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Inside this issue: Tuberculosis

- | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|
| Multidrug-resistant pulmonary tuberculosis treatment regimens and patient outcomes: an individual patient data meta-analysis of 9,153 patients. | 2 |
| Risk of progression to active tuberculosis following reinfection with <i>Mycobacterium tuberculosis</i>. | 2 |
| Identifying predictors of interferon-γ release assay results in pediatric latent tuberculosis: a protective role of <i>Bacillus Calmette-Guérin</i> A pTB-NET collaborative study. | 3 |
| Whole-genome sequencing of rifampicin-resistant <i>Mycobacterium tuberculosis</i> strains identifies compensatory mutations in RNA polymerase genes. | 3 |
| Surgical face masks worn by patients with multidrug-resistant tuberculosis. Impact on infectivity of air on a hospital ward. | 4 |
| 14-day bactericidal activity of PA-824, bedaquiline, pyrazinamide, and moxifloxacin combinations: a randomised trial. | 4 |
| Delamanid for multidrug-resistant pulmonary tuberculosis. | 5 |
| The immune reconstitution inflammatory syndrome after antiretroviral therapy initiation in patients with tuberculosis: findings from the SAPiT trial. | 5 |
| Fluorescein diacetate vital staining allows earlier diagnosis of rifampicin-resistant tuberculosis. | 6 |
| Predictive value of interferon-γ release assays for incident active tuberculosis: a systematic review and meta-analysis. | 6 |

Multidrug-resistant pulmonary tuberculosis treatment regimens and patient outcomes: an individual patient data meta-analysis of 9,153 patients.

Authors: Ahuja S D, et al.

Reference: PloS Med 2012;9(8): e1001300:doi:10.1371/journal.pmed.1001300

URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3429397/>

Comments: An individual patient data meta-analysis of observational data was conducted to assess the impact on outcomes of the type, number, and duration of drugs used to treat multidrug-resistant tuberculosis (MDR-TB). A total of 9,153 patients with MDR-TB from 32 observational studies were included in this analysis. Treatment success compared to failure/relapse or death was associated with later generation quinolones, (aOR: 2.7 [1.7–4.3]), ofloxacin (aOR:2.3 [1.3–3.8]), ethionamide or prothionamide (aOR: 1.7 [1.4–2.1]), use of four or more likely effective drugs in the initial intensive phase (aOR: 2.7 [1.9–3.9]), and three or more likely effective drugs in the continuation phase (aOR: 4.5 [3.4–6.0]).

Risk of progression to active tuberculosis following reinfection with *Mycobacterium tuberculosis*.

Authors: Andrews J R, et al.

Reference: Clin Infect Dis 2012;54:784-91

URL: <http://cid.oxfordjournals.org/content/54/6/784.long>

Comments: To assess the extent to which latent infection reduces the risk of progressive disease following re-exposure and reinfection, Andrews et al reviewed 18 prospective cohort studies of persons exposed to individuals with infectious tuberculosis that were published prior to the widespread treatment of latent tuberculosis to estimate the incidence of tuberculosis among individuals with latent tuberculosis infection (LTBI group) and without latent tuberculosis (uninfected; UI group). The weighted mean adjusted incidence rate of tuberculosis in the LTBI and UI groups attributable to reinfection was 13.5 per 1000 person-years (95% confidence interval [CI]: 5.0–26.2 per 1000 person-years) and that attributable to primary infection was 60.1 per 1000 person-years (95% CI: 38.6–87.4 per 1000 person-years). Individuals with latent tuberculosis had 79% lower risk of progressive tuberculosis after reinfection than uninfected individuals.

Identifying predictors of interferon- γ release assay results in pediatric latent tuberculosis: a protective role of Bacillus Calmette-Guérin A pTB-NET collaborative study.

Authors: Basu Roy R, et al.

Reference: Am J Respir Crit Care Med 2012;186:378-84.

URL: <http://ajrccm.atsjournals.org/content/186/4/378.long>

Comments: To investigate factors influencing results of Interferon- γ (IFN- γ) release assays in children, data from five sites across Europe comprising 1,128 children were pooled and analyzed. Age was positively correlated with a positive blood result (QuantiFERON-TB Gold In-Tube: odds ratio [OR], 1.08 per year increasing age [P<0.0001]; T-SPOT.TB: OR, 1.14 per year increasing age [P<0.001]). Prior BCG vaccination was associated with a negative IFN- γ release assay result (QuantiFERON-TB Gold In-Tube: OR, 0.41 [P < 0.001]; T-SPOT.TB: OR, 0.41 [P < 0.001]). BCG vaccination may be effective in protecting children against Mycobacterium tuberculosis infection

Whole-genome sequencing of rifampicin-resistant Mycobacterium tuberculosis strains identifies compensatory mutations in RNA polymerase genes.

Authors: Comas I, et al.

Reference: Nature Genetics 2012;44:106-10.

URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3246538/>

Comments: Studies have shown that drug resistance in bacteria is often associated with a fitness cost. However, some drug-resistance mutations are associated with little or no loss of fitness, and fitness cost might be reduced by compensatory evolution. Comas et al described a set of compensatory mutations in the RNA polymerase genes of rifampicin-resistant M. tuberculosis and reported that M. tuberculosis strains harboring these compensatory mutations showed a high competitive fitness in vitro and a relatively high clinical frequency across patient populations.

Surgical face masks worn by patients with multidrug-resistant tuberculosis. Impact on infectivity of air on a hospital ward.

Authors: Dharmadhikari A S, et al.

Reference: Am J Respir Crit Care Med 2012;185:1104-9.

URL: <http://ajrccm.atsjournals.org/content/185/10/1104.long>

Comments: To investigate whether surgical face masks worn by patients with multidrug-resistant tuberculosis (MDR-TB) reduce transmission, 17 patients with pulmonary MDR-TB at an MDR-TB ward in South Africa wore face masks on alternate days. Ward air was exhausted to two identical chambers, each housing 90 pathogen-free guinea pigs that breathed ward air either when patients wore surgical face masks (intervention group) or when patients did not wear masks (control group). Sixty-nine of 90 control guinea pigs (76.6%; 95% confidence interval [CI], 68–85%) became infected, compared with 36 of 90 intervention guinea pigs (40%; 95% CI, 31–51%), representing a 56% (95% CI, 33–70.5%) decreased risk of TB transmission when patients used masks.

14-day bactericidal activity of PA-824, bedaquiline, pyrazinamide, and moxifloxacin combinations: a randomised trial.

Authors: Diacon A H, et al.

Reference: Lancet 2012;380:986-93

URL: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(12\)61080-0/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61080-0/fulltext)

Comments: To assess early bactericidal activity (EBA) of various combinations of new anti-tuberculosis drugs, treatment-naive, drug-susceptible patients with uncomplicated pulmonary tuberculosis were randomised to receive bedaquiline, bedaquiline-pyrazinamide, PA-824-pyrazinamide, bedaquiline-PA-824, PA-824-moxifloxacin-pyrazinamide, or unmasked standard antituberculosis treatment as positive control. The mean 14-day EBA of PA-824-moxifloxacin-pyrazinamide (0.233 [SD 0.128]) was significantly higher than that of bedaquiline (0.061 [0.068]), bedaquiline-pyrazinamide (0.131 [0.102]), bedaquiline-PA-824 (0.114 [0.050]), but not PA-824-pyrazinamide (0.154 [0.040]), and comparable with that of standard treatment (0.140 [0.094]). One patient on PA-824-moxifloxacin-pyrazinamide was withdrawn because of corrected QT interval changes exceeding criteria pre-specified in the protocol.

Delamanid for multidrug-resistant pulmonary tuberculosis.

Authors: Gler M T, et al.

Reference: N Engl J Med 2012;366:2151-60.

URL: <http://www.nejm.org/doi/full/10.1056/NEJMoa1112433>

Comments: Delamanid (OPC-67683) is a nitro-dihydro-imidazooxazole derivative that inhibits mycolic acid synthesis of tuberculosis bacilli. In this randomized, placebo-controlled, multinational clinical trial, 481 patients with pulmonary multidrug-resistant tuberculosis were assigned to receive delamanid, at a dose of 100 mg twice daily (161 patients) or 200 mg twice daily (160 patients), or placebo (160 patients) for 2 months in combination with a background drug regimen according to World Health Organization guidelines. Among patients who received a background drug regimen plus 100 mg of delamanid twice daily, 45.4% had sputum-culture conversion in liquid broth at 2 months, as compared with 29.6% of patients who received a background drug regimen plus placebo ($P = 0.008$). Similar results were observed among patients who received the background drug regimen plus 200 mg of delamanid twice daily (41.9%, $P = 0.04$). Although no clinical events due to QT prolongation on electrocardiography were observed, QT prolongation was reported significantly more frequently in the groups that received delamanid.

The immune reconstitution inflammatory syndrome after antiretroviral therapy initiation in patients with tuberculosis: findings from the SAPiT trial.

Authors: Naidoo K, et al.

Reference: Ann Intern Med 2012;157:313-24.

URL: <http://annals.org/article.aspx?articleid=1355683>

Comments: To evaluate the immune reconstitution inflammatory syndrome (IRIS) relative to the timing of ART initiation in patients with HIV-related tuberculosis, 642 patients were randomly assigned to initiate ART within 4 weeks of tuberculosis treatment initiation (early integrated treatment group), within 4 weeks of completion of the intensive phase of tuberculosis treatment (late integrated treatment group), or within 4 weeks after tuberculosis therapy completion (sequential treatment group). Incidence of IRIS was 19.5, 7.5, and 8.1 per 100 person-years in the early integrated, late integrated, and sequential treatment groups, respectively. Incidence of IRIS was higher in the early integrated treatment group than in the late integrated (incidence

rate ratio, 2.6 [95% CI, 1.5 to 4.8]; $P < 0.001$) or sequential (incidence rate ratio, 2.4 [CI, 1.4 to 4.4]; $P < 0.001$) treatment groups.

Fluorescein diacetate vital staining allows earlier diagnosis of rifampicin-resistant tuberculosis.

Authors: Van Deun A, et al.

Reference: Int J Tuberc Lung Dis 2012;16:1174-9.

URL: <http://www.ncbi.nlm.nih.gov/pubmed/?term=Fluorescein+diacetate+vital+staining+allows+earlier+diagnosis+of+rifampicin-resistant+tuberculosis>.

Comments: To evaluate use of sputum smear fluorescein diacetate (FDA) vital staining to predict culture-defined failure and rifampicin (RMP) resistance, 1633 episodes of auramine smear defined late conversion and failure were analyzed. Negative FDA was 95% predictive of negative culture in patients on first treatment, and its positive predictive value was around 95% during re-treatment. FDA correctly identified 88–98% of all RMP resistance. FDA staining increased the proportion of tuberculosis patients put on second-line treatment without receiving the standard first-line retreatment regimen.

Predictive value of interferon-g release assays for incident active tuberculosis: a systematic review and meta-analysis.

Authors: Rangaka M X, et al.

Reference: Lancet Infect Dis 2012;12:45-55.

URL: [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(11\)70210-9/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(11)70210-9/fulltext)

Comments: A systematic review and meta-analysis was conducted to assess risk of development of active tuberculosis among individuals with positive results of interferon- γ release assays (IGRAs) and that of the tuberculin skin test (TST). Incidence rate ratios (IRR) for rates of disease progression were calculated. Incidence of tuberculosis during a median follow-up of 4 years (IQR 2–6) was 4–48 cases per 1000 person-years. Compared with test-negative results, pooled IRR was 2.11 [95% CI 1.29–3.46] for IGRA and 1.60 [0.94–2.72] for TST at the 10 mm cutoff. The proportion of IGRA-positive individuals in seven of 11 studies that assessed both IGRAs and TST was generally lower than TST-positive individuals.

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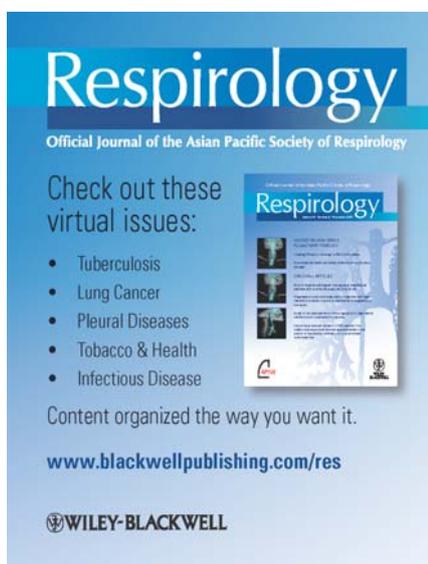
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