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INFECTIOUS DISEASES CORNER

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**Four Months of Rifampin or Nine Months of Isoniazid for Latent Tuberculosis in Adults.**
**D. Menzies, M. Adjobimey, R. Ruslami, A. Trajman, O. Sow, H. Kim, J. Obeng Baah, G.B. Marks, R. Long, V. Hoeppner, K. Elwood, H. Al-Jahdali, M. Gninafon, L. Apriani, R.C. Koesoemadinata, A. Kritski, V. Rolla, B. Bah, A. Camara, I. Boakye, V.J. Cook, H. Goldberg, C. Valiquette, K. Hornby, M.-J. Dion, P.-Z. Li, P.C. Hill, K. Schwartzman, and A. Benedetti. *N Engl J Med* 2018; 379:440-453.**

Tuberculosis constitutes a major health problem, with approximately 10.4 million new cases of tuberculosis worldwide reported in 2015. It has been estimated that one quarter of the global population has latent tuberculosis infection. Nowadays, given that enormous reservoir in mind, the treatment of latent tuberculosis infection is a key part of the elimination of tuberculosis strategies, world widely. A 9-month regimen of isoniazid is usually used to prevent active tuberculosis in persons with latent tuberculosis infection. However, this regimen has been associated with poor adherence rates and potentially severe adverse side effects, in terms of hepatotoxicity. In a trial conducted in nine countries, researchers randomly assigned adults with latent tuberculosis infection to receive treatment with a 4-month regimen of rifampin or a 9-month regimen of isoniazid for the prevention of confirmed active tuberculosis. The 4-month regimen of rifampin was not inferior to the 9-month regimen of isoniazid for the prevention of active tuberculosis and was related to a higher rate of completion of treatment and better safety outcomes.

**Management of KPC-producing Klebsiella pneumoniae infections.**
**M. Bassetti, D.R. Giacobbe, H. Giamarellou, C. Viscoli, G.L. Daikos, G. Dimopoulos, F.G. De Rosa, E.J. Giamarellos-Bourboulis, G.M. Rossolini, E. Righi, I. Karaiskos, M. Tumbarello, D.P. Nicolau, P.L. Viale, G. Poulakou, on behalf of the Critically Ill Patients Study Group of the European Society of Clinical Microbiology and Infectious Disease (ESCMID), Hellenic Society of Chemotherapy (HSC) and Societa Italiana di Terapia Antinfettiva (SITA). *Clin Microbiol Infection* 2018; 24:133-144.**

Klebsiella pneumoniae carbapenemase (KPC)-producing *K. pneumoniae* (KPC-KP), has become one of the most important contemporary pathogens, especially in endemic areas, such as the Mediterranean. Several new diagnostic technologies have recently become available to allow increased rapidity of microbiologic diagnosis, including matrix-assisted desorption ionization-time of flight mass spectrometry (MALDI-TOF MS), rapid immunochromatography, rapid enzymatic assays (such as the Carba NP test), single cell automated time-lapse microscopy and molecular biology based assays. Because monotherapy appeared to be associated with higher mortality rates compared to combination therapy for the targeted treatment of KPC-KP strains in observational studies, the use of combined regimens should be preferred in patients with severe KPC-KP infections. In combination treatment, meropenem may still be considered as an option for possibly enhancing bacterial killing, provided that the MIC of meropenem is 8 mg/L and that a high-dose and prolonged infusion regimen is administered. Other plausible antibiotics, include polymyxins (colistin and polymyxin B), tigecycline, aminoglycosides, fosfomycin and ceftazidime-avibactam. Optimal treatment duration for KPC-KP infections is unclear. In retrospective studies, a mean duration of 2 weeks of treatment was reported to be efficacious.

**Treatment of Infections by OXA-48-Producing Enterobacteriaceae.**
**Adam Stewart, Patrick Harris, Andrew Henderson, David Paterson. *Antimicrobial Agents Chemother* 2018; 62:e01195-18.**

Carbapenemase-producing Enterobacteriaceae (CPE) poses global public health threat in terms of antimicrobial resistance. OXA-48 and its variants are unique carbapenemases with low-level hydrolytic activity toward carbapenems, but

no intrinsic activity against expanded-spectrum cephalosporins. Despite the inability of OXA-48-like carbapenemases to hydrolyze expanded-spectrum cephalosporins, pooled isolates demonstrate high variable resistance to ceftazidime and cefepime, likely representing high rates of extended-spectrum beta-lactamase (ESBL) co-production. In vitro data from pooled studies, suggest that avibactam is the most potent beta-lactamase inhibitor when combined with ceftazidime, cefepime, aztreonam, meropenem, or imipenem. Avibactam is a diazabicyclooctane, a non-beta-lactam beta-lactamase inhibitor, which may have the ability to inhibit OXA-48 beta-lactamase by forming a stable covalent complex. Resistance to novel avibactam combinations, such as imipenem-avibactam or aztreonam-avibactam has not yet been reported in OXA-48 producers, although only a few clinical isolates have been tested. Although combination therapy is thought to improve the chances of clinical cure and survival in CPE infection, successful outcomes were seen in 70% of patients with infections caused by OXA-48-producing Enterobacteriaceae treated with ceftazidime-avibactam monotherapy. A carbapenem in combination with either amikacin or colistin has achieved treatment success in a few case reports, too. Uncertainty remains regarding the best treatment options and strategies for managing these infections. Newly available antibiotics such as ceftazidime-avibactam show promise; however, recent reports of resistance are really concerning. Newer choices of antimicrobial agents are truly required to combat this resistance problem.