

SEPAR continues to recommend 180 doses of isoniazid or the equivalent of 6 months treatment.¹ Treatment of tuberculosis infection with 6 months of isoniazid reduces the risk of developing the disease by 69%, a reduction that is noticeably less than the 93% reduction achieved with 9 months of isoniazid.² The ATS gives preference to 9 months of isoniazid treatment and only considers 6 as an acceptable alternative,³ one which cannot be used by patients with concomitant human immunodeficiency virus infection or those with fibrosis.¹ Neither can it be used by children, it should be added, especially those under 5,⁴ but this situation is not included in SEPAR's guidelines.¹

Claims have been made that the 6-month isoniazid treatment for tuberculosis infection is more cost-effective than the 9-month regimen,² but we agree with Rieder² in that "the primary decision that has to be taken in the selection of a regimen (curative or preventive) is efficacy; the second is effectiveness."

It follows that treatment of tuberculosis infection with isoniazid must be continued for at least 6 months² but that the maximum benefit possible for the patient will be achieved with the 9-month regimen, which is the one of choice.

Adverse iatrogenic effects with isoniazid are not common after 6 months of treatment,² and an additional 3 months of isoniazid exposes patients to hardly any more risk of damage, provided they are adequately monitored, while the risk of infection is reduced significantly. If isoniazid produces side effects (from hepatotoxicity) in the last 3 months of 9 months of treatment, such effects will reverse upon immediate suppression of isoniazid, as they do in the first 6 months of treatment, when hepatotoxicity is more common.²

In order to shorten treatment of tuberculosis infection, regimens have been studied that contain rifampicin, on its own or combined with isoniazid or pyrazinamide: rifampicin for 3 or 4 months, rifampicin and isoniazid for 3 months, and rifampicin and pyrazinamide for 2 months. These regimens have been tested in comparison with placebo or isoniazid (equivalence studies). We found that equivalence studies of 3 months of rifampicin, 4 months of rifampicin, and 3 months of rifampicin and isoniazid had been compared with the 6-month isoniazid regimen and not the 9-month one, and had shown a similar efficacy to 6 months isoniazid or, in the case of rifampicin alone, even slightly better efficacy.^{2,4,5} If these short course treatments of 4 months of rifampicin and 3 months of rifampicin and isoniazid already exist, why use a 6-month isoniazid treatment of similar efficacy, but not as short, knowing that with 3 months more (9 months of isoniazid) efficacy would increase from 69% to 93% (an increment of 35%)? The ideal is a short course with an efficacy which has not only been demonstrated to be similar to 6 months isoniazid but to 9 months isoniazid as well. These characteristics have only been found in 2 months rifampicin and pyrazinamide, but recent studies show that use of this treatment must be restricted due to its hepatotoxicity.^{2,6} In SEPAR's guidelines it states that 2 months of rifampicin and pyrazinamide, and 3 months

of rifampicin and isoniazid "have shown similar efficacy to the long course of isoniazid."¹ But are they comparing the 3-month course of rifampicin and isoniazid with a 6-month or a 9-month course of isoniazid?

We conclude, from the data available to date, that the 9-month isoniazid regimen must be recommended because it is efficacious, well tolerated and we are familiar with its use. Efforts must be made to insure maximum compliance, which experience has shown us is perfectly possible. The 6-month isoniazid regimen should not be recommended as there are other shorter courses with similar or better efficacy, such as 4 months of rifampicin and 3 months of rifampicin and isoniazid. In fact these regimens deserve to have an equivalence study with the 9-month isoniazid regimen (comparing the short course treatment of tuberculosis infection with the most efficacious regimen, 9 months of isoniazid) as recommended by the ATS.³

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1. Vidal R, Caylà JA, Gallardo J, Lobo A, Martín C, Ordoñez M, et al. Recomendaciones SEPAR. Normativa sobre la prevención de la tuberculosis. Arch Bronconeumol 2002;38: 441-51.
2. Rieder HL. Interventions for tuberculosis control and elimination. Proceedings of International Union Against Tuberculosis and Lung Disease. Paris, 2002; p. 17-35 and 127-45.
3. Comstock GW. How much isoniazid is needed for prevention of tuberculosis among immunocompetent adults? Int J Tuberc Lung Dis 1999;3:847-50.
4. ATS. Targeted tuberculin testing and treatment of latent TB infection. Am Respir Crit Care Med 2000;161:S221-S47.
5. Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: Code of Practice 2000. Thorax 2000; 55: 8876-901.
6. CDC. Public Health Dispatch: update: fatal and severe liver injuries associated with rifampicin and pyrazinamide. Treatment for latent tuberculosis infection. MMWR 2002; 51:998-9. 51.603

Comments on the Guidelines for the Prevention of Tuberculosis of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)

To the Editor: In the guidelines of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) on the prevention of tuberculosis,¹ treatment with rifampicin is recommended at a dosage of 15 mg/kg (maximum 900 mg) and isoniazid at a dosage of 15 mg/kg (maximum 900 mg), both drugs in a 3-times-per-week regimen (Table 7 of the SEPAR guidelines). The accepted dosage of rifampicin, however, is 10 mg/kg to a maximum 600 mg, the same as in a daily regimen, because higher dosages increase the chances of flu-like syndrome²; the accepted dosage of isoniazid in a 3-times-weekly regimen is also 10 mg/kg to a maximum 600 mg.²

Another aspect we would like to comment on is the authors' recommendation of 6 months of isoniazid in the treatment of tuberculosis infection. Maximum efficacy is known to be achieved when over 80% of the prescribed doses of 12 months of isoniazid has been administered² or when isoniazid has been continued for 9 months.³ The American Thoracic Society (ATS) and the Centers for Disease Control and Prevention recommend 270 doses of isoniazid over a period of 9 to 12 months,⁴ the optimal regimen as recognized by SEPAR in its guidelines.¹ Nevertheless,