

GUEST EDITORIAL

ISONIAZID AND THE LIVER

The discovery in 1951 of the antimycobacterial property of isonicotinic acid hydrazide (isoniazid, INH, INA) introduced into the therapeutic armamentarium one of the most effective tools ever known for the control of an infectious disease. In addition to efficacy it possessed the features of low toxicity, cost, and ease of oral administration with concomitant patient acceptance.

In the ensuing years the therapeutic value of isoniazid in the treatment of active tuberculosis has been proven abundantly in world-wide clinical use.

Soon after its introduction, studies suggested that it also possessed prophylactic potential. Extensive trials have clearly established that it is very effective in preventing tuberculosis infection from becoming active disease. In high risk groups morbidity has been consistently reduced by 50-75% over an extended period of years. As a result its prophylactic administration has become widespread. Its paucity of untoward reactions has been considered one of its outstanding advantages.

In the past few years, there has appeared to be an increasing number of instances of isoniazid-associated liver dysfunction.

Recently an Ad Hoc Committee on Isoniazid and Liver Disease, appointed by the U.S.P.H.S. Center for Disease Control to study data on isoniazid-associated liver disease and to advise on its future use as preventive treatment against tuberculosis, presented its report.

In brief, the committee concluded that liver disease can occur in patients receiving isoniazid but that the risk is very small—varying from 0 to 10 cases per 1,000 patients per year. The committee felt that no changes are warranted in the present use of the drug in treating active tuberculosis; and

that the present program of isoniazid preventive treatment and the guidelines for selection of recipients should not be modified at this time. However, the report did recommend that all preventive therapy candidates and recipients should be carefully screened and monitored at monthly intervals to detect incipient liver dysfunction. The report detailed the surveillance procedures.

In reaching a judgment as to whether or not to place a patient on preventive therapy the physician must weigh the risk of possible hepatic damage—the order of this has been mentioned above—against the risk of the development of active disease. The latter varies considerably in various high risk groups. In household contacts it is about 1 in 30 during the first year after discovery of the index case; there is a similar risk in recent converters of any age; and in persons with previously known, but now inactive tuberculosis who have not had adequate chemotherapy, the annual risk is about 1 in 75. One must also consider that while the risk of liver damage is present only during the year of preventive therapy, the risk of developing active tuberculosis in the absence of chemoprophylaxis remains a lifetime matter with hazard not only to the individual but to his family and close contacts—and thus to the community—health and cost-wise.

Isoniazid remains a powerful and very effective antituberculosis agent which merits continued therapeutic and prophylactic use even though liver dysfunction can be associated with its use. The individual and the community advantages of its use overbalance the rare possible untoward reactions.

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