Tuberculosis Treatment Interruptions—Ivanovo Oblast, Russian Federation, 1999

IN THE RUSSIAN FEDERATION, THE NUMBER OF TUBERCULOSIS (TB) CASES INCREASED FROM 45,000 (34 PER 100,000 POPULATION) IN 1991 TO 124,000 (85 PER 100,000 POPULATION) IN 1999.1 IN 1995, THE WORLD HEALTH ORGANIZATION (WHO) IMPLEMENTED A PILOT TB CONTROL PROJECT IN THE IVANOVO OBLAST OF THE RUSSIAN FEDERATION (1995 POPULATION: 1.3 MILLION), LOCATED 175 MILES NORTH EAST OF MOSCOW. THE PROJECT IS BASED ON THE FOLLOWING FIVE ELEMENTS OF THE WHO DIRECTLY OBSERVED TREATMENT, SHORT-COURSE (DOTS) STRATEGY FOR CONTROLLING TB: GOVERNMENT COMMITMENT, LABORATORY-BASED DIAGNOSIS, A RELIABLE SUPPLY OF ANTI-TB MEDICATIONS, DIRECT SUPERVISION OF STANDARDIZED TREATMENT, AND A RECORDING AND REPORTING SYSTEM THAT PERMITS EVALUATION OF TREATMENT OUTCOMES. IN MOST SETTINGS, IMPLEMENTING THIS STRATEGY HAS RESULTED IN CURE RATES OF ≥85%2,3; HOWEVER, LITTLE IMPROVEMENT OCCURRED IN CURE RATES IN IVANOVO AFTER IMPLEMENTATION OF THIS STRATEGY IN 1995.4,5 ALTHOUGH 17% OF THESE POOR OUTCOMES WERE ATTRIBUTED TO PRIMARY MULTIDRUG-RESISTANT TB (MDR TB) (I.E., TB RESISTANT TO AT LEAST ISoniaZID AND RIFAMPIN), OTHER FACTORS THAT MAY HAVE CONTRIBUTED TO POOR OUTCOMES, SUCH AS TREATMENT DELAY AND INTERRUPTION, WERE NOT QUANTIFIED. TO DETERMINE THE EXTENT OF TREATMENT INTERRUPTION AS A POTENTIAL CAUSE OF POOR OUTCOMES AMONG TB PATIENTS IN IVANOVO, CDC REVIEWED TB TREATMENT RECORDS FOR ALL NEWLY DIAGNOSED, NEVER-TREATED PULMONARY TB PATIENTS REGISTERED IN IVANOVO FROM APRIL THROUGH JUNE 1999. THIS REPORT SUMMARIZES THE RESULTS OF THAT ANALYSIS AND INDICATES THAT APPROXIMATELY ONE FOURTH OF HIGHLY INFECTIOUS TB PATIENTS INTERRUPTED TREATMENT FOR 2-8 WEEKS AND NEARLY ONE FOURTH INTERRUPTED TREATMENT FOR MORE THAN 8 WEEKS. ON THE BASIS OF THESE RESULTS, TB PROJECT STAFF HAVE INCREASED EFFORTS TO REDUCE TREATMENT INTERRUPTION THROUGH USE OF INCENTIVES.


DURING APRIL-JUNE, 115 NEWLY DIAGNOSED, NEVER-TREATED PULMONARY TB PATIENTS WERE REGISTERED; 54 (47%) WERE AFB SMER-positive. THE MEDIAN AGE OF THE SMER-positive PATIENTS WAS 43 YEARS (RANGE: 17-85 YEARS), AND 34 (63%) WERE MALE. NO PATIENTS WERE DOCUMENTED TO HAVE MDR TB BY SUBSEQUENT CULTURE AND SUSCEPTIBILITY TESTING. SUCCESSFUL TREATMENT OUTCOMES WERE DOCUMENTED FOR 31 (57%) SMER-positive PATIENTS. OF THE REMAINING 23 WITH POOR OUTCOMES, TREATMENT FAILED IN SIX (26%) PATIENTS, 12 (52%) DEFAULTED, AND FIVE (22%) DIED. OF THE PATIENTS WHO DIED, THREE DIED WITHIN 1 MONTH OF STARTING TREATMENT AND TWO DIED IN THE SECOND AND THIRD MONTHS OF TREATMENT, RESPECTIVELY.

TREATMENT INTERRUPTION OF 2-8 WEEKS OCCURRED AMONG 15 (28%) PATIENTS. OF PATIENTS WHO INTERRUPTED TREATMENT, 13 (87%) WERE MALE, AND 10 (67%) WERE AGED ≤50 YEARS. THE MEDIAN NUMBER OF INTERRUPTIONS PER PATIENT WAS TWO (RANGE: ONE-SIX). AMONG PATIENTS WHO INTERRUPTED TREATMENT, THREE (20%) INTERRUPTED DURING THE INTENSIVE PHASE, 10 (67%) DURING THE CONTINUATION PHASE, AND TWO (13%) DURING BOTH PHASES OF TREATMENT. THE MEDIAN DURATION OF ALL INTERRUPTIONS WAS 3 WEEKS (RANGE: 2-8 WEEKS); OF 30 INTERRUPTIONS, 20 (67%) WERE 2-3 WEEKS AND 10 (33%) WERE 4-8 WEEKS.

OF THE 31 AFB SMER-positive PATIENTS WHO COMPLETED TREATMENT, THE MEDIAN DURATION OF TREATMENT WAS 10 MONTHS (RANGE: 6-18 MONTHS). SIXTEEN (52%) COMPLETED 6 MONTHS OF PRESCRIBED MEDICATION WITHIN 6-9 MONTHS, EIGHT (26%) WITHIN 10-12 MONTHS, AND SEVEN (23%) WITHIN 13-18 MONTHS.

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veloping drug resistance or disease progression. However, interruptions of shorter duration also are of concern because patient adherence is important for treatment success and to prevent transmission.

In Ivanovo, the rates of treatment default and interruption were high. Approximately one third interrupted treatment during the intensive phase, when patients with a high bacillary load are at greatest risk for developing drug resistance and for spreading untreated disease in the community. Half of the patients interrupted treatment more than once, and the median duration of interruption was long, resulting in considerable delays in treatment completion and increasing the workload of staff responsible for tracking patients who interrupted or defaulted. Reasons for treatment interruption included both patient and program factors such as cost of transportation and length of hospital stay required for treatment.

The findings in this report are subject to at least three limitations. First, the sample size of the population was small, limiting statistical power to detect significant differences in outcomes among groups. Second, other risk factors (e.g., human immunodeficiency virus infection and excessive alcohol consumption) that may have affected the likelihood of both treatment interruption and poor outcomes could not be assessed in the treatment record review. Finally, not all patients were evaluated following treatment completion, and their final treatment outcome was not available.

On the basis of this study and another study examining reasons for treatment interruption, the TB project staff were encouraged to concentrate human and financial resources on treatment completion. To improve patient adherence and reduce treatment interruption, patients are now receiving food supplements or free transportation to the clinic. Aggressive efforts are being made to locate and restart treatment in patients who interrupt before completion. Vehicles, fuel, and public transportation passes have been provided to the TB project staff to enable them to find patients who interrupt treatment. Finally, health-care providers are receiving performance-based rewards if their patients complete treatment.

REFERENCES


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DURING THE 1990S, THE NUMBER OF tuberculosis (TB) cases increased dramatically in the Russian Federation, and the rise paralleled concomitant increases in TB-associated mortality. In November 1998, the World Health Organization (WHO), the U.S. Agency for International Development, and CDC, in collaboration with the Central Tuberculosis Research Institute of the Russian Academy of Medical Sciences and the Russian Ministry of Health, identified three regions as demonstration sites for implementing a WHO control strategy program of directly observed treatment short-course (DOTS). The program was designed to provide comprehensive TB care to both civilian and prison populations within each region (oblast), and periodic cohort analyses of treatment outcomes were recommended to evaluate its progress. This report summarizes evaluations of treatment outcomes for patients enrolled during the first 6 months of the project in Orel oblast and indicates that treatment success rates among TB patients in Orel were high. These findings support the use of DOTS as a control strategy in the Russian Federation.

Orel (1999 population: 900,000) is located approximately 200 miles southwest of Moscow. In 1999, the TB rate for Orel was 72 per 100,000 population, and 3.7% of newly diagnosed, smear-positive patients had primary multidrug-resistant TB (MDR TB) (i.e., TB resistant to at least isoniazid and rifampin). Case finding for TB followed existing national directives, which include the passive detection of symptomatic cases, active case finding among household contacts, and regular screening of groups considered to be at risk (e.g., prisoners, teachers, and health-care workers).

In the Russian Federation, TB is generally diagnosed by chest radiograph and clinical findings; however, in the oblasts where the demonstration projects have been implemented, smear microscopy and mycobacterial culture are used by clinicians to diagnose TB. In Orel, clinicians use the standard WHO-recommended short course chemotherapy regimen (isoniazid, rifampin, ethambutol, and pyrazidamine for 2 months followed by isoniazid and rifampin for 4 months) for patients not treated previously for TB.

Prospective data collection began in October 1999 on all Orel TB patients...
without a history of TB treatment. Sputum conversion and treatment outcomes for patients registered during October-December 1999 and January-March 2000 are presented in this report. Sputum conversion was defined as achieving three consecutive negative sputum smears and/or culture specimens from a previously positive patient. WHO/International Union Against Tuberculosis and Lung Disease definitions for six mutually exclusive treatment outcomes were used.3 Prison patients and retreatment patients (i.e., patients who had previously been treated for TB) were enrolled beginning in January 2000 and were included in the analysis of second quarter outcomes.

A total of 349 patients were enrolled in the study: 128 during October-December 1999, 164 during January-March 2000; 331 (95%) had pulmonary TB, and 265 (76%) were men. Mean age at diagnosis was 40 years (range: 15-89 years). Enrollment was higher in the second quarter, in part because of the inclusion of prisoners (n=39) and retreatment case-patients (n=6). Of the 310 civilian patients, 182 (52%) had positive smears or cultures for Mycobacterium tuberculosis before treatment, and 128 (41%) had negative bacteriologic findings; 146 (47%) reported having symptoms at TB diagnosis, and 164 (53%) were asymptomatic and were identified through routine screening. Culture confirmation of TB diagnosis was significantly higher in symptomatic patients than in those diagnosed through a screening procedure (77% versus 56%; p<0.001). In prisoners, routine biannual screening is mandatory. Fifteen (39%) prison case-patients had positive smears, and 20 (51%) were bacteriologically confirmed.

Of isolates from 179 culture-positive patients tested for susceptibility to five anti-TB drugs, 55 (31%) were resistant to streptomycin, 27 (15%) to isoniazid, 20 (11%) to kanamycin, five (3%) to rifampin, and five (3%) to ethambutol. Six (3%) patients had MDR TB, and all were civilians. MDR TB prevalence was 1% among patients with no history of previous TB treatment (five of 343) and 17% among retreatment cases (one of six).

Treatment success (i.e., patients with bacteriologically documented cure and those who completed treatment) was attained for 88% of new and 60% of retreatment TB patients. Among new, culture-positive pulmonary case-patients, 88% were either cured or completed treatment; this proportion declined to 81% for patients identified as smear-positive at diagnosis. Cure and completion rates among prisoners were high (97%), with no prison patients defaulting. Overall, case-fatality rates were high in Orel (5%), particularly among smear-positive patients (12%).

Reported by: B Kazeznyy, T Khoroshcheva, T Aptekar, Orel Oblast TB Dispensary, Orel; L Rybka, Central TB Research Institute of the Russian Academy of Medical Sciences; H Kluge, W Jakubowaski, D Pashkevich, World Health Organization, Moscow, Russia. International Activity, Div of TB Elimination, National Center for HIV, STD, and TB Prevention; and an EIS officer, CDC.

CDC. Editorial Note: The findings in this report indicate that treatment success rates among TB patients in Orel were high. Although rates for smear-positive patients during the first 6 months of the project were slightly lower than the WHO global target of 85%, these findings are consistent with expected success rates for a newly implemented DOTS project. The higher treatment success rates among Orel patients in whom asymptomatic TB was diagnosed using chest radiograph (without bacteriologic confirmation) compared with those with bacteriologic confirmation may reflect either early diagnosis of disease or incorrect diagnosis. The higher proportion of cases among prisoners identified through asymptomatic radiographic screening in Orel and the lack of defaulters in this group may account for their better outcomes compared with civilians.

The treatment success rates reported here were higher than those reported in the other project areas of the Russian Federation that implemented the DOTS strategy.3-7 Reasons for the higher treatment success rates in Orel may include earlier clinical presentation of patients and efforts by local staff to ensure that patients remained on treatment. Another factor may be the lower rates of MDR TB; studies in other areas of the Russian Federation have documented rates of 5%-22% in new TB patients.3-7 The higher proportion of deaths among Orel TB patients may indicate delays in treatment of TB disease, raising concern about sustained community transmission from unidentified infectious cases, the potential lack of education about TB symptoms in the general population, and the possibility of delayed recognition by physicians.

The public health system in the Russian Federation is struggling to control the newly re-emergent TB epidemic. Although the DOTS strategy is an inexpensive and effective method of TB control in other high-burden countries,1 the adoption of DOTS in the Russian Federation has begun only recently. Because aspects of the strategy depart from longstanding Russian TB control traditions, convincing TB physicians to adopt DOTS has been difficult. The findings in this report suggest that the successful implementation of DOTS in the Russian Federation is possible despite these historic differences in TB control, and that treatment success rates above the WHO global target of 85% can be achieved.

REFERENCES

*WHO treatment outcomes include bacteriologic cure of patients with a positive smear or culture before treatment and negative bacteriologic results at the end of therapy; treatment completion: patients who complete treatment without bacteriologic proof of cure or
Update: Assessment of Risk for Meningococcal Disease Associated With the Hajj 2001

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During late March and early April 2000, four cases of meningococcal disease caused by Neisseria meningitidis serogroup W-135 were identified among U.S. pilgrims returning from the Hajj in Saudi Arabia, their close contacts, and communities. These cases occurred as part of a larger epidemic in which approximately 400 cases caused by a similar and unusual strain were identified worldwide. The Hajj, an annual pilgrimage to the holy places of Islam, is attended by approximately two million persons from approximately 140 countries, including an estimated 15,000 from the United States.

After an outbreak of serogroup A meningococcal disease in 1987 associated with the Hajj, CDC recommended that U.S. pilgrims receive the quadrivalent meningococcal polysaccharide vaccine. This vaccine provides protection against disease caused by serogroups A, C, Y, and W-135; however, the vaccine may not affect asymptomatic pharyngeal carriage or a person’s ability to transmit disease. To assess the risk for meningococcal disease in 2001 among U.S. pilgrims, CDC conducted a study of pharyngeal carriage of N. meningitidis in departing pilgrims traveling to Saudi Arabia and of passengers returning from Saudi Arabia after the Hajj 1-2 weeks later.

After informed consent was obtained, pilgrims departing from John F. Kennedy International Airport (JFK), New York, on seven consecutive direct flights to Saudi Arabia during February 16-27, 2001, were asked to complete a questionnaire and provide an oropharyngeal swab for culture. During March 9-16, all disembarking passengers (i.e., pilgrims and nonpilgrims) on five consecutive direct flights from Saudi Arabia to JFK were similarly approached; 451 pilgrims were enrolled in the departing portion of the study and 869 passengers, including 727 pilgrims, were enrolled in the returning portion. Of the 27 N. meningitidis isolates recovered from 1320 passengers, 17 (63%) were nongroupable (i.e., a typically nonpathogenic strain); seven (26%) were serogroup W-135. Returning pilgrims were more likely to be carriers than departing pilgrims (2.6% versus 0.9%; p=0.04). None of the departing pilgrims carried serogroup W-135; however, six (0.8%) returning pilgrims were serogroup W-135 carriers (p=0.06). Among returning passengers, carriage of serogroup W-135 was similar among pilgrims and nonpilgrims (0.8% versus 0.9%; p=0.98).

Many returning passengers reported upper respiratory symptoms; 63% reported cough, 58% had sore throat, and 24% had fever during the 2 weeks before their return. Antibiotic use was reported by 396 (49%) of 811 returning passengers and was associated with decreased (although not significantly [2.1% versus 4.2%; p=0.09]) N. meningitidis carriage. The cause of this illness is not known; severe illness requiring hospitalization was not reported.

Because of the low rate of N. meningitidis serogroup W-135 carriage, antimicrobial chemoprophylaxis for all pilgrims was not recommended. Although overall carriage was low, the high proportion of serogroup W-135 carriage suggests continuing transmission in Saudi Arabia. Evidence of this transmission, combined with reports of cases of invasive disease among pilgrims returning to the United Kingdom who received only bivalent vaccine against serogroup A and C, suggests that U.S. pilgrims should continue to receive quadrivalent meningococcal polysaccharide vaccine before travel to the Hajj.

REFERENCES
3 available.

Publication of Surgeon General’s Report on Smoking and Health

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The Surgeon General’s report, Women and Smoking, was released on March 27, 2001. This report updates and expands the 1980 Surgeon General’s report, The Health Consequences of Smoking for Women, and examines various facets of smoking among women: patterns of tobacco use, health consequences of smoking, social and individual factors influencing cigarette smoking and smokeless tobacco use, and prevention and cessation programs and policies.


REFERENCES
1 available.