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Epidemiology of Tuberculosis in Remote Native Communities

SUMMARY

The incidence and mortality rates of tuberculosis among Indians living in the Sioux Lookout Zone in northwestern Ontario have declined over the past two decades. This 70-case series within the period 1975-1979 documents age-sex distribution, community distribution, sites of disease, signs and symptoms, bacteriologic status, X-ray findings, drug resistance and relapse rates, and effect of vaccination and chemoprophylaxis. Such information can also be used to evaluate the health care delivery system in general and the TB control program in particular. There are several policy implications in case-finding, treatment and prevention, especially in a setting such as the Sioux Lookout Zone, where both preventive and curative services are organized and delivered by the same agency. (Can Fam Physician 1982; 28:67-74).

SOMMAIRE

La fréquence de la tuberculose et les taux de mortalité observés chez les Indiens de la zone de Sioux Lookout, dans le nord-ouest de l'Ontario, ont baissé au cours des deux dernières décennies. Dans cette étude de 70 cas couvrant la période de 1975 à 1979, l'auteur étudie la distribution de la maladie par âge et par sexe, sa distribution dans les communautés, les points où elle apparaît, ses signes et ses symptômes, la situation bactériologique, les résultats des radiographies, la résistance aux médicaments, le taux des rechutes et les effets de la vaccination et de la chimioprophylaxie. Ces données peuvent aussi servir à évaluer le système de prestation des soins de santé en général et le programme de prévention de la tuberculose en particulier. La détection des cas, le traitement et la prévention comportent plusieurs implications de politique, en particulier dans les conditions de la zone de Sioux Lookout, où les services de prévention et de traitement sont organisés et assurés par le même organisme.

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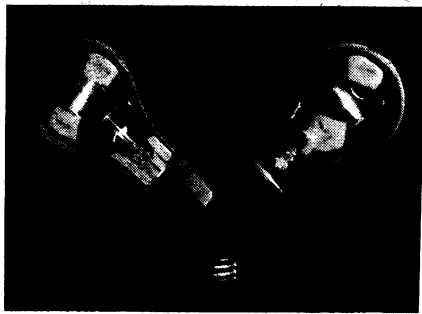
TUBERCULOSIS has been steadily decreasing in Canada. The incidence of new active and reactivated cases dropped from 93.9/100,000 in 1948 to 12.5/100,000 in 1978, while the mortality rate declined from 38.1/100,000 to 0.9/100,000 during the same period.

However, tuberculosis has by no means disappeared in this country and, unlike smallpox, its eradication still lies many years in the future. In the Canadian population, two subgroups contribute disproportionately to the tuberculosis problem: immigrants and native people. Indians and Inuit constitute only about 1.5% of the total Canadian population, but they contributed 17.5% of all active cases of tuberculosis in 1978.¹

In the late 1970s the incidence of tuberculosis among Canadian Indians and Inuit was about ten times that of

the general population—a rate comparable to that of Canada in the 1940s or those of some Third World countries today. While tremendous strides have been made in combating the problem, tuberculosis remains recalcitrant to the intensive control program organized by the Department of National Health and Welfare and other health agencies which serve native people. This state of affairs can be partly attributed to the low socioeconomic status of native communities in this country.

This paper reviews the clinical and epidemiological features of tubercu-



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Warnings and precautions - Since drowsiness may occur with pizotyline, sensitive patients should be cautioned against activities requiring rapid and precise response (i.e. driving an automobile or operating dangerous machinery) until their response to the drug has been determined. Since the effects of antihistamines can potentiate those of other drugs affecting the central nervous system, patients should be cautioned against drinking alcoholic beverages or taking hypnotics, sedatives, psychotherapeutic agents or other drugs with CNS depressant effects during pizotyline therapy. Administer pizotyline with caution to patients with narrow angle glaucoma or with urinary retention (e.g. prostatic hypertrophy).

Since it is desirable to keep drug administration to a minimum during pregnancy, pizotyline should be given only when the benefits derived from treatment exceed the possible risks to mother and fetus.

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After prolonged use, hepatotoxic effects might occur and patients should be advised to report for adequate laboratory evaluation.

Patients with diabetes, cardiovascular disease and known or suspected impaired renal or hepatic function should be given pizotyline with caution, and appropriate laboratory tests should be done at regular intervals.

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Side effects - Increased appetite, weight gain, and drowsiness are the most frequent side effects. An appropriate diet should be recommended by the physician for patients benefiting from the drug but gaining excessive weight. A gradual increase in the dosage of pizotyline is recommended to minimize or reduce the incidence of drowsiness. The following adverse effects have been observed less frequently in relation to the aforementioned reactions: fatigue, nausea, dizziness, headache, confusion, edema, hypotension, depression, weakness, epigastric distress, dry mouth, nervousness, impotence and muscle pain.

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losis in a region of isolated Cree-Ojibwa communities in northwestern Ontario. Statistical data over the past two decades were collected, and 70 cases which occurred in the period 1975-79 were analyzed in detail. Health services for this region's Indian population have been, and still are, chiefly the responsibility of a single agency. An excellent, comprehensive and up-to-date medical records system has been maintained, so data collection is complete and reliable.

The Study Area and Population

The Sioux Lookout Zone is a health service area operated by the Medical Services Branch of the Department of National Health and Welfare. It covers an area of some 380,000 sq. km of forests, lakes and swamps in the northwestern corner of Ontario north of the 50th parallel. Some 10,000 Indian people live in the Zone, about 8,000 of whom are in some 25 scattered, remote communities, while the other 2,000 inhabitants live in settlements along the railway and highway to the south and also in and around several predominantly non-native mining and logging towns.²

Health services are provided through a network of nursing stations and health stations staffed by outpost nurses and indigenous community health aides. The administrative centre of the Zone is the 70-bed Zone Hospital which has been in operation in the town of Sioux Lookout since 1949. A detailed description of the organization and delivery of health services and the changing pattern of health and disease in the Sioux Lookout Zone has been published elsewhere.^{3, 4}

Methods

Annual reports of the Sioux Lookout Zone, where available, were consulted to extract the relevant statistical information for the past 20 years.

Since 1975 a register of all known cases of tuberculosis in the Zone has been kept by the medical director. These cases were derived from various sources such as admissions to the Zone Hospital, the sanatorium in Thunder Bay, the respiratory disease unit in Winnipeg, and reports from other medical institutions and practitioners. From the list of names in the register,

the individual medical files were searched and the case summaries abstracted. Of the 72 known cases of active tuberculosis in Indians residing within the Zone's boundaries, detailed clinical information was available for 70 individuals.

What constituted a 'case' of tuberculosis was not always clearcut. Particularly uncertain were cases diagnosed solely on radiological and/or clinical grounds without bacteriological confirmation. For the purpose of this study, if a case was diagnosed (for whatever reasons) to be active tuberculosis and the patient put on a course of anti-TB chemotherapy, it was included. According to the classification scheme recommended by the American Thoracic Society,⁵ all cases in this series would fall into Class III "tuberculosis, infected, with disease; bacteriological status either positive or negative; chemotherapy status, terminated". If on subsequent review there was laboratory proof of the presence of another etiological agent, that case was removed from the register.

In this paper the term "reactivation" is defined in accordance with Statistics Canada usage,¹ i.e. "a case previously recorded as active but with a subsequent known period of inactivity and now active once more", while a new active case is one which has never been recorded as active. These terms should not be confused with "primary" and "post-primary" tuberculosis in clinicopathological discussions. It is unfortunate that post-primary or adult, chronic tuberculosis is sometimes also called "reactivation" tuberculosis.

Results and Discussion

Mortality

The decline in tuberculosis mortality rates since the 1950s is evident from Table 1. In the 1970s the mortality rate was so low that one or two deaths a year could make quite a difference in the annual mortality rate. With a population base of only 10,000, fluctuations from year to year were considerable.

Between 1972 and 1980 there were four deaths directly due to tuberculosis. Two of the deaths were due to drug resistant pulmonary tuberculosis while the other two were from tuberculous meningitis with delayed diagnosis.

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Occasionally reported: glossitis; oliguria; hematuria; tremor; vertigo; alopecia; and elevated BUN, NPN, and serum creatinine. Hematological changes occurring particularly in the elderly, are mostly transient and reversible (primarily, neutropenia and thrombocytopenia; less frequently, leukopenia, aplastic or hemolytic anemia, agranulocytosis, and bone marrow depression).

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In Enarson's study⁶ of TB deaths in British Columbia, half of the deaths were not diagnosed during life, yet most of these patients died in hospital and their mean length of stay was two weeks. Meningitis and miliary tuberculosis were noted to be particularly easy to miss. As health professionals become less familiar with the clinical diversity of tuberculosis due to inadequate training and exposure, preventable deaths due to tuberculosis will continue to occur.

TABLE 1
Tuberculosis Mortality Rates in the Sioux Lookout Zone: 1954-1980

Years	3-yr mean mortality rate (per 100,000 pop.)
1954-56	67.0
1957-59	54.3
1960-62	46.7
1963-65	24.2
1966-68	8.3
1969-71	NA*
1972-74	0.0
1975-77	6.4
1978-80	5.8

* Not available

Incidence

The mean annual incidence rates of new active and reactivated tuberculosis in the Sioux Lookout Zone during the 1970s are listed in Table 2.

The mean 1975-79 incidence rate was 137.9/100,000, which was higher than that for Canadian Indians (mean 1976-78 rate: 119/100,000) and all Canadians (mean 1976-78 rate: 13.3/100,000). Compared to the

1960s, some improvement in the Zone can be observed. The mean rate for 1965-68 was 246/100,000. This was lower than the rate for 1970-74 (288.2/100,000) but higher than that for 1975-79. During 1970-74 there was an epidemic in one community with 14 cases diagnosed in one year, causing an unusually high incidence when averaged out for the period.

The decline in mortality and morbidity rates in the post-War decades observed in the Sioux Lookout Zone paralleled that observed among Canadians and Canadian Indians nationally. However, in the late 1970s the mortality rate in the Sioux Lookout Zone was still about five times the national rate, while incidence was ten times the national rate. McKeown⁷ suggested that the decline in mortality from tuberculosis and other infectious diseases actually predated the availability of effective treatment and control measures. Perhaps the TB incidence and mortality among Indians in the Zone will approach that of other Canadians when their standard of living is raised to a comparable level—an objective which cannot be achieved through medical measures alone.

Reactivations

The percentage of reactivations among all active cases was 30% in 1975-79 in the Sioux Lookout Zone—little change compared to a decade previously (31% during 1965-68). It was, however, higher than the proportion among Canadian Indians and Canadians (both only about 13% in 1978).

About 1/3 of the cases had been inactive for under ten years, 1/3 between

TABLE 2
Incidence of New Active and Reactivated Tuberculosis in the Sioux Lookout Zone: 1970-1979

Year	Zone Indian population	No. of cases	Rate per 100,000
1970	8,847	16	180.9
1971	8,928	28	313.6
1972	9,381	23	245.2
1973	9,865	43	435.9
1974	9,802	26	265.3
1975	9,938	17	171.1
1976	10,328	17	164.6
1977	10,531	15	142.4
1978	10,611	15	141.4
1979	11,446	8	69.9
1970-74	5-year mean	27.2	288.2
1975-79	5-year mean	14.4	137.9

10 and 20 years, and the remaining 1/3 over 20 years. Those reactivated cases which had inactive intervals of over 20 years were cases which were probably not adequately treated before or during the early years of anti-tuberculosis chemotherapy. According to the follow up study by Grzybowski et al. of 1,000 TB patients discharged from sanatoria in Ontario during three different periods, those treated in the pre-chemotherapy era had a higher reactivation rate than those treated with some chemotherapy (but inadequately) in the early 1950s. The lowest risk of reactivation was observed among those who received proper chemotherapy in the mid-1950s.⁸

Age-Sex Distribution

Within the period 1975-79, 59.7% of the cases were men and 40.3% women. This was comparable to the ratio obtained for Canadians as a whole.

The age distribution of TB cases in the Sioux Lookout Zone is summarized in Table 3. About 1/3 of the active cases were under age 25, while among Canadians nationally only 19% of cases fell into this age group in 1978. If age-specific incidence rates are considered, the incidence rate of tuberculosis among the 15-24 years group in the Sioux Lookout Zone was 20 times that for Canadians of the same age group.

Community Distribution

The distribution of TB cases was not uniform across the Zone. Certain communities contributed to a large number of cases consistently over the years. There was no fixed pattern in terms of community size, proximity to white towns, or degree of social disintegration which these communities shared with one another. Some high-incidence

communities in the 1960s, however, have improved towards the end of the 1970s.

Site of Disease

The large majority of cases involved the respiratory tract. In the Sioux Lookout Zone, 59 of 70 patients (84%) in 1975-79 had respiratory tuberculosis. This was comparable to the 82% among all Canadians and 88% among Canadian Indians in 1978. There was little change compared to the period 1965-68 in the Sioux Lookout Zone (83%). It would be interesting to discover if the proportion of respiratory tuberculosis would decrease in the future as the general incidence of tuberculosis decreases.

The distribution of active cases by type and site, classified according to the International Classification of Diseases, 9th Revision, is given in Table 4.

Clinical Features

Of 59 patients who had tuberculosis involving the respiratory system (including pleural TB), 14 (24%) were asymptomatic. The distribution of symptoms is listed in Table 5.

These figures serve as rough guides only. How complete and accurate the patients' case records are depends on the patients' ability to recall events and the thoroughness of the physicians' history-taking and recording.

Among the classical symptoms usually associated with tuberculosis, cough and sputum were most frequently encountered. On clinical examination of the chest, abnormal findings were present in 30 patients (51%) with respiratory tuberculosis.

Compared to asymptomatic patients, symptomatic ones were more likely to be positive on smear and/or culture (chi-square 3.7, $p < 0.1$). As

bacillary cases pose the greatest threat to public health, it is somewhat reassuring to note that the great majority (32 of 38—84%) of such patients had symptoms which should alert the vigilant health worker to further investigations (Table 6).

Eleven patients had no demonstrable involvement of the respiratory system, while four had both respiratory and non-respiratory sites of disease. The clinical presentations were variable. There were no 'typical' features, and only a high index of suspicion and aggressiveness in diagnostic investigations resulted in their detection.

Bacillary Status

The most important investigation in any suspected case of tuberculosis is bacteriological examination of sputum and other relevant body secretions and specimens. Overall, the percentage of bacillary cases among Sioux Lookout Zone Indians, Canadian Indians, and Canadians was quite similar: 66, 70, and 71% respectively.

Since patients discharging bacilli act as sources of infection in the community, the World Health Organization recommended that only smear-positive cases be used as an epidemiological index to measure the extent of TB. For countries with limited resources, smear-positive cases should be the targets for case-finding and treatment.⁹ In Canada, efforts in case-finding are usually directed towards non-bacteriologically confirmed cases as well, and

TABLE 4
Distribution of Tuberculosis Cases by Type and Site: Sioux Lookout Zone 1975-79

Type and Site	No. of cases	%
Respiratory		
Primary	5	7.1
Pulmonary	46	65.7
Pleurisy	6	8.6
Larynx	2	2.9
Miliary	3	4.3
Other	1	1.4
Non-respiratory		
Meninges/CNS	2	2.9
Peritoneum	2	2.9
Bones/joints	2	2.9
Genitourinary	2	2.9
Peripheral lymph nodes	9	12.9
Note: one patient may have more than one site of disease, hence percentages do not add up to 100%.		

TABLE 3
Age Distribution and Age-Specific Incidence Rates of Active Tuberculosis Cases: Sioux Lookout Zone and Canada

Age Group	Sioux Lookout Zone 1975-79			Canada 1978		
	No.	%	rate/100,000	%	rate/100,000	
0-4	4	5.6	43	3.0	5	
5-14	6	8.3	36	5.2	4	
15-24	14	19.4	159	10.8	7	
25-44	20	27.8	174	27.2	12	
45-64	16	22.2	298	31.1	20	
65 & over	12	16.7	496	22.8	31	
All ages	72	100.0	138	100.0	13	

considerable resources expended in their treatment and follow-up.

Radiographic Findings

There were 46 patients with pulmonary tuberculosis. Four patients had positive sputa but their chest films were interpreted as normal. The remaining 42 patients had abnormal chest X-rays. Of these, 69% were bacillary. Cavitations were present in 43% of the abnormal films. The relationship between radiographic feature and bacillary status is demonstrated in Table 7.

Pulmonary TB patients with cavities on X-ray are more 'dangerous': almost 90% of them were bacillary, compared to only 54% among non-cavitary cases (chi-square 5.8, $p < 0.05$).

The use of X-rays in the diagnosis of tuberculosis is probably overrated. No radiographic picture is absolutely typical of tuberculosis and the hazards of observer error are well recognized. In the Sioux Lookout Zone series, chest X-rays were interpreted as normal in four of the 32 cases of culture-confirmed pulmonary TB cases. The false-negative rate was therefore about 12%. Had chest X-rays been used exclusively for diagnosis, these culture-positive cases would have been missed. On the other hand, a false-positive chest X-ray can lead to unnecessary treatment for tuberculosis while other treatable conditions are missed. During the five year period under study, two cases of North American blastomycosis and one case of pulmonary echinococcosis were initially treated unsuccessfully with anti-TB drugs before the correct diagnosis was made and the cases deleted from the TB Register.

The high degree of disagreement

among physicians reading chest X-rays was dramatically documented by the International Comparative Study on X-Ray Classification conducted in the 1960s. A high index of disagreement was found even in participants' responses to such fundamental questions as "Is this film abnormal?", "Is a cavity present?" and "Is there a need for medical action?".¹⁰

In the past, much reliance had been placed on survey chest X-rays in case-finding. This practice was slowly phased out, however, and by the mid-1970s community-wide X-ray surveys were no longer practised in the Sioux Lookout Zone. To illustrate the low cost-efficiency of survey X-rays in case-finding, in 1968, according to that year's Zone Annual Report, two cases were discovered from among 8,789 survey films. The yield was one case in over 4,000 films or 0.02%, and the two cases discovered accounted for only 6% of all active cases diagnosed that year.

Therapeutic Considerations

Except for two cases which were managed entirely on an outpatient basis, all tuberculosis patients during the period 1975-79 spent at least an initial period of variable duration in a hospital. The length of stay ranged from five days to 28 weeks. The mean length of hospital stay was 10.8 weeks in 1975; by 1979, this was reduced by half to 5.1 weeks.

In the early 1970s the standard regimen used in the Sioux Lookout Zone consisted of an intensive phase of triple therapy (streptomycin, isoniazid, and para-aminosalicylic acid) lasting

one to three months followed by double therapy for up to two years. In the latter part of the decade, rifampin and ethambutol, formerly second-line drugs, came into common use and PAS was phased out. The combinations used depended on the preferences of physicians and institutions. The duration of chemotherapy tended to shorten in more recent years to 12-18 months. Neither the short-course chemotherapy nor the intermittent supervised regimen was in use in the Zone during the study period.

The incidence of mycobacteria resistant to anti-TB drugs was six out of 45 culture-positive cases (13%). Three cases were of the 'primary' type of resistance, i.e. newly diagnosed, previously untreated cases. The other three were of the 'secondary' or 'acquired' type which had emerged in patients while undergoing chemotherapy. The primary resistance rate of 6.5% in the Sioux Lookout Zone was within the range reported in different parts of North America¹¹ and much lower than the rates encountered in many developing countries.

The second-line drugs such as capreomycin, ethionamide and pyrazinamide were used very rarely; within the study period they were given to only one patient.

While under a third of the 70 cases identified in the study period were reactivations at the time of diagnosis, when the 70 patients were followed longitudinally forward in time, seven patients relapsed by the end of 1980. 'Relapse' refers to the reappearance of bacilli in sputum (or other specimens) after a period of bacteriological

TABLE 5
Distribution of Symptoms Among Patients With Respiratory Tuberculosis

Symptom	No. pts.	%
Cough	33	56
Sputum	28	47
Hemoptysis	19	32
Fever	15	25
Weight loss	13	22
Night sweats	12	20
Chest pain	9	15
Dyspnea	8	14
None recorded	14	24

TABLE 6
Presence of Symptoms and Bacillary Status Among Patients With Respiratory Tuberculosis

	Bacillary	Non-Bacillary	Total
Symptomatic	32 (71%)	13 (29%)	45 (100%)
Asymptomatic	6 (43%)	8 (57%)	14 (100%)
Total	38 (64%)	21 (36%)	59 (100%)

TABLE 7
Bacillary Status of Pulmonary Tuberculosis Patients With Abnormal Chest X-Rays

	Bacillary	Non-Bacillary	Total
Cavitary	16 (89%)	2 (11%)	18 (100%)
Non-cavitary	13 (54%)	11 (46%)	24 (100%)
Total	29 (69%)	13 (31%)	42 (100%)

quiescence and accompanied by clinical deterioration. The high relapse rate of 10% among the 70 patients followed longitudinally for one to six years reflected the inadequacy of treatment supervision. In most trials of chemotherapy regimens, a relapse rate of more than 5% is generally considered as unacceptable. The isolation of Indian communities in the Zone and cultural barriers to Canadian health practices are probably contributory factors. However, with the presence of nursing stations in the larger communities and native health aides in the smaller ones, there should be no excuse. With an average of less than 15 cases of TB under treatment per year in the Zone in the late 1970s, adequate follow up and supervision of treatment should not cause any excessive drain on health workers' time.

To improve compliance, it is appropriate for the Sioux Lookout Zone to adopt the short course chemotherapy now in use in the United Kingdom¹² and recently recommended by the American Thoracic Society,¹³ based on extensive field trials in various parts of the world. Other advantages of short course chemotherapy—nine months of INH and rifampin with or without a third drug during the first two months—would include lessened demand on personnel time, cost reduction, and a lower risk of drug toxicity.

Preventive Measures

Two strategies are currently available to prevent tuberculosis: BCG vaccination and chemoprophylaxis with INH. Since the 1950s BCG vaccines have been administered to all newborn Indian babies in the Zone as a matter of policy. In the 70 cases of tuberculosis discovered during 1975-79, 18 patients (26%) had a definite record of previous BCG vaccination. This observation by itself is insufficient to evaluate the effectiveness of BCG. Without widespread use of BCG in the past two decades, the total number of active cases in the 1970s would perhaps be even greater.

In the literature eight major prospective controlled trials have been reported over the past three decades. Unfortunately the reduction in TB incidence varied widely—0-80%!¹⁴ One of the earliest trials conducted in the 1930s among eight American Indian tribes showed the highest protective effect.¹⁵ The most recent trial, one

which was started in south India in 1968 and designed to settle the question of BCG effectiveness once and for all, unfortunately showed negative effects after 7.5 years of follow-up.¹⁶

Although no longer recommended for the general population in North America,¹⁷ whether a case can still be made for universal use of BCG among the native Indian and Inuit population in Canada is debatable. Severe adverse reactions such as osteomyelitis, disseminated infection and death have never been reported in the Sioux Lookout Zone to the best of my knowledge. Complications such as local abscesses and lymphadenitis do occur from time to time, but these are of little consequence. Another criticism of BCG is the difficulty of interpreting tuberculin skin test among those vaccinated. However, current thinking regards large reactions (eg. over 15 mm) as unlikely due to BCG but should be managed as Mycobacterium tuberculosis infection. At any rate, BCG vaccination is still official policy of the Medical Services Branch's tuberculosis control program in native communities.

The other preventive strategy—INH prophylaxis—is less steeped in controversy. Contacts of active cases and people found to have recently converted or showing large reactions to tuberculin skin tests are generally put on prophylaxis for a year. The effectiveness of chemoprophylaxis is well established: Ferebee reviewed 13 controlled trials in seven countries,¹⁸ one of which was conducted among the Inuit in Alaska.¹⁹ In the Sioux Lookout Zone series, 11 of the 70 patients (16%) had a record of previous chemoprophylaxis. What could not be determined was the compliance of those people offered prophylaxis. This finding thus should not invalidate current recommendations for prophylaxis among certain selected groups.²⁰ As in treatment of active cases, health workers in the Sioux Lookout Zone must improve compliance through more intensive health education efforts. Even if compliance is expected to be poor, chemoprophylaxis should still be offered to those who meet the criteria, because even partial prophylaxis offers some protection. ●

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