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### Global Epidemiology

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#### Notice

This supplement is being published as a courtesy to the *MMWR* readership. The findings and conclusions in these papers represent the views of the authors and do not necessarily represent the views of CDC.

The material in this supplement originated at a meeting of the Training in Epidemiology and Public Health Interventions Network (TEPHINET) held in Beijing, China, during November 8–12, 2004. It was prepared for publication by the Coordinating Office for Public Health, Stephen C. Blount, MD, Director.

## Preface

Accurate epidemiologic information is essential for making good decisions about developing, implementing, monitoring, and evaluating health policies. To ensure the quality of information gathered, CDC created the Epidemic Intelligence Service (EIS) in 1951. Since then, approximately 32 countries have developed field epidemiology and allied training programs (FETPs) based on the EIS model, all sharing a common principle of training through service.

In the 1990s, work began to create a unified global network, and in 1999, the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) was formed. TEPHINET is dedicated to strengthening international public health capacity by enhancing competencies in applied epidemiology and public health practice. Nearly all of the 32 FETPs in the network began as partnerships between national ministries of health, the Division of Epidemiology and Surveillance Capacity Development (formerly the Division of International Health) of CDC's Coordinating Office for Global Health, and the World Health Organization (WHO).

This supplement to the *MMWR* highlights the work of epidemiologists who have graduated from TEPHINET member programs. The articles were developed from abstracts presented in Beijing, China, at the Third Global Scientific Conference of TEPHINET during November 8–12, 2004. Major funding for the conference was provided by the Bill and Melinda Gates Foundation. Approximately 230 field epidemiologists from 40 countries participated to share best practices and new ideas in field epidemiology, surveillance, response, and training. The reports selected for publication in this supplement focus on the contributions TEPHINET members and their trainees and graduates have made in surveillance of and response to emerging infectious diseases. They reflect the broad impact of the training programs.

Field epidemiology trainees studied major emerging problems of global concern (e.g., avian influenza in Thailand) and common outbreaks (e.g., salmonellosis and varicella in China). Trainees applied their skills to investigate occupational injuries in Zimbabwe, evaluate a tuberculosis control program in Kazakhstan, and adapt statistical methodologies used for industrial quality control to estimate vaccination coverage in India. The Canadian contribution highlights the application of epidemiologic methods to improve product safety for cochlear implants, and two papers discuss how to use case-control methodology to identify risk factors for brucellosis in Kyrgyzstan and neonatal tetanus in Uganda.

A key characteristic of TEPHINET members' training-through-service programs is their location in national ministries of health.

This enables TEPHINET to offer global and regional organizations access to public health professionals who conduct surveillance and respond to health threats. Network members serve more than half of the world's population, including the United States (Figure). Just as EIS provides critical personnel for the U.S. public health system, FETPs in TEPHINET provide essential staff to their own countries and regions.

As founding members of TEPHINET, WHO and CDC maintain close partnerships with the organization. With assistance from WHO and CDC, TEPHINET is piloting a continuing quality improvement process that is expected to lead to steady improvement in the quality of science and level of service that FETPs provide. In addition to its training and capacity building role, TEPHINET is a member of WHO's Global Outbreak Alert and Response Network (1) and provides experts for WHO investigative teams.

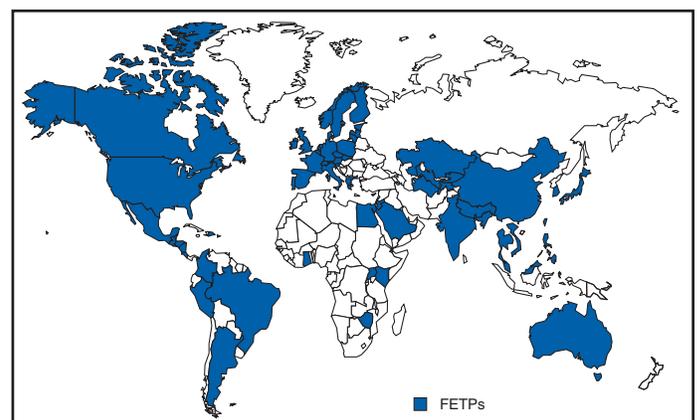
The new International Health Regulations require each nation to have competent public health personnel for epidemic surveillance and response (2). TEPHINET and its member programs will be major participants in achieving this goal. TEPHINET, WHO, and CDC are currently working together to create new FETPs in seven countries or regions worldwide.

Much of the work of FETP staff, trainees, and graduates is accomplished as they fulfill duties in their national public health systems and has not been published. Because of the value of this applied science, we are pleased at this opportunity to share a selection of the many excellent studies produced by TEPHINET member programs and their graduates.

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**FIGURE. Field epidemiology training and allied programs (FETPs), 2005**



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# Investigation of Avian Influenza (H5N1) Outbreak in Humans — Thailand, 2004

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## Abstract

**Introduction:** Beginning in late 2003, a substantial outbreak of influenza A (H5N1) virus spread among poultry in Thailand. On January 23, 2004, the Ministry of Public Health (MPH) detected the first confirmed human case of H5N1 infection in humans.

**Methods:** During February–November 2004, the MPH's Bureau of Epidemiology and provincial health offices worked together to investigate the H5N1 outbreak in humans. Two studies were conducted: a descriptive study to describe clinical manifestations and epidemiologic characteristic of the cases and a matched case-control study to determine risk factors for persons who might subsequently become ill with H5N1.

**Results:** A total of 16 patients with confirmed H5N1 were identified for the case-control study. Fever and respiratory symptoms predominated. Leucopenia and thrombocytopenia were present respectively in nine (100%) and four (44%) persons aged <15 years. Direct touching of unexpectedly dead poultry was the most significant risk factor (odds ratio = 29.0; 95% confidence interval = 2.7–308.2). Overall mortality was 75%; mortality for persons aged <15 years was 90%, compared with 57% for persons aged ≥15 years.

**Conclusion:** Avian influenza was more severe in children, who should avoid handling dead poultry during epizootics. Early avian influenza in children resembled the more common dengue fever, but presence of cough and absence of hemoconcentration distinguished avian influenza, which often progressed rapidly to acute respiratory distress syndrome, requiring intensive care.

## Introduction

In 1997, the first outbreak of avian influenza A (H5N1) in humans was reported in Hong Kong, and exposure to infected poultry was identified as the probable route of transmission (1–3). Since late 2003, this highly pathogenic virus has caused disease outbreaks in poultry in at least eight East Asian countries, and fatalities among humans have been attributed to the same virus in Cambodia, China, Indonesia, Thailand, and Vietnam (4,5). During December 2003–October 2004, a total of 17 cases of respiratory disease caused by H5N1 viruses were reported in Thailand; these cases coincided in time and place with the epizootic disease in poultry. Millions of persons in Thailand raise backyard chickens near their houses, which has increased concern about the potential for a substantial H5N1 outbreak in humans.

## Methods

During February–November 2004, the Bureau of Epidemiology (BoE) of the Ministry of Public Health (MPH) and

provincial health offices worked together to investigate the H5N1 outbreak in humans. Two studies were conducted: a descriptive study to describe clinical manifestations and epidemiologic characteristic of the cases and a matched case-control study to determine risk factors for persons who might subsequently become ill with H5N1.

## Descriptive Study

### Case Definition

Under Thailand's nationwide avian influenza surveillance system, which BoE initiated in December 2003, any patient admitted to a health-care facility with pneumonia or influenza-like illness who has a history of exposure to poultry is reported to BoE. For this study, a case was defined as H5N1 illness occurring in a person who had received a diagnosis of pneumonia or influenza-like illness and who had either a positive viral culture for H5N1 virus or confirmation of H5 strain by real-time reverse transcription-polymerase chain reaction (RT-PCR) (6,7).

## Laboratory Testing

Each patient was evaluated for H5N1 infection status at the time of hospital admission. Nasopharyngeal aspirates or nasopharyngeal swabs were collected and submitted to the Thai National Institute of Health or to Siriraj Hospital at Mahidol University for laboratory testing.

## Data Collection and Analysis

A standard form was used to collect information concerning clinical manifestations as recorded on medical records. Clinical manifestations and clinical progressions were analyzed using Epi Info 2002 version 2 (CDC, Atlanta, Georgia) and Excel (Microsoft, Redmond, Washington).

## Analytic Study

### Study Design and Sampling

A matched case-control study was conducted during the outbreak using the same case definition as the descriptive study. Population registers in the primary health-care unit of each village were used as the control sampling frame. Controls were selected matching village and age  $\pm 1$  year to each patient and then randomly selecting four controls for each patient. For one patient who was thought to have been infected through human-to-human transmission, four controls were selected from among health-care workers in the hospital to which the patient was admitted. A control was defined as any person who had no fever (i.e., temperature  $\geq 100.4^\circ\text{F}$  [ $\geq 38.0^\circ\text{C}$ ])  $\leq 7$  days before or after the onset of illness of the matched case-patient. With respect to exposure, unexpectedly dead poultry was defined as death of  $>10\%$  of all poultry in a farm or house within 1 day or  $>40\%$  within 3 days.

## Data Collection and Analysis

Interviews were conducted by physicians in BoE's Field Epidemiology Training Program. For persons who had died or were aged  $<12$  years, adult proxies were interviewed. A standard questionnaire was used to collect information regarding demographic characteristics, underlying diseases, exposure to other persons with suspected avian influenza, and activities related to poultry in the week before onset of illness in the matched case-patient. In the univariate matched analyses, the matched odds ratio (OR) and 95% confidence interval (CI) were calculated for each exposure using Epi

Info 2002 version 2. The Mantel-Haenszel summary chi square test was used for the matched data.

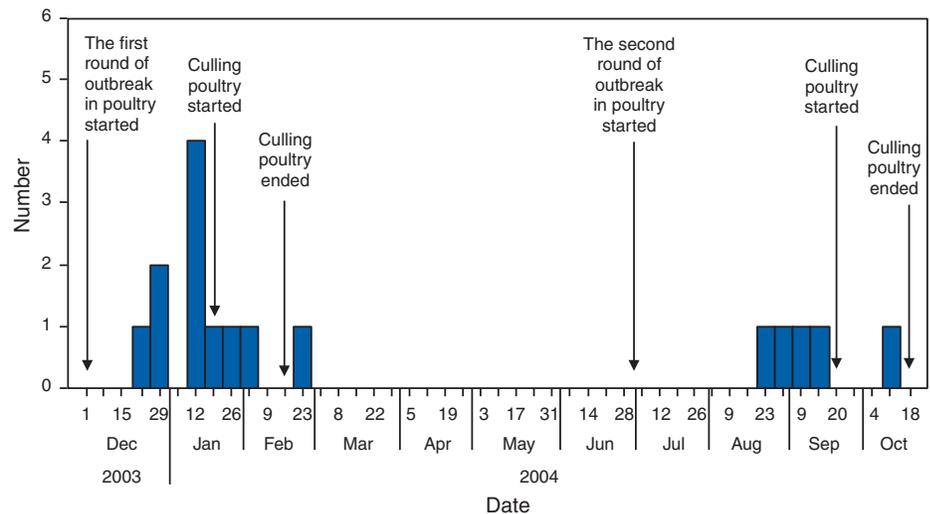
## Results

The outbreak in humans occurred in two episodes: January–March and August–October 2004 (Figure 1). Of 17 cases reported from the avian influenza surveillance system, one was excluded because of incomplete laboratory results; 16 patients with confirmed H5N1 infection were included in the study.

Patients lived in 11 provinces, primarily in central Thailand. Nine were male and seven female. Patients varied by age (range: 2–58 years; median: 13 years). Of the 16 patients included in the study, nine (56%) were aged  $<15$  years. Overall mortality was 75%; mortality for persons aged  $<15$  years was 90%, compared with 57% for persons aged  $\geq 15$  years (OR = 6.4; CI = 0.4–204.2).

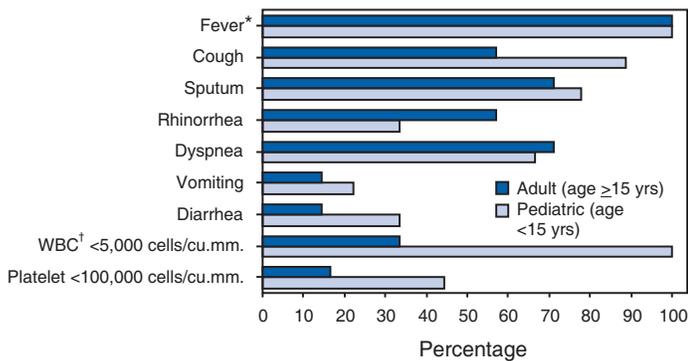
The incubation period varied (range: 2–8 days; median: 3 days). All patients had fever. Respiratory symptoms predominated, including cough (12 patients [75%]), sputum (12 [75%]), dyspnea (11 [69%]), and rhinorrhea (seven [44%]); four (25%) patients had gastrointestinal symptoms (Figure 2). All nine patients aged  $<15$  years had leucopenia (white blood cell count:  $<5,000$  cells/ $\text{mm}^3$ ; normal range: 5,000–10,000 cells/ $\text{mm}^3$ ), and four (44%) also had thrombocytopenia (platelet count:  $<100,000$  cells/ $\text{mm}^3$ ; normal range: 100,000–400,000 cells/ $\text{mm}^3$ ). The median hematocrit in persons aged  $<15$  years was 39% (range: 30%–41%). Clinical progressions demonstrated rapid progressive pneumonia and

**FIGURE 1. Number\* of persons with confirmed cases of avian influenza, by date of onset — Thailand, December 2003–October 2004**



\* N = 16.

**FIGURE 2. Clinical manifestations of influenza A (H5N1) patients from onset of illness to hospital admission, by symptom and age — Thailand, December 2003–October 2004**



\* Body temperature of >100.4°F (>38°C).

† White blood cell.

acute respiratory distress syndrome (ARDS) in all persons who died (Table 1). In the matched case-control study, case-patients and controls were similar with respect to the majority of variables (Table 2).

From the univariate matched analyses, direct touching of unexpectedly dead poultry yielded the highest odds ratio (OR = 29.0; 95% CI = 2.7–308.2). Having poultry die in or near the house or performing activities related to poultry was significantly associated with H5N1 disease (Table 3). No statistically significant difference was identified among patients reporting contact with persons with a suspected case of human avian influenza (Table 3).

## Discussion

The H5N1 outbreak in humans in Thailand during January–March and August–October 2004 affected primarily children. Overall mortality was high (75%). During the same period, mortality among persons with human cases in Vietnam was also high (80%) (8). These data suggest that the disease has become more severe than that reported in Hong Kong in 1997, in which mortality was only 33% (2). However, availability of early aggressive treatment in Hong Kong

**TABLE 1. Clinical progressions of influenza A (H5N1) patients, by symptoms and days after exposure to birds — Thailand, 2004**

Symptoms	No. of days	
	Median	Range
Onset of illness with fever,* cough, or rhinorrhea (n = 16)	4	2–8
Pneumonia (n = 13)	9	6–12
ARDS† (n = 12)	10	8–18

\* Defined as body temperature >100.4°F (>38°C).

† Acute respiratory distress syndrome.

**TABLE 2. Number and percentage of influenza A (H5N1) case-control study participants, by selected characteristics — Thailand, 2004**

Characteristic	Cases (n = 16)		Controls (n = 64)	
	No.	(%)	No.	(%)
Median no. of family members	4		5	
Median age (yrs)	14		14	
<b>Sex</b>				
Male	9	(56)	31	(48)
Female	7	(44)	33	(52)
<b>Smoking</b>				
Yes	2	(13)	9	(14)
No	14	(87)	55	(86)
<b>Chronic medical condition</b>				
Yes	2	(13)	10	(16)
No	14	(87)	54	(84)

in 1997 or mutation of the virus might explain this difference. During December 16, 2004–December 8, 2005, global mortality among persons with human cases was 29% (5).

Basic laboratory profiles in children indicated leucopenia and thrombocytopenia. These laboratory results in children led attending physicians initially to suspect dengue fever in the differential diagnosis. However, certain differences helped clinicians differentiate between H5N1 infection and dengue fever. In H5N1 cases, respiratory symptoms typically predominate, and case-patients did not exhibit hemoconcentration (7). The rapid progressive pneumonia and ARDS required physicians in the epizootic areas to be aware of the possibility of H5N1 infection before patients' illness progressed to severe pneumonia.

In the matched analyses, H5N1 disease was associated with recent exposure to sick or unexpectedly dead poultry, particularly direct touching of unexpectedly dead poultry. Only one patient was reported to have been exposed in a live poultry market. In contrast, the 1997 Hong Kong outbreak was related to exposure to live poultry market (2,9). A family cluster was recognized in Thailand in September 2004, probably as a result of person-to-person transmission during unprotected exposure to a critically ill index patient (10). Vietnam also reported probable human-to-human transmission in February 2004 (11). Moreover, in Hong Kong in 1997, a study demonstrated H5N1 infection among health-care workers exposed to a patient with H5N1 infection (12). The risk for person-to-person transmission of H5N1 virus might increase, either through viral mutation or reassortment. This emphasizes the need for strong surveillance, early detection, and intensive measures to protect unexpected person-to-person transmission.

The findings in this report are subject to at least five limitations. First, because a substantial number of patients had died, case interviews were conducted more frequently by proxy than

**TABLE 3. Number and percentage of reported exposures associated with influenza A (H5N1) infection, by type of exposure — Thailand, 2004**

Exposure	No. (%) of exposures		OR <sup>§</sup>	(95% CI <sup>¶</sup> )
	Case* (n = 16)	Control <sup>†</sup> (n = 64)		
Direct touching of unexpectedly dead** poultry	10 (63)	12 (19)	29.0	(2.7–308.2)
Dressing poultry	5 (31)	4 (6)	17.0	(1.6–177.0)
Having unexpectedly dead poultry around the house	8 (50)	9 (14)	5.6	(1.5–20.7)
Plucking poultry	4 (25)	3 (5)	14.0	(1.3–152.5)
Being ≤1 m away from dead poultry	10 (63)	16 (25)	13.0	(1.8–96.3)
Storing products of sick or dead poultry in house	7 (44)	3 (5)	9.3	(2.1–41.3)
Direct touching of sick poultry	8 (50)	(14)	5.6	(1.5–20.7)
Being ≤1 m away from sick poultry	9 (56)	14 (22)	3.8	(1.2–11.7)
Having contact with person with suspected or confirmed H5N1 illness	3 (19)	13 (20)	0.9	(0.2–4.4)
Visiting live poultry market	1 (6)	0		

\* H5N1 illness occurring in a person who received a diagnosis of pneumonia or influenza-like illness and who had either a positive viral culture for H5N1 virus or confirmation of H5 strain by real-time reverse transcription-polymerase chain reaction (RT-PCR).

† Selected by matching village and age ±1 year to a person with a case and then randomly selecting four controls for each case-patient.

§ Odds ratio.

¶ Confidence interval.

\*\* Death of >10% of all poultry in a farm or house within 1 day or of >40% of poultry within 3 days.

were control interviews. Second, recall bias might have occurred as a result of the public's high level of alarm. Third, exposure to poultry was part of the surveillance requirement, and results might have been biased toward these exposures. Fourth, because dengue serology was not documented for patients, combined dengue and H5N1 infections cannot be ruled out. Finally, matching one case patient with health-care workers rather than community controls might have introduced bias.

During and after performance of this study, multiple recommendations were provided to health-care workers. In areas that have unexpectedly dead poultry, clinicians should have a high index of suspicion for avian influenza in patients with acute respiratory illness and quickly distinguish between H5N1 and other viral infections (e.g., dengue fever) that have similar laboratory profiles in children. Persons (especially children) should avoid direct contact with unexpectedly sick or dead poultry and not store products from unexpectedly dead poultry in the home. When contact is unavoidable, persons should use personal protective equipment and wash their hands frequently. Long-term public health surveillance and control measures are needed to monitor for person-to-person transmission and the emergence of a potentially pandemic H5N1 influenza virus.

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# Occupational Injuries Among Workers in the Cleansing Section of the City Council's Health Services Department — Bulawayo, Zimbabwe, 2001–2002

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## Abstract

**Introduction:** During 2001–2002, a total of 97 occupational injuries occurred among workers in the cleansing section of the Bulawayo, Zimbabwe, City Council's Health Services Department. This report describes a study that was conducted to describe the nature of these injuries and determine the associated risk factors.

**Methods:** A retrospective, descriptive cross-sectional survey was conducted concerning occupational injuries incurred by workers in the cleansing section during 2001–2002. A total of 153 workers who had been in the section as of January 1, 2001, and 23 senior managers and section supervisors were interviewed, the occupational injury register was reviewed, and a walk-through survey was conducted to estimate risk factors.

**Results:** The occupational injury register indicated that during the study period, 62 workers sustained 67 injuries, including one that was fatal. Of these 67 injuries, 27 (40%) involved workers who sustained cuts inside a box-type refuse removal truck, and 11 (16%) involved workers who had sprained ankles and wrists as a result of improper lifting. Workers aged 18–25 years were more likely to incur an injury than workers aged >25 years. Working as a bin loader and not having received preemployment training were associated with injuries. None of the bin loaders had received preemployment training. Hazards identified during the walk-through survey included use of small jacks in workshops, contact with biologic and chemical materials on trucks and landfill sites, and poor use of protective clothing. Supervisors cited worker negligence as the main cause of injury, whereas 72 (84%) workers cited lack of adequate protective clothing as a source of injury, and eleven (7%) workers cited use of inappropriate equipment.

**Conclusion:** On the basis of the modifiable risk factors for injury identified in this study, the Bulawayo City Council drafted a new health and safety training manual. New recruits now receive training before starting work on refuse collection trucks.

## Introduction

Occupational injuries continue to be a serious but poorly documented problem in both developed and developing countries. The International Labour Organisation estimates that worldwide, workers sustain 250 million unintentional occupational injuries and an additional 330,000 fatalities annually (1). Reducing the number of injuries is one of Zimbabwe's top 10 health priorities (2). The highest numbers of occupational injuries in Zimbabwe occur in the construction, mining, and manufacturing industries. Service industries, including local government authorities, accounted for 1,707 (12%) of the 13,854 occupational injuries reported during 2000 (3).

The Bulawayo City Council Health Services Department (HSD) monitors the city's public health standards, including refuse disposal services provided by the cleansing section. During 2001–2002, a total of 97 injuries occurred among HSD workers, one of which was fatal (4). Of these 97 injuries, 67 (73%) occurred in the cleansing section, including the one fatality. After the City Council and employees expressed concern regarding the high incidence of occupational injuries in the section, a study was conducted to describe the nature of injuries and estimate the associated risk factors.

## Methods

Records of injuries that occurred during January 2001–December 2002 were reviewed, and a cross-sectional survey was conducted in the HSD cleansing section during June 2003 to determine demographic and personal risk factors associated with injuries. Of 188 eligible general workers, 153 (84%) were interviewed along with 23 senior managers and section supervisors. Of 62 workers who had an injury during the study period, 51 (82%) were interviewed. All participants were informed that the purpose of the study was to find risk factors and make recommendations to improve the work environment. Persons interviewed gave informed written consent. A walk-through survey of public restrooms, mechanical workshops, a landfill site, and the suburban refuse collection process also was conducted. A checklist adapted from CDC's National Institute of Occupational Health (5) and a form (Occupational Health and Safety Form OHS IAF 2003) created by the National Social Security Authority (NSSA) of Zimbabwe were used to identify environmental risk factors. Data were analyzed using Epi Info 2002 (CDC, Atlanta, Georgia). Univariate analysis, frequencies, prevalence odds ratios, and p values at 95% confidence intervals (CIs) were reported. A result with a value of  $p < 0.05$  was considered statistically significant.

## Results

### Results from Register of Occupational Injuries

The register of occupational injuries indicated that 62 workers were injured at least once during the study period; of 67 injuries that occurred, one was fatal (Table 1). The death occurred when a bin loader slipped and was run over by the back wheels of a refuse truck. Injuries occurred throughout the week with no association to day of week or hour of day.

Of the 51 injuries for which interviews could be conducted, 13 (25%) injuries were classified as major because they resulted in permanent scars and in loss of >3 working days, and 38 (74%) were minor. Only three of the 13 workers with major injuries received any compensation, and the amount they received was negligible (average: <\$1 U.S. per month). Data regarding whether the family of the deceased worker was receiving compensation were not available. HSD management is responsible for the initial assessment and forwarding of necessary documentation and referral of workers to NSSA for payment of compensation. Neither workers nor management appeared to understand the compensation system.

### Personal Risk Factors

The section workforce included 147 (96%) men and six (4%) women. Risk factors associated with suffering an injury were age 25 years (odds ratio [OR] = 3.2; CI = 1.6–9.2), working as a bin loader (OR = 3.6; CI = 1.1–4.8), not having received preemployment training (OR = 3.1; CI = 1.3–7.5), and subsequently rating the job as difficult to perform (POR = 2.9; CI = 1.1–7.7) (Table 2). Potential environmental hazards cited by workers included inappropriate equipment (cited by 30 [22%] workers), dust (22 [14%]), biologic material (20 [13%]), sharp objects (17 [11%]), and chemicals (15 [10%]). A total of 72 (84%) workers said provision of adequate personal protective equipment (PPE) would help in the prevention of injury. Another 11 (7%) workers said that provision of appropriate equipment could help in injury prevention. A total of 29 (20%) workers could not name any potential hazards.

### Environmental Hazards

A walk-through inspection revealed human waste on restroom floors. Workers were at risk for splashes into exposed eye and mouthparts because they did not wear goggles or face masks during cleaning of restrooms. Workshops were overcrowded, with dirty vehicles under repair. All workers wore

**TABLE 1. Number and percentage of occupational injuries among workers in the cleansing section of the Bulawayo City Council Health Services Department, by injury type and cause — Bulawayo, Zimbabwe, 2001–2002**

Type	Risk factor	No.	(%*)
Cut on hand, finger, thumb, or foot	Broken glass or sharp objects	27	(40)
Sprained ankle or wrist	Improper lifting or throwing technique, or running and disembarking from vehicle	11	(16)
Eye injury	Dust, liquid, chemicals, or smoke	8	(12)
Shoulder injury	Contact collision	8	(12)
Knee injury	Contact collision, slip, or fall	5	(8)
Laceration of leg or finger	Dog or scorpion bite	4	(6)
Sharp back pain	Excessive effort in lifting	3	(5)
Trunk injury	Run over by truck	1	(2)
<b>Total</b>		<b>67</b>	

\* Total might exceed 100% because of rounding.

**TABLE 2. Number and percentage of occupational injuries among workers in the cleansing section of the Bulawayo City Council Health Services Department, by selected characteristics — Bulawayo, Zimbabwe, 2001–2002**

Characteristic	Injured		Not injured		OR*	(95% CI†)
	No.	(%)	No.	(%)		
<b>Age group (yrs)<sup>§</sup></b>						
18–25	13	(25)	9	(9)	3.2	(1.2–9.2)
26–64	38	(75)	93	(91)		
<b>Marital status</b>						
Married	41	(80)	85	(83)	0.8	(0.3–1.5)
Not married	10	(20)	16	(17)		
<b>Medical condition</b>						
Yes	6	(12)	8	(8)	1.8	(0.6–5.7)
No	45	(88)	94	(92)		
<b>Education level</b>						
Secondary or above	33	(65)	46	(45)	2.2	(1.1–4.8)
Primary or none	18	(35)	56	(55)		
<b>Work position</b>						
Bin loader	43	(84)	54	(53)	3.6	(1.6–8.1)
Other	8	(16)	48	(47)		
<b>Length in service (yrs)</b>						
≤3	14	(27)	20	(20)	1.6	(0.7–3.4)
4–35	37	(73)	82	(80)		
<b>Preemployment training</b>						
No	41	(80)	58	(57)	3.1	(1.3–7.5)
Yes	10	(20)	44	(43)		
<b>Health and safety training</b>						
No	46	(90)	91	(91)	1.1	(0.3–3.9)
Yes	5	(10)	11	(11)		
<b>Job rating<sup>  </sup></b>						
Difficult (3–5)	45	(88)	73	(72)	2.9	(1.1–7.7)
Easy (1–2)	6	(12)	29	(28)		
<b>Knowledge of hazards</b>						
No	2	(4)	27	(26)	0.1	(0.02–0.5)
Yes	49	(96)	75	(74)		
<b>Total</b>	<b>51</b>		<b>102</b>			

\* Odds ratio.

† Confidence interval.

§ Age groups were classified on the basis of surveys, which indicated statistically significant patterns in the occurrence of injuries in three age groups (18–25, 26–55,

overalls, but none wore gloves to avoid contamination from materials left in refuse trucks. Mechanics used small jacks to lift trucks and were at risk for injury as a result of heavy equipment falling.

Two types of trucks were used for refuse collection: an old box-type truck and a modern hydraulic-compactor refuse-collection truck (Figure). The compactor has side steps on which bin loaders stand, and workers do not come into contact with rubbish. However, workers loading the box-type truck must lift bins above their shoulder level, and workers inside the truck come into direct contact with hazardous materials and are at risk for sustaining cuts to their legs, feet, or fingers while spreading out rubbish. Use of PPE was limited. Of 62

bin loaders observed during the bin-collection process, 27 (44%) had worn-out footwear, and 22 (32%) had overalls in bad condition. Only 17 (28%) wore respirator masks, and none wore head protection, although both are necessary to prevent injury. Workers are issued two pairs of overalls and a pair of boots twice annually. Heavy-duty gloves are issued every 2 weeks, and face masks are issued on demand.

Poor disposal habits of medical practitioners resulted in needles and bandages being present in refuse collection trucks, and uncovered biologic and chemical materials were observed at the landfill. Scavengers were observed at the dump site, which could cause unintentional injuries. Another hazard was that dust and noise were generated during the compacting process.

The presence of the hazards identified in the walk-through survey was confirmed by 23 senior managers and supervisors, who attributed injuries to the need for manual labor and to workers being careless and failing to follow the departmental safety protocol. However, no written documented safety protocol was identified. Supervisors also said that workers sold their allocation of work clothes.

Section supervisors who were directly responsible for the workers said that not much could be done in the section because of poor communication in the department and that directors did not welcome requests, especially those involving capital expenditure. Supervisors said risk could be reduced by providing modern equipment and adequate PPE and by reducing the workload.

## Discussion

Workers aged 18–25 years were more likely to suffer an injury than workers aged >25 years. Among workers in all industries, frequency of injuries has been demonstrated to decline with age (6). Younger workers might be more prone to injury because of their lack of experience and an inclination to take unnecessary risk.

Bin loaders were more likely to be injured than toilet or street cleaners. The absence of training at the beginning of employment was also identified as a risk factor. Bin loading involves handling of heavy loads and working with moving trucks. Workers should be trained in good lifting techniques and how to avoid vehicular accidents. Incidence of back injuries has been reduced substantially after training in proper lifting techniques (7).

**FIGURE. Box-type (top) and hydraulic compactor (bottom) refuse-collection trucks — Bulawayo, Zimbabwe, 2003**



**SOURCE:** Bulawayo City Council, Bulawayo, Zimbabwe, 2003

The findings in this report are subject to at least two limitations. First, a walk-through inspection might not have identified all hazards. Second, interview data were missing for 18% of persons with injuries and for 19% of persons without injuries. If these persons represent different distribution of risk factors than persons included in the study, ORs might be underestimated or overestimated.

## Conclusion

This report indicates the importance of keeping accurate records of the causes of injury so appropriate interventions

can be made to prevent future injuries. Injuries that occurred in the cleansing section during 2001–2002 could have been reduced or, in some instances, avoided by implementing appropriate interventions. As a result of these findings, the Bulawayo City Council has compiled a health and safety manual for use in the department. New recruits in the bin loading section are now trained before they start work. HSD was advised to provide proper jacks in its mechanical workshops and to devise a plan to gradually phase out the old refuse removal trucks. To reduce the risk for injury, small jacks and old box trucks should be replaced with modern hydraulic trucks, and proper use should be made of PPE.

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# Progress Toward Tuberculosis Control and Determinants of Treatment Outcomes — Kazakhstan, 2000–2002

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## Abstract

**Introduction:** In Kazakhstan, during 1995–2002, the annual notification rate per 100,000 population for new cases of tuberculosis (TB) increased from 67.1 to 165.1. Beginning in 1998, public health authorities have used the national case management strategy (DOTS) promulgated by the World Health Organization (WHO) to control TB. Intended goals of DOTS include achieving a cure rate of  $\geq 85\%$  for persons with newly detected pulmonary TB sputum-smear-positive (PTB+) cases and having PTB+ represent  $\geq 65\%$  of all PTB cases among adults. Surveillance data collected during 2000–2002 were analyzed to evaluate progress toward achieving these goals and identify factors associated with specific treatment outcomes.

**Methods:** Surveillance data included the following nonidentifiable information on persons with newly reported cases of PTB: dates of disease onset and treatment initiation; methods of diagnosis; treatment outcomes; HIV status; and selected demographic, socioeconomic, and behavioral characteristics. Cure rates and proportions of PTB+ cases were calculated on the basis of the TB case definition and treatment outcome classification format outlined in DOTS guidelines issued by WHO. Denominator data to calculate rates were obtained from the National Census Office of Kazakhstan. Logistic regression was employed to investigate factors associated with treatment outcomes using Epi Info version 3.2.

**Results:** During 2000–2002, a total of 65,011 new cases of PTB were detected in Kazakhstan. The average annual country-wide notification rate per 100,000 population was 146.0; provincial notification rates varied (range: 65.1–274.0). The countrywide cure rate for newly detected PTB+ was 72.2%; provincial rates varied (range: 65%–81%). Of 59,905 cases of PTB among adults during 2000–2002, a total of 26,804 (44.7%) were PTB+. Unfavorable treatment outcome of new PTB+ cases was associated with alcohol abuse, homelessness, and previous incarceration.

**Conclusion:** The cure rate for new PTB+ cases and the proportion of cases of PTB+ among all adults with PTB were below targeted goals. This might, in part, be explained by the 1998 adoption of DOTS. Improving program indicators requires evaluation of detection efforts, laboratory diagnostic capabilities, and adherence to treatment regimens, especially in provinces in which rates are high and among persons at high risk for unfavorable treatment outcomes.

## Introduction

In 1993, the World Health Organization (WHO) adopted a national case management strategy (DOTS) to reduce the increasing global burden of tuberculosis (TB), especially in developing countries (1). The five elements of the DOTS strategy are sustainable government commitment, quality assurance of sputum microscopy, standardized short-course treatment (including direct observation of therapy), regular supply of drugs, and establishment of reporting and recording systems (2,3). The goal of DOTS is to reduce TB morbidity and mortality and the chance of *Mycobacterium tuberculosis* developing resistance to primary treatment drugs (4). Target goals of TB control adopted in 1991 by the World Health Assembly (3) include  $\geq 70\%$  detection rate of the esti-

mated incidence of sputum-smear-positive pulmonary TB (PTB+) and  $\geq 85\%$  cure rate for newly detected PTB+ cases. The  $\geq 85\%$  cure rate was adopted on the basis of accumulated experience in Africa and certain districts of China (5,6).

Performance indicators in the DOTS program use the proportion detected of PTB+, which is the most infectious form of TB. PTB+ is associated with high mortality (7) and is the most effective form of TB to use for bacteriologic monitoring of treatment progress (8). The proportion of newly detected PTB+ cases among the total number of adults with PTB reflects the proper application of diagnostic criteria. In countries with a medium or high TB burden, when necessary laboratory resources are available and sputum smears for microscopy are taken from TB patients, PTB+ accounts for

>50% of all TB cases and >65% of new PTB cases in adults (3,9). Achieving a high (i.e.,  $\geq 85\%$ ) cure rate for PTB+ is a critical priority for TB-control programs (3,9). Failure to achieve this rate results in continued infectiousness and possible development of multidrug-resistant (MDR) TB, which is resistant to at least isoniazid and rifampicin (10,11).

During 1980–1994, the countrywide TB notification rate per 100,000 population decreased from 88.2 to 59.7. However, since 1995, notification rates have increased constantly, reaching 165.1 in 2002. TB mortality rates per 100,000 population decreased from 17.2 in 1980 to 10.6 in 1991. During 1992–1998, mortality rates increased, reaching 38.4 in 1998; however, rates decreased to 24.2 in 2002 (Kazakhstan Ministry of Health [MoH], unpublished data, 1980–2002). Increased TB mortality and morbidity have been attributed to socioeconomic changes and the deterioration of the health-care system in Kazakhstan after the country gained its independence from the former Soviet Union in 1991 (12,13).

To manage the increasing burden of TB in the country, in 1998, the Kazakhstan MoH adopted and implemented a new National Tuberculosis Program (NTP), whose objectives and target goals are in accord with the DOTS strategy (14). To implement the DOTS strategy in Kazakhstan, primary health-care physicians and TB specialists received training in case-detection policy, and laboratories were equipped with binocular microscopes. During 1997–2000, the number of sputum-smear examinations increased from 661,000 to 1,170,000 (Kazakhstan MoH, unpublished data, 2001).

Since 1998, a uniform TB surveillance system has operated in Kazakhstan. Beginning in 2000, all administrative territories collected surveillance data. In 2003, CDC conducted a study to evaluate NTP performance. Annual data for 2000–2002 were analyzed to describe patterns of PTB notification by person and place, assess progress toward achieving NTP target goals, and identify factors associated with unfavorable treatment outcomes.

## Methods

### Study Design

The MoH surveillance database in Kazakhstan was analyzed to estimate the PTB notification rate and describe NTP performance indicators that could be used to measure progress. Selection of appropriate progress indicators was guided by WHO recommendations (15). Two performance indicators were selected: the proportion of new PTB+ cases among reported cases of PTB among adults and the proportion of persons with newly detected PTB+ cases who were cured (3). Persons in the database, registered during 2000–2002, with

new PTB+ cases for which records for DOTS treatment regimen were completed by the time of the study were treated as members of a cohort that was used to study associations between treatment outcome and risk factors. The study was given institutional review board approval by the Kazakh State Medical University ethics committee.

### Study Definitions

Diagnostic categories for newly reported cases of PTB (both PTB+ and sputum-smear-negative PTB) and treatment outcomes\* for newly diagnosed PTB+ were defined in accordance with WHO guidelines (3). To study the associations among treatment outcome and risk factors, a new bi-level treatment outcome variable was defined on the basis of the DOTS outcome definitions: favorable (i.e., cured) and unfavorable (i.e., failed, died, or defaulted). Patients classified as having completed treatment or transferred out were excluded from the risk factor analysis because either information was lacking regarding alteration of sputum-smear status from positive to negative or they had been classified according to a new diagnostic category. Sociodemographic and behavioral variables in the surveillance database that were available for risk factor analysis included age, sex, place of residence, homelessness, employment status, employment in the medical profession, previous incarceration, and alcohol abuse. These variables were complete for >95% of records. Data were recorded by treating physicians at the time of TB diagnosis (5–10 days after hospital admission) on the basis of information provided by patients.

### Data Sources

By law, TB is a reportable disease in Kazakhstan. A standard notification form is completed by the treating physician and then entered into an electronic database when a patient receives a TB diagnosis in any TB treatment facility. The national TB surveillance database contains nonidentified information on cases among civilians from all 16 administrative regions (14 provinces and two large urban areas [Astana and Almaty]); data on prisoners and military personnel are not included in this database. During 2000–2002, a total of 99,111 extrapulmonary and pulmonary cases were registered

\* **Cure:** person who became sputum-smear-negative in the last month of treatment and on at least one previous occasion; **treatment failure:** person who continued to have sputum-smear-positive status at  $\geq 5$  months during treatment; **treatment completed:** person with PTB+ who completed treatment but whose condition was not consistent with the criteria for either cure or failure; **died:** person who died of any cause during treatment; **defaulter:** person who interrupted the treatment regimen for  $\geq 2$  consecutive months; and **transfer out:** person who moved to another health-care facility and was entered in a new diagnostic category (i.e., transfer in).

in the database; 65,011 (65.6%) were newly diagnosed PTB cases that were used for the descriptive analysis. Of these, 803 (1.2%) persons were excluded from the analysis because of lack of data on bacterioscopic investigation. Of 27,171 persons in the database with newly diagnosed PTB+, complete outcome data were available for 20,461 (75.3%) persons and were used for the risk factor analysis. Of these, 285 (1.4%) were children aged <15 years; because of these limited numbers, children were not included in the risk factor analysis. Population denominator data were obtained from the National Census Office of Kazakhstan.

## Statistical Analyses

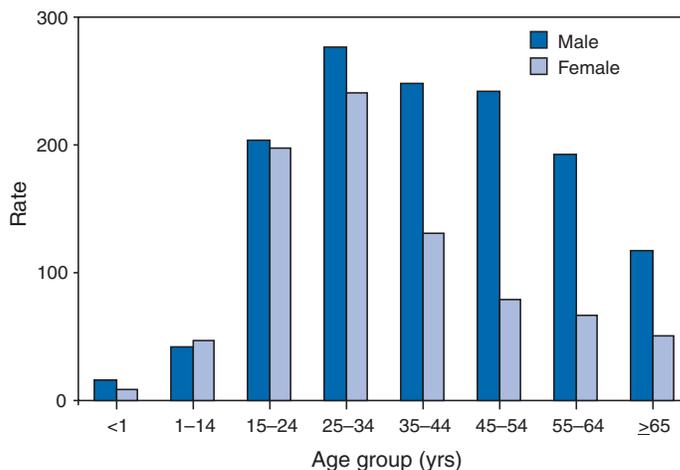
Data analyses were performed using Epi Info, version 3.2 (CDC, Atlanta, Georgia). Population estimates at midpoint of the 2000–2002 study period were used to calculate the average annual notification rates for new PTB by sex, age, and region. Chi-square tests were used to evaluate differences in notification rates and estimated target indicators by region. Logistic regression analysis was used to study associations between the study-defined treatment outcome variable and sociodemographic and behavioral risk factors. All variables that were significant at the two-sided  $\alpha = 0.05$  level in univariate analyses were included in the final multivariate logistic model; adjusted odds ratios (AORs) were used as measures of association.

## Results

### Descriptive Statistics

During 2000–2002, the countrywide average annual PTB notification rate was 146 per 100,000 population. Rates in urban and rural areas were similar (146.1 and 144.9, respectively). However, rates differed significantly ( $p < 0.001$ ) by region (range: 65.0 [Almaty City]–274.0 [Kzyl-Orda]). In general, the highest rates were observed in the country's western regions (Actobe, Atirau, Mangistau, and West Kazakhstan). Age-specific rate patterns were similar for men and women. The highest rates occurred among persons aged 25–34 years (men: 277; women: 241). Among persons aged  $\geq 25$  years, rates were consistently higher for men than for women (Figure). By region, significant differences were reported in the proportion of sputum-smear-positive cases among adults with newly reported PTB cases (range: 34.5% [Astana]–59.6% [Northern Kazakhstan]) ( $p < 0.001$ ) (Table 1); no region attained the goal of  $\geq 65\%$ . The cure rate for persons with new PTB+ cases varied (range: 65% [Eastern Kazakhstan]–81% [Almaty City]) ( $p < 0.001$ ) (Table 2). No region attained the goal of  $\geq 85\%$ . Among 99,111 persons with TB, 100 (0.1%)

**FIGURE. Average annual notification rate\* of new cases of pulmonary tuberculosis (N = 65,011), by age group and sex — Kazakhstan, 2000–2002**



\* Per 100,000 population.

**TABLE 1. Number of reported new pulmonary tuberculosis (PTB) and PTB smear-positive (PTB+) cases among adults, by region — Kazakhstan, 2000–2002**

Region	No. of new PTB cases	PTB+ cases	
		No.	(%)
North Kazakhstan	2,582	1,538	(59.6)
Kostanay	4,061	2,309	(56.9)
Almaty	4,337	2,147	(49.5)
Acmlensk	3,962	1,931	(48.7)
Almaty City	2,154	1,038	(48.2)
Jambilsk	3,716	1,715	(46.2)
Karaganda	5,494	2,455	(44.7)
Kzyl-Orda	4,525	1,979	(43.7)
Atirau	2,747	1,199	(43.6)
Mangistau	1,988	855	(43.0)
West Kazakhstan	3,247	1,361	(41.9)
Actobe	4,071	1,694	(41.6)
East Kazakhstan	5,398	2,196	(40.7)
Pavlodar	3,729	1,498	(40.2)
South Kazakhstan	6,122	2,277	(37.2)
Astana City	1,772	612	(34.5)
<b>Total</b>	<b>59,905</b>	<b>26,804</b>	<b>(44.7)</b>

human immunodeficiency virus (HIV)-infected patients were identified during the study period.

### Risk Factor Analysis

Among 20,176 persons aged  $\geq 15$  years, 547 (2.7%) patients had finished the treatment course but their sputum-smear status was unknown, and 650 (3.2%) patients were transferred out; both groups were excluded from the risk factor analysis. Of 18,979 patients included in the analysis, 4,422 (23.3%) had unfavorable treatment outcomes (i.e., died, failed, or defaulted). The proportion recorded as having an unfavor-

**TABLE 2. Number of new pulmonary tuberculosis sputum-smear-positive (PTB+) cases\* and cure rates, by region — Kazakhstan, 2000–2002**

Region	No. of new PTB+ cases	Cured	
		No.	(%)
Almaty City	834	676	(80.8)
South Kazakhstan	1,649	1,321	(80.1)
Kzyl-Orda	1,540	1,201	(78.0)
Astana City	359	272	(75.8)
Atirau	895	669	(74.9)
North Kazakhstan	1,288	962	(74.7)
West Kazakhstan	1,036	769	(74.2)
Jambilsk	1,285	937	(73.0)
Kostanay	1,867	1,353	(72.5)
Almaty	1,742	1,252	(71.9)
Acmlensk	1,500	1,070	(71.3)
Actobe	1,088	762	(70.1)
Mangistau	662	453	(68.4)
Karaganda	1,755	1,160	(66.1)
Pavlodar	1,236	804	(65.0)
East Kazakhstan	1,725	1,119	(64.9)
<b>Total</b>	<b>20,461</b>	<b>14,780</b>	<b>(72.2)</b>

\* Occurring among persons for whom complete treatment outcome data were available.

able outcome varied by age group. In univariate analyses, all studied variables were statistically significant at the 0.05 level and were included in the final multivariate logistic model. Unfavorable treatment outcomes for new PTB+ cases were associated with alcohol abuse, homelessness, previous incarceration, unemployment, being male, and urban residence. Being medical personnel was protective. AORs for unfavorable treatment outcomes increased with age (Table 3).

## Discussion

The high countrywide notification rate of new PTB cases (146 per 100,000 population for the 3-year study period) underscores the importance of controlling TB in Kazakhstan. Substantial regional differences were recorded; in certain areas (e.g., Kzyl-Orda, 274 per 100,000 population), the notification rate was approximately twice the national average. As in other countries, regional differences might result from different underlying socioeconomic conditions and the quality of the performance of local TB-control programs (16,17). Further research is needed to identify the reasons for regional differences, so corrective measures can be taken as needed.

The age-specific notification rate of new PTB cases was similar for children aged <15 years for both sexes. However, for persons aged ≥15 years,

notification rates were higher among males. Similar results have been reported in other countries (18–20). The reasons for this difference in TB notification rates are not known. No evidence exists that health-seeking behaviors are substantially different in countries of the former Soviet Union and could not have accounted for male-female differences. Genetic factors or transmission dynamics might explain this difference.

During 2000–2002, the proportion of PTB+ cases among the total number of new PTB cases among adults in Kazakhstan was 44.7% (program target: ≥65%). In certain areas, the proportion was lower (e.g., Astana-City: 34.5%; South Kazakhstan: 37.2%). The DOTS strategy was adopted recently (i.e., in 1998), and the quality of laboratory services and the application of the diagnostic criteria might not be up to the required standard, especially in certain areas.

Since the DOTS strategy was implemented, the supply of primary TB drugs in TB-treatment facilities has been adequate; consequently, this factor cannot explain the low cure rate for new PTB+ cases, especially in certain regions (e.g., East

**TABLE 3. Number and percentage of persons with new sputum-smear-positive pulmonary tuberculosis (PTB+) cases, by selected demographic characteristics and type of analysis — Kazakhstan, 2000–2002**

Characteristic	New PTB+ cases (N = 18,979)		Univariate (crude) analysis		Multivariate analysis	
	No.	(%)	COR* (95% CI)†	AOR§ (95% CI)		
<b>Residence</b>						
Urban	10,309	(54.4)	1.5	(1.4–1.6)	1.4	(1.3–1.5)
Rural¶	8,649	(45.6)	1.0		1.0	
<b>Sex</b>						
Male	11,938	(62.6)	1.5	(1.4–1.6)	1.2	(1.1–1.3)
Female¶	7,041	(37.4)	1.0		1.0	
<b>Alcohol abuse</b>						
Yes	762	(4.0)	3.2	(2.8–3.7)	2.1	(1.8–2.5)
No¶	18,203	(96.0)	1.0		1.0	
<b>Homeless</b>						
Yes	313	(1.7)	3.4	(2.7–4.3)	2.2	(1.7–2.7)
No¶	18,653	(98.3)	1.0		1.0	
<b>Previous incarceration</b>						
Yes	1,043	(5.5)	1.8	(1.6–2.1)	1.5	(1.3–1.7)
No¶	17,923	(94.5)	1.0		1.0	
<b>Unemployed</b>						
Yes	11,614	(61.2)	1.4	(1.3–1.5)	1.5	(1.4–1.6)
No¶	7,364	(38.8)	1.0		1.0	
<b>Medical personnel</b>						
Yes	229	(1.2)	0.5	(0.3–0.7)	0.6	(0.4–0.9)
No¶	18,736	(98.8)	1.0		1.0	
<b>Age group (yrs)</b>						
15–24¶	4,340	(23.0)	1.0		1.0	
25–34	5,316	(28.0)	1.4	(1.2–1.5)	1.3	(1.1–1.4)
35–44	4,324	(23.0)	1.9	(1.7–2.1)	1.7	(1.5–1.9)
45–54	2,723	(14.0)	2.4	(2.1–2.7)	2.1	(1.9–2.4)
55–64	1,376	(7.0)	2.2	(1.9–2.6)	2.3	(2.0–2.7)
≥65	900	(5.0)	2.3	(1.9–2.6)	2.8	(2.3–3.3)

\* Crude odds ratio.

† Confidence interval.

§ Adjusted odds ratio.

¶ Referent group.

Kazakhstan and Pavlodar, both 65%). Data were not available to explore reasons for the low cure rate (e.g., the prevalence of MDR-TB). The single study available indicated that high (14.2%) MDR-TB rates among new TB patients in Kazakhstan might contribute to a low cure rate in the country (21).

Unemployment and urban place of residence were highly prevalent (>54%) in the study group and associated with unfavorable treatment outcomes; this could have contributed to the low cure rate. Other factors (i.e., homelessness, history of incarceration, alcohol abuse, and age  $\geq 55$  years) had more effect on the unfavorable treatment outcome; however, their overall effect on the cure rate might have been limited because of low prevalence.

Among medical personnel, the protective odds ratio for unfavorable treatment outcome (AOR = 0.6) might be explained by their stricter adherence to treatment regimen. The high percentage of unfavorable treatment outcomes among persons aged  $\geq 55$  years was attributable to deaths from any cause; however, among persons in other age groups, the majority of unfavorable treatment outcomes were attributable to treatment failure.

Kazakhstan is in the beginning stage of an HIV epidemic. During 2000–2002, a total of 100 (0.1%) cases of HIV were identified among 99,111 persons with TB. The contribution of HIV infection to the TB burden is believed to be insubstantial.

The findings in this report are subject to at least one limitation. All study factors were measured by the treating physicians on the basis of patient self-reports. Patients might not have reported certain behaviors, particularly those regarded as socially unacceptable (e.g., alcohol abuse). As a result, the low prevalence of these behaviors among TB patients and their consequent low overall impact on the cure rate might reflect inaccurate self-reporting.

Continued evaluation is needed to improve performance of the TB program in Kazakhstan. Improving program indicators requires evaluation of detection efforts, laboratory diagnostic capabilities, and adherence to treatment regimens, especially in provinces where rates are high and among persons at high risk for unfavorable treatment outcomes, so recommendations for improvement can be offered as needed. In addition, laboratory quality control and quality assurance for TB culture should be further implemented in the country to assist in assessing the impact of MDR TB on the cure rate of PTB patients.

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# Estimation of Measles Vaccination Coverage Using the Lot Quality Assurance Sampling (LQAS) Method — Tamilnadu, India, 2002–2003

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## Abstract

**Introduction:** As part of the global strategic plan to reduce the number of measles deaths in India, the state of Tamilnadu aims at  $\geq 95\%$  measles vaccination coverage. A study was conducted to measure overall coverage levels for the Poondi Primary Health Center (PPHC), a rural health-care facility in Tiruvallur District, and to determine whether any of the PPHC's six health subcenters had coverage levels  $< 95\%$ .

**Methods:** The Lot Quality Assurance Sampling (LQAS) method was used to identify health subcenters in the PPHC area with measles vaccination coverage levels  $< 95\%$  among children aged 12–23 months. Lemeshow and Taber sampling plans were used to determine that the measles vaccination status of 73 children aged 12–23 months had to be assessed in each health subcenter coverage area, with a 5% level of significance and a decision value of two. If more than two children were unvaccinated, the null hypothesis (i.e., that coverage in the health subcenter was low [ $< 95\%$ ]) was not rejected. If the number of unvaccinated children was two or fewer, the null hypothesis was rejected, and coverage in the subcenter was considered to be good (i.e.,  $\geq 95\%$ ). All data were pooled in a stratified sample to estimate overall total coverage in the PPHC area.

**Results:** For two (33.3%) of the six health subcenters, more than two children were unvaccinated (i.e., coverage was  $< 95\%$ ). Combining results from all six health subcenters generated a coverage estimate of 97.7% (95% confidence interval = 95.7–98.8) on the basis of 428 (97.7%) of 438 children identified as vaccinated.

**Conclusion:** LQAS techniques proved useful in identifying small health areas with lower vaccination coverage, which helps to target interventions. Monthly review of vaccination coverage by subcenter and village is recommended to identify pockets of unvaccinated children and to maintain uniform high coverage in the PPHC area.

## Introduction

The goal of the World Health Organization's global measles strategic plan is to reduce by half the estimated number of measles deaths by 2005 compared with 1999 estimates (1). The target goal set by the Indian Ministry of Health and Family Welfare is to reduce measles mortality 66% by 2010 compared with 2000 estimates (2). Increasing, sustaining, and documenting high routine coverage is essential to achieve sustainable reduction of measles mortality.

The southern Indian state of Tamilnadu has set three objectives for its measles control program: 1) measles vaccination coverage of  $\geq 95\%$  through routine vaccination of children aged 9–12 months, 2) ring vaccination after occurrence of measles cases, and 3) treatment of ill persons to prevent com-

plications. To evaluate progress toward achieving the first objective, the Field Epidemiology Training Programme and local public health officials estimated coverage levels by using a Lot Quality Assurance Sampling (LQAS) survey (3). This evaluation was conducted for fiscal year 2002–2003 (April 1, 2002–March 31, 2003) to identify health subcenters with measles vaccination coverage of  $< 95\%$  among children aged 12–23 months and to estimate the overall measles vaccination coverage in the same age group in the primary health center area.

LQAS is a stratified random sampling method in which small samples randomly selected from each stratum are used to determine whether coverage in a stratum exceeds a specific threshold. Compared with the commonly used cluster survey

technique, LQAS can be used to identify areas with low vaccination coverage (3). The operational feasibility of LQAS to evaluate vaccination coverage among limited population units in India has been demonstrated (4,5).

## Methods

In April 2003, the LQAS survey was conducted in the Poondi Primary Health Center (PPHC) area, Tiruvallur District, Tamilnadu, India. This primary health center serves approximately 27,000 persons distributed in six health subcenter areas (approximately 4,500 persons per health subcenter).\*

### Sampling Methods

A simple random sample of the population served by PPHC was used, divided into six strata representing the six health subcenters. District health authorities expected measles coverage in the PPHC area to be  $\geq 95\%$ . A decision value ( $d$ ) of two nonimmunized children and an acceptable alpha value of 0.05 were set. On the basis of this information, sample size ( $n$ ) was estimated by using Lemeshow and Taber LQAS tables (6). A plan with  $n = 73$  was used; this single-stage sampling plan accepted an alpha error of 5%. In each health subcenter, the total number of eligible children (i.e., those aged 12–23 months) available was assumed to be 100. Within each stratum, 73 children were assessed for measles vaccination status, for an overall sample of 438 children in the PPHC area.

Each health subcenter included multiple villages. To determine the number of children to be selected in each village in each stratum, a list of villages was constructed for each stratum with the number of households and the cumulative number of households; 73 random numbers were selected using random number tables. Once the number of children had been determined for each village, researchers randomly selected as many households as children were needed. For each selected household, any eligible child was included. When no eligible child was identified in the house, the next houses to the right were surveyed until an eligible child was identified. When more than one eligible child was present in a house, only the youngest one was included. Children's ages were estimated using birth certificates or any other records showing the date of birth. When no written documentation was available, the age given by the mother or the guardian was used.

\* A primary health center is a basic health unit staffed by a medical officer and health team that provides integrated curative and preventive health-care services to a rural population of approximately 20,000–30,000 persons. A health subcenter is a peripheral outpost staffed by an auxiliary nurse midwife who provides primary health-care services (e.g., mother-and-child care, family planning, and vaccination) for a population of approximately 3,000–5,000 persons.

Only those children who received measles vaccination at age 9–12 months were considered vaccinated. The measles vaccination status of the child was obtained by reviewing vaccination cards if available or by interviewing the mother or guardian when cards were not available. Children were excluded from the survey if a parent or guardian was not available.

### Analysis of the Survey

Two analyses were conducted, an LQAS analysis in each stratum and a pooled analysis for the total sample. Card availability in subcenters varied (range: 7%–37%). The LQAS analysis in each stratum was based on testing a hypothesis. The null hypothesis ( $H_0$ ) was that the coverage in the health subcenter was  $< 95\%$  ( $H_0$ :  $p < 95\%$ , low performance). The alternate hypothesis ( $H_a$ ) was that the coverage in the health subcenter was  $\geq 95\%$  ( $H_a$ :  $p \geq 95\%$ , high performance). In each stratum of 73 persons, two (2.7%) persons were considered as the decision value (i.e., the threshold for analysis). In practice, when more than two of 73 children were identified as unvaccinated, coverage in the stratum was considered to be  $< 95\%$ . If no more than two unvaccinated children were identified, coverage in the stratum was considered to be  $\geq 95\%$ . All data were pooled to estimate overall total PPHC coverage. Overall measles vaccination coverage was calculated from the total number of eligible children vaccinated compared with the total number of eligible children surveyed. Because this was a simple random sample, with no design effect, best estimates and 95% confidence intervals (CIs) were calculated using standard methods.

## Results

### LQAS Analysis

In two health subcenters (Neyveli and Vellathukkottai), more than two children were unvaccinated, and vaccination coverage was considered to be  $< 95\%$  (Table). In the other four subcenters (Chitampakkam, Meyyur, Nambakkam, and Poondi), the number of unvaccinated children did not exceed two, and vaccination coverage was considered to be  $\geq 95\%$  (Table).

### Pooled Analysis

The pooled analysis was made on the basis of an overall sample of 438 children (73 from each subcenter). Of these, 428 (97.7%) had been vaccinated against measles, and overall measles vaccination coverage in Poondi was considered to be 97.7% (CI = 95.7%–98.8%) (Table).

**TABLE. Measles vaccination coverage, by health subcenter — Poondi Primary Health Center, Tiruvallur District, Tamilnadu, India, 2002–2003\***

Health subcenter	No. of children			Coverage	
	Surveyed	Vaccinated	Unvaccinated	LQAS <sup>†</sup>	Estimate (95% CI) <sup>§</sup>
Neyveli	73	69	4	<95%	NA <sup>¶</sup>
Vellathukkottai	73	70	3	<95%	NA
Meyyur	73	71	2	≥95%	NA
Chitampakkam	73	72	1	≥95%	NA
Poondi	73	73	0	≥95%	NA
Nambakkam	73	73	0	≥95%	NA
<b>Total</b>	<b>438</b>	<b>428</b>	<b>10</b>	<b>NA</b>	<b>97.7% (95.7%–98.8%)</b>

\* Fiscal year 2002–2003 (April 1, 2002–March 31, 2003).

<sup>†</sup> Lot quality assurance sampling.

<sup>§</sup> Confidence interval.

<sup>¶</sup> Not applicable.

## Discussion

This study determined that the overall vaccination coverage level in the PPHC area was 97.7%, which is consistent with the state target level of ≥95%. Two (33.3%) subcenters had coverage levels below the target level of ≥95%; these results were used to target interventions to these low-coverage areas.

LQAS techniques provide a rapid and simple determination of output quality and are used in industry for quality-assurance purposes. The strategy and goals of LQAS in the health field are similar to those in the manufacturing field (7). LQAS analysis is based on testing a hypothesis rather than on estimating a proportion. Because LQAS is based on stratified random sampling, results from lot samples can be combined to obtain a point estimate for the entire population, allowing for a small sample size. LQAS procedures were useful for identifying small health areas with lower measles vaccination coverage. This information, combined with further assessment of performance problems and timely corrective action, has been used to improve vaccination coverage in the district. LQAS techniques also could be used to assess performance as part of routine monitoring or supervisory activities of routine vaccination.

For a vaccination program to achieve its goal, a sufficient number of doses must be administered at the appropriate ages. Coverage levels are therefore a key process indicator of performance. Monitoring this indicator at the population level provides an overall assessment of program performance. Operational units with poorer coverage should be identified so performance can be improved (8). LQAS techniques are a particularly useful way of monitoring indicators of coverage, as these techniques provide a rapid and simple determination of output quality.

On the basis of the results of the study, an analysis of vaccination coverage by health subcenter and village during regular monthly review meetings was recommended to identify missed pockets of unvaccinated children and to continue efforts to maintain uniform high vaccination coverage in the PPHC area. The recommendation was followed by all the medical officers and helped them identify groups of unvaccinated children and improve the measles vaccination coverage. No outbreaks of measles were reported subsequently in the study area. However, measles surveillance was limited by the unavailability of long-term trend data, and the validity of the surveillance system has not been estimated.

The findings of this study are subject to at least one limitation. Vaccination cards were available for only 91 (21%) of 438 children surveyed, which could have resulted in overestimating measles vaccination coverage. The supply of vaccination cards was limited, and those parents who did receive cards often did not preserve them. To aid in future surveys, a sufficient quantity of vaccination cards should be made available to health workers in each health subcenter. This will facilitate monitoring and evaluation efforts. Health workers should be trained to understand the importance of the cards and how to use them properly, and families should be educated to understand the need to keep the cards in a safe place.

In December 2004, an outbreak of measles was reported in the Cuddalore district of Tamilnadu. Estimated measles vaccination coverage was approximately 96% (9), indicating that a measles outbreak can occur among a well-vaccinated population when a single-dose measles vaccination strategy is employed. A substantial measles outbreak also was reported during 1999–2000 in Sri Lanka, where single-dose measles vaccination coverage since 1996 was >90% (10). For future measles outbreaks in an area with a single-dose measles schedule to be prevented, a possible strategy to provide a second dose might be considered.

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# Bacterial Meningitis Among Cochlear Implant Recipients — Canada, 2002

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## Abstract

**Introduction:** In July 2002, a cluster of bacterial meningitis (BM) cases was identified among European cochlear implant recipients (CIRs), prompting Health Canada to conduct a retrospective cohort study to determine the rate of BM infection among Canadian CIRs and to identify risk factors for acquiring BM.

**Methods:** A survey was mailed to 1,432 Canadian CIRs who had received implants during January 1995–July 2002 to assess occurrence of postimplant BM infection. Data collection included demographics, episodes of meningitis, and vaccination status.

**Results:** A total of 1,024 (72%) surveys were completed. Median age of CIRs at implantation was 16 years (range: 7 months–81 years). Five (0.5%) cases of BM infection were reported (two pneumococcal, one meningococcal, and two of unknown etiology); one CIR died. Four cases occurred among children aged <18 years. Time between implantation and BM infection varied (range: 7 months–7.7 years; median: 11 months). The rate of BM infection per 1,000 person-years was 0.7 among CIRs aged ≥18 years and 2.9 among those aged <18 years. The proportion of CIRs vaccinated against pneumococcal and meningococcal disease was low (46% and 41%, respectively). Preimplant meningitis was identified as a risk factor for postimplant BM ( $p = 0.002$ ). No other risk factors evaluated were associated with an increased risk for BM infection.

**Conclusion:** CIRs have a high rate of postimplant BM infection. Preimplant BM infection was identified as a risk factor. Cases of BM infection might have been prevented through vaccination.

## Introduction

Meningitis is an inflammation of the lining of the brain's surface, often as a result of a bacterial or viral infection. Children aged <2 years are most at risk for meningitis. Among infants, early symptoms of meningitis include fever, irritability, lethargy, and loss of appetite. Among children and adults, other symptoms might include headache, stiff neck, photophobia, nausea and vomiting, and confusion or alteration in consciousness (1).

Cochlear implants are medical devices that electronically stimulate the auditory nerves in the cochlea (inner ear), allowing persons with severe hearing loss to perceive sound. In early July 2002, a cluster of cases of bacterial meningitis (BM) infection was identified among European cochlear implant recipients (CIRs) who had received an implant produced by manufacturer A (2). European implant surgeons had hypothesized that the cluster of BM infections they had observed among their patients might be related to a recently licensed cochlear implant device (device A) produced by manu-

facturer A (2). This device differed from other similar manufactured devices in that it had two components, an electrode array and a positioner, rather than a single electrode array. The positioner increased electrical signal transmission to the auditory nerve, particularly among patients with malformations of the cochlea. On July 23, manufacturer A issued a voluntary recall of the device in France (3). After discussions with the European regulatory authorities, manufacturer A subsequently issued a voluntary worldwide withdrawal of the device. On July 26, the two-piece device, which had been licensed for use in Canada in November 1998, was withdrawn from the Canadian market.

On July 29, Health Canada issued an alert warning that CIRs might be at greater risk for meningitis (4). Subsequently, the Immunization and Respiratory Infections Division of Health Canada (now the Public Health Agency of Canada) investigated the extent of BM infection among CIRs in Canada. To understand the magnitude of this problem in Canada, a retrospective cohort study was conducted. The three-

fold purpose of the investigation was to determine the rate of BM among CIRs in Canada, identify risk factors for postimplant BM, and recommend public health action based on investigation findings.

## Methods

The study cohort included all 1,432 recipients of cochlear implant devices in Canada with implant dates during January 1995–July 2002. Cohort members were identified using manufacturer implant registries. At the time of the study, two manufacturers were licensed in Canada. A case was defined as one occurring in a CIR who reported having BM infection since receiving an implant.

A self-administered questionnaire in both French and English was mailed to CIRs or, if deceased, their next of kin. The questionnaire was designed by modifying tools developed for a similar investigation in the United States (5). The survey was completed by the recipient or by a parent or guardian if the recipient was aged <16 years or was incapable of completing the survey. Questions addressed included cause of hearing loss, history of meningitis infection, vaccination status, and risk factors (e.g., household smoking, other children in the household, and otitis media infections). Questions were divided into two periods: before and after receiving a cochlear implant. Only nonnominal data were collected. Data were collected during November 25, 2002–March 31, 2003. To obtain the highest response rate possible to the mailed questionnaire, Dillman's Total Design Method for mailed surveys was followed, with certain modifications (6). Ethics approval for the study was obtained from Health Canada's Research Ethics Board.

Data were entered in EpiData 2.1a (The EpiData Association, Odense, Denmark, 2001–2002). Univariate and bivariate analysis, including relative risks and chi-square tests, were conducted using Epi Info 6.04d (CDC, Atlanta, Georgia). To determine if the introduction of the two-piece implant affected incidence of BM infection, data were stratified by implant manufacturer and date of implant (i.e., before and after January 1, 1999, when the two-piece implant device was licensed in Canada).

## Results

A total of 1,024 CIRs completed and returned the survey (overall response rate: 72%). Median follow-up time (from implant to BM infection or end of the study period) for CIRs was 42 months (Table 1). Among respondents, males and females were equally represented, and approximately half (n = 482) were aged <18 years. Manufacturers were repre-

**TABLE 1. Number and percentage of cochlear implant recipients (CIRs), by selected characteristics — Canada, 2002**

Characteristic	No.	(%)
<b>Age at time of implant</b>		
Pediatric (<18 yrs)	482	(47.5)
Adult (≥18 yrs)	532	(52.5)
Median: 16 yrs		
Range: 7 mos–81 yrs		
<b>Sex</b>		
Female	523	(51.1)
Male	501	(48.9)
<b>Implant manufacturer</b>		
A	391	(38.4)
B	628	(61.6)
<b>Date of implant</b>		
Before January 1, 1999	294	(35.2)
On or after January 1, 1999	541	(64.8)
<b>Bacterial meningitis before implant</b>		
Yes	71	(7.3)
No	905	(92.7)
<b>Bacterial meningitis after implant</b>		
Yes	5	(0.5)
No	984	(99.5)
<b>Received vaccination</b>		
Pneumococcal	432	(45.7)
Meningococcal serogroup C	381	(41.1)
Hib*	369	(40.0)
<b>Received vaccination before implant†</b>		
Pneumococcal	40	(11.6)
Meningococcal serogroup C	32	(10.9)
Hib	155	(55.4)
<b>Additional implanted devices‡</b>		
	33	(6.9)
<b>Cause of deafness</b>		
Acquired	408	(40.1)
Congenital	177	(17.4)
Other	200	(19.7)
Unknown	233	(22.9)
<b>Household smoker</b>		
	279	(22.9)
<b>Other household children</b>		
	275	(26.9)
<b>Child care attendance</b>		
	320	(31.5)

\* *Haemophilus influenzae* type b.

† Certain CIRs were not old enough to be eligible for vaccination before implantation.

‡ Includes middle-ear tubes and ventriculoperitoneal and endolymphatic shunts.

sented in proportion to their market share (approximately 33% for manufacturer A and 67% for a second manufacturer [manufacturer B]).

Among 98 CIRs who had an episode of meningitis infection before receiving a cochlear implant, 71 (72%) had infections that were bacterial. Of seven cases of meningitis reported after a cochlear implant, five (71%) were bacterial; the type of bacteria was reported for three cases. Two CIRs reported *Streptococcus pneumoniae* as the causative agent, and one reported *Neisseria meningitidis* (Table 2). None of the BM episodes occurred during the perioperative period (0–30 days postimplantation).

**TABLE 2. Cases of postimplant bacterial meningitis (BM) among cochlear implant recipients — Canada, 2002**

Age group (yrs)*	Sex	Preimplant BM	Postimplant BM			Outcome
			Type	Previous vaccination	Interval between implantation and infection	
1–4	Male	No	Pneumococcal	No	20 mos	Recovered
5–9	Female	No	Unknown	—†	7 mos	Recovered
10–14	Female	Yes	Meningococcal	No	11 mos	Died
15–17	Male	Yes	Pneumococcal	No	7 yrs, 9 mos	Recovered
65–70	Female	Yes	—	—	12 mos	Recovered

\* No cases occurred among persons aged 18–64 years.

† No data available.

The overall incidence of BM infection for this cohort was 1.8 per 1,000 person-years of observation (95% confidence interval [CI] = 0.6–4.2). Among CIRs aged <18 years, incidence was 2.9 (CI = 0.8–7.3); among CIRs aged <6 years, incidence was slightly lower (2.0; CI = 0.2–7.1). Incidence among adults aged ≥18 years was 0.7 per 1,000 person-years of observation (CI = 0.0–4.1).

Incidence of BM infection among adults aged ≥18 years before and after 1999 did not vary (2.2 and 2.0 per 1,000 person-years observation, respectively). Although not statistically significant, incidence of BM infection among persons aged <18 years was higher on or after January 1, 1999, than before (4.0 and 2.2 per 1,000 person-years, respectively). Among children aged <6 years, incidence was 1.5 (CI = 0.0–8.1) before 1999 and 3.1 on or after January 1, 1999 (CI = 0.1–17.2).

All five persons with BM infection had received meningococcal vaccine, and four had received pneumococcal vaccine. However, of the three persons for whom the causative agent was known, none had received vaccination against the implicated agent before the postimplant episode of meningitis.

Potential risk factors assessed for postimplant BM infection included a history of otitis media, household smoking, and children living in the household. None was statistically significant (Table 3). A previous episode of BM infection was identified as a risk factor for postimplant BM infection (relative risk [RR] = 23.1; CI = 3.2–197.3; *p* = 0.002). Having had other implanted devices was associated with an increased risk for BM infection; however, this association was not statistically significant (*p* = 0.081).

No difference in risk for BM infection by implant manufacturer was noted (*p* = 1.0). The cohort included recipients who had received the device with a positioner; however, the type of implanted device (with or without a positioner) was not well reported, and whether the positioner was an independent risk factor could not be determined.

**TABLE 3. Number of cases and relative risk for postimplant bacterial meningitis (BM) among cochlear implant recipients, by selected characteristics — Canada, 2002**

Characteristic	Postimplant BM		RR† (95% CI§)
	Yes (No. cases)	No (person-months*)	
<b>BM before implant</b>			
Yes	3	2,003	23.1
No	2	30,920	(3.2–197.3)
<b>Other implanted devices</b>			
Yes	2	3,380	6.0
No	3	30,573	(1.1–36.1)
<b>Otitis media after implant</b>			
Yes	2	5,336	3.2
No	3	25,750	(0.5–19.2)
<b>Child care attendance</b>			
Yes	1	11,402	0.4
No	4	17,593	(0.04–3.5)
<b>Implant manufacturer</b>			
A	2	11,685	1.3
B	3	22,383	(0.2–7.6)
<b>Child in household</b>			
Yes	1	9,139	0.7
No	4	25,086	(0.1–6.1)
<b>Household smoker</b>			
Yes	1	10,820	0.5
No	4	23,358	(0.1–4.8)

\* Number of months each study participant contributed to the study cohort.

† Relative risk, calculated by using the number of cases as the numerator and the number of person-months of observation for each person in the cohort as the denominator.

§ Confidence interval.

## Discussion

The rate of BM infection per 1,000 person-years among CIRs aged ≥18 years was 0.7, compared with 2.9 among CIRs aged <18 years. Results of a similar study of CIRs in the United States during the same period have been published (5). Incidence of BM infection among CIRs was 3.9 among U.S. children aged <6 years, compared with 2.0 among Canadian children in the same age group during the period when device A was on the market. Although different methodologies were used, certain key study questions were similar, allowing com-

parisons between the two studies. In Canada, no cases of perioperative BM infection were identified among CIRs, whereas in the U.S. study, the rate of perioperative BM infection was 2.1 cases per 1,000 procedures (5). Why incidence of perioperative infections is higher among CIRs in the United States is not known.

These findings of increased incidence of BM infection among CIRs aged <18 years since the device with the positioner was introduced in 1998 are similar to findings published previously (5). No increased risk for BM infection was identified among adult CIRs after the device with the positioner was introduced.

In Canada, surveillance of invasive diseases (e.g., meningitis) is organism specific and includes all forms of invasive disease. Incidence of invasive pneumococcal disease ranges from 11.6 to 17.3 per 100,000 population, whereas incidence of invasive meningococcal disease ranges from 0.6 to 1.6 per 100,000 population (7,8), compared with an observed incidence of 1.8 per 1,000 person-years among CIRs in this study.

CIRs have multiple potential underlying conditions that might increase their risk for BM infection above that of the general Canadian population. The ideal comparison group for CIRs would be a population of severe-to-profoundly deaf persons who do not have cochlear implants; however, such data are not available. During 1994–2001, the overall annual incidence of BM infection in the general Canadian population ranged from 3.2 to 3.7 per 100,000 population (9).

Preliminary study results were presented to Canada's National Advisory Committee on Immunization (NACI). In February 2003, NACI recommended that CIRs be considered at high risk for both *Haemophilus influenzae* type b (Hib) and invasive pneumococcal disease and should receive vaccination according to the high-risk schedule (10). In addition, CIRs, like all Canadians, should be up-to-date on all routine vaccinations, including meningococcal C conjugate vaccines. These vaccines are recommended for all Canadian children aged <5 years, adolescents, and young adults.

CIRs, their parents, and caretakers should be aware of the signs and symptoms of meningitis and seek medical attention if they occur. Medical professionals should be aware of the potential for BM infection among CIRs, be vigilant for the signs and symptoms of meningitis in this population, and educate their patients accordingly. Primary health-care providers of CIRs or persons considering cochlear implants should ensure that these persons are fully vaccinated according to NACI guidelines (10).

The findings in this report are subject to at least four limitations. First, the retrospective cohort was established by using manufacturer registry data that were likely incomplete

and that did not contain the most recent mailing address of every CIR in Canada. CIRs who did not register their implant devices were not included in the cohort. However, because incomplete mailing addresses were evenly distributed among the two implant manufacturers, no selection bias was likely introduced as a result. Second, as with all self-administered questionnaires, reported medical histories might not be accurate, particularly for adults who might have lost their hearing many years before receiving a cochlear implant. Third, medical details (e.g., type of meningitis and whether treatment was received for episodes of otitis media) were poorly reported. Response rates for medical details varied widely (range: 40%–80%) compared with responses to other questions (e.g., ever having otitis media, ever having meningitis, and cause of deafness [range: 90%–99%]). The cause of BM was based on self-report and was not verified with medical records. In addition, subtyping of bacteria that caused postimplant BM was not reported. The type might not have been vaccine preventable. Certain questions pertaining to vaccination history were misinterpreted. For example, Hib vaccine was often indicated as having been received yearly, indicating confusion between Hib vaccine and annual influenza vaccine. Finally, the study was conducted in English and French. CIRs who could not read either of these languages were systematically excluded from the cohort and might have BM at a different rate from CIRs who read English or French.

## Conclusion

In this study, CIRs had postimplant BM infection at a rate of approximately 1.8 cases per 1,000 person-years of observation. In addition, children with cochlear implants had BM infection at a higher rate than adults (2.9 and 0.7 per 1,000 person-years of observation, respectively). Because of the increased risk for BM infection among CIRs, health-care professionals should ensure that CIRs and persons considering cochlear implants are vaccinated against bacteria that commonly cause meningitis. The only risk factor identified for having postimplant BM was preimplant BM infection. CIRs and their families should be aware of the signs and symptoms of meningitis and seek prompt attention if they occur.

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## Risk Factors for Neonatal Tetanus — Busoga Region, Uganda, 2002–2003

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### Abstract

**Background:** Uganda has not achieved the 2005 neonatal tetanus (NNT) global elimination target set by the World Health Organization (WHO). The Busoga region has the highest recorded level of NNT incidence in Uganda. To understand the reasons for this high incidence, a study was conducted to identify NNT risk factors.

**Methods:** During March–May 2004, a matched case-control study was conducted in the Busoga region for a 2-year study period (2002–2003). Matching variables were sex, residence, and date of birth. A total of 24 cases of NNT (according to the WHO case definition) were identified from hospital records, and 96 community controls (children who survived the neonatal period) were selected.

**Results:** Bivariate analysis indicated that neonates with NNT were more likely to have been delivered outside a health facility, on an unclean surface, without use of gloves, or by unskilled attendants. Mothers of these neonates were less likely to report vaccination during previous pregnancies, administration of 2 doses of tetanus toxoid (TT) during the study pregnancy, or use of certain intravaginal substances (most commonly, herbs) at onset of labor. Multivariate analysis indicated that unclean delivery surfaces (odds ratio [OR] = 38.8; 95% confidence interval [CI] = 2.9–518.1) and primigravidae mothers (OR = 79.5; CI = 1.8–3,472.2) were associated with NNT. Administration of 2 doses of TT during pregnancy, vaccination during previous pregnancies, and intravaginal application of certain substances were protective against NNT.

**Conclusion:** These findings underscore the importance of having clean delivery surfaces and of mothers receiving 2 doses of TT during pregnancy. Implementation of these measures might help eliminate NNT from the Busoga region of Uganda.

### Introduction

Neonatal tetanus (NNT) is a fatal yet preventable disease that accounts for 14% of annual neonatal deaths worldwide (1). In 1997, a total of 248,000 NNT deaths occurred globally; 95,000 NNT deaths occurred in Africa, 4,600 of which occurred in Uganda (2). In 2000, the World Health Organization (WHO) targeted NNT for global elimination by 2005 (3). Uganda is one of the 57 countries that have not yet eliminated NNT. In Uganda, with 195 cases, the Busoga region has the highest NNT incidence (4). In 2002, the Uganda Ministry of Health (MoH) launched an NNT elimination campaign in Busoga. After the second round of mass tetanus toxoid (TT) immunization during the NNT elimination campaign, approximately 86% of women of reproductive age in all districts in the region had received 2 doses of TT (5).

A previous study attributed NNT in Busoga to unhygienic delivery practices, application of harmful substances on the umbilical cord, and lack of TT immunization among mothers but did not document the magnitude of risk associated with these factors (6). Worldwide, NNT has been associated with prenatal, perinatal, and neonatal factors, including unhygienic delivery and cord-care practices and lack of maternal TT immunization (7). Risk for contamination and subsequent occurrence of NNT remains high for several days after delivery until the baby's cord wound heals (8).

NNT cases continue to be reported in Busoga. For this reason, district health teams in the region recommended that a study be conducted to identify NNT risk factors as a basis for planning and implementing appropriate NNT elimination strategies.

## Methods

A community-based, matched case-control study was conducted to identify delivery and umbilical cord-care practices that predispose neonates to NNT and to compare maternal TT immunization status for both groups. The study was conducted during March–May 2004 in five districts that make up the Busoga region (Bugiri, Iganga, Jinja, Kamuli, and Mayuge). Respondents were the mothers of the neonates with NNT and matched controls.

Mothers of neonates with NNT were identified by screening NNT investigation forms from all hospitals in the Busoga region for January 2002–December 2003. A case was defined as confirmed NNT according to the WHO case definition (i.e., history of normal sucking and crying for the first 2 days of life, onset of illness at age 3–28 days, and inability to suck followed by generalized stiffness and/or spasms) occurring in a child born in the Busoga region during the study period (5). A control was defined as a child who had survived the neonatal period, who was matched for sex and date of birth (range:  $\pm 6$  months), and who lived in the same village as a neonate with NNT. A control was selected from each of the first four households closest to the home of a child with NNT that had a child consistent with the control definition. If a household had more than one eligible control, the child whose date of birth was closest to that of the neonate with NNT was selected. Multiple controls were selected to increase the power of the study (9). Children whose mothers did not live in the Busoga region at the time of delivery were excluded from the study.

The questionnaire used was adapted from the WHO NNT case investigation form (5). It was modified before the study was conducted on the basis of qualitative data about the most probable NNT risk factors collected from 80 mothers who participated in eight focus group discussions and interviews with eight traditional birth attendants. Questionnaires were pretested among 20 Jinja district mothers who were not part of the final study sample.

Trained interviewers used the pretested, interviewer-administered questionnaire to collect data on maternal sociodemographic characteristics, delivery practices, umbilical cord-care practices, and maternal TT immunization status. The delivery surface was categorized as clean or unclean; any surface other than a new plastic sheet or operating theater table was classified as unclean. The mother of a neonate with NNT was always interviewed before that of the controls to ensure accurate matching. The Uganda National Council of Science and Technology and Makerere University Institute of Public Health Higher Degrees Research and Ethics Committee approved this study, and all participating mothers signed consent forms.

Data were double-entered and validated by using Epi Info 6.04 (CDC, Atlanta, Georgia). Epi Info also was used for bivariate analysis; stratified Mantel-Haenszel analysis produced matched odds ratios (ORs) and 95% confidence intervals (CIs). For multivariate analysis, data were exported to SPSS 10.0 (Statistical Package for the Social Sciences for Windows, version 10.0; SPSS; Chicago, Illinois); conditional logistic regression was performed to identify the predictors for NNT. All variables entered in the model were dichotomized, with neonatal tetanus case (Yes/No) as the outcome variable. The initial logistic regression model included all variables that were statistically significant during bivariate analysis (e.g., delivery place, birth attendant, delivery surface, use of intravaginal substances, use of gloves, maternal TT status in study, and previous pregnancies). Other variables that were not significant on bivariate analysis but that are known risk factors for NNT (e.g., handwashing, type of cord-cutting tool, cord dressings, and cord tie used) and potential confounders (e.g., maternal age) also were included in the model. Measures of interest were adjusted ORs and CIs for NNT risk factors. Goodness of fit of the final model was tested by using Nagelkerke  $R^2$  value.

## Results

A total of 40 NNT cases were identified from the records, but only 24 mothers could be traced in the community. Full names were not available for three mothers, and addresses of nine mothers were not recorded in the hospital records. In four cases, parents had moved and could not be located. Four matched controls were selected for each of the 24 cases, for a total of 96 controls and a study sample of 120.

### Bivariate Analysis

The majority of neonates with NNT and controls had mothers who were aged  $\geq 20$  years, were currently married, and had attained at least a primary education (Table 1). The percentage of mothers who were primigravidae (i.e., this was their first pregnancy) was 25% for neonates with NNT and 12.5% for controls. The majority of mothers (17 [70.8%] of 24 neonates with NNT and 62 [64.6%] of 96 controls) had had one to four previous deliveries. No statistically significant associations were observed between maternal sociodemographic characteristics and NNT.

Maternal TT immunization status of the two study groups was compared (Table 2). Maternal TT immunization status was determined by history because only 12.5% of mothers whose neonates had NNT and 26% of controls had TT

**TABLE 1. Number and percentage of neonates with neonatal tetanus (NNT) and controls, by selected maternal characteristics — Busoga region, Uganda, 2002–2003**

Characteristic	Children with NNT		Controls		Matched OR* (95% CI†)
	No.	(%)	No.	(%)	
<b>Maternal age (yrs)</b>					
<20	3	(12.5)	16	(16.7)	0.7 (0.2–2.8)
≥20	21	(87.5)	80	(83.3)	1.0
<b>Marital status</b>					
Unmarried	4	(16.7)	10	(10.4)	1.9 (0.5–7.5)
Married	20	(83.3)	86	(89.6)	1.0
<b>Mother's education level</b>					
None/Primary	22	(91.7)	72	(75.0)	3.7 (0.8–16.9)
Secondary	2	(8.3)	24	(25.0)	1.0
<b>Mother's occupation</b>					
Agriculture related	8	(33.3)	25	(26.0)	2.0 (0.5–8.6)
Not agriculture related	16	(66.7)	71	(74.0)	1.0
<b>No. of previous deliveries</b>					
None	6	(25.0)	12	(12.5)	2.5 (0.8–8.4)
≥1	18	(75.0)	84	(87.5)	1.0

\* Odds ratio.

† Confidence interval.

immunization cards. Significantly fewer mothers of neonates with NNT (20.8%) than control mothers (66.7%) had received the recommended 2 doses of TT by the time of delivery (OR = 0.2; CI = 0.1–0.5;  $p = 0.0001$ ). Mothers of neonates with NNT also were less likely to have had TT immunization for previous births (OR = 0.1; CI = 0.02–0.3;  $p < 0.001$ ). The majority of mothers in both groups had received prenatal care during the study pregnancy, but this was not identified as being protective.

All four investigated delivery practices were associated with NNT (Table 2). Mothers of neonates with NNT were more likely than control mothers to have delivered outside health facilities and to have had unskilled birth attendants; 70.8% of these mothers had unskilled attendants, including traditional birth attendants (six of 24), friends or relatives (six of 24), and nursing assistants (five of 24). In contrast, only 31.3% of controls were delivered by unskilled attendants, including traditional birth attendants (12 of 96), friends or relatives (nine of 96), nursing assistants (four of 96), and self (five of 96). Doctors delivered no neonates with NNT and 3.1% (three of 96) of controls. The rest were delivered by midwives and nurses. Mothers of neonates with NNT were more likely than control mothers to have delivered on unclean delivery surfaces (e.g., mats, sacks, uncovered delivery beds, and uncovered floors). Certain mothers (three [12.5%] of 24 mothers of children with NNT and 36 [37.5%] of 96 controls) reported having applied substances into the vagina at onset of labor, a traditional practice in this region; mothers of neonates with NNT were less likely than control mothers to have used

intravaginal substances (most frequently herbs) (OR = 0.2; CI = 0.1–0.8) (Table 3). Bivariate analysis indicated that the only umbilical cord-care practice that was associated with NNT was the birth attendant not wearing gloves (OR = 3.8; CI = 1.1–13.1;  $p = 0.06$ ) (Table 2).

## Multivariate Analysis

The best fitting model for NNT risk factors explained 71.4% (Nagelkerke  $R^2$ ) of the variation observed in the outcome variable. Within this model, the mother receiving 2 doses of TT during the study pregnancy and a history of receiving TT in previous pregnancies were significantly protective ( $p = 0.007$ ) (Table 4). Receiving only 1 TT dose in study pregnancy was not protective and was excluded from the final model. Delivery on an unclean surface and primigravidae mothers were associated with increased risk for NNT. Use of intravaginal substances at onset of labor was significantly protective, with mothers of neonates with NNT less likely to have used them ( $p = 0.017$ ).

## Discussion

This study identified two risk factors for NNT and two protective factors in the Busoga region of Uganda: unclean delivery surfaces and primigravidae mothers. Unclean delivery surfaces were the most likely source of tetanus organisms, underscoring the importance of using clean delivery surfaces to prevent NNT. This finding concurs with results of other studies that identified unclean delivery surfaces as a risk factor for NNT (8,10). Children born to primigravidae mothers were at more risk for having NNT than those born to multiparous mothers. The association might be confounded by receipt of TT before pregnancy, which was not captured in this study.

Intravaginal application of local medicines (most commonly, herbs) at onset of labor is widely practiced as it is thought to ease labor by widening the birth canal. This traditional practice was negatively associated with acquisition of NNT, implying that it might have had a protective effect. This finding has not been reported previously and requires further clarification. Association might result from reporting bias, as a mother of a neonate with NNT conceivably might have withheld information about use of these substances for fear of being blamed for her child's illness. Alternatively, applying such substances immediately after bathing, as is the practice, might have ensured that clean hands were used, thus decreas-

**TABLE 2. Number and percentage of neonates with neonatal tetanus (NNT) and controls, by delivery practices, cord-care practices, and maternal tetanus toxoid immunization status — Busoga, Uganda, 2002–2003**

Characteristic	Neonates with NNT		Controls		Matched OR* (95% CI†)
	No.	(%)	No.	(%)	
<b>Maternal immunization status at delivery</b>					
<b>1 dose of TT§ in study pregnancy</b>					
Yes	13	(54.2)	85	(88.5)	0.1 (0.04–0.5 <sup>¶</sup> )
No	11	(45.8)	11	(11.5)	1.0
<b>2 doses of TT** in study pregnancy</b>					
Yes	5	(20.8)	64	(66.7)	0.2 (0.1–0.5 <sup>¶</sup> )
No	19	(79.2)	32	(33.3)	1.0
<b>TT in previous pregnancies††</b>					
Yes	9	(37.5)	76	(79.2)	0.1 (0.02–0.3 <sup>¶</sup> )
No	15	(62.5)	20	(20.8)	1.0
<b>Delivery practices</b>					
<b>Delivery place</b>					
Outside health facility	13	(54.2)	26	(27.1)	4.5 (1.4–13.1 <sup>¶</sup> )
Health facility	11	(45.8)	70	(72.9)	1.0
<b>Birth attendant§§</b>					
Unskilled	17	(70.8)	30	(31.3)	7.3 (2.1–16.9 <sup>¶</sup> )
Skilled	7	(29.2)	66	(68.8)	1.0
<b>Delivery surface¶¶</b>					
Unclean	12	(50.0)	14	(14.6)	6.7 (2.1–21.3 <sup>¶</sup> )
Clean	12	(50.0)	82	(85.4)	1.0
<b>Used intravaginal substances***</b>					
Yes	3	(12.5)	36	(37.5)	0.2 (0.1–0.8 <sup>¶</sup> )
No	21	(87.5)	60	(62.5)	1.0
<b>Cord-care practices</b>					
<b>Attendant washed hands</b>					
Yes	16	(72.7)	74	(78.7)	1.0
No	6	(27.3)	20	(21.3)	1.5 (0.5–5.0)
<b>Attendant wore gloves</b>					
Yes	16	(69.6)	80	(85.1)	1.0
No	7	(30.4)	14	(14.9)	3.8 (1.1–13.1 <sup>¶</sup> )
<b>Cutting tool</b>					
New razor blade	14	(63.6)	51	(58.0)	1.0
Scissors	8	(36.4)	37	(42.0)	0.7 (0.2–2.7)
<b>Thread cord tie</b>					
Yes	17	(70.8)	71	(74.0)	0.8 (0.3–2.4)
No	7	(29.2)	25	(26.0)	1.0
<b>Cloth cord tie</b>					
Yes	4	(16.7)	13	(13.5)	1.3 (0.4–4.7)
No	20	(83.3)	83	(86.5)	1.0
<b>Applied substance on cord</b>					
Yes	6	(25.0)	33	(34.4)	0.7 (0.3–1.7)
No	18	(75.0)	63	(65.6)	1.0
<b>Prenatal-care attendance</b>					
None	6	(25.0)	14	(14.6)	1.8 (0.6–5.3)
At least one visit	18	(75.0)	82	(85.4)	1.0

\* Odds ratio.

† Confidence interval.

§ Received ≥1 tetanus toxoid dose during study pregnancy.

¶ Statistically significant at 0.05 level.

\*\* Received ≥2 tetanus toxoid doses during study pregnancy.

†† Answered “yes” to question, “Were you ever immunised with TT in previous pregnancies or during the recent mass TT immunisation campaign?”

§§ Skilled = doctors, midwives, and nurses; any other = unskilled.

¶¶ Clean = only new plastic sheet or operating theatre; any other = unclean.

\*\*\* Answered “yes” to question, “Did you apply any substance into the vagina at onset of labor?”

ing the risk for contaminating the substances and the birth canal. This finding is contrary to the increased risk for NNT observed in other studies of pregnant women who had pre-delivery intravaginal exposure to ghee or coconut oil (8,11). Possibly the herbs used as intravaginal medications had antibacterial properties. Further research is required to determine if these herbs have such medicinal properties.

Absence of the mother receiving 2 doses of TT vaccination during pregnancy was identified as a risk factor for NNT, which concurs with findings of previous studies conducted in Uganda and Nigeria (6,11,12). The study indicated that <80% of all mothers in Busoga region had received recommended 2 doses of TT, which suggests that >20% of children born in the region are still at risk for having NNT because of low 2-dose TT coverage.

A discrepancy was noted between prenatal care attendance and maternal TT vaccination. Although approximately 75% of mothers of neonates with NNT had prenatal care, only half received ≥1 dose of TT, indicating that health-care workers are missing opportunities to vaccinate pregnant women. This finding has been documented previously (13–15). This discrepancy might result from mothers receiving prenatal care only when pregnancy is so far advanced that they can receive only 1 dose of TT before delivery.

The type of tool used to cut the umbilical cord was not identified as a risk factor for NNT. This finding is consistent with a previous study conducted in Senegal (16) and is probably attributable to the use of new razor blades and scissors. In addition, no mother reported having applied any harmful substance (e.g., cow dung or mud) to the newborn's cord wound. This suggests that a positive shift in cord-care culture has occurred among mothers in Busoga; certain unhygienic cord practices identified previously are no longer practiced (6). This change in cord-care practices might be attributable to widespread health education activities in this region, especially during recent mass NNT elimination campaigns. It also might result from public awareness of risk for acquisition of HIV associated with use of unsterilized instruments.

The findings in this report are subject to at least five limitations. First, use of unverified maternal TT vaccination histories might have biased study findings. Second, health education provided during the NNT elimination campaign might have introduced reporting bias; however, such bias would be

**TABLE 3. Percentage of mothers\* who used intravaginal substances at onset of labor, by type of substance used — Busoga region, Uganda, 2002–2003**

Substance	Mothers of children with neonatal tetanus	Mothers of controls
Herbs	67%	86%
Burnt snake skin or snail shells	33%	8%
Ghee	0	3%
Vaseline	0	3%

\* Mothers of children with neonatal tetanus: n = three; controls: n = 36.

**TABLE 4. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) for variables retained in the final multivariate model of risk factors for neonatal tetanus — Busoga region, Uganda, 2002–2003**

Variable	AOR	(95% CI)
<b>Parity</b>		
Primigravidae mothers	79.5	(1.8–3472.2*)
Mothers with previous births	1.0	
<b>Delivery surface†</b>		
Unclean	38.8	(2.9–518.1*)
Clean	1.0	
<b>Birth attendant§</b>		
Unskilled	9.0	(0.9–89.4)
Skilled	1.0	
<b>Used intravaginal substances¶</b>		
Yes	0.04	(0.003–0.6*)
No	1.0	
<b>Type of cord tie used</b>		
Thread	0.1	(0.014–1.1)
Other	1.0	
<b>2 doses of TT in study pregnancy**</b>		
Yes	0.05	(0.005–0.4*)
No	1.0	
<b>1 dose of TT in previous pregnancies††</b>		
Yes	0.04	(0.004–0.4*)
No	1.0	

\* Statistically significant at 0.05 level.

† Clean = only new plastic sheet or operating theatre; any other = unclean.

§ Skilled = doctors, midwives, and nurses; any other = unskilled.

¶ Answered “yes” to question, “Did you apply any substance into the vagina at onset of labor?”

\*\* Received  $\geq 2$  tetanus toxoid doses during study pregnancy.

†† Answered “yes” to question, “Were you ever immunized with tetanus toxoid in previous pregnancies?”

nondifferential. Third, recall bias might have occurred because mothers of neonates with NNT are likely to have a better recall of circumstances surrounding delivery and cord care than control mothers. Birth-date matching attempted to equalize recall difficulties for both mothers of cases and controls. Fourth, NNT status of participants could not be masked; however, nonmedical data collectors were employed to minimize interviewer bias. Finally, only 60% of mothers of neonates with NNT could be traced, which reduced study sample size. However, the matched case-control study design with four controls per case minimized the effect of this limitation.

## Conclusion

This study identified two risk factors for NNT: unclean delivery surfaces and primigravidae mothers. Protective factors were the mother receiving 2 doses of TT in current pregnancy, history of TT in a previous pregnancy, and application of intravaginal substances at onset of labor. Cord-care practices were not NNT risk factors.

On the basis of these findings, the following recommendations are offered:

- Health-care workers should routinely assess the TT status of all female patients of reproductive age and vaccinate them according to MOH vaccination guidelines.
- Health-care workers should educate mothers, especially primigravidae mothers, about the importance of receiving 2 doses of TT during pregnancy and the need to purchase clean delivery kits.
- MoH and district health teams (DHTs) should collaborate with social marketing organizations to provide pregnant women with clean delivery kits (containing gloves, cord ligatures, blade, plastic delivery sheet, and cotton wool) at a subsidized fee.
- DHTs should budget for clean delivery kits, which they should provide at no cost to mothers who cannot afford to buy.
- The possible prophylactic effects of application of intravaginal substances should be studied further.

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## Risk Factors for Brucellosis — Leylek and Kadamjay Districts, Batken Oblast, Kyrgyzstan, January–November, 2003

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### Abstract

**Introduction:** Brucellosis is a zoonotic disease that is associated with chronic serious sequelae in humans. During 1997–2002, the reported incidence of human brucellosis in Kyrgyzstan increased nearly twofold, from 20 to 36 per 100,000 population. In 2002, the highest incidence of brucellosis was reported in two rural districts of Batken Oblast: Leylek (106 per 100,000 population) and Kadamjay (80 per 100,000 population). During January–November 2003, trainees from the Applied Epidemiology Training program in Central Asia conducted a matched, hospital-based, case-control study to identify risk factors for brucellosis and describe the epidemiology of disease in these two districts.

**Methods:** Brucellosis cases were defined on the basis of epidemiologic, clinical, and laboratory criteria. During January–November 2003, a total of 100 persons with confirmed brucellosis were identified in the infectious disease wards of the two district hospitals; these persons were matched by age and date of admission to 100 controls who were admitted to other hospital wards for unrelated conditions. Data on socioeconomic and occupational factors and history of exposure to animals and animal products were collected by using a structured questionnaire. Conditional logistic regression was used to study the association between exposure variables and brucellosis.

**Results:** Among the 100 persons with confirmed brucellosis during the study period, 86 (86%) owned farm animals, and 45 (45%) became ill during April–May, the birthing season for farm animals. Multivariate analysis indicated that brucellosis was associated with exposure to aborted farm animals in the household (odds ratio [OR] = 29.8; 95% confidence interval [CI] = 4.4–203.4) and consumption of home-made milk products obtained from bazaars or neighbors (OR = 11.4; CI = 1.6–83.9). Knowledge of the mode of brucellosis transmission appeared to be protective against disease transmission (OR = 0.2; CI = 0.03–0.8).

**Discussion:** Exposure to aborted home-owned animals and consumption of home-made milk products obtained from bazaars or neighbors were identified as probable sources of human brucellosis infections in the study districts. This finding suggests that brucellosis spreads among farm animals in the area and that home-made milk products are not adequately pasteurized.

**Conclusion:** To reduce the burden of brucellosis in Batken Oblast, veterinary services should be improved, and health education programs should be increased. Implementing these measures should minimize exposure to farm animals and reduce the risk for infection from locally produced milk products.

### Introduction

Brucellosis is an infectious zoonotic disease that is associated with chronic debilitating infections in humans and reproductive failure in domestic animals (1). Although brucellosis occurs worldwide, it is more common in countries that do not have effective public health and domestic animal health programs.

Kyrgyzstan (estimated 2003 population: 4,892,808) is an almost entirely mountainous country in Central Asia that became independent in 1991 after the disintegration of the

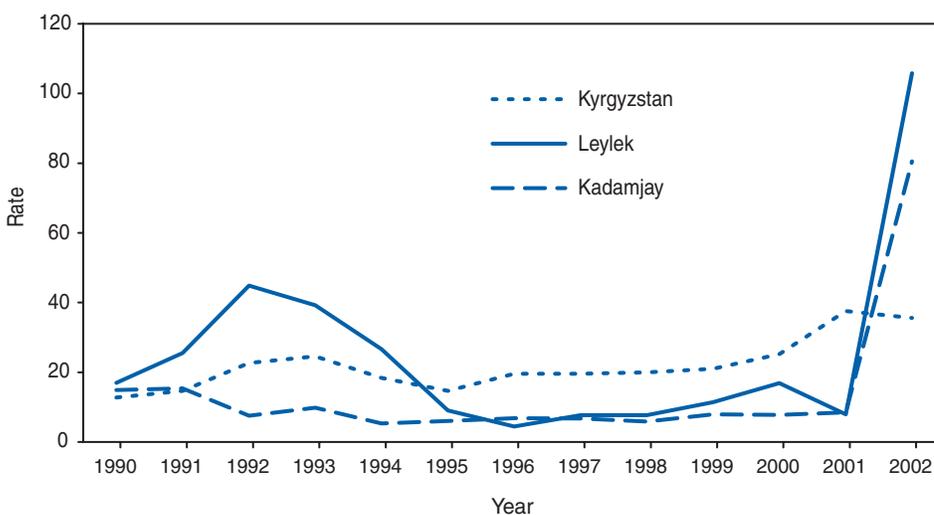
former Soviet Union. An estimated 3,180,000 (65%) persons live in rural areas. Agriculture accounts for 44% of the country's gross domestic product (GDP), and half of the country's agricultural GDP comes from the livestock subsector (2). Animal husbandry is the dominant form of agricultural production in the mountainous regions of Kyrgyzstan.

During the Soviet era, the collective-farm system that existed in the country accounted for the majority of livestock production; a high level of state veterinary and sanitary control was maintained over the livestock population and pro-

duction. The collapse of the Soviet Union in 1991 led to social changes and economic hardship that affected all government sectors. The state farming system disappeared, forcing families, especially those in rural areas, to raise farm animals themselves. These changes in the agricultural sector resulted in the loss of the state control over the livestock population and a drastic decline in the quality of veterinary services. In addition, as a result of deteriorating economic conditions, Kyrgyzstan was unable to maintain the health infrastructure inherited from the Soviet era, and the quality and availability of health services declined, especially in rural areas, where neither veterinary nor sanitary inspection agencies provide adequate health services (3,4).

Brucellosis can be transmitted to humans through contact with animals or their products; it is an occupational hazard to persons engaged in certain professions (e.g., veterinarians, slaughterhouse workers, and farmers) (5–7). During 1997–2002, countrywide incidence of human brucellosis increased substantially, from 20 to 36 cases per 100,000 population (Kyrgyz Ministry of Health [MoH], unpublished data, 2003) (Figure 1); during the same period, the State Veterinary Department did not report an increase in incidence of brucellosis in animals. The greatest increase in incidence during this 5-year period (from six to 68 cases per 100,000 population) was reported in Batken Oblast, a mountainous area in the southwestern part of the country. In two districts of this oblast, Leylek and Kadamjay, incidence of human brucellosis in 2002 was 106 and 81 per 100,000 population, respectively.

**FIGURE 1. Reported rate\* of brucellosis, by year — Leylek and Kadamjay districts, Batken Oblast, Kyrgyzstan, 1990–2002**



\* Per 100,000 population.

## Methods

During January–November 2003, in response to a request from the Kyrgyz MoH, trainees from the Applied Epidemiology Training Program in Central Asia conducted a hospital-based, matched case-control study in Leylek and Kadamjay districts of Batken Oblast to identify risk factors for brucellosis and describe the epidemiology of disease in these districts. During the study period, 100 persons with confirmed cases of brucellosis were identified in the infectious disease wards of the two district hospitals. A case was defined as illness occurring in a permanent resident of one of the two study districts who was admitted to either of the two local hospitals and who received a clinical diagnosis of brucellosis for the first-time on the basis of the following symptoms: fever ( $>99.5^{\circ}\text{F}$  [ $>37.5^{\circ}\text{C}$ ]) for  $>5$  days, headache and arthralgias, and Wright agglutination test dilution  $>1:100$ . A control was defined as a patient with no recent history of brucellosis who was a permanent resident of one of the two study districts and who was admitted to the same hospital with a noninfectious condition during the study period. One control per case was selected and matched by age ( $\pm 2$  years) and date of admission ( $\leq 2$  weeks of the brucellosis patient's date of hospitalization). The Schlesselman formula for matched case-control design was used to calculate sample size, with the following parameters: the significant level was set at 0.05, the desired power was 0.8, and the case-to-control ratio was 1:1. To adjust for confounding, 10% was added to the result. The total number of pairs needed was 100.

Informed consent was obtained from all study participants, and person-to-person interviews were conducted. Data on socioeconomic and occupational factors and on exposure to animals and animal products were collected by using a structured questionnaire. Clinical and laboratory data were abstracted from medical records. A period of 2 months before date of illness onset for cases and the same period for corresponding controls was used as the relevant time for measuring these variables.

Data management and analysis were performed using Epi Info, version 3.2 (CDC, Atlanta, Georgia). Conditional logistic regression was used to study the association between exposure variables and brucellosis. Potential risk factors were first assessed in the univariate analysis. All variables with *p* values of

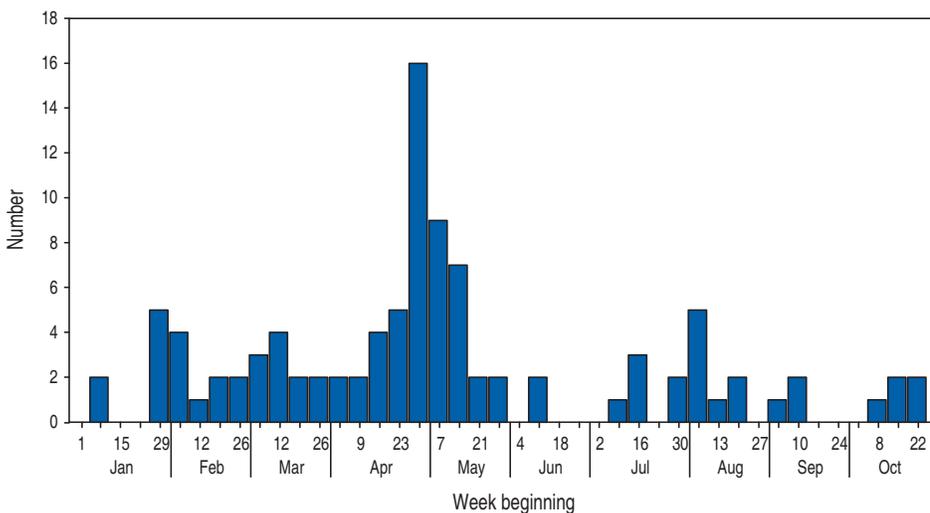
<0.2 in univariate analysis were selected for multivariate analysis. The stepwise method of model building was used to arrive at the final statistical model. A p value of  $\leq 0.05$  was defined as statistically significant.

## Results

Of 100 persons with brucellosis who participated in the study, 69 (69%) became ill during February–May; with the highest number of illnesses beginning during late April–early May (Figure 2). The age of ill persons varied (range: 1–75 years; mean: 32 years); 66 were males and 87 were of Kyrgyz nationality (Table 1). Twelve patients were collective farm workers; 86 patients reported owning farm animals at home, including cattle (n = 80), goats (n = 70), dogs (n = 50), and sheep (n = 49). Among the 86 persons with brucellosis who had farm animals at home, 70 (81%) cleaned barns, 60 (70%) assisted in animal delivery, and 22 (26%) slaughtered animals (Table 1).

Univariate analysis indicated that exposure to aborted animals (OR = 16.0; CI = 4.5–99.2), assistance in animal delivery (OR = 5.6; CI = 2.3–16.3), keeping goats at home (OR = 5.2; CI = 2.1–15.2), cleaning animal barns (OR = 3.0; CI = 1.1–9.2) and being of Kyrgyz nationality (OR = 2.4; CI = 1.1–5.6) were significantly associated with risk for having brucellosis; limited evidence in the univariate analysis suggested that milk products purchased in bazaars or from neighbors (OR = 1.7; CI = 0.9–3.2) might be associated with brucellosis.

**FIGURE 2. Number of brucellosis cases,\* by week of onset — Leilek and Kadamjay districts, Batken Oblast, Kyrgyzstan, January–October 2003**



\* N = 100.

Multivariate analysis indicated that exposure to aborted home-owned animals (OR = 29.8; CI = 4.4–203.4), exposure to home-made milk products purchased in bazaars or from neighbors (OR = 11.4; CI = 1.6–83.9), and being of Kyrgyz nationality (OR = 4.8; CI = 1.2–20.3) were independent risk factors for having brucellosis. Knowledge of the mode of brucellosis transmission was protective (OR = 0.2; CI = 0.03–0.8). Owning a cow at home was borderline associated with brucellosis (OR = 4.5; CI = 0.9–23.5) (Table 2).

## Discussion

Although brucellosis can occur any time, the majority of cases occurred during February–May 2003, which is the birthing season for farm animals. In this season, *Brucella* can be excreted in high numbers from infected animals, and the likelihood of exposure to infected animals increases. Similar trends have been observed in other countries (7,8).

Humans become infected with *Brucellae* by coming into contact with animals or animal products that are contaminated with these bacteria. Inadequately heated milk and other dairy products from infected animals are a primary source of infection (6,9,10). Person-to-person transmission of *Brucella* is extremely rare (1,10). In the two districts studied, exposure to aborted home-owned animals and eating home-made milk products purchased in bazaars or from neighbors were independent risk factors for having brucellosis. Being of Kyrgyz nationality was associated with brucellosis; this might be explained by residual confounding or to other unmeasured risk. Knowledge of the mode of brucellosis transmission was

protective, which underscores the importance of health education in preventing of brucellosis. Increased government efforts are necessary to improve education regarding risk factors for brucellosis transmission, especially in rural areas, where human contact with domestic animals is widespread.

Brucellosis in Batken Oblast is probably spread among home-owned animals, and home-made milk products obtained from bazaars or neighbors probably are not adequately pasteurized. The spread of brucellosis in farm animals might be attributable to the privatization of collective farms as a result of the changed political and economic situation in the country. Collective farm animals were distributed among small private farms; families who

**TABLE 1. Number and percentage of persons with brucellosis, by selected characteristics — Leylek and Kadamjay districts, Batken Oblast, Kyrgyzstan, January–November 2003**

Characteristic (n = 100)	No.	(%)
<b>Sex</b>		
Male	66	(66)
Female	34	(34)
<b>Nationality</b>		
Kyrgyz	87	(87)
Other	13	(13)
<b>Education</b>		
No formal	4	(4)
Primary	19	(19)
Secondary	61	(61)
Secondary special*	14	(14)
Postsecondary	2	(2)
<b>Type of domestic animal owned (n = 100)</b>		
Cattle	80	(80)
Goat(s)	70	(70)
Dog(s)	50	(50)
Sheep	49	(49)
Any	86	(86)
<b>Relative distribution of cases by type of exposure to animals (n = 86)</b>		
Cleaned barns	70	(81)
Assisted during delivery	60	(70)
Exposed to aborted animals in household	48	(56)
Milked cows	29	(34)
Sheared sheep	27	(31)
Slaughtered animals	22	(26)

\* Combines general education with specialized training in a professional field.

own these animals might disregard or not be aware of sanitary and health requirements necessary to prevent transmission of brucellosis to humans. A probable consequence of privatization of the animal sector is an increased volume of home-made animal food products with inadequate sanitary control over production.

Despite the increase in the number of registered human brucellosis cases, the State Department of Veterinary Services did not report an increase in the number of brucellosis cases among animals during the same period. This might reflect the inadequacy of veterinary services. In addition, persons who own their own animals might not seek veterinary service if needed because of fear that they might lose their source of income.

These findings were discussed by MoH staff and were presented at conferences attended by staff of international agencies (e.g., the World Bank and the Swiss Emergency Relief Agency). Public health and veterinary officials in Kyrgyzstan have determined that the best approach to reduce the country's brucellosis burden is to focus their resources on improving health education. Together with the nongovernment organization Rural Activists for Health, MoH has developed a prevention campaign that targets persons on rural privately owned farms with livestock. Prevention messages are delivered through the mass media and focus on use of protection methods (e.g., wearing

**TABLE 2. Risk factors for human brucellosis — Leylek and Kadamjay districts, Batken Oblast, Kyrgyzstan, January–November 2003**

Risk factors	Adjusted	
	OR*	(95% CI†)
Kyrgyz nationality	4.8	(1.2–20.3)
Kept cows	4.5	(0.9–23.5)
Kept goats	1.6	(0.4–6.5)
Cleaned animal barns	3.3	(0.6–17.3)
Sheared animals	0.4	(0.1–2.0)
Slaughtered animals	0.7	(0.1–3.1)
Was exposed to aborted animals in the household	29.8	(4.4–203.4)
Milked cows	0.5	(0.1–2.6)
Obtained milk products from bazaar or neighbor	11.4	(1.6–83.9)
Knew how brucellosis is acquired	0.2	(0.03–0.8)

\* Odds ratio.

† Confidence interval.

protective clothes, especially when assisting in delivery; not permitting children to have contact with animals; and having sick animals checked by a veterinarian) during contact with animals and adherence to adequate sanitary standards (e.g., boiling or pasteurizing) when processing milk and milk products. Brucellosis health education brochures and flyers are being distributed at infectious disease hospitals, local clinics, and health outposts. In addition, MoH has applied for a grant from the World Bank to fund brucellosis prevention efforts.

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## Salmonellosis Outbreak Among Factory Workers — Huizhou, Guangdong Province, China, July 2004

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### Abstract

**Introduction:** During July 9–14, 2004, an outbreak of gastroenteritis occurred among workers at an electronics factory in Huizhou, Guangdong Province, China; 199 cases were reported. A case-control investigation was initiated to identify the agent and the mode of transmission.

**Methods:** Stool samples were collected from 142 workers and food handlers and cultured for enteric pathogens. A questionnaire concerning meals and foods eaten in the factory cafeteria during July 11–13 was administered to 92 ill workers and 100 controls.

**Results:** Of approximately 2,000 workers who worked during the outbreak, 197 (10%) had illness consistent with the case definition. *Salmonella enteritidis* was identified from 44 (31%) of 142 stool samples collected from ill workers. Ill workers were more likely than controls to have eaten breakfast in the factory cafeteria during July 11–13. Of eight foods served at breakfast in the factory cafeteria, three were associated with illness: cake, bread (on July 12 only), and congee (i.e., rice porridge). Stratification of bread and congee exposure by cake consumption indicated that only bread eaten on July 12 was associated with gastroenteritis. The cake was baked on July 11, and a mixture that included raw eggs was poured on top; the cake was then stored at room temperature and served for breakfast on 3 consecutive days (July 11–13). The bread was stored together with the cake on July 11 and 12. No leftover food was tested.

**Discussion:** The investigation indicated that an outbreak of *S. enterica* serotype *Enteritidis* resulted from consumption of an unusual food vehicle (i.e., cake) that had been contaminated from a more typical source (i.e., raw eggs). The bread was stored at room temperature together with cake on which a mixture made from raw eggs had been poured. The bread was probably contaminated by contact with the cake.

**Conclusion:** Food handlers should be instructed that intact fresh eggs can harbor *S. enteritidis*, foods made from eggs must be cooked, and prepared food must be stored under refrigeration.

### Introduction

On July 13, 2004, a local hospital reported to the Huizhou City Center for Disease Control (CDC) that approximately 70 patients had been admitted that day to the hospital with gastroenteritis characterized by diarrhea, fever, nausea, and vomiting. All 70 patients were workers at a local factory that manufactured electrical products. Investigators from the Huizhou and Guangdong CDCs visited the hospital and the factory to identify the agent causing this outbreak. Initial interviews and review of medical records indicated that for the majority of patients, onset of gastroenteritis occurred during a 2-day period (July 12–13).

### Methods

A case of gastroenteritis was defined as illness occurring in either a factory worker or in a family member who ate a meal at the factory cafeteria during July 7–16 and who had diarrhea (two or more liquid stools per day) or fever  $>99.5^{\circ}\text{F}$  ( $>37.5^{\circ}\text{C}$ ) in addition to one of three symptoms: nausea, vomiting, or abdominal pain. Ill workers were identified from doctors' reports and from an announcement to workers. Stool samples were collected from 142 patients (136 workers and six food handlers) and 24 healthy food handlers. Stool samples were inoculated to *Shigella-Salmonella* agar and common agar culture of enteric bacterial pathogens, including *Shigella*, *Salmonella*,

and *Escherichia coli*. Slide agglutination tests were used to identify the suspected bacteria and later the serotype of *Salmonella*. As the investigation proceeded, other workers were learned to have sought treatment at a second local hospital.

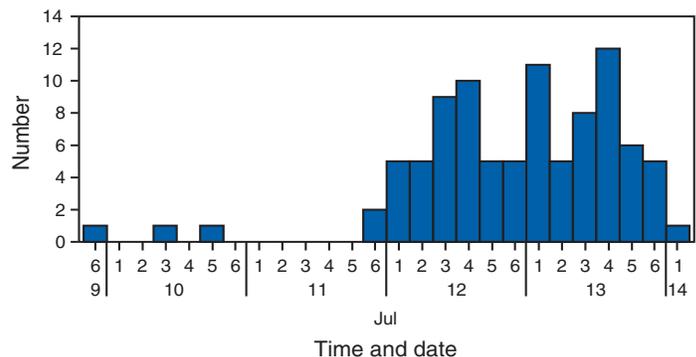
A case-control study was conducted to identify the probable vehicle of transmission; 92 ill workers from the two hospitals were selected as a convenience sample, and 100 factory workers with no symptoms of gastroenteritis were selected as controls. Controls lived in the same dormitory or were employed in the same workshop as the ill patients. Ill workers and controls shared similar demographic characteristics. During July 13–15, the workers were administered a standard questionnaire that collected demographic information and asked to state where and what they had eaten at each meal during July 11–13. Because patients reportedly ate all their recent meals in the factory cafeteria and drank only boiled water, the investigation focused on foods served in the cafeteria. Respondents were asked to identify which foods they had eaten for breakfast, lunch, and dinner and to report symptoms of gastroenteritis. Frequencies of exposure of ill workers and controls were compared for all meals. For meals associated with illness, exposures of different foods served were compared among patients and controls. Respondents who did not answer a specific question were not included in the analysis for that exposure. In addition, a field survey was conducted to identify whether anything had happened in the factory cafeteria that was associated with the outbreak, especially in the environment of the cafeteria and the food preparation process.

## Results

Of approximately 2,000 factory workers who worked during the 3-day outbreak, 197 (10%) had an illness consistent with the case definition. An additional two family members who also ate in the factory cafeteria became ill. Stool specimens from 44 (31%) of 142 ill workers yielded *Salmonella enterica* serotype Enteritidis. Of 92 patients interviewed in the case-control study, the most common clinical symptoms were diarrhea (80 [87%]), abdominal pain (72 [78%]), fever (61 [66%]), nausea (26 [28%]), and vomiting (17 [18%]). Onset of illness time was clustered from midnight July 11 through midnight July 13 (Figure). Patients' ages varied (range: 17–50 years; median: 25 years) and reflected the age distribution of the factory workforce. Between one and three cases occurred in each of the factory's 100 dormitories, each of which housed 15–20 workers.

A comparison analysis indicated that eating breakfast in the factory cafeteria during July 11–13 was significantly associated with having gastroenteritis (odds ratio [OR] range: 3.5–7.5) (Table 1). Eating lunch or dinner on these

**FIGURE. Number\* of cases of gastroenteritis among factory workers, by time† and date of illness onset — Huizhou City, Guangdong Province, China, July 9–14, 2004**



\* N = 92.

† 1 = 12:00 a.m.–3:59 a.m.; 2 = 4:00 a.m.–7:59 a.m.; 3 = 8:00 a.m.–11:59 a.m.; 4 = 12:00 p.m.–3:59 p.m.; 5 = 4:00 p.m.–7:59 p.m.; and 6 = 8:00 p.m.–11:59 p.m.

days was not associated with illness. Of 92 ill workers, 84 (91%) ate breakfast at least once during July 11–13. Time intervals between eating breakfast and onset of illness varied (range: 12–54 hours).

Eight food items were served each day at breakfast: cake, bread, congee (i.e., rice porridge), steam bread, meat-stuffed steam patties, fried rice, fried noodles, and boiled noodles. Eating cake, bread, or congee was associated with illness (Table 2). These three foods were not served at either lunch or dinner. The same cake was served on all 3 days and had the highest OR (OR = 19.0; 95% confidence interval [CI] = 7.4–47.0), whereas bread was associated with illness only on July 12 (OR = 8.9; CI = 2.9–27.0). On all 3 days, the OR for congee was lower (OR = 3.6; CI = 2.0–6.6) than that for cake

**TABLE 1. Number and percentage of workers exposed who ate meals at a factory cafeteria, by meal and date — Huizhou, Guangdong Province, China, July 11–13, 2004**

Meal/Date	No. of respondents		% exposed		OR*	(95% CI)†
	Case	Control	Case	Control		
<b>Breakfast</b>						
July 11	61	84	72	43	3.5	(1.7–7.0)
July 12	82	98	90	55	7.5	(3.3–17.0)
July 13	44	83	77	48	3.7	(1.6–8.3)
<b>Total</b>	<b>92</b>	<b>100</b>	<b>91</b>	<b>59</b>	<b>7.3</b>	<b>(3.0–18.0)</b>
<b>Lunch</b>						
July 11	58	82	64	80	0.4	(0.2–0.9)
July 12	79	93	77	77	1.0	(0.2–2.2)
July 13	28	64	61	67	0.8	(0.3–2.1)
<b>Total</b>	<b>92</b>	<b>100</b>	<b>80</b>	<b>81</b>	<b>1.0</b>	<b>(0.4–2.1)</b>
<b>Dinner</b>						
July 11	59	76	68	68	1.0	(0.4–2.1)
July 12	67	87	73	78	0.8	(0.3–1.7)
July 13	18	56	33	66	0.3	(0.01–0.8)
<b>Total</b>	<b>92</b>	<b>100</b>	<b>82</b>	<b>77</b>	<b>1.3</b>	<b>(0.6–2.8)</b>

\* Odds ratio.

† Confidence interval.

**TABLE 2. Number and percentage of workers exposed to *salmonellae* who ate breakfast at a factory cafeteria, by type of food eaten and date — Huizhou, Guangdong Province, China, July 11–13, 2004**

Food/Date	No. of respondents		% exposed		OR*	(95% CI†)
	Case	Control	Case	Control		
<b>Cake</b>						
July 11	27	32	37	6	8.8	(1.7–45.0)
July 12	69	53	41	8	8.4	(2.5–30.0)
July 13	34	39	59	0	∞	p<0.01
<b>Total</b>	<b>92</b>	<b>100</b>	<b>54</b>	<b>6</b>	<b>19.0</b>	<b>(7.4–47.0)</b>
<b>Bread</b>						
July 11	27	31	22	10	2.7	(0.5–16.0)
July 12	69	53	42	8	8.9	(2.9–27.0)
July 13	34	39	26	10	3.2	(0.8–14.0)
<b>Total</b>	<b>92</b>	<b>100</b>	<b>37</b>	<b>10</b>	<b>5.3</b>	<b>(2.4–12.0)</b>
<b>Congee</b>						
July 11	27	78	31	48	3.7	(1.2–12.0)
July 12	69	67	53	43	2.6	(1.2–5.5)
<b>Total</b>	<b>92</b>	<b>100</b>	<b>62</b>	<b>31</b>	<b>3.6</b>	<b>(2.0–6.6)</b>
<b>Steam bread</b>						
July 11–13	92	100	15	10	1.6	(0.78–3.8)
<b>Steam patty</b>						
July 11–13	92	100	12	12	1.0	(0.4–2.4)
<b>Fried rice</b>						
July 11–13	92	100	20	11	2.0	(0.9–4.4)
<b>Fried noodle</b>						
July 11–13	92	100	45	50	0.8	(0.5–1.4)
<b>Boiled noodle</b>						
July 11–13	92	100	13	15	0.9	(0.4–1.9)

\*Odds ratio.

†Confidence interval.

(OR = 19.0; CI = 7.4–47.0). The bread and cake were baked on the evening of July 10 and first served on July 11; they were then stored together in the same container. The bread was used up after breakfast on July 12 and replaced with newly baked bread on July 13. Cake that was left over on July 12 was served again on July 13. Congee was prepared fresh daily and was not in contact with the bread or cake. Flies were present in the kitchen, and food handlers seldom washed their hands while working.

To understand how three different foods could be associated with a single outbreak, investigators stratified the analysis of these three foods, comparing them alone and in combination to a single reference exposure (i.e., workers who had not eaten any of the three foods at any breakfast). This analysis indicated that cake eaten on any of the 3 days and bread served on July 12 were associated with illness (Table 3). Congee alone had no association with illness when eaten without cake but an OR of 53 if eaten with cake.

The cake and bread were baked at midnight July 10. Sela oil (a mixture prepared from raw eggs, sugar, vinegar, and water) was poured over the baked cake. On July 10 at midnight, the Sela oil was heated at approximately 104°F (40°C) and stored at room temperature (77°F–86°F [25°C–30°C]) for 3 hours before it was poured on the cake. Then the cake was stored at room temperature for another 4 hours until breakfast.

At breakfast, the cake and bread were placed on the same serving platter. After breakfast, the cake and bread were placed together in an open container, stored at room temperature for another 24 hours, and served for breakfast on July 12. The bread was completely eaten on July 12, but leftover cake was served on July 13. Congee was made fresh each morning by boiling rice in water for 1 hour and served while still hot. No cake or bread remained for culture. All eggs used to make the Sela oil were consumed before samples could be collected.

*Salmonella enterica* serotype Enteritidis was isolated from the stool specimens of 10 (33%) of 30 food handlers. Of the 10 food handlers infected with *S. enteritidis*, six (60%) had gastroenteritis (attack rate: 20%). Swabs from the hands of one food handler also yielded *S. enteritidis*.

## Discussion

The investigation indicated that an outbreak of *S. enterica* serotype Enteritidis resulted from consumption of an unusual food vehicle (i.e., cake) that had been contaminated from a more typical source (i.e., raw eggs). Sela oil poured on the cake was probably responsible for the initial contamination, and the cake was the source of the infection. The high risk for illness from eating both cake and congee, compared with the absence of risk for eating congee alone, indicates that the cake was the source of the infection. The congee might have had a synergistic effect on the occurrence of illness. The method of preparing congee (boiling rice in water for 1 hour) would not permit salmonella survival to occur once, let alone in three batches on 3 consecutive days. However, congee has a relatively high pH (6.4) and could neutralize stomach acid, thus permitting salmonellae from cake to reach the small intestine. In addition, congee could speed gastric emptying, leading to more of the ingested dose of organisms reaching the small intestine.

*S. enteritidis* was probably transferred from the cake to the bread by contact with a common serving platter or utensil, the hands of a kitchen worker, or flies. Storage for a sufficient time at room temperature then facilitated multiplication of *S. enteritidis* on the bread. Cross contamination without multiplication of *S. enteritidis* probably did not occur because this would have caused infection on any or all of the 3 days that the cake was served.

The key event in the outbreak was the preparation of the Sela oil. After initial contamination from either raw eggs or another source, both suitable temperature and nutrition were available for 3 hours for salmonellae to multiply before application to the surface of the cake. Once the oil was on the cake, suitable temperatures for growth of *S. enteritidis* continued for another 4 hours. By the time the cake was sold at breakfast

**TABLE 3. Stratified analysis comparing cake eaten on any of 3 days to bread eaten on July 12 and congee eaten during July 11–13, 2004 — Huizhou City, Guangdong Province, China**

Cake and bread eaten on July 12					
Cake	Bread	Case	Control	OR*	(95% CI†)
Yes	Yes	9	1	37	(4.4–826.0)
Yes	No	41	5	34	(11.0–111.0)
No	Yes	20	3	28	(6.9–129.0)
No	No	22	91		Reference
Cake and congee eaten during July 11–13					
Cake	Congee	Case	Control	OR*	(95% CI†)
Yes	Yes	39	2	53	(11.0–343.0)
Yes	No	11	4	7.5	(1.9–31.0)
No	Yes	18	29	1.7	(0.7–3.8)
No	No	24	65		Reference

\*Odds ratio.

†Confidence interval.

on July 11, it likely was contaminated. Additional incubation of the same cake for 24–48 hours is consistent with the continuing association of illness with the cake for 3 days.

The original contamination of the Sela oil with *S. enteritidis* probably came from the raw eggs. Intact shell eggs are known to become infected with *S. enteritidis* by vertical transmission (1–3). *S. enteritidis* is the only salmonella in chicken embryo that can be found inside eggs. One infected egg typically contains 10–20 *S. enteritidis* bacterial cells, but only a few eggs per 1,000 or even 10,000 become infected (3). Infected eggs are the most likely source of this outbreak. Other less likely possible sources of infection are a food handler having contaminated hands, flies, or other ingredients in the Sela oil.

Transmission of *S. enteritidis* in association with intact chicken eggs was first recognized in the United States in 1986 (4,5). Since then, it has been recognized worldwide (6,7). This is the first outbreak of *S. enteritidis* in China that has been attributed to raw eggs. However, salmonella surveillance and other outbreak reports suggest that *S. enteritidis* outbreaks occur more commonly than has been recognized previously. At approximately the same time as this outbreak, gastroenteritis outbreaks attributed to *S. enteritidis* occurred in two nearby cities (Hong Kong and Guangzhou City, Guangdong Province). Investigation of the Hong Kong outbreak implicated a mango pudding made from raw eggs (8). The Guangzhou outbreak was not investigated. In Hong Kong, salmonella surveillance has indicated that *S. enteritidis* isolations doubled during 1995–2000 whereas other serotypes remained stable (9). In 10 of China's 31 provinces that have conducted food surveillance, *S. enteritidis* is among the top seven salmonella serotypes isolated (10). In 2000, *S. enteritidis* was a leading cause of foodborne salmonellosis in the United States (11,12).

The findings in this report are subject to at least four limitations. First, no cake or eggs remained available for testing. Second, certain workers could not recall exactly which foods they

had consumed. Third, because of time constraints, ill patients and controls were selected by convenience and might not be representative of all persons. Finally, other possible routes of contamination (e.g., food handlers) could not be excluded.

## Conclusion

As a result of this investigation, changes were suggested in the methods of preparing Sela oil or any other sauce made from uncooked eggs. Heating the Sela oil to pasteurization temperatures (132.8°F [56°C]) for 30 minutes during preparation and storage of the prepared Sela oil or sauce under refrigeration should reduce the risk for salmonellosis. Food handlers should be instructed that intact fresh eggs might harbor *S. enteritidis*. Because direct use of raw eggs without cooking might cause salmonella contamination of food, food handlers should apply these guidelines to all foods made from eggs and store foods prepared with eggs under refrigeration. Researchers and health-care workers should investigate whether such outbreaks occur more frequently than has been reported previously.

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## Varicella Outbreak Among Primary School Students — Beijing, China, 2004

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### Abstract

**Introduction:** On June 9, 2004, a varicella outbreak was reported in a Beijing primary school affecting approximately 80% of children in one preschool classroom. An outbreak investigation was initiated to identify factors contributing to the high rate of transmission and to assess the effectiveness of control measures.

**Methods:** A varicella case was defined as onset of a generalized, vesicular pruritic rash lasting >4 days in a student at the school during January 1–June 26, 2004. Parents of all students in the four lowest grades (K–2) were questioned concerning varicella illness before January 1, 2004. Exposure and vaccination histories of 111 ill students and 120 control students with no history of varicella were compared.

**Results:** During January 1–June 26, 2004, of 1,407 students, 138 (9.8%) had varicella; 488 (35%) K–2 students had no history of varicella before the outbreak. In five classrooms in which attack rates (ARs) were high (>40%), a primary-case student had remained in school 2 days while ill with a rash. The secondary attack rate (SAR) in these classrooms was 21%, compared with 1.7% in classrooms in which the first ill student was sent home immediately (risk ratio [RR] = 10; 95% confidence interval [CI] = 3.7–29.0). A total of 111 (70%) ill students rode the school bus daily, compared with 120 (33%) control students (odds ratio [OR] = 4.9; CI = 2.7–9.0). A total of 73 (33%) ill students had a history of varicella vaccination before January 1, 2004, compared with 32 (69%) control-students (OR = 0.22; CI = 0.08–0.59).

**Conclusion:** Students who were not excluded from school on the first day of rash were key contributors to the spread of varicella in their classrooms. High susceptibility to varicella at school entry indicates that vaccination of susceptible students might be the only effective measure to control this recurrent problem.

### Introduction

Varicella has been a nearly universal disease of childhood. In temperate climates, nearly 90% of children had varicella by age 15 years before vaccine became available (1). Before 1995, when vaccine was licensed, an estimated 4 million cases of varicella occurred each year in the United States; approximately 100 patients died and 10,000 persons were hospitalized annually because of varicella and related complications (2). Because varicella is not a notifiable disease in China, statistics concerning hospitalization and death attributable to varicella are not available. However, since January 1, 2004, varicella outbreaks have been reported to the public health emergency reporting system. During January–June 2004, a total of 64 varicella outbreaks were reported, accounting for 20% of all communicable disease outbreaks reported in China; 58 (91%) varicella outbreaks occurred in schools. Varicella vaccine has been available commercially since 2003, but China has no programs to support routine varicella vaccination.

On June 9, the Chinese Center for Disease Control and Prevention (China CDC) was notified of a varicella outbreak in a primary school in a suburb of Beijing, affecting approximately 80% of children in certain classes. Since the school opened in 1999, varicella outbreaks have disrupted activities every year, despite a school policy to isolate students with a rash at home for 7 days. An outbreak investigation was initiated to identify factors contributing to the high rate of transmission and assess the effectiveness of control measures.

### Methods

A varicella case was defined as a generalized, vesicular pruritic rash in a school student lasting >4 days with onset during January 1–June 26, 2004. To identify cases, investigators reviewed records kept by the school doctor and absentee records kept by teachers, and teachers and doctors were questioned concerning rash illness among students. A questionnaire was

sent to the parents of any student identified as having a rash illness to collect information concerning the student's symptoms and the results of any physician consultation. Case determination was based on the results of all three sources. A primary case was defined as the first varicella case in a student with onset of rash to appear in a classroom. A secondary case was defined as any varicella case in a student with onset of rash 11–19 days after the onset of a primary case in the same classroom. A coprimary case was defined as a varicella case in a student with onset of rash  $\leq 10$  days after occurrence of a primary case in the same classroom. Secondary attack rates (SARs) were calculated by dividing the number of secondary cases by all students with no history of current or previous varicella minus those with primary and coprimary cases. SARs for classrooms in which the student with the primary case had been isolated immediately were compared with SARs for classrooms in which the student with the primary case had not been promptly isolated.

A case-control study was conducted; participants included all 123 students with varicella in grades K–2 and 123 controls selected randomly from all 365 students in grades K–2 with no history of current or previous varicella. Self-administered questionnaires were sent to parents of all 635 students in grades K–2. Questionnaires requested demographic information, illness characteristics, varicella vaccination history (including dates and place of vaccination), previous varicella disease history, and exposures to varicella. Parents were contacted by telephone to obtain missing information.

Responses were obtained for 111 (90%) of 123 students with varicella in grades K–2. The exposure histories of these students were compared with those of 120 control students. The number of controls selected for each classroom was proportionate to the number of varicella cases that occurred in the classroom (i.e., frequency matched). In two classrooms with high attack rates (ARs), an insufficient number of control students was available, and additional control students were selected at random from other classes in the same grade.

## Results

During January 1–June 26, of 1,407 students, 138 (10%) had a rash illness consistent with the case definition of varicella. Cases were identified in three ways: 1) the school doctor examined 77 students and recorded their temperatures; 2) a doctor in the community examined another 42 students; and 3) 19 students were identified from responses to parent questionnaires. In addition to a characteristic rash, 64 (46%) students had temperature  $\geq 99.5^\circ\text{F}$  ( $\leq 37.5^\circ\text{C}$ ); of these, 36 (56%) had a temperature  $\geq 100.4^\circ\text{F}$  ( $\geq 38^\circ\text{C}$ ). Four (2.9%) students

had a secondary skin infection. Cases occurred in all eight grades and in 21 (60%) of 35 classrooms. Higher ARs were reported among students aged 3–8 years in the four lower grades (K–2) (Table). Although cases began to appear in January, the outbreak was not evident until mid-April, peaked in May, and ended with the closing of school on June 30. Distinct peaks of cases occurred at 15-day intervals during April–June (Figure 1). Over the course of this outbreak, teachers' records indicated that 1,090 days of absenteeism resulted from varicella illness, equivalent to 8 days of school missed per ill child.

Further analysis was limited to 488 (77%) of 635 K–2 students in 15 classrooms who did not have varicella before January 1, 2004. The AR in this group was 25%; analysis of ARs by classroom identified two distinct groups: 10 classrooms with ARs  $< 15\%$  and five classrooms with ARs that were substantially higher (40%–80%). In all classrooms with ARs  $> 40\%$ , one or more ill students had remained in school  $\geq 2$  days while ill with a rash. These classrooms had new teachers who were not familiar with the school's isolation policy. In

**TABLE. Number of varicella cases among primary-school students, by grade levels — Beijing, China, January 1–June 26, 2004**

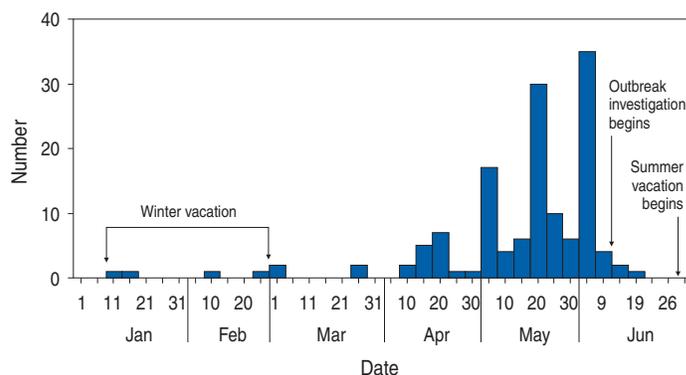
Grade	Age group (yrs)	No. of students	No. of cases	AR* (%)
K <sup>†</sup>	3–5	63	7	11.0
P <sup>§</sup>	5–6	194	68	35.0
1st	6–7	213	16	7.5
2nd	7–8	165	32	19.0
3rd	8–9	210	3	1.4
4th	9–10	214	7	3.3
5th	10–11	185	3	1.6
6th	11–12	163	2	1.2
<b>Total</b>	<b>3–12</b>	<b>1,407</b>	<b>138</b>	<b>9.8</b>

\* Attack rate.

<sup>†</sup> Kindergarten.

<sup>§</sup> Prefirst (between K and first grade).

**FIGURE 1. Number of varicella cases detected among children in a primary school, by date of rash onset — Beijing, China, January 1–June 26, 2004**

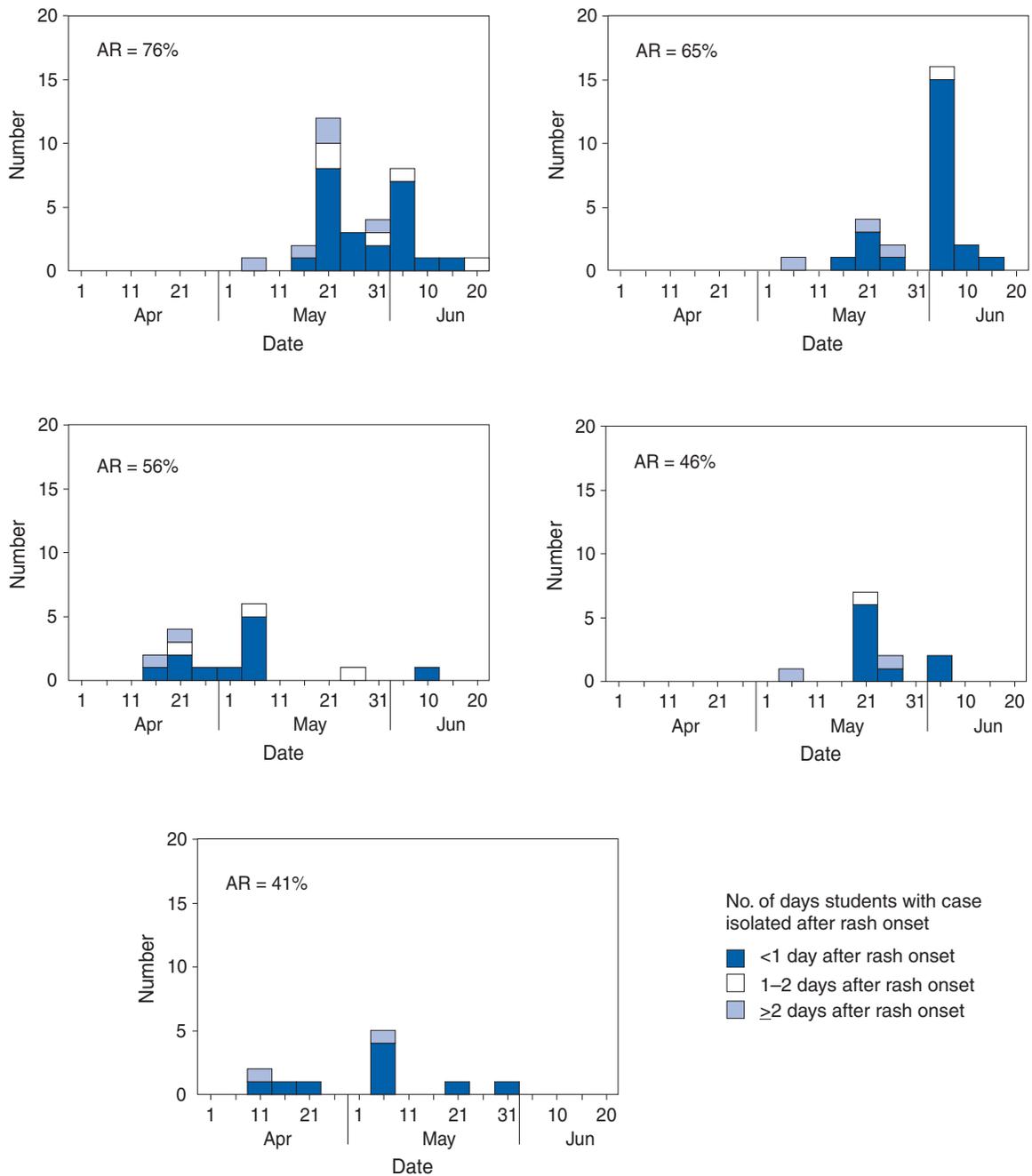


each of these five classrooms, outbreaks began with a student who was allowed to stay in school for  $\geq 2$  days while having a vesicular rash. Lax isolation continued during the second generation of cases in these classroom outbreaks, and tertiary cases followed (Figure 2).

In the five classrooms in which the student with the primary case was isolated only after  $\geq 2$  days of rash, the SAR

was 21% (34 of 163) compared with 1.7% (four of 235) in seven classrooms in which the first student with varicella rash was isolated immediately (in three classrooms, no cases occurred) (risk ratio [RR] = 10; 95% confidence interval [CI] = 3.7–29.0). In three classrooms in which a single student with a primary case was not isolated, the SAR was 26% (29 of 111) (RR = 12; CI = 4.4–34.0) compared with those

**FIGURE 2. Number of varicella cases for five primary-school classrooms with attack rate (AR) of >40%, by date of rash onset — Beijing, China, April 1–June 20, 2004**



classes for which cases were isolated immediately. In the two classrooms with several coprimary cases, the SAR was 9.6% (five of 52) compared with the classrooms with only isolated cases (RR = 5.2; CI = 1.5–19). Finally, the five classes in which a single student with a primary case was not isolated did not differ from other classrooms regarding crowding, availability of handwashing, activities involving close personal contact, or the sharing of items that might act as fomites (e.g., towels, eating utensils, and cups).

Complete responses were obtained from 111 (90%) students with varicella and from 120 (98%) control students. The case-control study in grades K–2 demonstrated that 78 (70%) ill students used the school bus every day, compared with 39 (33%) control students (odds ratio [OR] = 4.9; CI = 2.7–9.0); 24 (33%) ill students had a history of varicella vaccination before January 1, 2004, compared with 22 (69%) controls (OR = 0.2; CI = 0.1–0.6). This excludes responses for 38 ill students and 88 controls whose parents could not provide the date and place of varicella vaccination or were otherwise uncertain. Stratification of bus riding and vaccination by classrooms or grade resulted in adjusted ORs that were not appreciably different from the crude OR and that indicated no difference in effect between high- and low-incidence classrooms (classroom-adjusted OR = 4.3; CI = 2.3–8.5 for bus riding, and 0.24; CI = 0.1–0.7 for vaccination). Parent questionnaires indicated that only two ill students were known to have had contact with an ill neighbor before onset of varicella rash.

## Discussion

High ARs (40%–80%) in classes from which students with rash were not sent home immediately are characteristic of transmission among siblings in the home setting and in primary schools before availability of vaccination (1). In this outbreak, two factors contributed to high ARs. First, 77% of K–2 students had no evidence of protection by natural immunity. Second, ill students were not isolated promptly, leading to continuing exposure to varicella for several days and ARs >40%. The estimated 77% susceptibility for children aged 3–8 years in this school is consistent with the 30% prevalence of varicella infection in children in Shanghai aged 3–6 years in 1998 (3).

A factor that could contribute to high susceptibility for varicella illness is the number of families with only one child as a result of China's one-child-per-family policy, which has been in effect since 1979. By 2001, of approximately 291 million families in China, approximately 130 million (44%) had only one child, and 102 million (35%) had two children (4). Preschool children often lack older siblings who could

acquire varicella at school or in the community and subsequently infect these more sequestered toddlers and preschoolers at home. Moreover, child care centers and other concentrations of susceptible infants and toddlers are rare in China. Under Chinese law, mothers receive 6 months of paid postmaternity leave to care for their infants. Thereafter, working parents customarily entrust their children to grandparents or other older relatives until age 3 years, when the children are old enough to attend kindergarten. Consequently, the possibility of exposure of preschool children to natural varicella in the home or community is substantially reduced, resulting in high prevalence of susceptibility at school entry.

Similar high rates of susceptibility to varicella might be widespread among students in lower grades in China. Vaccinating susceptible students at school entry might be the most effective control method. To be effective, vaccination coverage will need to be >95% because transmission might be sustained in schools with vaccination coverage of 67%–95%.

Other recommended measures include home isolation of students with a rash (5,8). In this outbreak, prompt isolation was associated with lower ARs. However, a high SAR has been reported in a school despite universal isolation from class at rash onset; in that investigation, because ill students in all classrooms were isolated promptly, the effect of isolation could not be compared with the absence of isolation (9). Isolation is only a temporary measure that simply delays but does not prevent varicella illness (1).

To stop this outbreak, investigators recommended adding vaccination to isolation. However, because the investigation was conducted near the end of the term, the school could not implement this recommendation before the school year ended. Because varicella outbreaks in schools are a common occurrence in China, a more effective plan might be to vaccinate susceptible students when they begin school rather than to isolate them after an outbreak has begun. Beginning in 2005, students at this school will be vaccinated at the beginning of the school year.

In 2003, the Chinese Food and Drug Administration licensed the Oka-strain varicella vaccine for children aged >12 months (11). However, varicella vaccine is not included in national or provincial vaccination programs. A major obstacle to widespread varicella vaccination in China is the high cost of this vaccine, which is 10 times more expensive than rubella vaccine and 75 times more expensive than measles vaccine. As of 2002, only 131,730 (23%) children in Shanghai aged <6 years had received varicella vaccine (10). Another possible contributing factor is that parents might not be aware of the availability of vaccine or the need to isolate ill children at home.

The findings in this report are subject to at least three limitations. First, information on vaccination and previous history of varicella disease is subject to recall bias and other reporting errors on the part of the parents. Vaccination history in particular suffered from a high nonresponse rate or responses of “can’t remember” or “unknown.” Accordingly, only the protective effect is discussed and not vaccine effectiveness or effects on classroom-specific ARs. Second, because 94% of controls and all ill students participated in the study, selection bias was likely minimal. Finally, why two classrooms in different grades had multiple coprimary cases is unknown. Exposure in these classrooms might have led to an earlier, mild primary case that was missed by the teachers and thus was not identified. Mild varicella with sparse rashes can occur in vaccinated children; these mild infections can be transmitted to others and have been implicated in transmission in other school outbreaks (5,7). When cases are missed by school staff and parents, isolation measures are not taken.

## Conclusion

Although no deaths or severe complications occurred in this outbreak, varicella is a highly contagious disease that can be fatal (11). In this outbreak, the low level of naturally acquired immunity was the principal factor underlying the high ARs recorded. Failure to isolate ill students also contributed to high ARs in five classrooms. Vaccination was available and protective, but the decision to vaccinate was left to parents.

Universal vaccination at school entry might be the only reliable method of controlling varicella. In addition to preventing deaths, vaccination might also reduce hospitalizations from other varicella-related complications (12). More parents would be likely to have their children vaccinated if they understood the effectiveness of vaccine and the consequences of varicella illness. A stronger policy to encourage varicella vaccination in schools in China should be developed. Careful assessment of the cost of vaccine compared with the cost of

disruption of school activities would be valuable in assisting provinces, educational authorities, and individual schools in developing a vaccination policy.

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