Pulmonary Involvement and Leptospirosis, Greece

To the Editor: Since the leptospirosis outbreak associated with pulmonary hemorrhage in Nicaragua in 1995 (1), pulmonary manifestations of leptospirosis are often recognized in many countries; reported incidence has ranged from 20% to 70% (2–4). The severe pulmonary form of leptospirosis is accompanied by pulmonary hemorrhage, which directly results in high death rates (2.5). In Greece (population 11 million), leptospirosis cases in humans occur every year, usually from June to November (summer and autumn), with a peak in August. The annual incidence rate of the disease is 3 cases per 1 million population (6). Clinical presentation varies from a flu-like syndrome to Weil disease, which includes jaundice, renal failure, and hemorrhagic complications. Studies on leptospirosis in Greece have been limited, and no reports have focused on pulmonary involvement.

During 1998–2007, we tested samples from 650 patients with suspected leptospirosis or hemorrhagic fever with renal syndrome (i.e., hantavirus infection). Various hospitals of northern Greece sent these samples to our laboratory (a World Health Organization Collaborating Center for Reference and Research on Arboviruses and Hemorrhagic Fever) for analysis. Because both diseases are endemic to Greece and have similar clinical, epidemiologic, and seasonal characteristics (7), all samples sent to our laboratory for testing either for leptospirosis or for hantavirus infection are always tested for both (8).

Leptospirosis was confirmed for 123 patients, 10 (8.1%) of whom died (Table). For 72 case-patients, paired samples were available. A commercial ELISA (Leptospira IgG/IgM, Institute Virion/Serion GmbH, Würzburg, Germany) was used to detect immunoglobulin (Ig) G and IgM against Leptospira spp. A nested PCR, which amplifies a 289-bp fragment of the 16S rDNA gene, was used to detect bacterial DNA (9). IgM concentrations >20 U/mL indicated acute infection. Samples with borderline results were tested in parallel with a second sample taken from the patient 1 week later. IgG concentrations were considered only for paired samples, and a case was considered as acute leptospirosis when a ≥4-fold titer rise of IgG, or IgG seroconversion, was detected. When samples were taken before the sixth day of illness, initial diagnosis was achieved by PCR. In 6 of 10 fatal cases, leptospirosis was diagnosed only by PCR because antibodies were not detectable. Epidemiologic and clinical information for patients was collected from chart review, following a protocol approved by the medical school review board.

All 123 patients resided in northern Greece. Most (82.1%) were male; patients were 6–83 years of age (me-
Table. Leptospirosis cases and pulmonary involvement, Greece, 1998–2007

| Year | No. cases (no. fatal cases) | No. cases with pulmonary involvement (no. fatal cases) |
|------|-----------------------------|-----------------------------------------------------|
| 1998 | 12 (0)                      | 0 (0)                                               |
| 1999 | 9 (2)                       | 3 (0)                                               |
| 2000 | 7 (1)                       | 1 (0)                                               |
| 2001 | 11 (0)                      | 1 (0)                                               |
| 2002 | 13 (2)                      | 4 (2)                                               |
| 2003 | 13 (1)                      | 6 (1)                                               |
| 2004 | 20 (3)                      | 10 (3)                                              |
| 2005 | 14 (1)                      | 3 (1)                                               |
| 2006 | 17 (0)                      | 5 (0)                                               |
| 2007 | 7 (0)                       | 2 (0)                                               |
| Total| 123 (10)                    | 35 (7)                                              |

Pulmonary involvement seems to be common and associated with a high death rate for patients with severe leptospirosis cases in our setting. Clinicians in Greece should include leptospirosis in the differential diagnosis of syndromes with associated pulmonary manifestations.

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