Nitrate Reductase Assay for Drug Susceptibility Testing of Mycobacterium tuberculosis

In their recent article, Kristian Ångeby et al. (4) reported a novel test for drug susceptibility testing of Mycobacterium tuberculosis. However, it should be clarified that this method was previously published in 1989 (3) by Emil Kalfin, (National Institute for Lung Diseases, Sofia, Bulgaria) and Andreas Engibarov (National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria). It is not clear where and when the test was first developed but it is apparent that Dr. Kalfin experimented with the methodology for some time prior to its publication. Since 1989, this assay has been used routinely by several diagnostic tuberculosis laboratories in Bulgaria, where the method is known as “the test for nitrate reductase activity” or as “the biochemical test” for assessment of drug susceptibility of M. tuberculosis.

During the period of 1998 to 2000, we modified and improved the nitrate reductase assay by experimenting with the use of a crystalline nitrate reductase reagent described by Lampe (5) and Warren (6). This crystalline reagent is reported to be less toxic and has a longer shelf life than the Griess reagent. We tested this new version of the assay on 31 clinical isolates of M. tuberculosis collected at Iskrez Hospital, Bulgaria, and two reference strains, M. tuberculosis ATCC35822 and H37Rv, using rifampin (40 

We are grateful to Ruth McNerney from London School of Hygiene and Tropical Medicine for helpful review of the manuscript.

REFERENCES


Authors’ Reply

We read with great interest the letter by Panaïtov and Kantardjiev referring to our recently published paper (2). Unfortunately we were not aware of the use of this technique in Bulgaria and the recommendation of it by Kalfin and Engibarov in a Bulgarian guideline for microbial diagnosis of mycobacterial drug sensitivity, and the use of sensitivity tests in tuberculosis control programs (1). Unfortunately we were not aware of the use of this technique in Bulgaria and the recommendation of it by Kalfin and Engibarov in a Bulgarian guideline for microbial diagnosis of mycobacterial drug sensitivity, and the use of sensitivity tests in tuberculosis control programs (1).

However, we find it very promising that the nitrate reductase assay has been in routine clinical use for more than a decade in several Bulgarian microbiological laboratories, and it is unfortunate that the extensive experience of this assay in Bulgaria is not available to the scientific community. Nevertheless, we are happy that this technique has been applied much more than we thought.

Even though we have not yet had the time to test it, we believe that the use of crystalline reagents as suggested by Panaïtov and Kantardjiev, leading to a simplified test performance and a prolonged shelf life, will further improve the potential of this easy-to-perform, rapid, and inexpensive susceptibility test. We look forward to seeing the results from Bulgaria—and other settings—in international jour-
nals and welcome scientific collaboration in this field in the future.

REFERENCES


K. A. Kristian Anègy*
Lisbeth Klintz
Sven E. Hoffner
Department of Bacteriology
Swedish Institute for Infectious Disease Control
171 82 Solna, Sweden

*Phone: 46-8-457 24 73
Fax: 46-8-30 17 97
E-mail: kristian.angeby@smi.ki.se