# Note

## ISONIAZID PROPHYLAXIS AMONG ALASKAN ESKIMOS: A Final Report of the Bethel Isoniazid Studies[1, 2]


**Summary**

As a result of numerous trials, isoniazid prophylaxis was shown to be effective in preventing tuberculosis in many different populations and under a variety of conditions. However, the duration of the protective effect has been of some concern. In a previous report, the protective effect of isoniazid prophylaxis among Alaskan Eskimos was shown to persist through the fifteenth year after its administration. In this final report, the protective effect is shown to persist for more than 19 years. The magnitude of the effect is related to the amount of isoniazid taken. The results of the study are consistent with the hypothesis that the decrease in risk of tuberculosis produced by isoniazid preventive therapy is lifelong.


Isoniazid administered daily for 1 year has been shown to be effective in preventing tuberculosis in many different populations and under a variety of conditions (1). However, the duration of this protective effect has been of some concern since the earliest preventive therapy trials were reported.

Theoretically, the effect of isoniazid could be only a temporary suppression of the growth of tubercle bacilli that would render them incapable of causing disease during and immediately after therapy. Thereafter, the disease-producing capability of these organisms might be restored. If this were the case, tuberculosis case rates among isoniazid recipients would be expected to be lower than case rates among placebo recipients only during the period of isoniazid administration and shortly thereafter. Subsequently, the tuberculosis case rate among isoniazid recipients should be equal to or even greater than the rate in the placebo group. On the other hand, if tubercle bacilli harbored by infected persons are killed or otherwise rendered incapable of causing disease by isoniazid, or are decreased sufficiently in numbers so that the bodily defenses of most persons can handle the surviving bacilli, the drug's protective effect should be lifelong, assuming that "exogenous" reinfection does not occur.

In a previous publication we reported that the effectiveness of isoniazid prophylaxis among Alaskan Eskimos had persisted through the fifteenth year after its administration (2). This final report extends our observations to slightly longer than 19 years. It deals with 2 topics: (*1*) the duration of effectiveness if isoniazid prophylaxis, and (*2*) the relationship of subsequent tuberculosis case rates to the amount of isoniazid taken in 2 Alaskan chemoprophylaxis programs.

These 2 programs among Eskimos in the Bethel area of Alaska were part of the extensive studies of isoniazid prophylaxis conducted by the U.S. Public Health Service. These investigations have been previously described in detail (3, 4). In December 1957, the first program, a placebo-controlled trial of isoniazid prophylaxis, was initiated using a recommended dosage of 4 to 8 mg of isoniazid per kg of body weight once per day for 1 year. Because isoniazid was successful in decreasing case rates among persons receiving this medication, it was offered in the same dosage to all residents of the area (including those who participated in the first program) in a second program that was begun in 1963.

In this report, the study population is limited to persons who participated in both of these programs to some extent, who took only one medication (placebo or isoniazid) in the first program, and who were not being treated for tuberculosis at the time of the second program. Slightly more than one fifth of the study group are known to have been previously treated for tuberculosis, most of them before the start of the first program. Although it was not possible to determine details of treatment because of the considerable number of widely scattered institutions involved in treatment of Alaskans in the 1950s, it can safely be assumed that many and perhaps most of the previously treated group had had isoniazid included in their treatment regimens. It is also likely that in recent years a few other study subjects received ison-


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[2] Requests for reprints should be addressed to Technical Information Services, Bureau of State Services, Center for Disease Control, Atlanta, Ga. 30333.