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

To the editor: We greatly appreciate the critical review and comments on the Guidelines for the Prevention of Tuberculosis made by Pina et al as they have led us to think over the points they consider debatable.

The first question they raise concerns the dosages of intermittently administered

rifampicin (R) and isoniazid (H) for chemical prophylaxis or tuberculosis infection treatment. In the first place we ought to point out that these intermittent regimens are hardly ever used in Spain; in particular, R is not usually prescribed, as it would only be recommended for persons who are contacts of patients resistant to H and in the exceptional circumstances of patients who can not follow a daily regimen of 4R. We agree that the dose of R that is usually recommended is 600 mg, but in intermittent treatments failure to take a single dose or to absorb it properly would render the treatment ineffective. Treatment is more likely to be successful with a dose of 900 mg and there is only a slight increase in risk for the very infrequent "flu-like syndrome." However, we would accept replacing 900 mg with 600 to 900 mg.

The dose of 15 mg/kg with a maximum of 900 mg of H in intermittent chemical prophylaxis is recommended by the American Thoracic Society (ATS) both in intermittent treatment and for prevention.[1,2]

Secondly, the duration of treatment in chemical prophylaxis using H is a very controversial subject that will soon be resolved by the regular use of shorter treatment regimens using 2 drugs. Such regimens have higher adherence rates and are therefore more effective. The 1994 North American guidelines issued jointly by the ATS, the Centers for Disease Control and Prevention, and the Infectious Diseases Society of America recommended that treatment should last 6 months, as did the writers of the 1992 Spanish consensus report for the control of tuberculosis and the recommendations of the Research Unit on Tuberculosis of Barcelona.[3] However, the 2000 ATS Guidelines already recommended a treatment regimen of 9 months. This change of policy is based on Comstok's[4] theoretical re-evaluation of the results of 2 studies carried out in the 1960s. One of the studies dealt only with persons presenting untreated fibrotic lesions and reported the successful prevention of re-infection in 69% of patients using 6H and in 93% using 12H. The other study focused mostly on analyzing the total amount of H taken. A policy change was not endorsed by the British Thoracic Society (BTS) in its latest recommendations[5] or by a recent Spanish consensus conference. We still think that a 6-month course of treatment, as is given to the source case with very similar results, is more recommendable.[5] However, treatment may be extended from 6 to 9 or 12 months in individual cases when the prescribing physician thinks it appropriate, given that less than 6 months is not to be recommended and more than 12 months is not necessary.

In any case the 2000 ATS Guidelines on which Pina et al. have based their observations, have several disputable points. In the first place, they replace the term "chemical prophylaxis" with "latent tuberculosis infection treatment," arguing that the word treatment is more forceful and persuades the patient to be more compliant. However in many cases it could have negative repercussions on healthy contacts by leading them to believe that they are ill and need to isolate themselves. Furthermore, we think that the addition of "latent" is unnecessary. Consequently, we have continued to use both "chemical prophylaxis" and "tuberculosis infection treatment" as synonyms.

The SEPAR guidelines also recommend a short treatment protocol using 2 drugs: R and pyrazinamide (Z), 2 RZ, which is giving an unacceptable rate of severe hepatotoxicity unless patients are monitored very frequently[6]; but the 3RH regimen advocated by the BTS[5] as equally effective, better tolerated, and more easily administered is not even mentioned.

Finally we would like to point out that, in the future, chemical prophylaxis or tuberculosis infection treatment should be based on short courses of therapy as it is unrealistic to expect persons without symptoms to follow preventive treatments lasting 9 months or more (longer than the treatment given to people who are sick). This is particularly true given that it is unlikely that most of these people will develop tuberculosis.

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2. ATS. Targeted tuberculin testing and treatment of latent TB infection. Am J RespirCrit Care Med 2000;161:S221-S47.
3. Grupo de Estudio de Contactos de la Unidad de Investigación en Tuberculosis de Barcelona. Documento de consenso sobre el estudio de contactos en los pacientes tuberculosos. Med Clin (Barc) 1999;112:151-6.
4. Comstock GW. How much isoniazid is needed for prevention of tuberculosis among immunocompetent adults? Int J Tuberc Lung Dis 1999;3:847-80.
5. Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: Code of Practice 2000. Thorax 2000; 55:887-901.
6. CDC. Fatal and severe liver injuries associated with rifampicin and pyrazinamide treatment for latent tuberculosis infection. MMWR 2002;51:998-99.