ISONIAZID PROPHYLAXIS IN AN UNDEVELOPED AREA[1]

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(Received for publication August 10, 1962)

Introduction

The remarkable therapeutic effectiveness of isoniazid led the U.S. Public Health Service, among others, to study its usefulness as a prophylactic agent against tuberculosis. After large-scale animal studies had shown that isoniazid could prevent tuberculosis under laboratory conditions (1, 2), controlled field trials were initiated among humans. A primary consideration in selecting populations for field trials was the expectation that their risk of developing serious tuberculosis would be high. But it was also important to study isoniazid prophylaxis under conditions similar to its potential application in tuberculosis control programs. Thus, the first trial by the Public Health Service cooperative groups involved children with asymptomatic primary tuberculosis (3); the second, household associates of persons with active tuberculosis (4, 5); and the third, patients in mental institutions (6). The fourth trial, in the Bethel area of Alaska, was designed to test the prophylactic usefulness of isoniazid among entire communities in an undeveloped area with a serious tuberculosis problem.

Background of Study

The Bethel Hospital Service area, shown in figure 1, lies in southwestern Alaska, north of the Alaskan peninsula but south of the Arctic Circle. Encompassing the entire drainage area of the Kuskokwim River as well as that of the lower Yukon, its area of 98,116 square miles is exceeded by that of only eight states of the United States. The locations of the 28 villages participating in the trial are shown in figure 2. All are within the sixteenth and twenty-fourth election districts, which together roughly correspond to the combined deltas of the Yukon and Kuskokwim Rivers—a flat, nearly treeless expanse where meandering rivers and countless lakes compete with tundra and bog as the dominant features of the landscape.

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The economy of this area is still largely based on fishing, hunting, and trapping. Few families have cash incomes exceeding $3,000 per year, and the purchasing power of the dollar is considerably diminished by the expense of transportation. Goods are brought to Bethel by freighter twice each summer and by daily air service from Anchorage. Transportation from Bethel to other villages in the study area is mostly by boat and small float planes in the summer and by dog team and ski-equipped planes in the winter. Almost all houses are now constructed of wood, but are very small. Two-thirds have only one room, although the average household consists of six persons. With such cramped quarters in a climate that discourages ventilation, conditions are favorable for the spread of respiratory infections among these friendly, gregarious people.

Until very recently, tuberculosis had no rival as the principal health problem of the Bethel natives. In 1956, 2 per cent of the population was first reported to have active tuberculosis (7). A year later, a tuberculin testing survey revealed an average annual infection rate of 8 per cent (8), a rate higher than any reported in the tuberculosis campaigns conducted by the World Health Organization after World War II (9). Even with the recent dramatic improvement in the tuberculosis situation, the infection rate in 1960 was more than ten times greater than the estimate for the rest of the United States (10).

Obviously, the Bethel area population met the selection criterion of high tuberculosis rates. But still other features of the area made a field trial attractive. In 1954, the enormity of the tuberculosis problem among Alaskan natives prompted the health authorities to embark on an intensive control program with considerable emphasis on ambulatory chemotherapy. This program was undertaken as a demonstration by the Arctic Health Research Center of the Public Health Service, supported by funds first from the Bureau of Indian Affairs and later from the Division of Indian Health of the Public Health Service (11). By 1957, the tuberculosis control