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Revision of the case definition for sputum smear positive pulmonary TB
Background document

Current international policy for case detection

The World Health Organization (WHO) in its first "Framework for Effective Tuberculosis Control" [1] defined sputum smear-positive tuberculosis as follows:

1. Tuberculosis in a patient with at least two initial sputum smear examinations (direct smear microscopy) positive for acid fast bacilli (AFB+), or
2. Tuberculosis in a patient with one sputum examination positive for AFB+ and radiographic abnormalities consistent with active pulmonary tuberculosis as determined by the treating medical officer, or
3. Tuberculosis in a patient with one sputum specimen positive for AFB+ and culture positive for AFB+.

In a subsequent joint publication WHO, the International Union against Tuberculosis and Lung Disease (The Union) and the Royal Netherlands Tuberculosis Association (KNCV) confirmed the definition [2].

Proposed new definition

With the prerequisite of a functional external quality assurance (EQA) system with blind rechecking, the proposed definition is "a patient with one or more initial sputum smear examinations positive for acid fast bacilli (AFB)".

It should be noted that the definition of bacteriological failures has not been reviewed; hence, no change in the definition of failure cases is proposed at this stage.

Rationale for laboratory diagnosis of tuberculosis by sputum microscopy based on a single positive smear

1. Sensitivity and specificity of acid-fast microscopy

More than 30 years ago, international studies performed in India and Singapore demonstrated that the first two examinations can detect as much as 95% of sputum 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 [3] (references 1, 2, 4, 5, 6 listed in Toman's Tuberculosis, page 49).

A systematic review of studies that quantified the diagnostic yield of each of the three sputum specimens was performed 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 (IY2)), 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 (IY3), 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 (IY2) was 11.9%, while the incremental yield of the third specimen (IY3), when the first two specimens were negative, was 3.1% [4].
Pos X X = 85.8%
Neg Pos X = 11.9%
Neg Neg Pos = 3.1%

In a recent study conducted in Kenya, Bonnet *et al* compared several approaches for case definition on 644 TB suspects where it was concluded that using one positive smear result out of two specimen examinations increased the sensitivity of smear microscopy as compared to that of an actual TB case definition by 14.1% while the specificity remains unchanged. Therefore, the proposed definition will allow less false-positive results with no increase in false-negative results. In addition, the study demonstrated that lowering the threshold for defining a positive smear lead to the reduction of patients' visit to clinics and to laboratory workload [5].

2. Minimizing the errors

The rationale for recommending two positive smears for the diagnosis of a pulmonary TB case was to minimize the laboratory errors such as suboptimal quality of reagents, clerical deficiencies and poor record keeping. However, the international community now believes that a functional EQA system with blind rechecking of smears and support supervision with a regular feedback mechanism will identify a large number of shortcomings and subsequently be able to resolve any errors [6].

False-positive and false-negative results may be due to poor quality of sputum samples, deficiencies in the preparation, staining, or examination of the smear[3]. Proper training on sputum smear microscopy together with wide implementation of EQA will address possible suboptimal microscopy performances.

3. Laboratory experts' opinion

In an expert consultation, held in 2005 for improving the Diagnosis of Tuberculosis through optimization of sputum microscopy, one of the final recommendations was: *"The requirement for two positive smears to define a smear positive case should be urgently reviewed by the relevant authorities"*.

Based on the results of the systematic review and the recommendations of the expert consultation, the Subgroup on Laboratory Capacity Strengthening (SLCS) in their fourth annual meeting in November 2006, recommended to the WHO to consider a policy revision. The TB case definition should be revised to consider that one positive smear microscopy result is sufficient to diagnose a case of pulmonary tuberculosis.

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Since then, a number of key meetings and workshops were held where the TB case definition was discussed. These meetings included the meeting of the SLCS, an expert group meeting organized by the UNION held in Belgium and a technical expert workshop held in The Netherlands. Recent scientific evidence [4,5] was reviewed and it was concluded that where a functional EQA for smear microscopy is in place, the finding of a single AFB in at least one single sputum smear examination in a TB suspect would satisfy the criterion to report a patient as having "sputum smear-positive tuberculosis" and to subsequently start treatment.

4. Official request

After reviewing the scientific evidence and recent meeting reports the Directors of the technical organizations The Union, KNCV, CDC, RIT/JATA, Supranational laboratories and other laboratory experts, support and officially request the proposed definition change.

Recommendation to the STAG

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

1. Endorse the definition change of new sputum smear positive pulmonary TB case. The new definition will be based on the presence of AFB in only one sputum sample in those countries with a functional EQA system.

2. The definition of a bacteriological failure remains unchanged and should not be affected by this recommendation.

References

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