

Fruit bats in the genus *Rousettus* are widely distributed throughout Southeast Asia, South China, and the entire Indian subcontinent and have had positive serologic results for Ebola viruses in these regions (7–9), indicating that these bats play a role in the circulation of filoviruses in Asia. The possibility of new emerging filovirus-associated diseases in the continent emphasizes the need for further investigation of these animals.

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## Increase in Lymphadenitis Cases after Shift in BCG Vaccine Strain

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**To the Editor:** Bacillus Calmette-Guérin (BCG) vaccine is one of the most commonly used vaccines for tuberculosis (TB) worldwide (1). The original BCG strain was developed in 1921. Numerous strains have since been developed, and 5 strains, including Danish SSI 1331 (Statens Serum Institute, Copenhagen, Denmark), account for >90% of BCG vaccine used. Each strain has unique characteristics and a different reactogenicity profile (2). The most common severe adverse events related to BCG vaccination are nonsuppurative and suppurative lymphadenitis.

In the country of Georgia, BCG vaccine is administered routinely to infants (estimated coverage 96%); the National Center for Disease Control and Public Health receives its vaccine supply from the United Nations Children’s Fund and is responsible for countrywide distribution. Before 2012, Russian BCG-I (Bulbio, Sofia, Bulgaria) and Danish SSI 1331 strains were used (~50% each). Shortly after a change to exclusive use of the Danish 1331 strain during 2012–2013, an increasing number of BCG-related lymphadenitis cases were reported to the National Center for Tuberculosis and Lung Diseases (NCTLD). We aimed to quantify the increase in cases of BCG lymphadenitis and to evaluate clinical management of the cases. The Institutional Review Boards of Emory University (Atlanta, GA, USA) and the National Center for Disease Control and Public Health approved the study.

Medical chart abstraction was conducted for all infants with BCG lymphadenitis either reported to the NCTLD or found by inquiry of pediatricians at the largest children’s hospital in the country during January 2012–July 2013. We used national surveillance data to obtain the number of live-born infants.

BCG vaccine is given intradermally over the deltoid muscle on the left arm to infants within 5 days after birth at the maternity hospital. BCG lymphadenitis was clinically

defined as ipsilateral axillary lymph node enlargement developing within 2 years after vaccination. If the patient was brought for care to the NCTLD, a sample was obtained through aspiration for acid-fast bacilli smear; culture; and, if necessary, drug-susceptibility testing (3). Although treatment was at the discretion of clinicians, national TB program treatment guidelines did not include management of BCG-related adverse events.

During 2007–2011, six cases of BCG lymphadenitis were reported to the NCTLD. During the 19-month study period, we found 23 cases of BCG lymphadenitis: 15 reported to the NCTLD and 8 diagnosed at the Tbilisi children's hospital and ascertained by inquiry (Table). In all cases, a 0.05-mL dose of Danish SSI BCG vaccine (series 111003A and 111021A) was used. The 15 infants from the NCTLD were vaccinated at 8 maternity hospitals: 6 in Tbilisi and 2 in outside regions. A total of 14,230 live-born infants were registered at hospitals reporting BCG lymphadenitis in 2012. Based on the following calculation—16 cases/(14,230 live-born infants × 96% vaccination coverage)—the estimated prevalence of BCG-related suppurative lymphadenitis in 2012 was 1.12 cases per 1,000 infants.

Median time from BCG vaccination to onset of lymphadenitis was 5 months (range 1–15 months). No patients had systemic signs or symptoms.

After a change in BCG vaccine strains in Georgia to the exclusive use of BCG SSI vaccine, we found a substantial increase in the known prevalence of BCG-associated lymphadenitis. We found 23 cases of BCG-associated lymphadenitis during a 19-month period, ≈4 times the number of reported cases during the prior 5 years, when multiple vaccine strains were used. The estimated prevalence of suppurative lymphadenitis (1.12 cases/1,000 infants) was higher than the expected rate of <1/1,000 given by the manufacturer (4). Our rate is probably an underestimation, given a mainly passive system of surveillance. Prior studies in various countries have similarly shown increased BCG lymphadenitis with the introduction of the BCG SSI vaccine (5–7).

We found different approaches to treatment of BCG-associated lymphadenitis depending on where care was received. Physicians at the NCTLD prescribed first-line anti-TB medications, including pyrazinamide, whereas patients managed at the children's hospital were treated with either surgical excision or a conservative watch-and-wait approach. Although no official treatment guideline exist for suppurative BCG-associated lymphadenitis, a recent meta-analysis found no benefit to using anti-TB medications (8). Furthermore, *Mycobacterium bovis* is inherently resistant to pyrazinamide. A randomized controlled trial found needle aspiration to improve rates and speed

**Table.** Characteristics of 23 infants with BCG lymphadenitis, Georgia, January 2012–July 2013\*

| Hospital, infant no.      | Characteristic† |               |                         |                                 |         |         |            |                    |
|---------------------------|-----------------|---------------|-------------------------|---------------------------------|---------|---------|------------|--------------------|
|                           | Sex             | Date of birth | Age at presentation, mo | Size of axillary lymph node, mm | Culture | Surgery | Drugs used | Treatment outcome‡ |
| NCTLD, n = 15             |                 |               |                         |                                 |         |         |            |                    |
| 1                         | F               | 2012 Jan 9    | 5                       | 20                              | Pos     | No      | R, I, P    | Completed          |
| 2                         | M               | 2012 Dec 19   | 5                       | 14                              | ND      | No      | R, I, P    | Completed          |
| 3                         | F               | 2012 Jul 2    | 9                       | 40                              | NA      | No      | R, I, P    | Completed          |
| 4                         | F               | 2012 May 31   | 12                      | 28                              | NA      | No      | R, I, P    | Completed          |
| 5                         | M               | 2012 Jul 25   | 4                       | 15                              | NA      | No      | R, I, P    | Computed           |
| 6                         | F               | 2012 Aug 16   | 1                       | 15                              | NA      | No      | R, I, P    | Defaulted          |
| 7                         | M               | 2012 Feb 7    | 2                       | 22                              | NA      | No      | R, I, P    | Completed          |
| 8                         | M               | 2011 Nov 28   | 3                       | 24                              | NA      | No      | R, I, P    | Defaulted          |
| 9                         | M               | 2012 Jul 9    | 2                       | 18                              | NA      | No      | R, I, P    | Defaulted          |
| 10                        | M               | 2012 Aug 7    | 7                       | 23                              | NA      | Yes     | R, I, E    | Unknown            |
| 11                        | M               | 2012 May 10   | 4                       | 56                              | NA      | No      | R, I, P    | Completed          |
| 12                        | M               | 2012 Nov 13   | 6                       | 60                              | NA      | No      | R, I, P    | Completed          |
| 13                        | M               | 2012 Oct 1    | 2                       | 11                              | Pos     | Yes     | R, I       | Completed          |
| 14                        | M               | 2012 Feb 22   | 9                       | 24                              | NA      | No      | R, I, P, E | Completed          |
| 15                        | F               | 2012 Feb 24   | 5                       | 15                              | NA      | Yes     | R, I, P    | Complete           |
| Pediatric hospital, n = 8 |                 |               |                         |                                 |         |         |            |                    |
| 1                         | F               | 2013 Jan 28   | 4                       | 25                              | ND      | Yes     | None       | Unknown            |
| 2                         | M               | 2012 Jun 15   | 8                       | 20                              | ND      | Yes     | None       | Unknown            |
| 3                         | M               | 2012 Mar 25   | 15                      | 17                              | ND      | Yes     | None       | Unknown            |
| 4                         | M               | 2012 Jan 28   | 6                       | 21                              | ND      | Yes     | None       | Unknown            |
| 5                         | M               | 2013 Jan 28   | 4                       | 21                              | ND      | Yes     | None       | Cured              |
| 6                         | M               | 2012 Jun 28   | 8                       | 25                              | ND      | Yes     | None       | Unknown            |
| 7                         | M               | 2013 Mar 28   | 5                       | 15                              | ND      | No      | None       | Cured              |
| 8                         | F               | 2013 Jun 8    | 1                       | 17                              | ND      | No      | None       | Cured              |

\*BCG, bacillus Calmette-Guérin vaccine; Pos, positive; E, ethambutol; I, isoniazid; P, pyrazinamide; R, rifampin; NA, not available; ND, not done; NCTLD, National Center for Tuberculosis and Lung Diseases.

†For all patients, type of BCG strain used was Danish SSI (Statens Serum Institute, Copenhagen, Denmark).

‡Defaulted is an outcome definition applied by the tuberculosis program when a patient misses treatment for 2 consecutive months and is considered lost to follow-up.

of healing of suppurative nodes and is the only evidence-based effective treatment (9). Surgical excision remains controversial because of potentially high rates of significant scarring (10). For nonsuppurative lymphadenitis, a watch-and-wait approach is recommended because most resolve rapidly (8).

Given our findings, the National TB Program in Georgia subsequently created a management protocol. This protocol recommends no intervention for nonsuppurative lymphadenitis and needle aspiration for suppurative local lymphadenitis.

In summary, we found an increasing rate of BCG-associated lymphadenitis after a shift to exclusive BCG SSI vaccine use in Georgia. Countries with a BCG vaccination policy should have a clear protocol on management of BCG vaccine-related adverse events to avoid inappropriate treatment in children.

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## Fatal Accelerated Cirrhosis after Imported HEV Genotype 4 Infection

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**To the Editor:** Hepatitis E is a viral hepatitis that is endemic in many developing countries. In its classic form, it results from ingesting fecally contaminated water that carries hepatitis E virus (HEV), and it frequently resolves without treatment. When hepatitis E is imported to the United States, it originates mainly from persons who have acquired HEV genotype 1 infection from South Asia (1). We report imported HEV genotype 4 infection (Technical Appendix Figure, panel A) in a patient during which cirrhosis and fatal hepatic decompensation ensued.

The patient was a 68-year-old man of Chinese ethnicity who had been a California resident since 1985. He sought treatment for mild jaundice in April 2013 in Hong Kong, where he had been staying for 7 weeks. Sixteen years before, he had undergone orthotopic liver transplantation at Stanford University Medical Center (Palo Alto, California, USA) for hepatitis B cirrhosis. Since then, he had received entecavir and tacrolimus for maintenance and had been vaccinated against hepatitis A virus. Until his current illness, routine liver function tests had not indicated hepatic dysfunction (values in November 2012: alanine aminotransferase 2 IU/L, aspartate aminotransferase 24 IU/L, alkaline phosphatase 67 IU/L, total bilirubin 0.5 mg/dL).

When the patient returned to the United States, 3 weeks after onset of jaundice, the initial work-up showed the following values: alanine aminotransferase 149 IU/L, aspartate aminotransferase 59 IU/L, alkaline phosphatase 193 IU/L, total bilirubin 2.8 mg/dL (online Technical Appendix Figure, panel B, <http://wwwnc.cdc.gov/EID/article/21/9/15-0300-Techapp1.pdf>). Hepatitis B virus DNA and anti-nuclear antibodies were not detected, and the tacrolimus level was stable. Ultrasound revealed a normal transplanted liver. A liver biopsy specimen showed mild portal, biliary, and lobular inflammation and early biliary injury (Figure,