BRIEFING NOTES

Issue No 000002 November 2001.

Drug resistance: a novel low cost rapid test.

DFID TB KNOWLEDGE PROGRAMME

Background

Drug resistant strains of tuberculosis pose a serious threat to efforts to control the disease. Increased numbers of drug resistant cases have been reported in many settings, including high burden low-income countries in Asia, Africa, Latin America and the former USSR. Current methods of detecting drug resistance are slow and cumbersome. Simple, low cost tests are needed both for rapid case detection and monitoring incidence at local and national levels. Rapid identification of drug resistant disease would enhance interventions to limit transmission. A novel low cost test for screening isolates for resistance to the major anti-tuberculosis drug rifampicin has been developed at the London School of Hygiene & Tropical Medicine. The test is to undergo further evaluation in Asia and Africa.

Principle of test

The test utilises mycobacteriophage D29 (phage), a lytic virus that infects mycobacteria. The phages are able to infect and replicate in live *Mycobacterium tuberculosis* bacilli but all viral replication is blocked in the presence of the major TB drug rifampicin, an ansamycin that inhibits synthesis of bacterial mRNA. However, rifampicin resistant strains of tuberculosis continue to support phage replication and so successful phage infection in the presence of the drug indicates that a rifampicin resistant strain of bacteria is present.

Outline of test

The test is performed in the wells of a microtitre plate. A suspension of the bacteria is incubated with drug overnight, phages are then added and infection allowed to proceed for one hour. Phage replication is detected following overnight incubation with *M. smegmatis*, a fast-growing environmental mycobacteria. The end point is either by viewing plaques in the bacterial lawn or via a colour reaction in the well of a microtitre plate.

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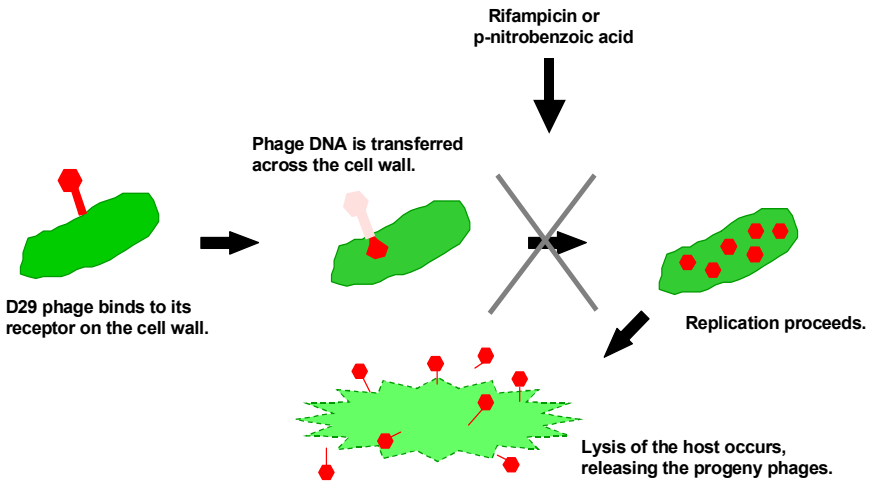
Principle of phage drug resistance test.



Advantages of Test

- The test is rapid (results within 48hr) and simple to perform.
- The test uses a microplate format, which facilitates the screening of large numbers of isolates.
- The end point is visual, specialist equipment other than that required for tuberculosis culture is not required.
- A confirmatory test has been incorporated to exclude false positive results due to MOTTS.
- Phage stocks may be maintained in-house reducing the necessity to import reagents and keeping costs low.

KEY PUBLICATION

McNerney R, Kiepiela P, Bishop K S, Nye P and Stoker NG. Rapid screening of *Mycobacterium tuberculosis* for susceptibility to rifampicin and streptomycin. Int J Tuberc Lung Dis. 2000 4 (1) 69-75.

This work is funded by the Department for International Development. U.K.

Published by the TB Knowledge Programme, which is funded by the Department for International Development, UK. Please send all correspondence to: Alexandra Coldham, Clinical Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK.
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