Tuberculosis Outbreak Investigation of a U.S. Navy Amphibious Ship Crew and the Marine Expeditionary Unit Aboard, 1998

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A Marine deployed aboard a U.S. Navy amphibious ship had smear-positive, cavitary pulmonary tuberculosis (TB). Contact investigation ultimately found 21 active cases of TB among sailors and Marines who were aboard the affected ship. Approximately 3 months lapsed between onset of the source patient's illness and appropriate diagnosis and treatment. During the contact investigation, 3,338 persons received tuberculin skin tests and 712 were identified as new latent tuberculosis infection cases. Four persons diagnosed with latent tuberculosis infection developed active TB because of poor compliance with treatment. After personnel disembarked from the ship, persistent efforts to identify persons with active disease and latent infections were successful in controlling further spread of tuberculosis in military units and local communities. The *Mycobacterium tuberculosis* bacteria isolated from the source patient and 16 of the other active cases were susceptible to all drugs commonly used to treat TB.

Introduction

Following a period of resurgence of tuberculosis (TB) in the United States that began in the mid-1980s and peaked in 1992, its incidence has steadily declined to an annual rate of 5.8 cases per 100,000 persons in the year 2000, the lowest ever recorded in the United States.[1] The combined TB rate for the Navy and Marine Corps has generally been lower than the national rate (Fig. 1), but was higher in 1998 and 1999 due to the outbreak described in this report.[2-5] Navy ships, with crews living in closed spaces that have controlled ventilation systems, have historically presented ideal settings for transmission of TB infection.[6] In 1987, a contact investigation found 216 members of the crew of the USS Saipan to be infected, a conversion rate of 24.5%.[6] In 1966, a contact investigation found 48% of the USS Richard Byrd's company were infected from exposure to a sailor with cavitary TB.[7]

Described in this report is a large outbreak of tuberculosis that occurred among the crew and the Marine Expeditionary Unit (MEU) personnel deployed aboard an amphibious ship. Aggressive public health measures were applied during the consequent contact investigation and helped limit the outbreak to only those persons exposed aboard ship, with one exception. Stopping the spread of TB depends on identifying and treating persons with active disease, followed by identifying persons with latent tuberculosis infection (LTBI) in subsequent contact investigations and providing prophylactic therapy.[7] The challenges presented to the Navy physicians, nurses, and corpsman involved in this outbreak are representative of challenges faced in the ultimate eradication of tuberculosis across all populations within the United States.

Background

The ship on which the TB outbreak occurred is a large amphibious ship of the LHD class with a crew of approximately 1,000 personnel. When deployed it serves as lead ship of an Amphibious Ready Group composed of three ships and the Marines aboard. The mission of an Amphibious Ready Group is to serve as a mobile base of operations for a MEU. A MEU has approximately 2,200 personnel organized into four groups: a Command Element, a Battalion-Landing Team, an Air-Combat Element, and a Service and Support Group. Most MEU personnel, approximately 1,350 persons, were based aboard the outbreak ship; the remainder were aboard either an LPD class ship (350 Navy crew/450 Marines) or an LSD class ship (290 crew/250 Marines).

Source Patient History

The source patient was a 21-year-old white male Marine who was a member of the Battalion-Landing Team element of the Marine Expeditionary Unit. He lived in a berthing area with approximately 100 other Marines where sleeping compartments are stacked four high. A review of his medical records showed that he last had a tuberculin skin test (TST) in January 1997, with a reading of 0 mm interpreted as "negative."

In late May 1998, he sought care for a dry cough of 1-month duration that had just begun to be productive of sputum. He also noted at that time that he was becoming short of breath while exercising. Evaluation included a chest X-ray that showed a bilateral diffuse infiltrate pattern without associated effusions or loculations. Of note, earlier in the month he received two TSTs, the first (routine) one resulting in a reading of a 16-mm reaction, which prompted a second confirmatory test that was read as 0 mm. The second TST result was accepted because it was thought that the initial TST injection was improperly performed by an inexperienced person. Based on the patient's symptoms, chest X-ray, and physical examination, he was diagnosed with "atypical pneumonia" and treated with a 5-day course of azithromycin.

He returned twice in June for follow-up and was treated with an albuterol inhaler for exercise-related dyspnea. He did not improve and was re-evaluated on the last day of June. Chest X-ray showed diffuse interstitial infiltrates, and laboratory findings included erythrocyte sedimentation rate 55, hemoglobin 11.5, white blood count 8.6, hematocrit 35.7, red blood cell count 4.42, and platelet count 361. Sputum Gram stain showed few white blood cells, few Gram-positive diplococci, and few

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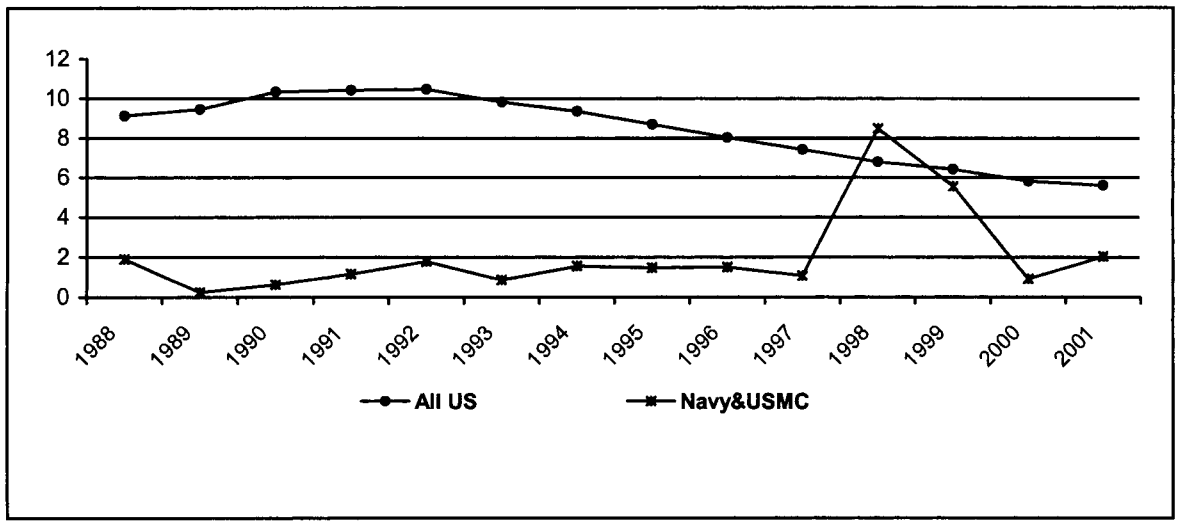

Fig. 1. Active TB case rates per 100,000 population: U.S. national rate and combined U.S. Navy-Marine Corps rate, 1988–2001.

epithelial cells and he was again treated for atypical pneumonia, this time with a 14-day course of azithromycin. Sputum culture was positive for *Streptococcus pneumoniae* sensitive to all antibiotics. A week later, the patient returned for follow-up reporting that he was feeling better, his cough was becoming less productive, but he had been waken by chills the night before. Lung examination was remarkable for a few end-expiratory wheezes in the left lower lobe. Assessment was resolving pneumonia and the plan was to complete the course of antibiotics.

On July 20, he was admitted to the ship's hospital for surgical treatment of a perianal abscess. The night after the procedure he became febrile, spiking a temperature of 105°F and was started on triple antibiotic therapy (ampicillin, gentamycin, metronidazole). He remained on the ward until the ship arrived in port on July 25, at which time he was transported to the local naval hospital.

Active pulmonary tuberculosis was diagnosed on July 27 and treatment with isoniazid, rifampin, ethambutol, and pyrazinamide was initiated. Chest roentgenograms obtained aboard the ship and at the hospital were reviewed and found to be consistent with tuberculosis, showing evolution of a cystic cavitary lesion in the apex of the right lung. Three sputum smears contained acid-fast bacilli interpreted as too numerous to count. The patient's sputum cultures contained *M. tuberculosis* that was susceptible to all antituberculous drugs. Medical record review and interview of the source patient indicate that he had probably had active pulmonary tuberculosis since mid-April.

A contact investigation of all MEU personnel was begun on July 29. The ship, which had subsequently traveled to its homeport of Norfolk, Virginia, was notified and a contact investigation was done among the ship's crew. In the course of the investigation, another 20 active TB cases were eventually identified, but only 1 of these cases had a sputum smear that contained acid-fast bacilli (interpreted as 2-plus positive).

Methods

We defined a patient with an active case of TB as any person who had been aboard the ship between February 1, 1998 and August 1, 1998 and had sputum or tissue cultures that were positive for *M. tuberculosis* or chest roentgenogram and clinical findings consistent with pleural TB.[8,9] We defined a case of LTBI as a positive TST result in a person from the same populations who had no previous documented positive test result. All TSTs were administered with 5 tuberculin units using the Mantoux method and were read by trained Navy corpsmen, nurses, and physicians. Because this was an outbreak investigation, a tuberculin skin reaction with induration of at least 5 mm was considered positive.[8,9] Testing was done in two stages, initial testing and follow-up testing done 3 months later on all personnel who initially tested negative.[8,9]

Also, persons in two other exposure categories, social contacts and occupational contacts, were investigated. Social contacts of any active TB case included friends, family members, and any other persons sharing a household. Occupational contacts were defined as any person who cared for an active TB case identified as part of this investigation.

Statistical analyses were done comparing each group's rate of active TB and LTBI with the rate for the remainder of the population considered. Confidence Intervals of 95% on the relative risk were obtained using EpiInfo 2000 (Centers for Disease Control, 2000). Mantel-Haenszel χ^2 test or Fisher's exact test (two-tailed) was used for contingency tables.

Results

Contact Investigation

From May 1998 to July 1999, 21 persons who were either Navy amphibious ship crew or members of the Marine unit aboard developed active tuberculosis. Sixteen of the active cases were male and 5 were female. Fourteen were from the Marine unit and seven were ship's crew. Sixteen had pulmonary tuberculosis and the other five had pleural disease. Eight patients were hospitalized; none died. All active TB cases were either ship's crew or Marines who were part of the deployed MEU; none were social or occupational contacts of the source patient.

Berthing areas for Marines aboard the ship are cramped and crowded. All MEU personnel aboard all three ships of the Amphibious Ready Group were screened. The ship a MEU member

TABLE I

FREQUENCY AND RELATIVE RISK OF DEVELOPING A POSITIVE TST AMONG SHIP'S CREW, MARINE EXPEDITIONARY UNIT, AND COMMUNITY CONTACTS

Group	Persons Tested, *n*	Persons with Positive TSTs, *n* (%)[a]	Relative Risk (95% confidence interval)	*p*
Ship's crew (LHD)	934	171 (18.3)	0.85 (0.73, 0.99)	0.040
MEU personnel aboard outbreak ship (LHD)	1,304	447 (34.3)	3.01 (2.61, 3.48)	0.000
MEU personnel aboard LPD	436	28 (6.4)	0.28 (0.20, 0.41)	0.000
MEU personnel aboard LSD	245	5 (2.0)	0.09 (0.04, 0.22)	0.000
Community contacts	319	16 (5.0)[b]	0.22 (0.13, 0.35)	0.000

[a] Includes 21 active cases.

[b] Of the 16 cases of LTBI, only 1 was exposed to the source case.

was berthed on was recorded during the screening process. A number of personnel "cross-decked" (switched ships) during the deployment or were sent back to the United States for other medical or administrative reasons; therefore, a comprehensive record of ship assignments was not possible. The best estimate of MEU personnel who were assigned only to the outbreak ship is 1,347. Of these members, 43 were "prior reactors" who had received appropriate treatment for previously positive TSTs. The remaining 1,304 received TSTs of which 447 (34.3%) were positive (Table I). Of the 447 positive tests, 42 (9.4%) were identified during the 3-month follow-up round of testing.

The total number of MEU personnel tested was 2,085, with 525 (25.2%) positives, including 56 identified during follow-up testing. Screening results of MEU personnel berthed on the other two Amphibious Ready Group ships are also shown in Table I. Follow-up TST results could not be confirmed on 130 personnel because of transfers to other commands or discharge from military service.

All ship's crew were screened. Of the 1,019 crew members, 85 were prior reactors and the remaining 943 received TSTs, of which 171 (18.3%) were positive (Table I). Of the 171 positive tests, 39 were identified during the follow-up round of testing.

TSTs were done on 59 other social and occupational contacts of active cases at the MEU's home base, of which 3 were positive. Of these, only one could be directly linked to the source case, a naval hospital nurse who cared for him. Two hundred sixty TSTs were completed in the Norfolk area on other persons who had been aboard the ship, including civilians and midshipmen. Family members and close contacts of subsequently identified cases were tested and 13 of these were determined to be positive. The total number of social and community contacts tested was 319, of which 16 (5.0%) were positive.

MEU personnel aboard the outbreak ship were three times more likely (relative risk, 3.01 [2.61, 3.48]) to become a LTBI case when compared with the ship's crew, MEU personnel aboard other ships, and community contacts (Table I). For active TB, Table II shows that MEU personnel aboard the outbreak ship were again much more likely to become a case (relative risk, 2.97 [1.20, 7.33]).

The large MEU population was examined further in its component units. Table III shows that Battalion-Landing Team personnel were twice as likely to become a LTBI case, relative risk, 2.29 (1.92, 2.74), than the remainder of MEU personnel. There were also 10 active TB cases in the Battalion-Landing Team (Table IV), with a relative risk of 1.87 (0.59, 5.93) compared to the remainder of MEU personnel, although this was not statistically significant.

Culture Results

There were 18 positive cultures from outbreak-related active cases, including 1 from the source patient. All outbreak-related strains were susceptible to isoniazid, rifampin, and other antituberculous agents, although one patient's culture was interpreted to have intermediate susceptibility to isoniazid and full susceptibility to the other antituberculous agents. Three patients diagnosed as active cases had pleural disease with negative cultures. Several cases were reported to have identical pulsed field gel electrophoresis patterns by the Virginia State reference laboratory, but the majority of positive cultures were not submitted for this testing.

TB Treatment Program

At the time of this outbreak in 1998, the Navy Tuberculosis Control Program routinely recommended isoniazid (INH) prophylaxis (300 mg/day for 6 months) for persons diagnosed with

TABLE II

FREQUENCY AND RELATIVE RISK OF DEVELOPING AN ACTIVE TB CASE AMONG SHIP'S CREW, MARINE EXPEDITIONARY UNIT, AND COMMUNITY CONTACTS

Group	Persons Tested, *n*	Active TB Cases, *n* (rate/100,000)	Relative Risk (95% confidence interval)	*p*
Ship's crew (LHD)	934	7 (749)	1.23 (0.50, 3.05)	0.649
MEU personnel aboard outbreak ship (LHD)	1,304	14 (1,074)	2.97 (1.20, 7.33)	0.013
MEU personnel aboard LPD	436	0	0 (0.00, 1.52)	0.100[a]
MEU personnel aboard LSD	245	0	0 (0.00, 2.91)	0.400[a]
Community contacts	319	0	0 (0.00, 2.17)	0.258[a]

[a] Fisher's exact result.

TABLE III

FREQUENCY AND RELATIVE RISK OF DEVELOPING A POSITIVE TST AMONG MARINE EXPEDITIONARY UNIT COMPONENTS

Group	Persons Tested, *n*	Persons with Positive TSTs, *n* (%)[a]	Relative Risk (95% confidence interval)	*p*
Battalion-Landing Team	1,194	396 (32.8)	2.29 (1.92, 2.74)	0.000
Air-Combat Element	418	75 (17.9)	0.66 (0.53, 0.83)	0.000
Service and Support Group	259	26 (10.0)	0.37 (0.25, 0.53)	0.000
Command Element	214	28 (13.1)	0.49 (0.35, 0.70)	0.000

[a] Includes 14 active cases.

LTBI who were younger than 35 years of age.[9] Under that guidance, persons older than 35 years of age who developed a positive TST were not offered INH prophylaxis. Current Navy policy, adopted in 2001 to correspond with current recommendations in the Centers for Disease Control Core Curriculum on Tuberculosis, requires consideration of treatment for all persons who develop a positive TST regardless of age.[8] While undergoing LTBI treatment, naval personnel are required to follow-up monthly with their primary care provider for an interview, examination, and medication refill.

Of the 601 latent TB infections identified in the contact investigations on the outbreak ship, all were started on 300 mg/day INH. The rate of completion of treatment was not determined due to difficulty tracking and following the many personnel who transferred or left military service. However, it is important to note that four persons developed active pulmonary TB due to poor compliance after being started on INH treatment. A Marine admitted to not taking his daily isoniazid dose, although no specific reason was described in the medical record, and he developed active disease within 60 days of being started on INH. One sailor developed fever and chest pain 3 months after supposedly beginning the prophylaxis program, but when diagnosed with active pulmonary TB, it was discovered that although she reported full compliance to Navy Medical personnel during each monthly follow-up, she was actually not taking the medication at her mother's direction. Another sailor took INH for the initial 6 weeks, then stopped and discarded her refills while faking compliance for the next 5 months and was diagnosed with active pulmonary TB 3 months later. A third sailor took INH for 1 month, stopped for 1 month, resumed for 4 months then quit, and was diagnosed with active pulmonary TB 4 months later.

All active TB cases diagnosed in this outbreak were treated with the standard four-drug regimen recommended in the Centers for Disease Control Core Curriculum: INH, 300 mg/day for 6 months; rifampin, 600 mg/day for 6 months, with pyrazinamide 15–30 mg/kg per day and ethambutol 15–25 mg/kg per day for the first 2 months.[8]

Discussion

This study illustrates that TB remains a significant threat to the health and readiness of Navy and Marine Corps personnel, particularly in the shipboard environment. Prompt diagnosis and treatment of the source case would have prevented the infection of a large number of personnel and would have also reduced the magnitude of medical resources necessitated by the outbreak investigation and the treatment of those infected. Also preventable were the active TB cases that resulted from poor compliance with LTBI treatment.

Among a population of 2,238 personnel, 21 cases of active tuberculosis occurred in this outbreak, 14 among Marine Corps personnel and 7 among Navy personnel. Six hundred eighty-four LTBIs were identified among MEU and ship personnel and other close contacts. Active case rates ranged from 1074 (MEU) to 749 per 100,000 population (Ship's crew), which were, respectively, 873 and 609 times greater than the active TB case rate that the combined Navy-Marine Corps population experienced over the previous 10 years (1.23 cases per 100,000 population).[2] The actual frequency of TB cases for the Navy-Marine Corps averaged 8.4 annually from 1988 to 1997, ranging from 2 cases reported in 1989 to 15 cases reported in 1988.[2]

A highly infectious source patient was identified. Close contact with the source patient was associated with both an increased risk for becoming infected and for developing active tuberculous disease. Overall highest LTBI rate and active TB case rate (34.3% and 1,074 per 100,000) and relative risks (2.97 and 3.01) were found among Marines assigned to the outbreak ship. Within the MEU population, Battalion-Landing Team personnel (the source patient's unit) were twice as likely to develop an active TB case or become a LTBI case.

In the *Morbidity and Mortality Weekly Report* publication of 1994, "Guidelines for Preventing the Transmission of Tuberculosis in Health Care Facilities,"[10] two of the basic preventive approaches recommended in particular would have limited the transmission of disease to others aboard ship. The first, "ensure early identification, diagnostic evaluation, and effective treat-

TABLE IV

FREQUENCY AND RELATIVE RISK OF DEVELOPING AN ACTIVE TB CASE AMONG MARINE EXPEDITIONARY UNIT COMPONENTS

Group	Persons Tested, *n*	Active TB Cases, *n* (rate/100,000)	Relative Risk, (95% confidence interval)	*p*
Battalion-Landing Team	1,194	10 (838)	1.87 (0.59, 5.93)	0.282
Air-Combat Element	418	3 (718)	1.09 (0.30, 3.88)	1.000[a]
Service and Support Group	259	1 (386)	0.54 (0.07, 4.13)	1.000[a]
Command Element	214	0	0 (0.00, 3.19)	0.385[a]

[a] Fisher's exact result.

ment of patients who may have infectious TB,"[10] would clearly have prevented many of the active cases and LTBIs. In the United States, patients with newly diagnosed tuberculosis transmit the disease to an average of only 1.5 other persons.[11] However, recent studies show that up to 10% of patients with tuberculosis were highly infectious and probably accounted for most instances of transmission, as in this outbreak.[12] Military medical care providers, from junior corpsmen to senior medical officers, must consider TB in the differential diagnosis when evaluating a patient who complains of persistent cough, even if the patient appears young and otherwise healthy. TSTs should be placed and read by individuals experienced in the technique and equivocal results or missed readings should lead to an immediate repeat of the test. Delays in TB diagnosis in the shipboard environment can rapidly lead to compounding of problems, as demonstrated by this outbreak. Additionally, between 5% and 10% of newly infected persons who do not receive prophylaxis eventually develop tuberculosis.[13-16] Approximately one-half of these cases develop within 2 years of infection; the remainder occur in later years, often remote from the time of infection.[15] In this outbreak, four persons developed active pulmonary TB because of poor or noncompliance with the appropriate treatment, INH prophylaxis.

The second relevant approach recommended by "Guidelines for Preventing the Transmission of Tuberculosis in Health Care Facilities" is "developing, installing, maintaining, and evaluating ventilation and other engineering controls to reduce the potential for airborne exposure to *M. tuberculosis*."[10] A promising engineering control is the use of ultraviolet germicidal irradiation (UVGI). Not only would installation of ultraviolet lamps in the ventilation systems of ships lower the risk of TB transmission, they would also lower the transmission risk of other viral, bacterial, and fungal respiratory pathogens, while also controlling fungal growth in the ventilation systems. Viruses are more susceptible to UVGI than bacteria, while bacterial spores are more resistant.[17] Considering the huge expenditure of resources associated with this outbreak and the emerging threat of attack with biological agents, the potential for UVGI systems to decrease respiratory disease rates and the feasibility of their installation aboard ships should be investigated by the Navy.

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