients (Dixon *et al.*, 1957), very few failed to take their P.A.S. because of its unpleasant gastrointestinal side-effects. Spontaneous complaints were rare, and on direct questioning only 8% of this series admitted ever having had any such symptoms. Those who had experienced this trouble had usually overcome it by taking the drug with food. A small series of 61 patients visited unexpectedly mid-month gave 89% positive results with the blotting-paper test.

Tests were done on undiluted urine as described by Simpson (1956), on diluted urine as described by Dixon *et al.* (1957), and with blotting-paper as described above.

Tests on 319 Out-patients at End of P.A.S. Therapy

Undiluted Urine:				
Definite positive	..	..	..	106 (33%)
Precipitate sufficient to obscure the result	..	..	..	64 (20%)
Diluted Urine: positive	..	..	..	115 (36%)
Blotting-paper: positive	..	..	..	124 (39%)

A further assessment of the blotting-paper test was carried out on a small series of in-patients. They comprised 13 having P.A.S. 5 g. 12-hourly, and 18 having P.A.S. 3 g. eight-hourly. On the day of the test the latter group missed one dose in order that the tests could be continued for 10 hours after the last dose of the drug. Urines were tested every two hours, and all were positive up to and including those collected 10 hours after they had had their P.A.S.

COMMENT

Of the tests on undiluted urine it was found that 20% produced precipitate in such quantities as to obscure their interpretation. The tendency is to call these positive, yet in this series it was found that only a third of them gave positive results with either of the other two tests used.

The test on diluted urine is not so sensitive as the blotting-paper test, and is more difficult to carry out. The difficulty is not great, but the test is time-consuming, which may be of importance in a busy clinic.

The blotting-paper test described can be performed very rapidly, is easily read, and is sensitive enough for the practical purpose of determining whether or not the patient is adhering to the regime of P.A.S. prescribed for him.

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