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DIAGNOSIS OF TUBERCULOSIS IN CHILDREN: CHALLENGES AND OPPORTUNITIES

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Childhood tuberculosis is an important public health problem in resource constrained settings, but continues to be neglected by physicians and policy makers. Diagnosis is particularly challenging in infants and children for many reasons. Children generally do not produce or expectorate sputum, making it difficult to obtain appropriate samples for analysis. Families generally do not collect and transport respiratory specimens properly. The disease is generally paucibacillary and mycobacteria are shed intermittently, reducing the yield (compared to adults). The hallmark radiological signs (such as pulmonary cavity) are rarely seen in childhood tuberculosis. Further physicians often treat children without confirming the diagnosis. The twin burdens of HIV infection and rising resistance among mycobacteria add further challenges to diagnosis. The mainstay of tuberculosis diagnosis rests on demonstration of acid fast bacilli (AFB) in biological samples (induced sputum, gastric aspirate/lavage, nasopharyngeal aspirate, lymph node aspirate, etc.). However staining with conventional methods yields results in only about 30% confirmed cases. Mycobacterial culture yield is also extremely low, but is somewhat improved by using liquid culture media. Clinical scoring systems have poor sensitivity and specificity; with limited diagnostic validity for treatment decisions. Radiological diagnosis rests on demonstration of one of three signs viz. hilar/paratracheal lymphadenopathy, military shadows and a fibrocavitary lesion, but these findings are rare. Tuberculin test and

serological assays are two frequently misused tests. The former cannot distinguish infection from disease (hence has limited value in endemic settings) and the latter is unreliable and is discouraged by national and international guidelines. Even interferon gamma release assays (IGRA) have no value in endemic settings. Recent molecular diagnostic tests have raised hopes of better diagnostic platforms. The Xpert MTB RIF system (GeneXpert) is the most promising among these. A series of systematic reviews shows that GeneXpert is superior to microscopy, but inferior to culture (sensitivity ~60%, specificity >95%). This is a setback because although a positive test result is helpful to start treatment, a negative test does not rule out tuberculosis. Further, GeneXpert sensitivity is considerably lower in smear microscopy negative cases (compared to smear positive cases). However, a significant advantage is the rapid identification of rifampicin resistance. Other diagnostic techniques undergoing evaluation in children include: loop-mediated isothermal amplification (LAMP), and LED microscopy. However, children are excluded from the majority of global research studies on newer diagnostic platforms. In summary, diagnosis of childhood tuberculosis is difficult, and needs considerable time and effort. A step-wise approach can increase diagnostic confirmation in this difficult public health problem.

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