Tüberküloz Laboratuvarında Yaşanan Sorunlar

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Tıbbi Mikrobiyoloji AD.

Sunum Planı

- Tüberküloz lab.dan beklentiler
- TB lab sorunları
  - Fiziki alt yapı ve güvenlik
  - Analiz öncesi
  - Analiz
  - Analiz sonrası
- Son söz- hayallerimiz

TB laboratuvarları nasıl olmalı?

25.10.2015 tarih ve 25913 sayılı resmi gazetede yayınlanan "**Tüberküloz Laboratuvarlarının Çalışma Usül ve esaslarına dair Tebliğ**" gereğince bu laboratuvarlardaki tüm süreçler standartlara uygun olarak yürütülmelidir

Fiziki alt yapı ve güvenlik

Laboratuvar alanlarının yetersiz olması

- ✓ Laboratuvar büyüklüğü
  - ✓ Kişi başına yaklaşık 25-30 m^2 alan ve/veya çalışanlar arasında 1,5 m mesafe güvenli kabul ediliyor
  - ✓ Aydınlatma ve ergonomi

- ✓ Yetersiz aydınlatma
- ✓ Ergonomik olmayan düzenleme

MMWR 6, 2012

Fiziki alt yapı ve güvenlik

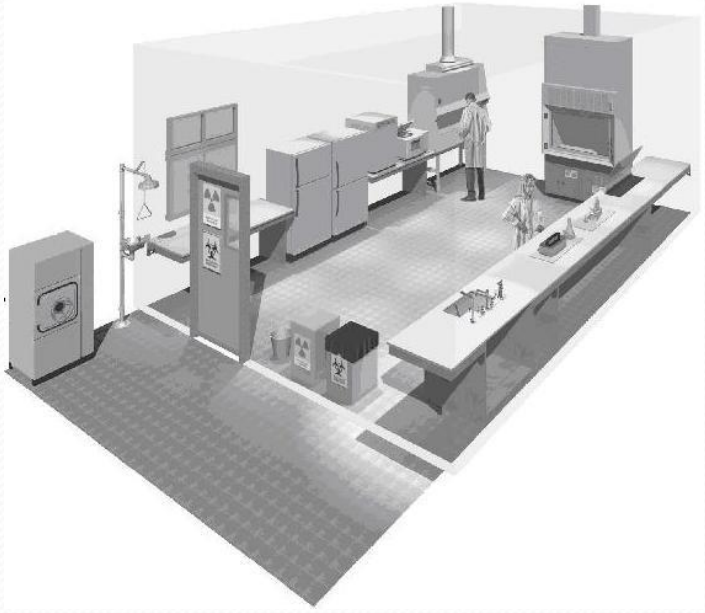
Laboratuvara kontrolsüz giriş-çıkış

- ✓ Laboratuvarda uygun giriş sınırlaması olmalı
  - ✓ Kilitli kapı, yetkilendirilmiş giriş
  - ✓ Biyolojik tehlike işareti
  - ✓ Biyogüvenlik düzeyi bilgisi
  - ✓ Acil durumlar için ulaşılacak isim ve telefon numarası

Fiziki alt yapı ve güvenlik

Laboratuvar güvenliğinde eksiklikler

- ✓ Laboratuvar tasarımı
  - ❖ Düzey I ve II için;
    - ✓ BGD-2 koşulları
    - ✓ Temizden kirliye iş akışı
  - ❖ Düzey III için;
    - ✓ çift basamaklı giriş,
    - ✓ pencereler açılmaz,
    - ✓ izlenebilir negatif basınçlı ortam,
    - ✓ merkezi havalandırma/hava akımı çalışanları ve işlemlenen örnekleri koruyacak biçimde yönlendirilmiş olmalı



Fiziki alt yapı ve güvenlik

Giysi dolapları lab'da

- ✓ Laboratuvar alanı ofis alanlarından fiziksel ve işlevsel olarak ayrılmalı

Lab dolaplarında gıda bulundurulması ve lab'da tüketilmesi

Alan kısıtlılığından lab'ın dinlenme ve ofis alanı olarak da kullanılması

Fiziki alt yapı ve güvenlik

- ✓ Yangın, Deprem gibi afetlere yönelik önlemler

Odadaki dolap ve cihazların duvara sabitlenmemesi

Yangın alarmı yok

Acil yangın çıkışı işaretleri konmamış

Yangın söndürücüler kontrol edilmiyor

Kimyasalların kullanım ve saklama kurallarına yeterince dikkat edilmemesi

Fiziki alt yapı ve güvenlik

- ✓ Kişisel koruyucu donanım (KKD) kullanımı

Uygun olmayan KKD

Bilgi eksikliği

Fiziki alt yapı ve güvenlik

- ✓ Laboratuvar donanımı

Donanım temininde güçlük, uygun olmayan kullanım

Sağlık çalışanı enfeksiyonu

Analiz Öncesi
Örnek Yönetimi

- ✓ Örnek alma ve taşıma prosedürleri olmalı
- ✓ Balgam çıkarma talimatı ve hastalara bilgilendirme olmalı
- ✓ Talimat zamanlama, kap, uygun sıcaklık, uygun miktar bilgisini içermeli

Özellikle balgam örneklerinin lab'a yakın tuvaletlerde çıkarılması

Örnek kayıpları

Uygunsuz örnekler

Örneklerin karışması

Örnek yönetimi

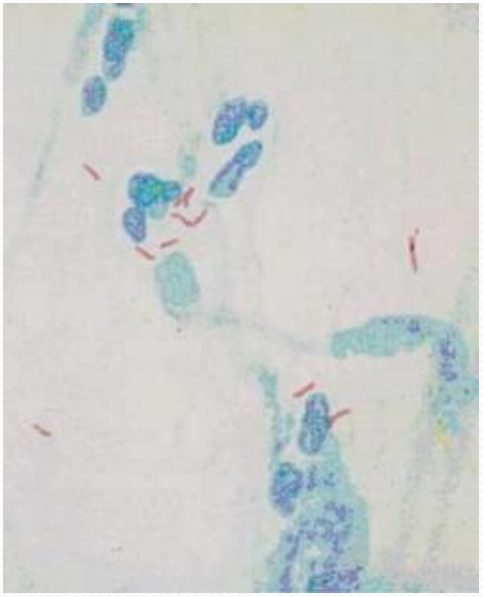
- ✓Numuneler +4 C'de bekletilmeli (BOS ve kemik iliği hariç)
- ✓İdrar bekleyecekse santrifüj edilip sediment PBS ile sulandırılarak bekletilmeli
- ✓Nötralize edilmemiş AMS bekletilmemeli

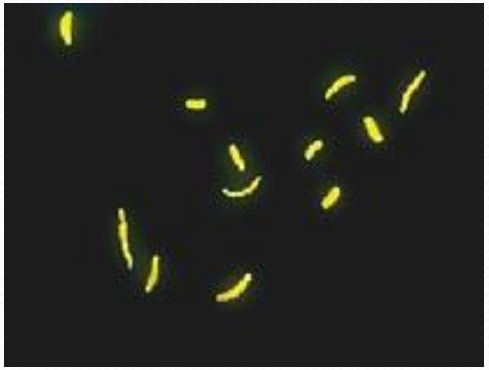
Örnek gönderme ve saklama kurallarına uyulmuyor

Analiz

Direkt Mikroskopi

- ✓ Hızlı, ucuz ve kolay bir yöntem
- ✓ 24 saat içinde sonuç verilir!..
- ✓ Karbol fuksin Boyama
  - ✓ Erlich Ziehl Neelsen (EZN)
  - ✓ Kinyoun
- ✓ Floresan Boyama
  - ✓ Fluorokrom (Auromin-Rhodamin)





INT J TUBERC LUNG DIS 11(9):946–952

WORKSHOP REPORT

Critical appraisal of current recommendations and practices for tuberculosis sputum smear microscopy

C. Gilpin, S. J. Kim, R. Lumb, H. L. Rieder, A. Van Deun, for the Working Group on Sputum Smear Microscopy*

Internation… …ease, Paris, France

SUMMARY

…National Tuberculosis Programmes and other health authorities. In particular, allocation of sufficient resources for rechecking and integration of laboratory supervision must be ensured. Countries must make better investments in the purchase of high quality microscopes and laboratory supplies. To address the human resource crisis, personnel without specific laboratory schooling can, in principle, be trained to respond to immediate needs for TB diagnostic microscopy services. Periodic reporting on acid-fast smear examinations is highly desirable for regular monitoring and a more balanced provision of supplies.

KEY WORDS: acid-fast smear; diagnosis; microscopy; laboratory services; tuberculosis

✓Örnek kalitesi, miktarı ve sayısı sonucu etkiler

✓İki örnek yeterli olabilir

✓Üçüncü örnek duyarlılığı %2-5 arttırabilir

SPUTUM SMEAR MICROSCOPY for …fast bacilli (AFB) is of vital clinical and epidemiological importance in the diagnostic process for tuberculosis … in both affluent low-incidence countries[1] and … burden countries with limited resources.[2] The detection of AFB in pulmonary secretions identifies those patients with the greatest potential for transmission of *Mycobacterium tuberculosis*.[3–5] Sputum smear microscopy offers the triple advantages of speed, simplicity and low cost.[6] In many countries with a high burden of TB, it is the most appropriate and most accessible diagnostic tool.[7] An effective mechanism for quality assurance (QA) is required to maintain the national TB laboratory network in optimal condition, providing accurate, reliable and timely results, so as to generate ongoing confidence in the service.[8]

SPECIMEN COLLECTION, TRANSPORT AND CONCENTRATION

* Working Group on Sputum Smear Microscopy: P Angra (Centers for Disease Control and Prevention, Atlanta, Georgia, USA), M Becx-Bleumink (World Health Organization, Dhaka, Bangladesh), S Endo (Japan Anti-Tuberculosis Association, Tokyo, Japan), C Gil-

Öneri→

- ✓ Teksif duyarlılığı %6-9 arttırmakta (özgüllükten %1-3 kayıp olabilir)
- ✓ Floresan mikroskopi %10 daha duyarlı

Duyarlılık %20-80

Canlı- ölü basil ayrımı yapılamamakta

Tür tanısı hakkında fikir vermez

Steingart KR. Lancet Infect Dis 2006;6:570-81

Mikroskopide sorunları nasıl fark edebiliriz?

- ✓Pozitif ya da negatif yayma sayısının beklenen orandan yüksek olması
- ✓Farklı hastalara ait ardışık yayma pozitifliği
- ✓Yayma pozitif örneklerin kültürde üremesi
- ✓Yayma negatif örneklerin kültürde yoğun olarak üremesi

Kalite göstergelerini kullanalım

Analiz

Kültür

- ✓Güncel kılavuzlar en az bir sıvı, bir de katı besiyerinin birlikte kullanılmasını önermekte

Katı besiyerlerinde özellikle geç üreme

Kan ve kanlı örneklerde üretmede zorluk

Antimikrobiyaller bazı mikobakterilerin üremesini önleyebilmekte

Ticari hazır kitlerin kullanımı iş yükünü ve kontaminasyonu azaltmıştır

Kültürde sorunları nasıl fark edebiliriz?

- ✓ Kontaminasyon oranları gözden geçirilmeli
- ✓ %2'nin altında → dekontaminasyon aşırı
- ✓ %5-8'den fazla→ besiyeri kontaminasyonları/ yetersiz bir dekontaminasyon yöntemi
- ✓ Seri pozitifliklere dikkat
- ✓ Örnek tipi de yol gösterici
- ✓ Mikroskopi pozitifliğine göre beklenenden daha az oranda (%90'nın altında) kültürde üreme olması

Kalite göstergelerini kullanalım

Analiz
MTBC/TDM ayrımı

- Düzey 3 laboratuvarlarda yapılır
- Fenotipik yöntemler olarak üreme özellikleri, biyokimyasal testler ve immünokromotografik yöntemler kullanılmaktadır

Üreme özellikleri yeterli değil
Biyokimyasal testler zaman alıcı, zahmetli, değerlendirmesi güç testler
Taze kültür pasajı gerektirirler
Kesin sonuç vermeyebilirler
Biyolojik risk düzeyi yüksektir

Kumar *et al. BMC Research Notes* 2011, **4**:79
http://www.biomedcentral.com/1756-0500/4/79

BMC Research Notes

TECHNICAL NOTE Open Access

MPT 64 Antigen detection for Rapid confirmation of *M.tuberculosis* isolates

Vijay GS Kumar[1*], Tejashree A Urs[2] and Rajani R Ranganath[3]

Duyarlılık ve özgüllükleri çok yüksek (%100)

Abstract

Background: A new rapid Immunochromatographic test kit(SD MPT64TB Ag Kit) [illegible]ntigen in *M. tuberculosis* isolates using mouse monoclonal MPT 64 Antibody developed by SD Bioline, South Korea was evaluated for rapid identification of *M. tuberculosis* isolates. We also assessed the sensitivity, specificity and predictive values of this kit. The test kit has an excellent sensitivity, specificity, negative predictive value & positive predictive value. This rapid method is found to be a reliable, rapid and cheaper me[illegible]d for confirming MTB culture isolates in resource poor laboratories. Material/methods: 54 culture isolates of *M. tuberculosis* in broth & on LJ medium, 12 Non mycobacterial isolates, 10 Non tubercular (NTM) rapidly growing Mycobacteria isolated from pus & 5 smear positive sputum samples were tested for detection of MPT64 antigen using the SD Bioline immunochromatography (ICT)test kit. H37 RV strain was employed as the positive reference control.

Findings: H37 RV strain showed the presence of MPT64 antigen band. Similar band was formed in all the 54 MTB isolates tested proving 100% sensitivity. MPT64 band formation was not detected in any of the other test isolates which proved the 100% specificity of the test kit. Both PPV & NPV were 100%.

Conclusion: Tuberculosis is a global pandemic. Rapid identification of MTB culture isolate is very important for drug susceptibility testing. MPT 64 TB Ag detection ICT kit is a rapid, reliable method; it can be a substitute for the molecular identification methods.

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0095-1137/11/$12.00 doi:10.1128/JCM.02243-10

Evaluation of the Rapid MGIT TBc Identification Test for Culture Confirmation of *Mycobacterium tuberculosis* Complex Strain Detection[▽]

hızlı kromatografik testlerle tanımlama 1 saatte mümkün

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ng-Lan Yu,[3] and Ruwen Jou[3]*

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aboratory of Mycobacteriology, Research and Diagnostic Center, Centers for
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Received 8 November 2010/Returned for modification 7 December 2010/Accepted 20 December 2010

A culture confirmation test for the detection of *Mycobacterium tuberculosis* complex strains that uses a lateral-flow immunochromatographic assay to detect the MPB64 antigen, the MGIT TBc identification (TBc ID) test, has been developed. We evaluated the performance of the TBc ID test in the detection of the *M. tuberculosis* complex in 222 primary-positive liquid cultures. We compared these results to those of nucleic acid-based identification and conventional biochemical tests. The validity of the TBc ID test was determined, and all of the nontuberculous mycobacteria (NTM) and *Nocardia* species t detection limit of the TBc ID test was 5 × 10[5] CFU/ml, and for IS*6110* re the *M. tuberculosis* and *M. africanum* cultur were found to be positive cultures were negative. With the exception of 1 contaminated culture, th tained 171 (77.5%) *M. tuberculosis* isolates, 39 (17.6%) NTM species, and culture-positive isolates harbored a 63-bp deletion at position 196 of the *mp* positive predictive values, and negative predictive values of the TBc ID t respectively. Furthermore, the approximate turnaround time for real-time sample preparation), while for the TBc ID test it was less than 1 h. We su identification of *M. tuberculosis* in liquid culture using the TBc ID test subculture followed by identification using biochemical methods.

Genotipik yöntemler;

- ✓PCR restriksiyon enzim analizi

Ekipman, donanım ve deneyimli personel gerekli

- ✓Ters hibridizasyon testleri"Line Probe Assay
- ✓NAAT

-Silik bantlar
-Test tekrarı – Maliyet artışı
-Test süresi uzun 6-8 saat

INNO-LIPA Rif TB (LIPA)

(Inno-Genetics NV, Ghent, Belgium)

BioMed Central

Research article

Open Access

A commercial line probe assay for the rapid detection of rifampicin resistance in *Mycobacterium tuberculosis*: a systematic review and meta-analysis

Maureen Morgan[†1], Shriprakash Kalantri [illegible] Madhukar Pai[*1,4]

Background: *Mycobacterium tuberculosis* is a leading c[illegible] resistant tuberculosis (MDR-TB) infectiousness is freque[illegible] control TB. The conventional tuberculosis drug susceptibility[illegible] they are not rapid. The INNO-LiPA Rif. TB ® (LiPA) is a commerci[illegible] rapidly detect rifampicin resistance, a marker of MDR-TB. Although Li[illegible] results, its overall accuracy has not been systematically evaluated.

Methods: We did a systematic review and meta-analysis to evaluate the accuracy[illegible] detection of rifampicin-resistant tuberculosis among culture isolates and clinical specimens. [illegible] searched Medline, Embase, Web of Science, BIOSIS, and Google Scholar, and contacted authors, experts and the manufacturer. Fifteen studies met our inclusion criteri[illegible] these, 11 studies used culture isolates, one used clinical specimens, and three used both. We used a summary receiver operating characteristic (SROC) curve and Q* index to perform meta-analysis and summarize diagnostic accuracy.

Results: Twelve of 14 studies that applied LiPA to isolates had [illegible]nsitivity greater than 95%, and 12 of 14 had specificity of 100%. The four studies that applied LiPA directly to clinical specimens had 100% specificity, and sensitivity that ranged between 80% and 100%. The SROC curve had an area of 0.99 and Q* of 0.97.

Conclusion: LiPA is a highly sensitive and specific test for the detection of rifampicin resistance in culture isolates. The test appears to have relatively lower sensitivity when used directly on clinical specimens. More evidence is needed before LiPA can be used to detect MDR-TB among populations at risk in clinical practice.

kültür izolatlarında duyarlılık ve özgüllük; %95-100

direkt örneklerde duyarlılık %80-100

GenoType MTBDR assay

(Hain Lifescience, Nehren- Germany)

BioMed Central

Research article

Open Access

Direct susceptibility testing for multi drug resistant tuberculosis: A meta-analysis

Freddie Bwanga[1,2,3], Sven Hoffner[2,3], Melles Ha[illegible]3 and Moses L Joloba*[1]

Background: One of the challenges facing the tuber[illegible] resource-limited settings is lack of rapid techniques for dete[illegible] drug resistant tuberculosis (MDR TB). Results obtaine[illegible] testing methods come too late to influence a timely [illegible] tests directly applied on sputum samples are needed. This[illegible] and time to results of four direct drug susceptibility test[illegible] testing for detection of resistance to rifampicin and isoniazid i[illegible] included two in-house phenotypic assays – Nitrate Reductase [illegible] Observation Drug Susceptibility (MODS), and two commercially ava[illegible] MTBDR and Genotype® MTBDR*plus* (Hain Life Sciences, Nehren, Germa[illegible]

Methods: A literature review and meta-analysis of study reports was performe[illegible] software was used to analyse the reports and tests for sensitivity, specificity, and area under summary receiver operating characteristic (sROC) curves. Heterogeneity in accuracy estimates was tested with the Spearman correlation coefficient and Chi-square.

Results: Eighteen direct DST reports were analysed: NRA – 4, MODS- 6, Genotype MTBDR® – 3 and Genotype® MTBDR*plus* – 5. The pooled sensitivity and specificity for detection of resistance to rifampicin were 99% and 100% with NRA, 96% and 96% with MODS, 99% and 98% with Genotype® MTBDR, and 99% and 99% with the new Genotyp[illegible]MTBDR*plus*, respectively. For isoniazid it was 94% and 100% for NRA, 92% and 96% for MODS, 71% and 100% for Genotype® MTBDR, and 96% and 100% with the Genotype® MTBDR*plus*, respectively. The area under the summary receiver operating characteristic (sROC) curves was in ranges of 0.98 to 1.00 for all the four tests. Molecular tests were completed in 1 – 2 days and also the phenotypic assays were much more rapid than conventional testing.

Conclusion: Direct testing of rifampicin and isoniazid resistance in *M. tuberculosis* was found to be highly sensitive and specific, and allows prompt detection of MDR TB.

Rifampisin için duyarlılık ve özgüllük: %99

İzoniazid için %96-100

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2011, p. 3068–3070 Vol. 49, No. 8
0095-1137/11/$12.00 doi:10.1128/JCM.00718-11

Cepheid GeneXpert MTB/RIF Assay for *Mycobacterium tuberculosis* Detection and Rifampin Resistance Identification in P... with Substantial Clinical Indications of Tub... Smear-Negative Microscopy Re...

Panayotis Ioannidis,* Dimitrios Papaventsis, Simona Karabela, Stavi...
Ekaterini Raftopoulou, Eythymia Konstantinidou, Ioanna Mari...

National Reference Laboratory for Mycobacteria (NRLM), Sotiria Chest Diseas...

Received 11 April 2011/Returned for modification 19 May 2011/Accepted 5 Ju...

The GeneXpert MTB/RIF assay was evaluated with microscopically negative and p...ive pulmonary and extrapulmonary specimens from patients with substantial clinical indications for tuberculosis. For the pulmonary samples, the sensitivity, specificity, and positive and negative predictive values were 90.6%, 94.3%, 93.5%, and 91.7%, and for the extrapulmonary samples, they were 100%, 91.6%, 50%, and 100%, respectively. For microscopically negative specimens, the respective values were 86.3%, 93%, 79%, and ...6%. The assay correctly detected rifampin resistance in all but one specimen, which harbored a mixed population. The GeneXpert assay was highly effective for tuberculosis diagnosis and identification of rifampin-resistant strains in smear-negative samples.

AKC
- Duyarlılık:%91
- Özgüllük: %94
- PPD:%94
- NPD:%92

AKC DIŞI
- Duyarlılık:%100
- Özgüllük: %92
- PPD:%50
- NPD:%100

...ublic health problem, ...ident cases and 1.3 ...The emergence and ...y (XDR) drug-re... (MTBC) strains ...ol (11). In order to ...nsitivity and diagnostic ...NAA) tests have been in... ...sitivities are high for specimens that are aci... ...us (AFB) microscopy positive but lower ganisms, making the assay suitable for use near patients in settings with limited biocontainment facilities (1).

A prospective study was conducted between September 2009 and May 2010 at the National Reference Laboratory for Mycobacteria (NRLM), Athens, Greece, in order to assess the performance of the Xpert MTB/RIF assay in AFB-negative respiratory and nonrespiratory specimens in a routine hospital laboratory setting. Specimens were selected from patients with strong clinical indications for TB. A small number of AFB-positive specimens was also included to serve as positive con-

Ulusal tüberküloz tanı rehberi (UTTR) de yüksek TB kuşkusu olan yayma negatif olgular ve akciğer dışı TB kuşkulu olgulara moleküler test uygulanmasını önermektedir!..

Örnekteki basilin homojen dağılmaması, yeterli nükleik asit elde edilememesi veya ortamda çoğalmayı engelleyen faktörlerin bulunması durumunda yalancı negatif
Örnek kontaminasyonunda yalancı pozitif

Canlı ve cansız bakterileri ayıramamakta,
Maliyetli

OPEN ACCESS Freely available online

PLoS one

Commercial Nucleic-Acid Amplification Tests for Diagnosis of Pulmonary Tuberculosis in Respiratory Specimens: Meta-Analysis and Meta-Regression

Daphne I. Ling[1], Laura L. Flores[2], Lee W. Riley[1,3], Madhukar Pai[4]*

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Tanısal doğruluk yetersiz
Tek başına konvansiyonel testlerin yerini alamaz

*B*ic accuracy of nucleic-acid amplification tests (NAATs) for ore consistent results than in-house assays. Previous meta- ble estimates of sensitivity. However, reasons for variability in erformed a meta-analysis on the accuracy of commercial NAATs to y factors that are associated with higher accuracy. ***Methodology/*** rom searching the literature. We found 402 articles that met our eligibility tudies from 105 articles that reported NAAT results from respiratory specimens were included. The pooled sensitivity was 0.85 (range 0.36–1.00) and the pooled specificity was 0.97 (range 0.54–1.00). However, both measures were significantly heterogeneous ($p<.001$). We performed subgroup and meta-regression analyses to identify sources of heterogeneity. Even after stratifying by type of commercial test, we could not account for the variability. In the meta-regression, the threshold effect was significant ($p=.01$) and the use of other respiratory specimens besides sputum was associated with higher sensitivity. ***Conclusions/Significance***. The sensitivity and specificity estimates for commercial NAATs in respiratory specimens were highly variable, with sensitivity lower and more inconsistent than specificity. Thus, summary measures of diagnostic accuracy are not clinically meaningful. The use of different cut-off values and the use of specimens other than sputum could explain some of the observed heterogeneity. Based on these observations, commercial NAATs alone cannot be recommended to replace conventional tests for diagnosing pulmonary TB. Improvements in diagnostic accuracy, particularly sensitivity, need to be made in order for this expensive technology to be worthwhile and beneficial in low-resource countries.

Serolojik Testler

- ✓ Özellikle gelişmekte olan ülkelerde çok sayıda ticari serolojik test mevcut
- ✓ Akciğer ve akciğer dışı organ tüberkülozlarında kullanılıyor

Steingart KR. Thorax 2007; PLoS Med 2007

OPEN ACCESS Freely available online PLoS MEDICINE

Commercial Serological Tests for the Diagnosis of Active Pulmonary and Extrapulmonary Tuberculosis: An Updated Systematic Review and Meta-Analysis

Karen R. Steingart[1], Laura L. Flores[2,3], Nandini Dendukuri[4], Ian Schiller[4], Su[5,6] Ramsay[8], Philip C. Hopewell[2,3], Madhukar Pai[4]*

1 Department of Health Services, University of Washington School of Public Health, Seattle, Wash Care Medicine, San Francisco General Hospital, University of California, San Francisco, Californi University of California, San Francisco, California, United States of America, 4 Department of Montreal, Chest Institute, Montreal, Quebec, Canada, 5 Department of Pathology, New Y America, 6 Department of Microbiology, New York University Langone Medical Center, New York, New York, United States of America, 8 UNICEF/UNDP/World Bank/WHO Spe Organization, Geneva, Switzerland

Duyarlılıklar (%0-100)
Özgüllükler (%31-100)
(Akc dışı %59-100)
Mikroskopinin yerini alabilecek yeterlilikte değil

Abstract

Background: Serological (antibody detection) tests for tuberculosis (TB) are w a World Health Organization policy process, we performed an updated systematic accuracy of commercial serological tests for pulmonary and extrapulmonary TB with a focus on the relevance tests in low- and middle-income countries.

Methods and Findings: We used methods recommended by the Cochrane Collaboration and GRADE approach for rating quality of evidence. In a previous review, we searched multiple databases for papers lished from 1 January 1990 to 30 May 2006, and in this update, we add additional papers published from that perio 29 June 2010. We prespecified subgroups to address heterogeneity and summarized test performance using bivar andom effects meta-analysis. For pulmonary TB, we included 67 studies (48% from low- and middle-income countries) with 5,147 participants. For all tests, estimates were variable for sensitivity (0% to 100%) and specificity (31% to 100%). For anda-TB IgG, the only test with enough studies for meta-analysis, pooled sensitivity was 76% (95% CI 63%–87%) in smear-positive (seven studies) and 59% (95% CI 10%–96%) in smear-negative (four studies) patients; pooled specificities were 92% (95% CI 74%–98%) and 91% (95% CI 79%–96%), respectively. Compared with ELISA (pooled sensitivity 60 5% CI 6%–65%]; pooled specificity 98% [95% CI 96%–99%]), immunochromatographic tests yielded lower pooled sensitivity (53%, 95% CI 42%–64%) and comparable pooled specificity (98%, 95% CI 94%–99%). For extrapulmonary TB, we included 25 studies (40% from low- and middle-income countries) with 1,809 participants. For all tests, estimates were variable for sensitivity (0% to 100%) and specificity (59% to 100%). Overall, quality of evidence was graded very low for studies of pulmonary and extrapulmonary TB.

Conclusions: Despite expansion of the literature since 2006, commercial serological tests continue to produce inconsistent and imprecise estimates of sensitivity and specificity. Quality of evidence remains very low. These data informed a recently published World Health Organization policy statement against serological tests.

Please see later in the article for the Editors' Summary

TDM izole edildiği durumlarda klinik olarak etken kabul edilip edilmemesi de kritik bir konu

Risk faktörleri;

- ✓ Altta yatan hastalık, immün sistemi baskılayan bir hastalığın varlığı
- ✓ Deri bütünlüğünü bozan aletlerin bulunması

- ✓ TDM'lerde balgamda ARB pozitifliğinin yüksek olması anlamlıdır
- ✓ Balgam için birden fazla örnekte kültürde üreme olması ve steril alanlardan alınan örneklerde tek bir kültürde üreme olması anlamlıdır
- ✓ *M. gordonae, M. xenopi, M. fortuitum, M. mucogenicum, M. terrae* kompleks, vb. sıklıkla çevresel patojendir
- ✓ Balgamda herzaman anlamlı değilken venöz kateterli bir hastanın kanında tespit edildiğinde sepsisle ilişkilendirilir

Analiz
İDT

- ✓ Düzey 3 laboratuvarlar birinci seçenek İDT' lerini uygular
- ✓ İkinci seçenek ilaçlar için İDT leri Ulusal Referans Laboratuvarı'nca uygulanmaktadır
- ✓ Kültürün saf olması gerekli
- ✓ Ticari sıvı yöntemlerde direnç saptandığında kontaminasyon olmadığı doğrulanmalı

Katı besiyerinde İDT geç sonuç vermekte
Katı besiyerinde pirazinamid duyarlılığının test edilmesi standart değildir

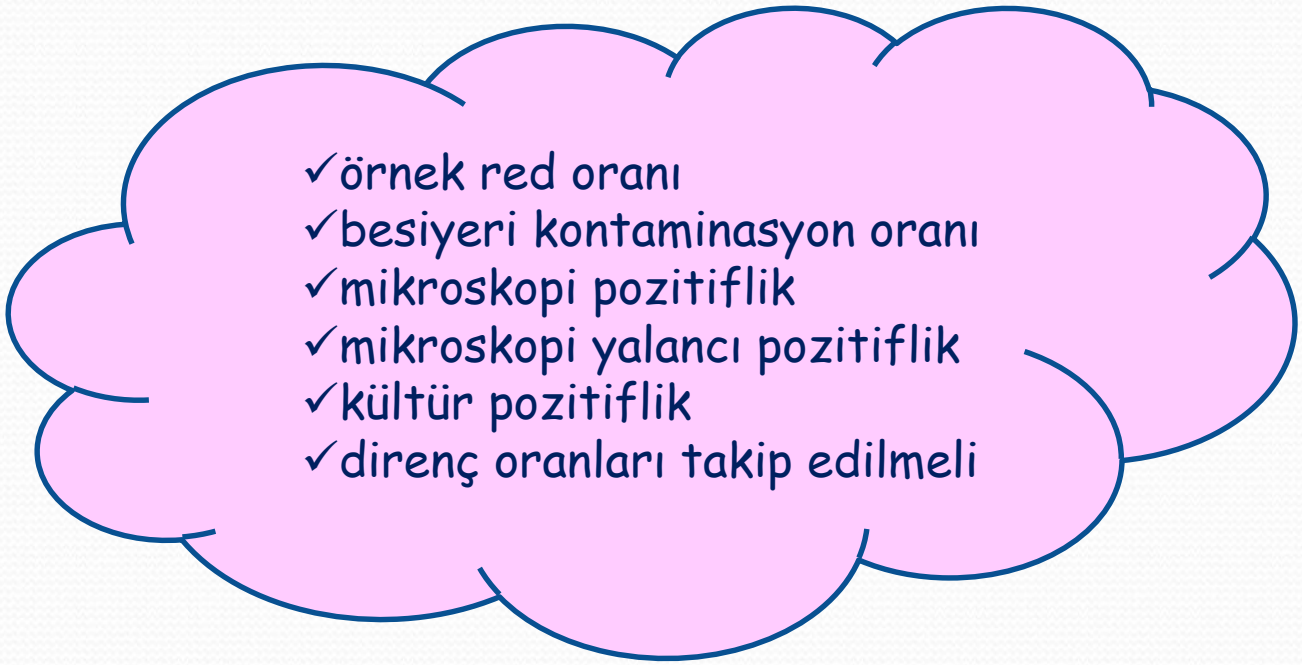
İDT Öneri

Xpert MTBC/RIF uygulanması mikroskopi, kültür ve İDT ihtiyacını ortadan kaldırmaz

- ✓ ÇİD-TB kuşkusunda Xpert MTBC/RIF testi DSÖ'nün ilk tanısal testi olarak güçlü önerilerinden

Laboratuvar uygulamaları

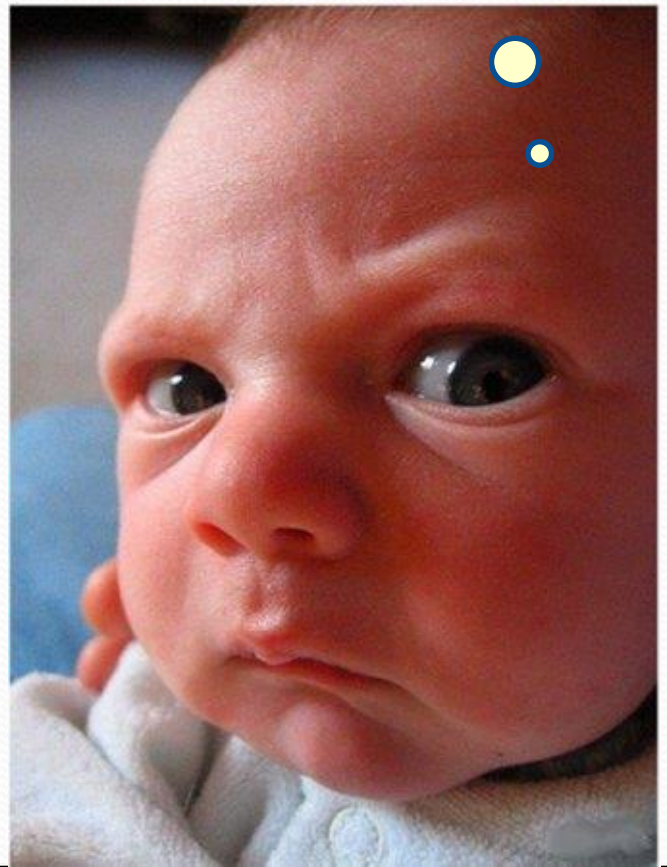
- ✓ Kalite göstergeleri



Analiz Sonrası

Sonuçların geç çıkması
Kritik değer bildirimlerinde sıkıntı

- ✓Uygun zamanda sonuçları raporlandırmak önemli
- ✓Ortalama sonuçlanma süreleri;
  - ✓Mikroskopi 24 saat
  - ✓Moleküler tanı 72 saat
  - ✓Kültür pozitifliği 21 gün
  - ✓İDT 30 gün



TB tanısında laboratuvarda yaşanan sorunların giderilmesinde

- ✓Ulusal Tüberküloz Tanı Rehberine göre çalışmak
- ✓Kalite güvencesini sağlamak (kalite göstergeleri kullanmak ve KK kurallarına uymak)
- ✓Klinisyen ile işbirliği yapmak büyük önem taşımaktadır

Laboratuvar tanısında hayallerimiz

- ✓ **Hızlı, güvenilir hasta başı testlerinin geliştirilmesi**
  - ✓ Biyomarker çalışmaları mevcut, ancak henüz uygun test geliştirilmedi
- ✓ YİD-TB'u da içerecek şekilde **ilaç direncinin hızlı tanısı** için uygun testlerin geliştirilmesi ve yöntem geçerliliğinin kanıtlanması

- ✓ Direkt bakı negatif Akc TB
- ✓ Akc dışı TB
- ✓ Çocukluk çağı TB'da tanı süresini kısaltacak algoritmlerin geliştirilmesidir

Teşekkürler…