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Tuberculosis in Chronic Care Homes

SUMMARY

Caucasian Canadians are in the tertiary phase of a 300-year tuberculosis epidemic. In this phase, the pattern of disease over the age spectrum is low in the young and middle-aged groups and rises to four times this rate in the elderly. The concentration of the elderly in chronic care homes (CCHs) magnifies the tuberculosis problem by increasing case rates another four times above the rate of elderly persons living separately, and 20 times above the overall Canadian rate. In spite of effective drugs with cure rates of over 95%, tuberculosis in the institutionalized elderly continues at an alarming rate. The difficulty lies in case finding. The prevailing attitude is that tuberculosis is no longer a problem. Surveillance programs are rudimentary. Between 35% and 40% of active cases in CCHs are the result of primary infection, mimicking bacterial pneumonia clinically and radiographically. In this target group of high-incidence tuberculosis, surveillance of residents is necessary, and the diagnosis needs to be considered in antibiotic-unresponsive pneumonia and in fever of unknown origin. (*Can Fam Physician* 1987; 33:1231–1235.)

RÉSUMÉ

Les Causaciens canadiens vivent la période tertiaire d'une épidémie de tuberculose qui remonte à 300 ans. Au cours de cette période, la distribution caractéristique de la maladie dans les différents groupes d'âge s'avère faible chez les groupes jeunes et d'âge moyen et les taux vont jusqu'à quadrupler chez la personne du troisième âge. La concentration de personnes âgées dans les centres d'accueil amplifie le problème de la tuberculose avec un nombre de cas quatre fois supérieur à celui des personnes vivant séparément et vingt fois supérieur à la population canadienne en général. Malgré l'efficacité des médicaments dont les taux de guérison dépassent 95%, la tuberculose, chez les patients placés en institution, continue d'évoluer à un rythme alarmant. La difficulté réside dans l'identification clinique de cas. L'attitude la plus répandue en ce moment veut que la tuberculose ne constitue plus un problème. Les programmes de surveillance sont rudimentaires. Dans les centres d'accueil, de 35% à 40% des cas actifs sont le résultat d'une infection primaire, simulant une pneumonie bactérienne tant sur le plan clinique que radiologique. Dans ce groupe cible où l'incidence de tuberculose est élevée, il est nécessaire de surveiller les pensionnaires et de considérer les besoins diagnostiques tant pour les cas de pneumonie qui ne répondent pas à l'antibiothérapie que pour une fièvre d'origine inconnue.

Key words: tuberculosis, elderly, chronic care homes

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WITH DECREASING CASE rates of tuberculosis, with the discovery of effective drugs to cure tuberculosis and to prevent active disease in infected persons, and with the implementation of bacillus Calmette-Guerin (BCG) vaccination programs, the eradication of tuberculosis was expected. A generation has passed, and tuberculosis is still much in evidence. Twenty-two thousand new cases were reported in the United States[1] and 2,400 cases in Canada,[2] both in 1984. These continuing cases are the subject of increasing concern by persons and agencies responsible for tuberculosis control.[1,3,4]

Background

A tuberculosis epidemic will run its course in about 300 years from beginning to end.[5] For Caucasians, the epidemic began about 300 years ago with the birth of the Industrial Revolution. The route of transmission of tubercu-

lous infection is primarily by aerosol droplet expectoration by an infected source, inhaled by a susceptible host.[6] The move by agrarian Europeans to the industrial centres, to supply the labour requirements of industry, led to the conditions of crowding required for epidemic transmission of tuberculosis infection. The epidemic was under way.

The primary phase of the tuberculosis epidemic is characterized by rapidly increasing infection, active case rates, and death rates. The secondary phase is characterized by increased infection rates, peak and decline of active case rates, and accelerating decline in death rates. The tertiary phase is characterized by declining infection and active case rates, and low death rates.

The natural history of the tuberculosis epidemic is explained by increasing group immunity. With the death of each susceptible person, the remaining group will have a higher proportion of persons resistant to disease.[5]

Each phase is characterized by a different pattern of active case and death rates over the age spectrum. The tertiary phase has an age as compared to an active case distribution characterized by low rates in the very young. The rates gradually rise with age and rise steeply among persons over 60.[5] The Canadian distribution in 1984 is characteristic (Table 1).[2] The overall Canadian active case rate was 9.4.[2] (Rates are recorded per 100,000 unless specified.) As shown in Table 1, case rates in groups of persons under age 40 were eight or fewer; in the over 50 age groups, they were 11 or more, rising to 33 in the 75+ age group, four times the rate in the under 40 age groups!

Among Canadians, as among Americans, tuberculosis is a disease of the elderly. In the United States, in 1979, 29% of all cases of tuberculosis occurred in persons 65 years and older,[7] who comprised 11% of the American population.[8] In Saskatchewan, in 1985, 30% of all cases of tuberculosis occurred in persons 65 years and older,[9] who comprised 12% of the Saskatchewan population.[10]

The Chronic Care Home Dilemma

Infection and active case rates are unlikely to rise in the absence of changes in host resistance or in factors, such as crowding, which increase the transmission of infection.[5]

Increased crowding, which raises the number of infected and active cases under one roof, occurs in the elderly population who live in chronic care homes. Therefore, chronic care homes raise the rate of tuberculosis which, in Canada, is already a disease of the elderly. Hypothetically, infection and active case rates should be higher in the elderly living in chronic care homes compared to the elderly living in individual homes.

A survey of chronic care homes in Arkansas confirmed this hypothesis.[11] Twelve per cent of newly admitted residents were infected (tuberculin skin test measured $\geq$ 10 mm induration). Twenty-one per cent of long-term residents were infected. Longitudinal studies revealed that 5% of uninfected residents were infected each year.[11, 12] The active case rate in those residents who were infected prior to admission was 600 (compared to 60 for all Arkansas); in those who were infected after admission, it was 1,500. The overall active case rate in chronic care residents was 234, four times the rate for the elderly in the entire state!

In Saskatchewan, 10,000 persons over age 65 (11.6%) live in chronic care homes. A 10-year retrospective survey of active cases of tuberculosis in chronic care homes identified 21 cases, for a case rate of 21.[13] Two cases (10%) were discovered at autopsy. This rate was no different from the provincial rate of 19 for this age group.[9] Furthermore, all active cases in chronic care homes were activations of remote infection. The proportion of long-term Saskatchewan chronic care residents who were infected (20%) was the same as for Arkansas. These factors strongly suggest that additional cases of active tuberculosis exist in chronic care homes, but are not identified.

Pathogenesis of Tuberculosis

Tuberculosis is transmitted by aerosol droplet nuclei.[6] When the droplet nuclei are inhaled in sufficient number by a susceptible host, a primary infection develops.[14] The site is in the well-ventilated portion of the lung, the bases. The bacilli multiply freely in the first several weeks before eliciting a host response. This phase is accompanied by hematogenous seeding of bacilli.[15] When host cellular immunity develops, an inflammatory response develops in the lung (pneumonitis) and in the draining lymph nodes which, together, form a Ghon complex. In a great proportion of hosts, the infection resolves spontaneously. Many of the bacilli, particularly the hematogenously seeded bacilli, remain viable for many years. In some hosts, the bacilli begin to replicate at some time, but in whom or when cannot be predicted. This replication occurs mostly in areas of high oxygen tension, the apices of the lung. (Tubercle bacilli are obligate aerobes.) This is the secondary infection which results from the activation of dormant organisms in the host.[16]

Problems with the Diagnosis of Tuberculosis

It is generally believed that tuberculosis is under control, and that active cases which develop are all found, readily treated, and cured with effective drugs. This is a self-fulfilling expectation. For example, Saskatchewan records about 140 active cases each year. On average, there-

Table 1
Active Case Rates over the Age Spectrum Canada 1984

Age	0–4	5–14	15–24	25–34	35–44	45–54	55–64	65–74	75+
No. per 100,000	4	2	5	8	8	11	15	23	33

Source: See reference 2.

fore, each of the 1,400 physicians in Saskatchewan sees one active case of tuberculosis every 10 years. Understandably, the probability of their considering tuberculosis as a diagnosis is small.

It is generally believed that adult pulmonary tuberculosis presents as upper-lobe apical and posterior segmental acinar and/or cavitary disease. This is so in over 95% of cases identified in Saskatchewan.[9] Ten to 15 per cent of residents newly admitted to chronic care homes are infected. When they develop tuberculosis, the pulmonary lesions are characteristically apical and/or cavitary. In Arkansas, such lesions accounted for 63% of the cases of tuberculosis. Thirty-seven per cent of the active cases developed in recently infected residents, the majority of whom presented with lower-lobe pneumonia, hilar adenopathy, or pleural effusions without acinar disease.[11] Fever, which is present in most of these cases, is a clinical sign. These are presentations of primary tuberculosis and do not present with the typical radiographic appearance or clinical signs of adult tuberculosis. In this setting, the diagnosis of tuberculosis is easily overlooked and is probably frequently missed. Since 85%–90% of chronic care residents are not infected on admission, they are susceptible to infection and the stage for a tuberculosis epidemic is set. Active tuberculosis in these patients will present with atypical clinical and radiographic findings: atypical for adult tuberculosis, but typical of primary tuberculosis.

In Saskatchewan, regulations governing surveillance for tuberculosis in chronic care homes call for screening of staff with tuberculin skin tests and chest radiographs to protect residents. There is no requirement for screening residents. Since residents are, on average, 25 years older than staff and outnumber staff two to one, the risk of a resident being infected by another resident is significantly greater than the risk of residents being infected by staff. Therefore a policy of staff screening only will result in active cases of tuberculosis being missed in residents.

All these factors explain the Saskatchewan chronic care experience with tuberculosis in which cases are missed. Two of the 21 active cases discovered were diagnosed at autopsy. Eleven were pulmonary, and 10 of these were sputum-smear positive and therefore contagious; all 11 were culture positive. These patients presented with typical adult clinical and radiographic disease. No primary infections were seen, although they undoubtedly exist. Tuberculosis resulted in the death of seven (33%) of these 21 residents.

Tuberculosis-Surveillance Policy

Tuberculosis surveillance in chronic care homes clearly requires the screening of residents as well as of staff. Resident screening requires tuberculin skin testing on admission using 5 tuberculin units (TU) of purified protein derivative (PPD-S).[17] All residents with reactions less than 10 mm are retested within one to two weeks to identify booster responses.[11, 18]

Skin testing in non-reactors (< 10 mm induration) is repeated annually. Chest radiographs are obtained on all tuberculin reactors (≥ 10 mm induration) and all residents with cough or sputum, irrespective of tuberculin status. Sputum for acid-fast bacilli (AFB) is obtained from residents with cough or sputum at the time of admission, irrespective of tuberculin status. Subsequently, it is obtained again, together with a chest radiograph, if cough or sputum persists for more than one month, or if lower lobe radiographic and/or clinical pneumonia fails to respond to the usual antimicrobial agents.

Treatment of Tuberculosis

Active cases

The recommended treatment for tuberculosis is nine months of daily isoniazid (INH) 5 mg/kg/day, to a maximum of 300 mg/day, and Rifampin (RMP) 10 mg/kg/day, to a maximum of 600 mg/day. Ethambutol (EMB) 15 mg/kg/day is added for four to eight weeks for possible resistance.[19, 20]

In the majority of treated cases, the culture becomes negative after three months.[20] For those persons whose sputum cultures continue to grow AFB after three months, drug treatment should continue for six months after cultures are negative.[19] For this reason cultures should be repeated monthly until they are negative.

If, because of drug-resistant organisms or intolerance, either INH or RMP cannot be used, the drug regimen will require pyrazinamide (PZA) 30 mg/kg/day, EMB, or streptomycin, or a combination, in addition to INH or RMP, and the duration may have to be extended to 18 months. In the presence of INH or RMP resistance, 25 mg/kg/day of EMB may have to be used.[19] In cavitary disease, an additional drug should be used. Toxicities affect about 10% of users. These are listed in Table 2.

Prevention

Preventive therapy for tuberculosis is possible because of INH, which was introduced in 1952. It is safe, inexpensive, can be taken orally, and is

Table 2
Treatment of Tuberculosis

Commonly Used Drugs	Daily Dosage	Toxicity	Comments
Isoniazid	5 mg/kg	Peripheral neuritis, hepatitis, dermatitis, fatigue	Bacericidal to intracellular and extracellular organisms
Rifampin	10 mg/kg	Hepatitis, fever, purpura	Same as INH Orange urine Interferes with the action of estrogens
Streptomycin	12 mg/kg	8 nerve damage, renal damage, dermatitis	Bactericidal to extracellular organisms only
Pyrazinamide	30 mg/kg	Hyperuricemia, hepatotoxicity	Bactericidal to intracellular organisms only
Ethambutol	15-25 mg/kg	Optic neuritis (rare)	Bacteriostatic to intra- and extracellular organisms

bactericidal. Its use has satisfactorily demonstrated the reduction of active tuberculosis in infected persons by 50%–90%.[21]

The major factor determining the degree of protection is compliance. In a closed population with directly observed therapy, protection rates of up to 94% have been achieved.[11]

Not every infected person without active disease qualifies for chemoprophylaxis. Individualized decisions are considered for several categories which are based primarily on the relative risk of developing clinical disease as compared to the risk of toxicity. The most worrisome effect of INH is hepatotoxicity. The frequency of this effect is age related.[22] It is < 0.3% in the under age-35 category, 1.2% in the 35–49-age category, and 2.3% in the over age-50 category. If, and only if, the probability of developing clinical disease is greater than that of developing hepatitis, INH chemoprophylaxis is recommended.

The average age of Saskatchewan residents in chronic care homes is over 70 years.[13] Therefore INH chemoprophylaxis could be justified in a subgroup of residents in whom the probability of clinical disease is greater than 2.3%. Such a group exists in recent tuberculin converters. For clinical purposes, this means persons with documentation of tuberculous infection within the past two years. In this group active disease develops in 5%–20% of persons.[23] When the decision to administer INH chemoprophylaxis is made, arrangements for careful review of the presence of toxic effects are included. This will ensure the identification of those persons in whom INH will need to be withdrawn.

Bateriologic rationale for chemotherapy. Four factors influence the chemotherapeutic regimen of tuberculosis:[24, 25]

- M. tuberculosis is an obligate aerobe. Its metabolic activity is proportional to the ambient oxygen tension.
- M. tuberculosis has a slow rate of growth. Its mean-replication time is 20 hours.
- M. tuberculosis has a high rate of mutation to drug resistant forms. One organism in $1 \times 10^5 - 1 \times 10^7$ will be resistant to one drug.
- The site of action of a drug (Table 2).

There is evidence to support the hypothesis that there are several pools of M. tuberculosis with varying metabolic rates in persons with active disease.[25] This evidence is based on the oxygen requirements of the bacilli and on the efficacy of individual drugs:

- rapidly replicating, continuous growth, extracellular pool; (These conditions exist in lung cavities in which the oxygen tension is high.)
- slowly replicating, intermittent spurts of growth, extracellular pool; (These conditions exist in areas of caseous necrosis.)
- slowly replicating, intermittent growth, intracellular pool; (These conditions exist inside macrophages.)
- dormant pool. (These occur in areas of fibrosis in the lungs and all over the body.)

Because of the replication time of 20 hours, only one daily dose of drugs is prescribed, in preference to divided doses. Because of the high rate of mutation, at least two drugs are prescribed in active disease to prevent the emergence of resistant bacilli. The probability that a single mycobacterium will be resistant to two drugs is assumed to be equal to the product of the probabilities of resistance to the individual drug (e.g., $1 \times 10^6 \times 1 \times 10^6 = 1 \times 10^{12}$ organisms). It is very rare to have more than 1×10^{12} organisms in human disease. Therefore administering two drugs to fully sensitive organisms will prevent the development of resistance.[19, 20, 24]

Because of selective action any two drugs prescribed are not always two which act on the same pool of organisms. INH and RMP are active both intra- and extracellularly. Because of this property and because they are both bactericidal, they represent the best and most effective combination. PZA acts only intracellularly in an acid medium, and streptomycin acts only extracellularly in an alkaline medium. Both are bactericidal. If both these drugs are prescribed, each acts selectively on a different pool of organisms, PZA on the intracellular pool, and streptomycin on the extracellular pool. Therefore the conditions for resistant organism formation still exist in each pool, since each drug acts on a separate pool, and the two function as one. Used together, they are as effective as either INH or RMP, but not as desirable. EMB is bacteriostatic to both intra- and extracellular organisms. It prevents replication of organisms, but does not kill them. The killing is done by the macrophages. It is a slower process, and a longer course of treatment is required if EMB is one of only two drugs used.

Anti-tuberculous drugs are active only on replicating organisms. Therefore rapidly replicating organisms are killed most rapidly. Cavitary organisms, which are present in large numbers ($10^7 - 10^9$ organisms) because of their rapid replication, are killed most rapidly. This fact explains why sputum-smear positive (contagious) patients become non-contagious within two weeks,[26] and over 90% become culture negative within three months when INH and RMP are used in combination.[19, 20] Prolonged treatment (an additional six months for a total of nine months) is required to ensure that the slowly replicating extracellular and intracellular organisms are killed.[24]

The ideal drug combination is INH and RMP daily for nine months.[20] If resistance is suspected, EMB is added until sensitivities are reported. If resistance is confirmed, and only INH or RMP can be used with EMB, an 18-month course of treatment is required.

Chemoprophylaxis is the treatment for clinically inactive tuberculosis. The number of organisms is small (< 10^5),[24] and organisms are probably active in intermittent bursts only. This means that INH can be used alone without developing resistant organisms. It is efficacious in decreasing the proportion of infected persons who develop active disease when taken daily for one year.[11, 21]

Conclusions

There is no question about the efficacy of the available drug regimens for the treatment of tuberculosis. Active tuberculosis is curable. Tuberculous infection is preventable.

In a closed population such as that of a chronic care home, this result is achievable. It has not been achieved. The difficulty lies in case finding. The tuberculosis rate in unselected chronic care residents is over 200 and over 1,500 in selected residents. When viewed in the context of the case rate in Saskatchewan at the height of the tuberculosis epidemic in 1930, when case rates were 76, there is strong reason to take steps to find all active cases and to prevent infected persons from

developing active disease. Such steps require surveillance of residents and staff, a carefully developed treatment plan, and educational programs for physicians and nurses who are responsible for the medical care of residents. The elderly in chronic care homes are a group with a high incidence of tuberculosis which needs to be targeted by tuberculosis-control programs. ◉

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