Proposed reduction of number of smears for the diagnosis of pulmonary TB: background document

Current international policy for case detection

The current international policy on TB case detection recommends the examination of three sputum smears for the diagnosis of pulmonary tuberculosis (PTB). The present definition of a smear positive case is "Tuberculosis in a patient with at least two initial sputum smear examinations (direct smear microscopy) positive for acid fast bacilli (AFB+)" \(^1, 2\).

New policy based on two sputum smears

In countries with functional EQA system and human resource crisis, WHO proposes the following:

1. The reduction of number of specimens examined for screening of TB patients from three to two specimens.

2. If two smears are negative, then the suspect should follow the algorithm for sputum negative cases.

Rationale

Incremental yield of the third smear

International studies performed in India and Singapore more than 30 years ago demonstrated that the first two examinations can detect as much as 95% of sputum smear and culture positive cases. Indian studies illustrated that the first specimen was positive in about 85% of culture positive cases, while the second specimen was positive in an additional 10% of cases. (references 1, 2, 4, 5, 6 listed in Toman's Tuberculosis, pg 49) \(^3\).

The members of the Subgroup of Laboratory Capacity Strengthening (SLCS) and laboratory TB experts believed that an additional sample would provide extra precautions to diminish laboratory errors such as suboptimal quality of reagents, clerical deficiencies and poor record keeping. However, a functional EQA system with blind rechecking of smears and support supervision with a regular feedback mechanism would identify a large number of shortcomings and subsequently be able to resolve errors.

A systematic review of studies that quantified the diagnostic yield of each of the three sputum specimens was performed by Mase et al in 2005 and 37 eligible studies were included in the review. For the purpose of the review, a sputum smear-positive case was defined as a positive result in at least one of the three specimens. If the first specimen was positive, then the results of the subsequent two specimens were irrelevant (positive XX) and if the first specimen was negative and the second positive (incremental yield of the second specimen (IV2)), then the result of the third specimen was irrelevant (negative-positive X). If the first and second specimens were negative, then the incremental yield of the third specimen (IV3), if positive, was calculated (negative-negative-positive). The results of the systematic review clearly demonstrated that the average percentage of all cases was detected with the first sputum specimen, which was 85.8%. With the second sputum specimen, the average incremental
yield (IV2) was 11.9%, while the incremental yield of the third specimen (IV3), when the first two specimens were negative, was 3.1%.

A second analysis of data from a study involving 42 laboratories conducted by Rieder et al in four high-burden countries showed that the incremental yield from a third sequential smear ranged from 0.7 to 7.2%.

In a recent prospective study conducted in Kenya, Bonnet et al. compared several approaches for number of sputa examined to diagnose pulmonary TB cases. In addition, the study demonstrated that decreasing the number of smears examined for the detection of new pulmonary TB cases lead to a reduction of patient's visit in a clinic and laboratory workload by one third.

Positive impact on human resource crisis

Furthermore, the Global Plan to Stop TB, 2006-2015 recognizes that the weak health system (and particularly the health workforce crisis) is one of the greatest challenges to TB control and indeed to the achievement of the MDGs in general. The challenge is particularly great in sub-Saharan Africa, where the direct and indirect effects of the HIV epidemic exacerbate the human resource crisis. In most countries, but particularly in sub-Saharan Africa, the laboratory services have long been neglected and may be considered to be among the weakest components of the very fragile health system. Examining only two smears could alleviate the workload of laboratories particularly in countries with a high microscopy workload and with human resources shortage.

Decrease patients' and care providers' costs and poverty alleviation

The Global Plan to Stop TB, 2006-2015, supports patients, particularly poor patients, facing economic barriers in accessing TB control services and those patients with TB in developing countries face long and costly pathways to diagnosis. In 2000, Walker et al, showed that the average cost per case detected was US$ 5 for first smear, US$ 8 for second smear and US$ 11 for third smear.

Increase case finding and decrease defaulting

It is expected that microscopic analysis of two sputum smear samples will improve case findings through enhanced quality of service, decreased time for diagnosis and initiation of treatment and decreased number of patients dropping out of the diagnostic pathway. The rate of smear-positive cases dropping out of the pathway between submitting the first sputum and starting treatment is estimated to be 15% in Zambia.

International standard for tuberculosis care

The proposed new policy for the reduction of number of smears examined is not in contradiction with the International Standard for TB Care (ISTC) which states that "all patients (adults, adolescents, and children who are capable of producing sputum) suspected of having pulmonary tuberculosis should have at least two, and preferably three, sputum specimens obtained for microscopic examination. When possible, at least one early morning specimen should be obtained."
It should be noted that the ISTC also states "in some settings, because of practicality and logistics, a third specimen may be useful".10

**Proposed criteria for recommending two sputum analysis**

The reduction of the number of specimen examined for screening TB patients from three to two specimens should only be recommended in countries and settings with a well established laboratory network and a fully functional EQA programme for smear microscopy including on-site evaluation with the feed-back mechanism. Countries who do not want to introduce the new two smears policy or with no functional EQA system can use the actual three smears policy.

**Recommendation to the STAG**

Based on recent evidence and the recommendations of the laboratory subgroup and partner organizations we request the STAG members to endorse the recommendation:

1. To reduce the number of specimen to be examined for screening of TB cases from three to two.

2. If two smears are negative, then the suspect should follow the algorithm for sputum negative cases.

**References**


5. Rieder HL, Chiang CY, Rusen ID. A method to determine the utility of the third diagnostic and the second follow-up sputum smear examinations to diagnose tuberculosis cases and failures. INT J Tuberc Lung Dis 2005;9(4):384-391

6. Bonnet M, Ramsay A, Gagnidze L, Githui W, Guerin PJ, Varaine F. Reducing the number of sputa examined, and thresholds for positivity: An opportunity to optimize smear microscopy. Accepted for publication, Int J Tuberc Lung Dis

