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References


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Biological Warfare in the 17th Century

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To the Editor: In an article that reviews evidence of a plot to use plague to break the siege of Candia during the Venetian–Ottoman War of the 17th century, Dr. Thalassinos and her colleagues (1) identify an incident previously unknown to historians of biological warfare. However, the authors’ effort to broaden the context for biological weaponry is undermined by a reference to an often repeated allegation for which no credible evidence exists: namely, that during a siege occurring in the Swedish–Russian War of 1710, the Russians catapulted bodies of plague victims into the Swedish-held city of Reval.

Danish historian Karl-Erik Frandsen conducted a careful study of the plague outbreak affecting the Baltic area during 1709–1713 and found no evidence to support this allegation (2). Plague was first detected in Reval on August 10, 1710, while the army from Russia was still approaching the city. Reval was not besieged, and the Russians merely camped outside the city while attempting to isolate it. The army dumped corpses into a stream that flowed into Reval, but evidence does not show that the dead were plague victims, nor does evidence exist that clarifies whether the intent was contamination of the water supply or disposal of bodies. Original accounts provide no evidence to suggest that Russians hurled bodies into the city, much less plague-infected bodies. Frandsen estimates that about three quarters of the 20,000 persons in Reval died during the outbreak (2).

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Intentional introduction of disease has been rare (3). Consequently, the incident identified by Thalassinou and her colleagues arouses readers’ interest and inspires speculation.

References


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Bifidobacterium longum Subspecies infantis
Bacteremia in 3 Extremely Preterm Infants Receiving Probiotics

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To the Editor: Metaanalysis of randomized trials that tested different probiotics showed a reduction of ≈50% in necrotizing enterocolitis and all-cause death in preterm infants (7). Use of probiotics is increasing worldwide (2,3), and cases of probiotic sepsis were not reported among >5,000 infants in an updated review (7).

In Norway, a consensus-based protocol recommending prophylactic probiotic supplementation for preterm infants at highest risk for necrotizing enterocolitis (gestational age <28 weeks, birthweight <1,000 g) was introduced in 2014. After considering the safety profile, we investigated use in preterm infants of a widely used combination of oral probiotics (Infloran; Laboratorio Farmacéutico Specialità Igienico Terapeutiche, Mede, Italy) that contained 10^6 Lactobacillus acidophilus (ATCC 4356) and 10^6 Bifidobacterium longum subspecies infantis (ATCC 15697).

B. longum is a microaerotolerant, anaerobic bacterium susceptible to many antimicrobial drugs (Table). This bacterium is a rare cause of neonatal infections; until 2015, only 2 Bifidobacterium bacteremia cases in premature newborns had been reported (4,5).

A total of 290 extremely preterm infants received oral probiotics during April 2014–August 2015 in Norway. Three patients were given a diagnosis of B. longum bacteremia: 2 patients in a neonatal unit in which 17 patients were given oral probiotics and 1 patient in a neonatal unit in which 31 patients were given oral probiotics (Table).

All 3 infants had respiratory distress syndrome and received mechanical ventilation after birth. Enteral feeding with human milk was begun on day 1. Oral probiotics (½ capsule, 1×/d) were given during the first week of life and increased to 1 capsule/day after 4–7 days.

We identified B. longum in blood cultures by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Billerica, MA, USA). Whole-genome sequencing (MiSeq, Illumina, San Diego, CA, USA) and comparative analysis of nucleotide-level variation by using variant cell format in SAMtools (http://samtools.sourceforge.net) showed that all 3 blood culture isolates and a B. longum strain cultured from an oral probiotic capsule were identical.

Patient 1 had sepsis and severe hypotension 8 days after birth. A blood culture was prepared, and the patient was given antimicrobial drugs and vasoactive support. Abdominal distention, gastric residuals, and feed intolerance developed the next day, but the patient was cardiorespiratory stable. On day 12, abdominal radiographs showed pneumoperitoneum. Surgery showed multiple ileal perforations and bowel necrosis. Histologic analysis showed classical features of necrotizing enterocolitis. The patient received an ileostoma and improved after treatment with antimicrobial drugs. Blood culture was positive for gram-positive rods, which were identified as B. longum. Subsequent clinical course was uneventful.

Patient 2 had apnea, bradycardia, and temperature instability 12 days after birth. A blood culture was prepared, and the patient was given antimicrobial drugs. Blood culture was positive for gram-positive rods, which were identified as B. longum. Use of oral probiotics was discontinued. The patient recovered rapidly, and subsequent clinical course was uneventful.

Patient 3 had sepsis and necrotizing enterocolitis 9 days after birth. Ultrasound showed free abdominal fluid. A blood culture was prepared, and the patient was given antimicrobial drugs. Surgery showed 2 separate bowel perforations, and