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## Urine Color Testing and Isoniazid Monitoring

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To the Editor:

We read the article by Eidlitz-Markus et al (March 2003)<sup>1</sup> and the accompanying editorial<sup>2</sup> with great interest. We agree about the importance of improving patient adherence to antituberculous therapy and acknowledge the potential benefits of using the Arkansas method for monitoring compliance by testing a urine sample for breakdown products of isoniazid. However, we have severe reservations about this method, especially if used by a family physician. The method used involves using prepared stock solutions, including that of potassium cyanide, and adding varying numbers of drops of these reagents to a urine sample.<sup>3</sup> The risks involved in handling and storing such reagents in physicians' surgeries and other extralaboratory environments is very significant.

We therefore took these reagents and enclosed them inside a patented plastic testing device (SafeTube; University of Birmingham; Birmingham, UK), which safely contains the toxin reagents before use and seals the urine and reactants after use, with the testing kit disposed of in a "sharps" bin. This also reduces the likelihood of exposure to urine samples, which may be infected with viruses such as HIV. The testing device contains a 2-mL syringe for measuring a specific volume of urine, which is then added to tableted reagents and mixed, with a sample positive for isoniazid metabolites turning dark blue in a matter of seconds and a stable result present at 5 min.

We have evaluated this test in a busy hospital tuberculosis outpatient clinic, recruiting patients who were receiving daily therapy with isoniazid, and the vast majority (97%) receiving it in combination with rifampicin. In a cross-sectional study to compare this new test with the visual appraisal of the presence of orange staining of the urine from rifampicin, we collected urine samples from 131 patients. Of these, only 48% had orange-stained urine. The time interval from the last reported dose varied from 40 min to 23 h. Positive test results for isoniazid were obtained from 94.6% of patients, with the remaining seven patients (3.4%) producing a color change indicating partial or noncompliance, so indicating failure to abide by treatment instructions.<sup>4</sup>

This figure is much lower than the 28.5% nonadherence found by Eidlitz-Markus et al,<sup>1</sup> but his patients were all being treated for latent tuberculosis infection, whereas our patients were largely being treated for active tuberculosis disease. We therefore welcome the problem of nonadherence being highlighted, but we think we have a much more convenient, more safe, and less technically demanding method than the assay using wet chemistry. Our studies indicated that the new test was a useful guide for patients who required extra monitoring and further education as to the importance of taking their drugs every day, or those who required directly observed treatment.

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To the Editor:

We read with great interest the letter of Drs. Whitfield and Cope about their method to check metabolites of isoniazid in urine in a patented plastic testing device (Safe Tube; University of Birmingham; Birmingham, UK). We agree that although the cost of the Arkansas method<sup>1</sup> is very cheap (\$0.06),<sup>2</sup> some of its reagents may be dangerous to sick children or debilitating old patients. If safety precautions to prevent the contact of patients with these reagents cannot be taken, the new method should be considered. We did not receive information whether the new test was empirically checked and compared to the original Arkansas method, and how long after the last dose received by the patient the test was done.

A double-controlled study, comparing the two methods with the same urine samples, should be done. If the new test will be found to be as informative as the Arkansas method, it has a safety superiority over the Arkansas method.

The cost is an important factor, as tuberculosis is increasing all over the world, especially among low-income patients with HIV.<sup>3</sup> The cost of the new test is higher and should be considered. The two described methods are part solutions to increase adherence and improve the medical education of patients with tuberculosis infection.

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