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Epidemiology

**Passive smoking and tuberculosis**

Authors: Leung CC et al.


URL: [http://archinte.ama-assn.org/cgi/content/abstract/170/3/287](http://archinte.ama-assn.org/cgi/content/abstract/170/3/287)

Comment: The relationship between passive smoking and development of tuberculosis was assessed in a prospective follow-up cohort of 15,486 female never-smokers, aged 65–74 years, with adjustment for other baseline characteristics. Passive exposure to second-hand tobacco smoke in the household was independently associated with obstructive pulmonary disease (odds ratio 1.43, 95% confidence interval 1.16 – 1.77) and diabetes mellitus (OR 1.13, 95% CI 1.02 – 1.26) at baseline, and with the development of active tuberculosis (hazard ratio 1.49, 95% CI 1.01 – 2.19) on prospective follow-up. Thus, passive exposure to environmental tobacco smoke, like active smoking, can also increase the risk of developing active tuberculosis, reiterating the importance of tobacco control in tuberculosis programmes.
Development of extensively drug-resistant tuberculosis during multidrug-resistant tuberculosis treatment

Authors: Shin SS et al.


URL: http://ajrccm.atsjournals.org/cgi/content/full/182/3/426

Comment: For clinical and public health reasons it is clearly important to prevent amplification of drug resistance from multidrug-resistant tuberculosis (MDR-TB) to extensively drug-resistant tuberculosis (XDR-TB). A retrospective analysis was performed of 608 consecutive patients receiving treatment for MDR-TB. Bilateral and cavitary lesions were associated with a greater than 3-fold increase in risk of failure or non-completion of treatment. Prior exposure to a second-line injectable drug was associated with a greater than 3-fold risk, and each additional month, during which a patient failed to take at least 80% of their prescribed drugs, was associated with an additional 20% risk of developing XDR-TB. Thus, early and rapid diagnosis of MDR-TB, followed by timely commencement of appropriate chemotherapy under programmatic settings is mandatory to prevent the worsening of drug-resistance scenarios.

HIV co-infection in multidrug- and extensively drug-resistant tuberculosis results in high early mortality

Authors: Gandhi NR et al.


URL: http://ajrccm.atsjournals.org/cgi/content/full/181/1/80

Comment: From 2005 through 2007, two hundred and seventy-two cases of multidrug-resistant tuberculosis (MDR-TB) and 382 cases of extensively drug-resistant tuberculosis (XDR-TB) were diagnosed in Tugela Ferry, South Africa. HIV co-infection rates were found to be 90% and 98%, respectively. One-year mortality was 71% for MDR-TB patients and 83% for XDR-TB patients, with death occurring within 30 days of collection of sputum for examination, in 40% and 51% of patients, respectively. Although the one-year mortality rates improved from 2005 to 2007, these rates still appear to be very high, especially within the first 30 days. Thus, early diagnosis of HIV related drug-resistant TB, and prompt initiation of second-line anti-tuberculosis therapy and anti-retroviral treatment are clearly warranted.
Diagnosis

**Response to Rv2628 latency antigen associates with cured tuberculosis and remote infection**

Authors: Goletti D et al.


URL: [http://www.eur.ersjournals.com/content/36/1/135.full](http://www.eur.ersjournals.com/content/36/1/135.full)

Comment: Generally speaking, interferon-gamma release assays based on RD1 antigens do not discriminate well between recent infections and remote infections due to *Mycobacterium tuberculosis*. In a study involving 16 individuals with remote infections and 23 subjects with recent infections, as well as 15 healthy control subjects, 50 patients with active tuberculosis and 45 patients with cured tuberculosis, subjects with remote infections had significantly higher interferon-gamma whole blood responses to the *M. tuberculosis* latency antigen Rv2628 than individuals with recent infections, those with active tuberculosis and control subjects. The proportion of responders was also 5-fold higher. These findings, not only suggest a protective role for the immune response to this latency antigen, but also indicate the potential usefulness of this response for tracing tuberculosis contacts.

**Evaluation of quantitative IFN-γ response for risk stratification of active tuberculosis suspects**

Authors: Metcalfe JZ et al.

Reference: Am J Respir Crit Care Med 2010; 181: 87-93.

URL: [http://ajrccm.atsjournals.org/cgi/reprint/181/1/87](http://ajrccm.atsjournals.org/cgi/reprint/181/1/87)

Comment: Among 660 active tuberculosis suspects, the odds of active disease increased by 7% for each doubling of interferon (IFN)-gamma level. Higher quantitative interferon-gamma levels added clinical value to a prediction model incorporating conventional risk factors, and correctly re-classified 32% of tuberculosis suspects into higher or lower risk categories. However, such benefit may be attenuated in centres with high levels of clinical experience. Thus, it appears that the predictive accuracy of quantitative interferon-gamma levels should be evaluated in other settings. These findings would be of value in the application of interferon-gamma response to the diagnosis of active tuberculosis.

**Direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-Cut needle biopsies for pleural tuberculosis**

Authors: Koegelenberg CF et al.


URL: [http://thorax.bmj.com/content/65/10/857.full](http://thorax.bmj.com/content/65/10/857.full)

Comment: Among 89 patients suspected of having tuberculous pleuritis, either four or more Abrams needle biopsies followed by four or more Tru-Cut needle biopsies, or vice versa, were performed with ultrasound assistance, after randomization. Pleural biopsy specimens obtained with an Abrams needle yielded pleural tissue in 91% of patients, with a diagnostic sensitivity of 81.8%, whereas the Tru-Cut needle yielded tissue in 78.7% of patients (p = 0.015), with a diagnostic sensitivity of 65.2% (p = 0.022). Thus, an Abrams needle would be preferred to a Tru-Cut needle, for investigating possible cases of tuberculous pleuritis under ultrasound guidance.
Efficacy of a 6-month versus 9-month intermittent treatment regimen in HIV-infected patients with tuberculosis

Authors: Swaminathan S et al.
URL: http://ajrccm.atsjournals.org/cgi/content/full/181/7/743
Comment: A randomized clinical trial was conducted comparing two intermittent anti-tuberculosis drug regimens, administered for 6 months and 9 months, respectively, for treatment of tuberculosis in HIV-infected patients. While there was a similarly favourable response to therapy in both groups, bacteriological recurrences occurred significantly more frequently in the “6-month” group (15% vs 7%, p <0.05). By 36 months, 36% of patients in the “6-month” group and 35% of patients in the “9-month” group had died. Among the patients who failed to respond to chemotherapy, all developed acquired rifamycin resistance, with the main risk factor being baseline isoniazid resistance. Thus, some HIV-infected patients are likely to require more than 6 months of therapy for tuberculosis. Daily regimens should be administered rather than intermittent regimens.

Timing of initiation of antiretroviral drugs during tuberculosis therapy

Authors: Abdool Karim SS et al.
Comment: The optimal timing for commencing antiretroviral therapy during antituberculosis treatment remains uncertain. In an analysis of patients assigned to start antiretroviral therapy either during antituberculosis treatment (in two integrated-therapy groups), or after the completion of antituberculosis treatment (in one sequential-therapy group), there was an observed reduction in the rate of death in the combined integrated-therapy groups, as compared with the sequential-therapy group – a relative reduction of 56% (hazard ratio = 0.44, 95% confidence interval 0.25 – 0.79). Thus, the initiation of antiretroviral therapy significantly improved survival and the findings provide support for integration/collaboration between tuberculosis and HIV services.
Treatment outcomes among patients with extensively drug-resistant tuberculosis: systematic review and meta-analysis

Authors: Jacobson KR et al.
URL: [http://www.journals.uchicago.edu/doi/full/10.1086/653115](http://www.journals.uchicago.edu/doi/full/10.1086/653115)
Comment: This analysis was based on a literature search that yielded 13 observational studies covering 560 patients. Among these patients, 43.7% were cured or completed treatment and 20.8% died. Random effects meta-analysis and meta-regression showed that studies in which a higher proportion of patients received a later-generation fluoroquinolone reported cure or completion of treatment more frequently. This potentially important observation suggests a possible role for later generation fluoroquinolones, such as moxifloxacin and levofloxacin, in the treatment of extensively drug-resistant tuberculosis, and this should be more systematically evaluated in clinical trials.

Early bactericidal activity and pharmacokinetics of PA-824 in smear-positive tuberculosis patients

Authors: Diacon AH et al.
URL: [http://aac.asm.org/cgi/content/abstract/54/8/3402](http://aac.asm.org/cgi/content/abstract/54/8/3402)
Comment: PA-824 is a novel nitroimidazo-oxazine that has been developed for the treatment of tuberculosis. A randomized study was undertaken to evaluate its safety, tolerability, pharmacokinetics and extended early bactericidal activity. PA-824 demonstrated dose-linear but less than dose-proportional increases in serum concentrations at dosages from 200 – 1000 mg daily. A dose of 1200 mg conferred no additional exposure compared to 1000 mg. The mean daily falls in bacillary colony-forming-units were equivalent over the dosage range of 200 – 1200 mg. The drug also appeared to be well tolerated and safe. Further evaluation of the optimal dosage appears warranted.