Leptospirosis, a disease caused by pathogenic spirochetes of the genus *Leptospira*, is considered the most common zoonosis in the world and has recently been recognized as a re-emerging infectious disease among animals and humans and has the potential to become even more prevalent with anticipated global warming. Since 1970, occupational exposure accounting for 30-50% of human cases and recreational activities are recognized as important causes of disease. Reclamation of wastelands, deforestation, drainage congestion, water logging and changes in agricultural technology are also important factors for its spread in present times. The outbreaks of leptospirosis have been reported from coastal Gujarat, Maharashtra, Kerala, Tamil Nadu, Andhra Pradesh, Karnataka and Andaman periodically.

In the last decade, there has been a rapid rise in the incidence of leptospirosis in north India. In rural areas, high-risk groups are farmers and animal husbandry staff. In urban India, outbreaks are reported during monsoon due to flooding. The infection is probably transmitted to human when wading through stagnant rainwater contaminated by infected urine of animals. The organism enters the body when mucous membranes or abraded skin come in contact with contaminated environmental sources. Virulent organisms in a susceptible host gain rapid access to the bloodstream through the lymphatics, resulting in leptospiremia and spread to all organs. The incubation period is usually 5-14 days. During acute infection, leptospires multiply in the small blood vessel endothelium, resulting in damage and vasculitis. The major clinical manifestations of the disease are believed to be secondary to this mechanism, which can affect nearly any organ system.

The disease was first described by Larrey in 1812 among Napoleon’s troops at the siege of Cairo, and was initially believed to be related to the plague. Adolph Weil (1886) published his observations. Leptospirosis in humans is characterized by an acute febrile illness followed by mild self-limiting sequelae but at times causes more severe, and often fatal, multi-organ involvement. The clinical manifestations are highly variable. In general, the disease presents in four broad categories: (i) a mild, influenza-like illness; (ii) Weil’s syndrome characterized by jaundice, renal failure, haemorrhage and myocarditis with arrhythmias; (iii) meningitis/meningoencephalitis; (iv) pulmonary haemorrhage with respiratory failure. In mild illness, patients have fever, myalgia but do not have jaundice. Almost 90% of patients have this type of illness. Weil’s syndrome is severe form of the disease, characterized by jaundice and is usually associated with involvement of other organs. About 5-10% of patients have this type of manifestations. Many case reports, clinical series and descriptions of outbreaks have documented pulmonary involvement in leptospirosis. Direct involvement of the lung by the organism, inflammatory mediators, and vasculitis, all have been incriminated as cause of pulmonary involvement. It is difficult to differentiate pulmonary alveolar haemorrhage from ARDS radiologically. The virulence factors in leptospires are poorly understood. Some serovars tend to cause mild disease and others severe disease. Patient factors such as old age and multiple underlying medical problems are often associated with more severe clinical illness and increased mortality. Subsequent sequelae depend on the serovar involved and the health, nutritional status, and age of the patient, as well as the rapidity of definitive and supportive treatment.

In the present issue of journal, Chauhan V, et al have described profile of patients of leptospirosis from Shimla. Much of north India is subject to humid, subtropical climate where flooding and unseasonal precipitation, suitable for survival and transmission of leptospirosis, are not uncommon. Clinical expertise and awareness with availability of laboratory tests have increased the recognition of patients with leptospirosis all over India. However, Rickettsial diseases are important public health problem in addition to malaria, leptospirosis, viral hepatitis and dengue hemorrhagic fever in patients presenting with fever and jaundice in Himachal Pradesh. Presence of leptospira antibody by rapid tests or positive IgM ELISA in patients with clinical illness resembling leptospirosis make the case as probable leptospirosis. PCR detects antigen and is promising on both sensitivity and specificity, but is expensive and is most useful when patients present within four days of fever. Microscopic agglutination test (MAT) is the gold standard serologic test because of its unsurpassed diagnostic specificity. The main advantage is that serovars can be identified which is of epidemiological importance. However, MAT is only performed in reference laboratories and requires acute and convalescent samples for diagnostic confirmation. Even in centres with laboratory facilities, since serological tests become positive only after one week, clinicians should continue treating suspected cases of leptospirosis on an empirical basis. All suspected leptospirosis cases having feature of organ dysfunction such as hypotension, oliguria, jaundice, breathlessness, bleeding tendencies or altered level of consciousness should be immediately shifted to higher centre, whether positive or negative with rapid immunodiagnostic test. In the present study there was no mortality and only one patient required mechanical ventilation. Icterus and thrombocytopenia are markers of severe leptospirosis. Hypotension, myocarditis, cardiopulmonary arrest and adrenal haemorrhages are some of the features of more severe leptospirosis. Acute respiratory distress syndrome (ARDS) has been reported as one of causes of death. In patients with ARF, oliguria is a significant predictor of death. Other predictors of death are hypotension, hyperkalemia, high leucocytes count, alveolar infiltrates on chest X-ray, and abnormalities of ECG. Serum amylase levels are often raised significantly in association with ARF.

Leptospirosis is treated primarily with antimicrobial therapy. In uncomplicated infections that do not require hospitalization, oral doxycycline has been shown to decrease duration of fever and most symptoms. Hospitalized patients are treated with
intravenous penicillin therapy. Third-generation cephalosporins are effective as well in the treatment of acute disease. Once-daily administration and the extended spectrum of ceftriaxone against bacteria provide additional benefits over intravenous penicillin. Treatment with effective antibiotics should be initiated early in leptospirosis. The benefit of antibiotics after the fifth day of the disease is controversial. However, most clinicians treat with antibiotics regardless of the date of onset of the illness. Major improvements in the prognosis of severe leptospirosis have been made in recent decades, due to aggressive supportive care for organ failure, including advances in renal replacement therapy and non-invasive mechanical ventilation. The evidence for use of steroids in ARDS due to other causes is conflicting, but pulse therapy with high dose of methyl prednisolone is found to be useful when used in early ARDS due to leptospirosis.

Even cyclophosphamide has been used with success in cases of severe pulmonary hemorrhage in leptospirosis, but toxic adverse effects of such drugs are to be considered while using them in critically ill patients who often have concomitant sepsis and supportive therapy with colony stimulating factor may be required to counter leucopenia produced by the drug. There are isolated case reports of use of recombinant activated protein C (rAPC)-drotrecogin alfa in patients of tropical infections, including leptospirosis with multi-organ dysfunction syndrome (MODS), however further studies are warranted and caution has to be exercised in cases of leptospirosis as pathogenesis of disease involves bleeding and coagulopathy.

A number of leptospirosis outbreaks have occurred in the past few years in various places all over the world and in India. Some of these have resulted due to natural calamities such as cyclone and floods. Few of the patients develop various complications due to involvement of multiple organ systems. In such patients, the case fatality ratio could be about 40% or more. Increased awareness amongst physicians about protean manifestations of leptospirosis, and early institution of antimicrobial therapy pending diagnostic confirmation will help prevent mortality associated with complicated disease. Doxycycline is reported to give some degree of protection to exposed individuals from non-endemic areas. Even if it does not always prevent infection in endemic area, it can reduce the severity of the disease and thus mortality and morbidity. On-going studies in future will answer some queries regarding the evidence-based role of antibiotics and other interventions in patients with severe disease and MODS.

References