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Popular Article

Leptospirosis: A Worldwide Zoonosis

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Abstract

Leptospirosis (also called: Weil's disease) is an acute anthropo-zoonotic infection of worldwide significance caused by spirochaete Leptospira interrogans. In developing countries large outbreaks have occurred in urban slums and following floods. Various factors influencing the animal activity, suitability of the environment for the survival of the organism and behavioural and occupational habits of human beings can be the determinants of incidence and prevalence of the disease. Individuals from developed nations are also exposed to the infection as a result of international travel and greater participation in certain outdoor recreational activities. Rapid tests may not be sufficiently sensitive in early disease and culture facilities are not widely available. The control of leptospirosis is largely dependent on general hygienic measures and rodent control. An effective human vaccine is still not available.

Introduction

Weil, Professor of Medicine at Heidelberg (1886) whose name has been given to the disease in humans first described this disease, which is caused by *Leptospira interrogans*, serovar *icterohaemorrhagiae* or *copenhageni*. Leptospires had been seen at that time, but were not cultured and were named *Spirocheta interrogans* by Stimson as early as 1907, in silver-stained preparations of liver from a patient believed to have died of yellow fever, the viral origins of which were then unrecognized. The patient really had Weil's disease. Its contagious nature and microbial origin were proved independently, first in Japan *(Spirochaeta icterohaemorrhagiae)* in 1915, and soon after in Germany (*Spirochaeta icterogenes*) by Uhlenhuth and Fromme. Both groups isolated, cultivated and described pathogenic Leptospires. Later, a saprophytic leptospira found in fresh water was described in 1914; it was named *Spirochaeta biflexa*. Noguchi proposed the name 'Leptospira' (thin spirals) in 1918, following detailed microscopical and cultural observations. Yanagawa and Faine (1966) showed that Leptospires were analogous to other bacteria in structure and that

characteristic antigens are associated with structural elements. Consequently, Leptospirosis researchers became concerned with serological classification, based on absorption and cross agglutination of antisera. ELISA methods were developed to analyse non agglutinating as well as agglutinating antigens.

Epidemiology

Leptospirosis is a worldwide zoonosis. According to the occupational groups involved and the nature of the disease presentations, different names have been used, e.g. seven-day fever found commonly in Japan, Cane cutter's disease in Australia, Rice field Leptospirosis in Indonesia and Fort Bragg fever, which appeared as an outbreak in the US. Weil's disease, which is one of the severe forms of this disease, occurs in many countries, including India and other South-East Asian Countries, China, continental Europe and England. Leptospirosis exists in all the five inhabited continents and in a large number of countries. It occurs in tropical, subtropical and temperate zones. In November 1961, an outbreak of Leptospirosis occurred among 186 US Army Troops in the canal zone who had engaged in a jungle exercise 10 to 13 days earlier.

Pathogenesis

The most frequent sources of infection are urine, kidneys, surface water, mud and soil. Leptospires are presumed to enter via small abrasions or other breaches of the surface integument. They may also enter directly into the bloodstream or lymphatic system via the conjunctiva, the genital tract in some animals, the nasopharyngeal mucosa, possibly through a cribriform plate, the lungs following inhalation of aerosols, or through an invasion of the placenta from the mother to the foetus at any stage of pregnancy in mammals. Drinking or inhalation of contaminated water following immersion can also cause leptospirosis. Pathogenic leptospira rapidly invade the bloodstream after penetrating skin or mucous membranes. The primary lesion in leptospirosis is disruption of the integrity of the cell membrane of the endothelial cells lining small blood vessels in all parts of the body. Capillary leakage and haemorrhages result. These effects can be attributed to the action of a glycoprotein (GLP) toxin of leptospires. Widespread petechial haemorrhages are apparent in all organs and tissues, particularly the lungs, omentum and pericardium. Ischaemia from damage to blood vessels in the renal cortex leads to renal tubular necrosis, particularly of the proximal convoluted tubules. The resulting anatomical damage causes renal failure that can be fatal. Liver cell necrosis caused by ischaemia and destruction of hepatic architecture leads to the characteristic jaundice of the severe type of leptospirosis. Blood clotting mechanisms are affected by liver failure, aggravating the haemorrhagic tendencies. There may also be thrombocytopenia.

Clinical Symptoms

The incubation period for leptospirosis is usually 7 to 12 days, but it can range from 2 to 20 days. The onset of anicteric leptospirosis is abrupt and is characterized by fever, headache, severe myalgia, chills with rigors, prostration and sometimes, circulatory collapse. The septicaemic (or first) phase

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lasts 3 to 7 days. Fever is high and remitting. Headache is intense, unremitting and possibly throbbing. Anorexia, nausea, vomiting and abdominal pain occur in most patients. The most common physical finding is conjunctival suffusion in the absence of purulent discharge. Other signs include masculopapular skin rash, pharyngeal injection, lymphadenopathy, splenomegaly, hepatomegaly, and muscle tenderness. The symptoms are prominent for 4 to 7 days during the septicaemic stage, at which time defervescence due to lysis occurs. Leptospires can be isolated from the blood and the CSF during this phase.

Diagnostic Techniques

Direct Evidence

1. Demonstration of leptospires or their products:

Microscopy (Dark-field microscopy, Phase contrast microscopy)
Silver staining
Immunofluorescence, Immunoperoxidase
DNA hybridisation, Polymerase chain reaction

2. Isolation of leptospires:

Serovar specific ELISA; Blood, Urine, CSF, Body fluids and tissues

3. Animal Inoculation

Indirect Evidence

1. Detection of antibodies to leptospira:

Genus specific tests
Macroscopic agglutination test (MSAT), Indirect fluorescent antibody test (IFAT)
Indirect haemagglutination test (IHA), Counter immuno electrophoresis (CIEP)
Complement fixation test (CFT)

Newer techniques

ELISA, Microcapsule agglutination test (MCAT), Lepto-Dipstick
Serogroup/serovar specific tests
Microscopic agglutination test (MAT)
Serovar specific ELISA

Treatment

Penicillin or **doxycycline** are still the antibiotics commonly used to treat leptospirosis. Penicillin has been shown to shorten fever and period of renal dysfunction. Other antibiotics which may be effective include the macrolides, other beta-lactams and aminoglycosides. A recent multicentre, open randomised trial in Thailand involving 69 patients with confirmed leptospirosis showed that a three-day course of azithromycin is as effective as a seven-day course of doxycycline. Patients on azithromycin had less adverse effects.

Prevention & Control

General hygienic measures including avoidance of contact with potentially contaminated water, wearing protective clothing and footwear and rodents' control are the mainstay of prevention. Farm and domestic animals may be vaccinated. Currently there is still no effective vaccine for human use.

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