

Leptospirosis is everywhere, just have to know what to look for. But how?

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Over the past decade, leptospirosis has become increasingly recognized as a globally important infectious disease [1], perhaps the most common zoonosis worldwide. Leptospirosis is a serious disease, with case fatality rates ranging to 20% or higher [2]. *Leptospira* are one of four groups of spirochetes causing (human) human disease, the others being *Treponema pallidum*, the agent of syphilis, relapsing fever *Borrelia* spp., and Lyme Disease *Borrelia* spp. In contrast to the other spirochetes pathogenic for humans, pathogenic *Leptospira* live both in mammalian hosts and free in the environment. Humans contract leptospirosis through mucosal or percutaneous exposure to leptospire in environments contaminated by the urine of chronically infected animal sources. The most common animals implicated as sources of leptospiral transmission are peridomestic or agricultural rodents, dogs, pigs, and cattle. Environmental conditions are an important influence on the incidence of leptospirosis: the disease is rare in deserts [3], common in warm, humid tropical areas, and seasonal rains and severe weather are associated with increased frequency of disease [4, 5]. Leptospirosis is found in a wide variety of environmental contexts, in industrialized and developing countries, and in urban and rural contexts [1, 6].

Despite being common, the diagnosis of leptospirosis is often not made unless a patient presents with textbook manifestations, such as fever plus jaundice and renal failure. Leptospiral infection most often has minimal or no clinical manifestations [7]. Of cases in which fever develops, as many as 90% are undifferentiated febrile illnesses. Clinicians in developed countries may fail to recognize that leptospirosis transmission occurs in the urban setting because it is incorrectly perceived to be a rural disease [8]. In developing countries, laboratory facilities may be inadequate for diagnosis despite a high prevalence of disease. Nonetheless, where the disease is looked for, it is commonly found. Of substantial clinical importance, the syndrome of leptospiral pulmonary hemorrhage has emerged in recent years, in diverse places around the world [5, 9-11].

With this background, the readers of the *Swiss Medical Weekly* should find interest in the report of

Esen et al. in this issue. These investigators report their retrospective experience with 72 hospitalized patients diagnosed with leptospirosis in a referral hospital in the agriculture region of Samsun, Turkey. Previously, the authors showed that peridomestic rats, *Rattus* spp., common in urban and agricultural areas within the Samsun region, often were infected with pathogenic *Leptospira* [12], demonstrating the potential for rat-related leptospirosis transmission here.

It is worth briefly describing Samsun to understand the epidemiological context in which the investigators carried out their study. Samsun is an ancient and storied locale, found at the nexus of two river deltas abutting the Black Sea in north Turkey. According to myth, the river delta east of Samsun was the location of the tribe of Amazon women, a group of female warriors. (Nowadays we know the Amazon region of South America as another leptospirosis-endemic region.) In modern times, Ataturk began modern Turkey's war for independence at Samsun. These days, Samsun is a port town and quiet agriculture region with some tourism.

The major take-home message from this study is that wherever leptospirosis is sought, it is found. While Esen et al. analyze the relationship of clinical and laboratory findings to prognosis, the most interesting aspect of study is the surprisingly high frequency of pulmonary involvement in their patients. It would seem that this syndrome was not well recognized in this region; this lack of recognition of pulmonary involvement in leptospirosis is common worldwide. In contrast to reports such as that from Salvador, Brazil, where Weil's disease was found to be the major manifestation of severe leptospirosis in the absence of pulmonary involvement [6], more than 70% of the patients in the present study had respiratory symptoms; more than 30% of patients reported by Esen et al. had pulmonary infiltrates on chest x-ray. The syndrome of leptospiral pulmonary haemorrhage has to be considered when patients present with grave febrile illness and haemoptysis in an appropriate epidemiological context.

Two important issues continue to confront clinicians regarding leptospirosis. The first is how to reliably establish the diagnosis. The most common

way to diagnose leptospirosis is through serological tests, either the microscopic agglutination test (MAT) which detects serovar-specific antibodies, or a solid phase assay using the non-pathogenic *L. biflexa* serovar Patoc I as antigen, which detects genus-specific antigens. MAT optimally requires paired acute and convalescent serum samples; Patoc antigen-based assays may be more sensitive for the detection of IgM antibodies in some regions than others [13], and IgM antibodies can persist for many months, raising questions about whether a positive IgM result accurately identifies a current infection. In regions where leptospirosis is common, there may be a substantial proportion of people with relatively high MAT titers (1/400 or even greater), or high titers may remain stable without a diagnostic 4-fold rise. MAT results usually come too late to the clinician to be of much utility. Therefore, serological tests remain suboptimal for clinical use in diagnosing leptospirosis. The most promising diagnostic methods are those that demonstrate the presence of the organisms. Culture is difficult for a variety of reasons [1]. Molecular techniques to detect the presence of leptospiral DNA in blood, urine or spinal fluid are clearly the most sensitive and specific [1, 14]; the use of these modalities is precluded by cost and technical factors in non-reference laboratories. The recent development of leptospiral antigen detection methods is promising, but such approaches need to be fully evaluated in settings where the predominant leptospiral strains may not be detected [15].

The second issue of importance to clinicians is how to prevent leptospirosis in patient populations at risk. A classic study of U.S. soldiers in Panama showed that weekly doxycycline can prevent infection. However, such an approach is not tenable in highly endemic regions [16]. Veterinary vaccines of variable utility are available for dogs, cattle and pigs, comprised of whole killed cells. Such vaccines have not been approved in Western industrialized countries, although they are apparently used in China, Korea and Cuba [17, 18]. Substantial work is ongoing to develop recombinant protein-based anti-leptospiral vaccines [1, 19].

Leptospirosis is a common infectious disease that requires common clinical sense to identify classic presentations, but a high degree of suspicion is needed to consider the diagnosis in patients with appropriate exposure histories, and in cases of fever accompanied by pulmonary haemorrhage.

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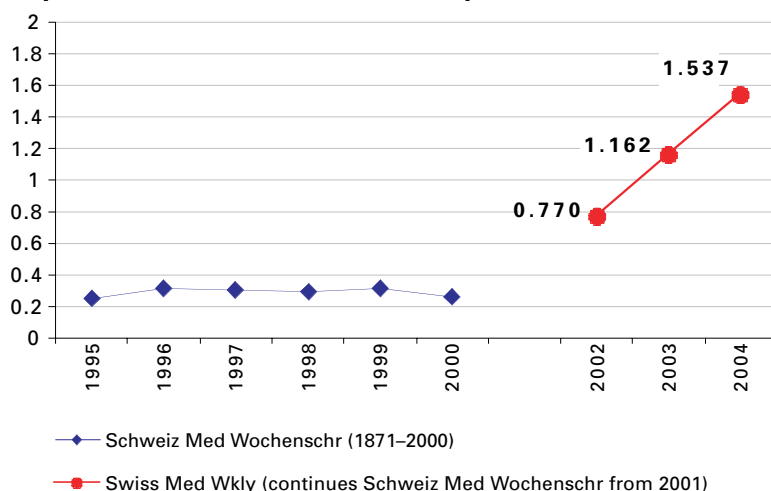
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