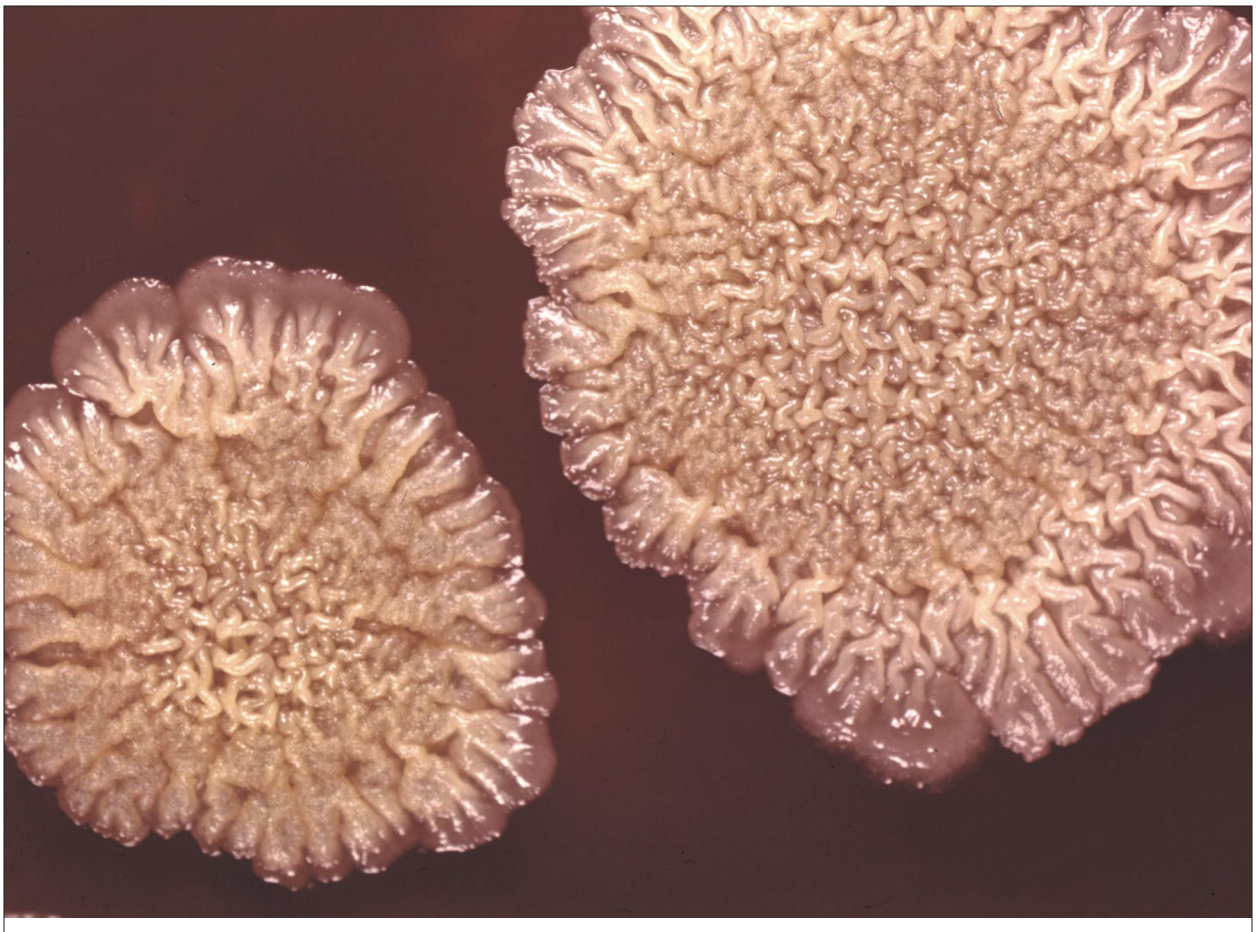

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Leptospirosis: Epidemiology and Usuel Manifestations

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ABSTRACT

Human leptospirosis can be a difficult infection to describe, as the symptoms can vary dramatically between patients. Some symptoms are extremely common, but only a small number of patients will experience the severe life-threatening illness known as Weil's disease. The severity of the infection depends on the age and general health of the patient, plus the serovar (strain) of bacteria involved and the number of bacteria that entered the patient's body. In severe types the illness develops and progresses rapidly, leading to organ failure and often death if not treated with intervention and support.

Key words: Leptospirosis, epidemiology, symptoms, infectious disease

INTRODUCTION

Leptospirosis is an emerging infectious disease and one of the most widespread zoonoses in the world (Levett, 2001). The clinical course in humans ranges from mild to lethal with a broad spectrum of symptoms and clinical signs. Leptospirosis is underreported in many countries because of difficult clinical diagnosis and the lack of diagnostic laboratory services.

Human infections vary from asymptomatic to severe. The clinical presentation varies from patient to patient; many cases are mild or asymptomatic and go unrecognized. In humans, leptospirosis is usually a biphasic illness. The first phase, called the acute or septicemic phase, usually begins abruptly and lasts approximately a week (Goldstein and Charon, 1988). This phase is characterized by nonspecific signs. The second phase of leptospirosis, called the immune phase, is characterized by the development of anti-Leptospira antibodies and the excretion of the organisms in the urine (Adler and Faine, 1978). This phase can last up to 30 days or more, but does not develop in all patients. During the immune phase, the patient becomes ill again. This disease occurs as two clinically recognizable syndromes: the anicteric leptospirosis (80-90% of all cases) and the remainder icteric leptospirosis (Farr, 1995). The diagnosis is confirmed by laboratory tests, but these are not always available. For these reasons, leptospirosis is neglected and underreported. Early diagnosis and the ability to differentiate leptospirosis from other diseases is important to reduce the risk of more serious infection or mortality (Cumberland *et al*., 1999). In cases of

particularly virulent serovars or patients with poor health, the infection follows a different pattern and the patient develops very rapid and severe symptoms from the start, without much of a remission. In this review the epidemiological features and usual manifestations of leptospirosis are being described in detail. Moreover, depending on these epidemiological data specific preventive measures are being suggested in order to reduce the risk of the disease transmission.

EPIDEMIOLOGY

Leptospirosis in humans is caused by infection with pathogenic spirochetes classified as Leptospira interrogans which is subdivided into serogroups and serotypes (serovars) (Ellinghausen *et al*., 1981) is acquired through contact with animal reservoirs or an environment contaminated by their urine (Faine *et al*., 1999). Some leptospiral serovars are commonly associated with particular animal reservoirs; thus the prevalence of different leptospiral serovars within a human population depends on the reservoirs present and the serovars they carry (Bharti *et al*., 2003). However, no association has been found between infecting serovar and severity or manifestations of clinical symptoms (Merien and Perolat, 1996; Yersin *et al*., 1998). Scientific studies have consistently indicated that rats are the most significant carriers and transmitters of leptospirosis globally, although other domestic and wild animals are potential reservoirs of the bacteria (Sarkar *et al*., 2002; Villanueva *et al*., 2010). Several *Leptospira* serovars and serogroups that circulate among rats have already been identified (McBride *et al*., 2007).

Leptospirosis is a zoonosis of worldwide distribution (WHO, 1999), endemic mainly in countries with humid subtropical or tropical climates and has epidemic potential (Everard *et al*., 1992; Ratnam, 1994). It often peaks seasonally sometimes in outbreaks and is often linked to climate change. In addition to the environmental attributes of slums, low socio-economic classification has been found to independently contribute to the risk of human infection (Reis *et al*., 2008). A pattern of disease seasonality has been described with a peak incidence occurring in summer or fall in temperate regions and during rainy seasons in warm-climate regions (Esmaeili *et al*., 2009). Ecologic studies of urban epidemics of leptospirosis identified that cases geographically clustered in these areas of poor sanitation and flooding during periods of heavy rainfall (Barcellos and Sabroza, 2000, 2001).

Human leptospirosis is endemic and epidemic in some parts of the world such as South and Central Americas (Trevejo *et al*., 1998; Ko *et al*., 1999), India (Jena *et al*., 2004) and Southeast Asian (Laras *et al*., 2002). In the Dom-Tom significant variations from one year to another reflect advantage of poor access to diagnosis. However, a resurgence of disease is observed in patients with recreational water probably correlated to the individual and preventive measures group (Weil, 1886).

The endemic nature is due to geographical and climatic conditions, the number of cases estimated by the World Health Organization (WHO) in the humid tropical climate is 10 per 100,000 inhabitants per year, or 0.01% of the population (OMS, 2007).

Among the states and insular territories of the region, Hawaii and New Caledonia have published detailed data on the local epidemiology of this disease (Katz *et al*., 2002). Few and often old, studies were conducted in other islands like French Polynesia (Gendron *et al*., 1992), the Marquesas Islands (Rougier *et al*., 1984) and Vanuatu (Perolat and Reeve, 1992). The risk of infection depends on exposure, leptospirosis has been well described in Australia and New Zealand as an occupational disease affecting livestock farmers and slaughterhouse workers (Thornley *et al*., 2002; Terry *et al*., 2000). Farmers, veterinarians and abattoir workers are professionally exposed

to Leptospira-infected animals such as cattle or pigs. This situation is important for various professional groups such labourers, chicken seller, fishmongers, butchers, worker in the bath (Haraji *et al*., 2011b). Freshwater-related sports are a potential risk in summer and throughout the year in tropical countries (Vinetz, 2001) where the disease is endemic. These include ingestion of contaminated food and water or by broken skin and mucous membrane contact with contaminated water and soil (Vijayachari *et al*., 2008). Leptospires can gain entry into humans through cuts and abrasions in the skin, through intact mucous membranes (nose, mouth, eyes) and perhaps through waterlogged skin (Jaureguiberry *et al*., 2005). They may occasionally enter the human body via the inhalation of droplets of urine or via drinking-water. Leptospirosis in humans is always acquired from an animal source; human-to-human transmission is for practical purposes non-existent and the disease is regarded globally as a zoonosis. Leptospirosis in humans can vary in severity according to the infecting serovar of Leptospira and the age, health and immunological competence of the patient. It ranges from a mild, influenza-like illness to a severe infection with renal and hepatic failure, pulmonary distress and death (the classical Weil's disease).

USUAL MANIFESTATIONS

The diagnosis of leptospirosis should be considered in any patient presenting with an abrupt onset of fever, chills, conjunctival suffusion, headache, myalgia and jaundice (Aliyan *et al*., 2006).

On examination, the most characteristic sign after the pain muscle is bilateral conjunctival suffusion, accompanied rule of a generalized hyperem. More rarely, macular rash, maculopapular, purpuric or urticarial transient can be observed, usually on the trunk or pretibial position in 10% of patients (Fraser *et al*., 1973). The pharynx is sometimes congestive. Hepatomegaly, splenomegaly and diffuse lymphadenopathy have been reported in 10% of cases (Faine and Adler, 1984).

Case fatality rates approaching 20% have been reported. A more recently recognised respiratory manifestation involves severe pulmonary edema and hemorrhages which have been the main cause of death in some epidemics. As with mild leptospirosis, chronic, long-term sequelae have been reported, but frequently not investigated fully. The host and microbial factors which may lead to long-term persistence are unknown. Leptospirosis of either type in pregnancy (Shaked *et al*., 1993) carries the risks of intrauterine infection and fetal death. Leptospirosis typically performs a triad of liver, Renal and meningeal.

The diagnosis is more difficult when patients present with symptoms of cough, dyspnoea, nausea, vomiting, abdominal pain (Granito *et al*., 2004), diarrhoea, arthralgias and a skin rash (Mansour-Ghanaei *et al*., 2005).

During hepatic Achievement jaundice appears between the 4th and 6th day of illness (with extremes of 2 to 9 days) and evolves rapidly (Haraji *et al*., 2011a), reaching its maximum in the space of one week. It comes in a quarter of cases of hepatomegaly sensitive. Hyperbilirubinemia is predominantly conjugated and can reach 60 to 80 mg L^{-1}, although it often remains lower 20 mg mL^{-1}. A moderate increase in transaminase and gamma-glutamyl transferase is commonly observed (Arean, 1962). The decreased levels of prothrombin is rare during the leptospirosis and generally reflects a lack of Vitamin K (Farr, 1995). Death is often caused by liver failure and we attends the complete recovery of liver injury (Brouqui *et al*., 1990).

Leptospirosis is characterized by fever, renal and hepatic insufficiency (Abd-El-Latif *et al*., 2007), Clinically, cough (25 to 70% of cases), hemoptysis (3 to 25%) and dyspnea (16%) constitute the most common pulmonary symptoms which are dominated by a cough (Chauhan *et al*., 2010), shortness chest pain and hemoptysis rarely revealing which can be life-threatening, acute

pancreatitis (Kaya *et al*., 2005), Encephalomyelitis (Chandra *et al*., 2004), Hypomagnesemia (Spichler *et al*., 2008), Myocarditis occurs most often by simple electrocardiographic changes, Supraventricular arrhythmias (fibrillation atrial flutter) and ventricular (ventricular extrasystoles, tachycardia or ventricular fibrillation) have been described (Ciuchi-Nicolau, 2010), Neuroretinitis (Ghosh *et al*., 2011), Meningoencephalitis (Vivek and Padmakumar, 2004), Pancytopaenia (Bee *et al*., 2003). Clinical signs are quite variable; most cases are probably inapparent. However, human mortality from its severe forms-Weil's syndrome and severe pulmonary hemorrhage syndrome is relatively high with rates of over 10 and 50%, respectively, even when optimal treatment is provided. Clinical differential diagnosis is required between leptospirosis and severe influenza, viral meningitis, acute abdominal conditions or glomerulonephritis. It may also mimic many other diseases, e.g. dengue fever (Mohammad *et al*., 2008), typhoid, viral hepatitis and other viral haemorrhagic diseases. Icterus (jaundice) is a relatively common symptom in leptospirosis but is also found in many other diseases involving the liver such as various forms of hepatitis.

Once the possibility of leptospirosis has been considered, appropriate diagnostic tests and clinical management should be instituted.

The MAT is the gold standard for serology and is used to identify the most probable serovar or serogroup that has caused an infection. Other techniques such as the ELISA can detect different classes of antibody but may be subject to false positive reactions and will require confirmation of these results by the MAT.

PREVENTION

At present there are few effective prevention measures for leptospirosis. Currently, there is no human vaccine available against leptospirosis. Human leptospirosis can be controlled by reducing its prevalence in wild and domestic animals.

Severe cases of leptospirosis should be treated with high doses of intravenous penicillin. Less severe cases can be treated with oral antibiotics such as amoxycillin, ampicillin, doxycycline or erythromycin. Third-generation cephalosporins, such as ceftriaxone and cefotaxime and quinolone antibiotics also appear to be effective (Green-McKenzie and Shoff, 2010; Suputtamongkol *et al*., 2004). Since some outbreaks have been associated with drinking of contaminated water, water purification should be implemented. Prevention and control measures should be focused on the infection source (Koutis, 2007). Rodent-vector control (Massawe and Makundi, 2011) preferably through the use of slow acting rodenticides and improved hygiene may be some of the measures for diminishing the risk of leptospirosis transmission. Occupational hygiene (in sewers, farmers and other high risk groups) that includes the use of water proof shoes and gloves is fundamental for preventing human leptospirosis.

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