Tuberculosis (TB)

TB diagnostics and laboratory strengthening - WHO policy

The use of liquid medium for culture and DST, 2007

WHO recommends, as a step-wise approach:

1. The use of liquid medium for culture and DST in middle- and low-income countries.

2. The rapid species identification to address the needs for culture and drug susceptibility testing (DST).

Taking into consideration that liquid systems will be implemented in a phased manner, integrated into a country specific comprehensive plan for laboratory capacity strengthening and addressing the following key issues:

1. **Appropriate biosafety level;**
2. **detailed customer plan describing guarantees and commitments of the manufacturer;**
3. **appropriate training of staff;**
4. **maintenance of infrastructure and equipment in laboratories;**
5. **quick transportation of samples from the peripheral to the culture laboratory;**
6. **rapid communication of results.**

1.

Detailed background information
pdf, 340kb

Use of Liquid TB culture and drug susceptibility testing (DST) in low- and medium- income settings

International TB laboratory experts and representatives of partner organizations recommend the use of TB liquid culture and DST in low income settings. Liquid culture systems are the standard of care for TB diagnosis and patient management in industrialized countries.

Liquid culture and DST systems are more complex and sensitive than solid culture and DST media. Increased bacterial contamination and an increased frequency of nontuberculous mycobacterial (NTM) isolation must

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be addressed. A rapid method to differentiate M. tuberculosis complex from other mycobacterial species is essential.

Background

Laboratory diagnosis of TB largely relies on the direct microscopic examination of sputum specimens. However, the technique, although specific, has low and variable sensitivity and cannot identify drug-resistant strains. Mycobacterial culture is more sensitive but growth of TB bacilli on traditional solid medium requires 4-8 weeks and consequently delays appropriate treatment in the absence of a confirmed diagnosis.

Expanding culture capacity is urgently needed to address challenges due to the epidemics of HIV-associated TB and drug resistant TB, especially in resource-limited settings.

Liquid culture systems reduce the delays in obtaining results to days rather than weeks. For DST, the delay may be reduced to as little as 10 days, compared to 28-42 days with conventional solid media. Liquid systems are more sensitive for detection of mycobacteria and may increase the case yield by 10% over solid media. With increased sensitivity and reduced delays, liquid systems may contribute significantly to improved patient management.

Liquid systems are, however, more prone to contamination by other micro-organisms. In experienced laboratories, approximately 5-10% of specimens cannot yield results because of contamination. Procedures to prevent cross -contamination (due to carryover of bacilli from positive to negative specimens) should also be strictly followed, especially where more positive specimens are processed in high-incidence countries.

Phased implementation

The decision to implement a liquid culture and DST system should be based on need and be consistent with a country’s plan for TB laboratory capacity strengthening and expansion. Such plans should be considered only in countries with a strong network of quality-assured microscopy.

In most circumstances, the first priority would be to implement the system in the NRL, assuming that the NRL is currently supervising quality-assured (QA) microscopy of the laboratory network and performing QA TB culture and DST. This would provide valuable experience that could be applied if a decision were made to scale up the system. In those countries where a liquid culture and DST system is currently in use at the NRL, the decision to scale up should be informed by the accumulated experience at the NRL with the liquid culture system.

Subsequent expansion of liquid culture and DST capacity would logically be to regional TB culture and DST laboratories. The extent of scale up should be determined by need and availability of funding, and again consistent with a national laboratory plan.

Species identification

It is imperative that all mycobacterial isolates be speciated at least to the level of M. tuberculosis complex vs. NTM. When using liquid culture, with the expectation that time-to-detection will be significantly reduced, it is also imperative that a rapid and affordable method of species identification be used. Where identification of NTM is needed, standard biochemical tests or other methods can be considered.

Key issues for WHO

Ministries of Health and their partners urgently require guidance from WHO on the use of liquid culture and other means to improve diagnostic capacity. Based on an expert consultation organized by WHO (26 March 2007) with key experts and agencies in this field, and building on recent comprehensive review of available evidence regarding the efficacy, effectiveness and feasibility of implementing liquid culture technology in high TB burden settings, recommendations were made.

Recommendations

1. Adoption of liquid culture systems should be decided by Ministries of Health in the context of a comprehensive and detailed country plan for TB laboratory capacity strengthening.

2. Country plans for expansion of TB culture and drug-susceptibility testing (DST) should be based on a strong network of quality-assured microscopy, the cornerstone for TB diagnosis.

3. Laboratories should have demonstrated experience in culture and DST using conventional methods.

4. Phased implementation is recommended with the National Reference Laboratory (NRL) as a first priority and further scale-up to regional laboratories based on the NRL experience and consistent with the national country plan.

5. Adequate infrastructure and equipment should be provided, especially regarding laboratory biosafety. Specimen processing for culture purposes has to be performed in appropriate Biological Safety Cabinets (BSCs), at least in Biosafety Level 2 (BSL2) facilities. Processing of cultures for conventional species identification, subculturing and phenotypic DST must be performed in BSL3 facilities [Ref. 9], since culture suspensions required for these activities generate highly infectious aerosols with a high concentrations of TB bacilli. The successful establishment, staffing and maintenance of BSL3 laboratories is demanding and costly.

6. Commercial liquid culture systems must include a detailed commercial sales contract which guarantees ample and continuous supply, optimal shipment conditions and logistics for custom clearance.

7. A customer support plan should detail measures that guarantee - by the supplier - equipment installation, maintenance, reparation and provision of training, training materials and technical support.

WHO will include the use of liquid culture in all relevant technical documents (e.g. Standard Operational Procedures, training material for culture and DST) and will support countries in assessing their needs and building capacity to use liquid cultures.

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