Immunorestitution disease after HAART

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The treatment of human immunodeficiency virus (HIV) infection has undergone considerable change in the past few years. Protease inhibitors and non-nucleoside-analogue reverse-transcriptase inhibitors, when used as part of combination drug regimens (known as highly active antiretroviral therapy or HAART), can profoundly suppress viral replication and rapidly replenish CD4+ cells. Use of this potent combination therapy has been associated with dramatic decrease in incidence of new opportunistic events, decline in morbidity and mortality due to AIDS [1]. Recently, it is even suggested that primary and secondary prophylaxis against P. carinii pneumonia can be safely discontinued in patients who have improved immunologic function while on HAART [2]. However, paradoxical reactions and clinical deterioration have been well described in AIDS patients who have preexisting opportunistic infection and immunologic improvement after receiving HAART. Immune reconstitution following antiretroviral therapy can be accountable for this phenomenon.

Definition

Immunorestitution disease (IRD) is defined as an acute symptomatic or paradoxical deterioration of a (presumably) preexisting infection that is temporally related to recovery of the immune system and is due to immunopathological damage associated with the reversal of immunosuppressive processes, such as withdrawal of corticosteroid, recovery of the neutrophil count from chemotherapy, engraftment after bone marrow transplantation, or HAART for AIDS [3]. The prexisting microbial infection could be either asymptomatic or mildly symptomatic.

In a literature review of IRD, it was found that the organisms in HIV-infected patients with IRD included M. tuberculosis (35.4%), M. avium complex (18.7%), M. xenopi (2.1%), Cryptococcus species (8.4%), CMV (29.1%), HBV (2.1%), and HCV (2.4%) [3]. The median interval between initiation of HAART and the onset of IRD for mycobacterial/fungal infection and viral infection were 11 days and 42 days respectively. However, there was no reported case of pyogenic bacterial infection in IRD.

As the mycobacterial and CMV infection are the commonest causes of IRD in the HIV-infected patient, it would be good to use them as examples to illustrate the features of IRD in HIV-infected patients.

Mycobacterial Infection

Transient worsening of tuberculous symptomatology and lesion following anti-TB therapy has been well described in HIV-negative patients. This phenomenon was also seen in HIV-seropositive TB patients receiving both antiretroviral therapy (ARV) and anti-TB therapy. It was found that paradoxical responses occurred frequently (35-46%) [4,5] and were more temporally related to the initiation of ARV than to the initiation of anti-TB

therapy (mean SD:1511 days versus 109 72 days) [4]. The paradoxical responses included fever, worsening pulmonary infiltration, pleural effusion and, intrathoracic and cervical lymphadenopathy. The majority of patients who experienced paradoxical responses had their tuberculin skin tests conversion from negative to strongly positive after ARV. These observations suggest that a paradoxical response associated with enhanced tuberculin skin reactivity may occur after the initiation of ARV in HIV-infected TB patients.

Elizabeth et al reported 5 HIV-infected patients presented with high fever, leucocytosis and evidence of lymph node enlargement within 1-3 weeks of starting ARV. Lymph node biopsy confirmed that focal lymphadenitis resulted from unsuspected local or disseminated M. avium complex (MAC) infection. These prominent inflammatory responses to previously subclinical MAC infection were associated with leucocytosis and with an increase in the absolute lymphocyte count [6]. Other clinical presentations in the cases of mycobacterial disease include abdominal pain, hepatosplenomegaly and skin lesion.

CMV Infection

AIDS-related CMV retinitis occurs primarily in patients with CD4 counts of 50 cells/uL and almost always in patients with CD4 counts of less than 200 cells/uL at the time of diagnosis. Mark et al described IRD of CMV retinitis in five HIV-infected patients who had absolute CD4 counts of less than 85 cells/uL between 5 and 24 weeks before retinitis was diagnosed. At the time that CMV retinitis was diagnosed, absolute CD4 counts were more than 195 cell/uL. The diagnosis was made 4-7 weeks after starting HAART. Ocular manifestations of CMV disease included visual loss and fundoscopic changes of inflammatory retinitis, vitritis, papillitis and macular edema. All five patients responded well to anti-CMV therapy 17].

Development of IRD

The development of IRD requires appropriate tissue burden of preexisting pathogens, virulence of the organism and recovery of immune system from immunosuppressive state [3]. Patients with a high microbial load or infected with virulent microbe will usually die during the immunosuppressive state. On the other hands, patients with low microbial load or infected with less virulent microbes will present subclinically only.

Management of IRD

The use of appropriate antimicrobial is the cornerstone for the management of IRD. NSAID and steroid may provide symptomatic control and may reduce the inflammatory damage induced by immunorestitution after starting HAART. The role of other immunotherapy such as immunoglobulin and cytokines is still uncertain. Finally, awareness of the disease by physicians is ultimately important for making diagnosis and management of IRD.

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Changing epidemiology of meningococcal infection in Hong Kong

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Meningococcal meningitis and septicemia are notifiable infections in Hong Kong. The causative organism, Neisseria meningitidis, is a Gram negative diplococci that has at least 13 serogroups based on its polysaccharide capsule. The common serogroups that cause human disease are A, B, C, W-135, and Y. Meningococcal infection has a 5-15% case fatality rate even with modern therapy. Septicemia carries a poorer prognosis than meningitis. About 10% of survivors suffer neurologic sequelae (e.g., deafness, seizures). In overseas studies, 5-10% of the population may harbor N. meningitidis in the nasopharynx without symptoms. Overcrowding, active and passive smoking, and recent upper respiratory tract infection increase the risk of developing disease. Susceptibility is higher among children aged <4 years, patients with asplenism, complement deficiency, or iron overload.

During 1995-99 in Hong Kong, a total of 16 cases of meningococcal infections were reported to the Department of Health, the annual number ranging from 2-5 cases. There were no outbreaks or localised clusters. The reported incidence rates were between 0.03 per 100,000 and 0.08 per 100,000, which are very low compared with Western countries (e.g., 2 per 100,000 in the U.K). More cases occurred during March, April, and August; no cases occurred from September through December. 13(81%) of the 16 cases during this period were local cases. 6 (38%) occurred in children aged <4 years. 10 (63%) were meningococcal meningitis and 6 (37%) had meningococcal septicemia. Of the 8 cases where serogroup information was available or partially available, 4 were serogroup B, 2 were serogroup A, and 2 belonged to non-B serogroups.

During January 2000 through July 2001, the reported incidence has increased. There were 14 cases in 2000 and 10 cases during the first 7 months in 2001. All of them were sporadic cases; the majority (79%) remained local. No age-shift was apparent. Unlike 1995-99, 5 cases occurred during October and November of 2000. Although the reported incidence of meningococcal infection is rising, it is still far below epidemic thresholds recognised in the U.S., Australia, and by the World Health Organisation.

Another important trend is that serogroup W-135 is clearly emerging. There were 3 cases with serogroup W-135 in 2000, and 5 cases during January through July 2001. 7 (88%) of these 8 serogroup W-135 infections were local cases. In 2000-01, serogroup W-135 caused an international outbreak as pilgrims to Hajj (Saudi Arabia) brought the strain to many countries, including the U.K., France, Norway, and Singapore. However, most of the cases with serogroup W-135 in Hong Kong reported no contact with Hajj pilgrims. Thus, serogroup W-135 may have become established locally.

The above changes in epidemiology have implications on prevention and control. One needs to monitor signs that increase the chance of an outbreak, such as an abrupt rise in incidence or an age-shift from young children to adolescents. Early case detection is paramount to prevent secondary spread, especially in institutions. Close contacts of a sporadic case should receive chemoprophylaxis (e.g., rifampicin, ceftriaxone, ciprofloxacin) as soon as possible. Close contacts include those who eat and sleep in the same place with the case-patient, children attending the same day care center, and anyone directly exposed to patient's oral secretions. Health care workers who are not exposed to the patient's oral secretions (e.g., mouth resuscitation, endotracheal intubation) are not considered close contacts, and they do not require chemoprophylaxis in general.

Another issue to consider is vaccination. While chemoprophylaxis to close contacts will suffice for the management of sporadic infections, vaccination may be required to terminate an outbreak or localised cluster should they appear. Due to the local emergence of serogroup W-135, the quadrivalent polysaccharide vaccine (A, C, W-135, Y) will be more useful than the bivalent polysaccharide vaccine (A, C). The former has a protective efficacy of 85-100% in older children and adults. It has been made a health requirement for arrivals to Hajj by the Ministry of Health of Saudi Arabia. However, this vaccine is not suitable for inclusion into routine childhood immunization because it provides limited efficacy of short duration in young children.

A new conjugate bivalent (A, C) meningococcal vaccine was introduced in the U.K. in 1999 for routine childhood immunisation. This vaccine confers a stronger immunogenic response in infants and young children, and is expected to provide a longer duration of immunity than its polysaccharide equivalent. Serogroup A, C, Y, and W-135 meningococcal polysaccharides have been chemically conjugated to protein carriers, and clinical trials evaluating these vaccines are ongoing.

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Creutzfeldt-Jakob disease: infection control measures

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Creutzfeldt-Jakob disease (CJD) is a fatal neurodegenerative disease with an incidence of approximately 1 in a million population worldwide[1]. It is traditionally categorised as sporadic, familial or iatrogenic cases. The patients remain asymptomatic, usually up to decades, and usually die within 1 year of illness onset. A new variant form of CJD (nvCJD) has been recognized recently. It differs from CJD in epidemiology, pathology and geographical distribution. Particular consideration in infection control should be taken because nvCJD patients may harbour more infectivity in peripheral tissues than the sporadic CJD patients. At present, there are no effective vaccines, reliable diagnostic methods nor proven treatment. The causative agent is a self-replicating infectious protein called prion which is extremely resistant to conventional sterilization and disinfection procedures[2].

Infection control measures

There is no evidence of occupational transmission of CJD to health care workers. Guidelines are available from the World Health Organisation [3] and other health care professional bodies e.g. Center of Disease Control and Prevention (CDC) of the United States, Advisory Committee of Disease Prevention Spongiform Encephalopathy Advisory Committee of the United Kingdom [4,5]

Risk evaluation in healthcare settings

CJD are not known to be transmitted by contact from person to person but iatrogenic infections have been documented. In risk evaluation, three parameters are considered: (1) probability of the patient developing CJD, (2) the level of infectivity in tissues/fluid, (3) the nature or the route of exposure. Persons with confirmed or suspected CJD are the highest risk group. Recipients of human pituitary hormones, dura mater graft or corneal transplants, persons who have undergone surgery with contaminated neurosurgical instruments and members of families with CJD are considered to be “at risk”. From studies in animal models, infectivity is highest in the central nervous system, specifically the brain, spinal cord and the eye. Infectivity of cerebrospinal fluid (CSF), kidney, liver, lung, lymph nodes and spleen is considered to be low. There has also been experimental transmission via dental pulp tissues and intracerebral inoculation of blood components in animals. Comparing with the brain, the optic nerve tissue, the lymphoreticular tissues (tonsil, spleen, lymph nodes) and the retina in nvCJD cases have levels of PrPSc of 25%, 15% and 2% respectively[6]. Therefore, concerns for the probable role of dental procedures, blood transfusion and ophthalmic equipment in the spread of infections are raised[7,8].

Infection control procedures in the ward

For the care of CJD patients in the ward, there are no special requirements other than the standard universal precautions currently practised. Isolation of

patients is not required. General nursing procedures and clinical waste disposal can be performed according to current practices.

Extra precautions are required when performing procedures involving blood and body fluids e.g. lumbar puncture, biopsies, injections. The staff should wear disposable protective gloves, clothing, goggles as appropriate; needles should be put into sharps box and all disposed of by landfill. In Hong Kong, tissues only are incinerated, all other materials are disposed of by landfill. Spillage of blood or body fluids should be disinfected with 1% sodium hypochlorite (10,000ppm available chlorine) for 30 minutes and the materials used to absorb the spill should be disposed of by landfill. All tissue specimens, eye aspirates and CSF should be clearly labeled "biohazard". This also applies to tissues fixed with alcohol, formalin or glutaraldehyde which, paradoxically, actually stabilise the infectivity.

Infection control procedures for surgery

The procedure should preferably be at the end of the list to allow cleaning. Team members should wear appropriate protective clothing including plastic apron, impermeable gowns, mask, gloves, goggles.

Disposable drapes and dressings, and where possible, disposable instruments should be used. All used instruments should be placed directly into a clearly labeled rigid container for special treatment (see below). Expensive instruments used on patients with suspected diagnosis can be quarantined pending confirmation of diagnosis. These instruments require cleaning with gloved hands and decontamination (see below) before storage in rigid sealed containers.

It is recommended that only those instruments used on low risk tissues of at risk patients can be decontaminated for reuse. Procedures that are currently identified as suitable are porous load steam sterilization at 134-137C for a single cycle of 18 minutes, immersion in sodium hypochlorite (20,000 ppm available chlorine) or 2M sodium hydroxide for 1 hour, and, for histological samples, immersion in 96% formic acid for 1 hour. Combination of heat and chemical decontamination is preferred if feasible. It is recognized that destruction of heat-resistant surgical instruments that come in contact with high infectivity tissues as described in the WHO guidelines, albeit the safest and most unambiguous method, may not be practical or cost effective.

Occupational exposure

Scrubbing of exposed areas should be avoided. Exposed intact skin should be cleaned with soap and water. Exposed mucous membrane should be irrigated with saline or water. In the case of sharps injury or abrasions, bleeding should be encouraged; the wound should be washed with soapy water and then covered with waterproof dressing. It is necessary to keep records of occupational exposure for at least 20 years.

Handling of dead bodies

According to the Hong Kong guidelines[9], the body should be put in a sealed impermeable, plastic bag prior to removal. Embalming and hygienic preparation are not allowed and viewing in funeral parlour is allowed only if no necropsy is performed. Cremated remains can be considered to be sterile. Exhumed bodies should be considered as having the same infectivity as at the time of burial.

For post mortem, full examination should be avoided. Disposable protective devices and instruments should be used. Where the skull is opened or there is CSF leakage, the bag should be lined with materials to absorb any fluid.

Tonsillectomy

Adenotonsillectomy is a common operation usually performed in children and instruments are reused many times. Since PrPsc are detectable in lymphoreticular tissues during the early asymptomatic incubation period of nvCJD, the United Kingdom Department of Health has mandated that all tonsillectomy procedures be carried out with single-use instruments.

Blood transfusion

Although there is no evidence that CJD can be transmitted by transfusion of blood or blood products, measures for restricting blood donation are becoming more stringent. Recipients of human growth hormone before 1989 or recipients of other human-derived pituitary hormones before 1993 are deferred in the U.K.

The U.S Food and Drug Administration has revised its current guidance, specific changes will be implemented by May 2002. These include the deferral of donors who have stayed in the U.K. for a cumulative period of 3 months from 1980 to 1996 (currently 6 months) or for a cumulative period of 5 years or more in France; or have received a blood transfusion in the U.K. since 1980. From October 2002, those who have spent a cumulative total period of five years or more in Europe since 1980 will also be deferred. However, these measures are still controversial and are not acceptable to all the regulatory bodies.

Conclusion

Prion diseases are rare and hence do not pose major infection control problems. Routine standard precautions are recommended for caring patients with CJD or related diseases. Because of the extreme resistance to conventional disinfection procedures and the considerable uncertainties about prion diseases, nvCJD in particular, infection control measures tend to be conservative and controversial. With the accumulation of more information, we can expect further modification to the management of infected patients and contaminated equipment in the near future.

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Leptospirosis

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The recent incident of leptospirosis occurring in Hong Kong has hit the news headline and drawn the attention of public. There is also a resurgence of international interest to this disease as a result of outbreaks associated with El Nino phenomenon and flooding. In fact, it is not something new. The recognition of this disease as an occupational hazard has been described in ancient Chinese literature, and the syndrome of icteric leptospirosis was first reported by Adolf Weil more than 100 years ago. It was in 1915 that the causative agent was identified by two independent groups of researchers in Germany and Japan.

Classification & taxonomy

Leptospira are Gram-negative spirochaetes. Traditional method of classification is by serologic means. It is a phenotypic classification and segregates Leptospira into two different species, i.e. L. interrogans, which is pathogenic, and L. biflexa, which is saprophytic. Both species are subdivided further into different serovars.

Epidemiology

Leptospirosis is believed to be the most widespread zoonosis in the world. It is more common in warm-climate places & developing countries. Disease was maintained in nature by chronic infection of renal tubules in maintenance hosts, most of which are small mammals. Distinct geographical variations in maintenance hosts & the serovars they carry were observed. The routes of acquisition were thought to involve the followings: abrasions & cuts in skin, contact through mucous membrane or conjunctiva, invasion through intact skin after prolonged immersion in water, inhalation of aerosols or contaminated water, ingestion of contaminated water, animal bites and possibly human to human. Three categories of 'at-risk' activities were reported in literature, namely occupational exposure (farmers, veterinarians, abattoir workers, meat inspectors, rodent control workers, sewer workers, miners, soldiers, septic tank cleaners, fish farmers, canal workers, farmers, sugar cane cutters, etc), recreational activities (swimming, canoeing, rafting, fresh water fishing, caving, etc) and avocational circumstances (bare foot walking in damp conditions, gardening with bare hands, contamination of drinking water, etc).

Pathogenesis

Two major mechanisms are involved in pathogenesis of leptospirosis, namely toxin production and immune mechanisms. The toxins identified are lipopolysaccharides (LPS), haemolysin, sphingomyelinase, phospholipase C, pore-forming protein, antiphagocytic component of outer envelope and outer membrane proteins. Immune mechanisms that have been described are immune complex mediated inflammation, which are involved in the

development of interstitial nephritis and uveitis; autoantibodies that include anti-platelet antibodies, anticardiolipin antibodies and anticytoplasmic antibodies (ANCA); and apoptosis via stimulation by LPS with induction of tumor necrosis factor (TNF)-α; generation.

Clinical features

The clinical manifestations of leptospirosis are highly variable. Over 90% of patients who had initial exposure presented with self-limiting systemic illness; mild or subclinical infections were also observed for those who have frequent exposure. On the other hand, severe, potentially fatal illness accompanied by any combination of liver failure, renal failure and pneumonitis with bleeding diathesis was well documented. Severe disease in human is frequently due to serovar icterohaemorrhagiae. The specific serovars involved depend largely on geographic location and ecology of maintenance hosts, e.g. serovar lai is common in Southeast Asia. Clinical presentation of leptospirosis is biphasic. Following an incubation period of 5 to 14 days, the leptospiraemic phase sets in and lasts for about 1 week. This is followed by immune phase, which is characterized by antibody production & excretion of leptospira in urine. Complications usually develop during the second week of illness, associated with localization of leptospira within tissue. Depending on the severity of the disease and the predilection of organ involvement, different forms of manifestations were described.

(1) Anicteric leptospirosis. It is characterized by a febrile illness of sudden onset, associated with chills, headache, myalgia, abdominal pain, conjunctival suffusion, and transient skin rash. It lasts about 1 week, but fever may recur after a remission of 3 to 4 days. Aseptic meningitis may occur at this stage and the reported incidence was up to 25%. Mortality is virtually absent. Differential diagnoses for anicteric leptospirosis comprise viral exanthem, HIV seroconversion illness, dengue fever, glandular fever, Hantavirus infection, rickettsiosis, typhoid fever, brucellosis, and malaria.

(2) Icteric leptospirosis. It involves 5 to 10% of cases infected by leptospira, with mortality rate ranges from 5 to 15 %. Following an initial phase of illness similar to those patients with anicteric leptospirosis, there is abrupt onset of high fever and rapid progression to liver failure, renal failure, pneumonitis, cardiac arrhythmia or circulatory collapse, often preceded by few days' of improvement. Liver damage results from injury of liver capillaries in the absence of frank hepatocellular necrosis. Clinically, hepatosplenomegaly can be found in about 25 % of cases. Bilirubin may be disproportionally elevated, in face of moderate rise of transaminase and mildly elevated alkaline phosphatase (ALP) level. Hypoprothrombinaemia is uncommon and the MM fraction of creatine kinase (CK) may be grossly elevated. Renal damage is the result of interstitial nephritis and it manifests clinically as abrupt onset of renal impairment with rapid progression to oliguria. It is frequently associated with jaundice and often accompanied by thrombocytopenia without evidence of disseminated intravascular coagulopathy. Oliguria is a predictor of mortality. Pulmonary damage may occur in the absence of

renal or liver failure and results in pulmonary haemorrhage. It presents as cough, dyspnea, haemoptysis, and adult respiratory distress syndrome. Radiographic changes include diffuse small opacities which may coalesce and pleural effusion. Dyspnoea and radiological evidence of alveolar infiltrate are poor prognostic indicators. Cardiac damage may take the form of myocarditis, coronary arteritis and aortitis, and presents with features of heart failure, arrhythmia & sudden circulatory collapse. It is strongly associated with pulmonary involvement in several case series.

(3) Ocular involvement. Acute cases of leptospirosis may present with conjunctiva) suffusion, whereas uveitis often persists for long time and is thought to be the result of immune phenomenon.

(4) Other complications. Infection in pregnancy is associated with abortion and fetal death. Other reported complications include cerebrovascular accident, rhabdomyolysis, thrombotic thrombocytopenic purpura, acalculous cholecystitis, erythema nodosum, epididymitis, nerve palsy, Guillian Barre syndrome, and reactive arthritis. Possibility of chronic infection, like those produced by other spirochaetal infection, was suggested. However, other than uveitis, objective evidence is lacking to support this view currently.

Laboratory findings

In anicteric leptospirosis, the white cell count (WCC) ranges from below normal to moderate elevation. There is often a slight elevation of transaminase, ALP and bilirubin level. Urinalysis may reveal proteinuria, sterile pyruria, microscopic haematuria, hyaline & granular casts. Lumbar puncture (LP) findings consists of normal to slightly elevated cerebrospinal fluid (CSF) pressure, normal glucose, normal or slightly elevated protein, and elevated WCC with lymphocyte predominance. In severe cases, there would be elevated WCC with left shift, thrombocytopenia, renal impairment, deranged liver function with disproportional rise of bilirubin, and grossly elevated CK.

A number of methods are currently available for establishing the diagnosis of leptospirosis. Microscopic demonstration of the organism by means of dark field microscopy and immunofluorescence or other appropriate staining may be used for body fluid like blood, urine, and CSF. It has the disadvantage of being insensitive and non-specific. ELISA based techniques for antigen identification is sensitive and dipstick method is available. It is convenient, simple to perform and allows a rapid diagnosis to be made, but the applicability of this test is restricted by the vast numbers of serovars present and geographical variation in terms of seroprevalence. Isolation and culture of leptospira is tedious and requires the use of special semi-solid medium containing 5-fluorouracil. The organism is slow growing, and the specimen is examined weekly with dark field microscopy for 13 weeks before being discarded. Samples suitable for culture during the first week of illness include blood, CSF, and dialysate. Urine sample can be collected for culture from the beginning of second week onwards, and the duration of excretion varies.

Only a limited number of laboratories can perform the identification of the leptospira by serological or molecular techniques. Serological diagnosis by means of microscopic agglutination test (MAT) is still regarded as the gold standard. Antibodies start to appear in blood about 5 to 7 days after onset of illness. Titre following acute infection may be extremely high and take months or even years to fall to low level. On the other hand, seroconversion may rarely be delayed for many weeks after recovery. The situation is further complicated by the presence of 'anamnestic response'. For those who have serological evidence of past infection by another serogroup, there may be a rise of antibody titre against the previous serogroup that precede for weeks or even months the rise of antibody titre against the current serogroup. The Centre of Disease Control and Prevention (CDC) adopts a case definition of 'an antibody titre of greater than 200 with clinically compatible illness'. However, the cut-off value of the antibody titre will largely depend on seroprevalence locally. Molecular methods of diagnosis that are currently under study include polymerase chain reaction (PCR), restriction endonuclease (REA), restriction fragment length polymorphism (RFLP), and pulse field gel electrophoresis (PFGE).

Treatment

Outpatient management is usually sufficient for those with mild symptoms. LP is required sometimes for relief of headache. Patients with more severe symptoms should be admitted for observation and management in intensive care unit is mandatory for those with icteric leptospirosis. Support of organ functions is an essential component of management for those patients with severe disease. Leptospira are sensitive to many antibiotics in vitro. However, only a limited number of studies have successfully demonstrated the benefits of antibiotic treatment. The drugs of choice for severe disease are Penicillin 1.5MU q6h IV or Ampicillin 0.5 - 1 gm q6h IV. For mild disease, Doxycycline 100mg BD PO or Amoxycillin 500mg q6h PO are effective. One should watch out for Jarisch-Herxheimer reaction during treatment.

Vaccination and chemoprophylaxis

Immunity following the infection is largely humoral and strongly restricted to the homologous serovar or closely related serovars. Vaccination has limited success so far and one needs to give vaccine containing the dominant local serovars. Doxycycline 200 mg once weekly for prophylaxis has been shown to be efficacious in military personnel. Doxycycline chemoprophylaxis may be practical for short-term high-risk exposures.

Conclusion

Leptospirosis is an emerging infection that threatens the population living in areas with warm climate and exposed to risk of flooding or engaged in those 'at-risk' activities. Because of its non-specific initial presenting features, a high index of suspicion is required in order to arrive at the diagnosis early.