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Review Article

REVIEW ON LEPTOSPIROSIS IN ANIMALS AND HUMAN

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ABSTRACT

Leptospirosis is a contagious disease which infects both animals and humans. It is caused by bacteria called Leptospira. It can affect almost all mammals. Regular contact with the environment is a major risk factor, Laboratory testing for leptospiral infections is important both for diagnosis and management of the patients. Definitive diagnosis of leptospirosis is made by culture of Leptospira spp. from clinical samples such as blood or urine, or by the reference serological assay, the microscopic agglutination test (MAT). Infections in humans are known to occur primarily when individuals come in contact, directly or indirectly, with urine containing viable leptospires from rodents, or by ingestion of contaminated food or water. Several factors, such as age, sex, season, geographical location, and occupation have been associated with human leptospirosis The clinical presentation varies from patient to patient; hepato-renal failure, myocarditis, severe pulmonary hemorrhage with respiratory distress and meningitis are some of the syndromes reported commonly. Antibiotic treatment early in the illness may shorten the duration of fever and hospitalization for severe cases, penicillin is the preferred drug. For allegoric patients or less severe cases, Doxycycline, ampicillin or erythromycin can be given.

INTRODUCTION

Leptospirosis is a contagious disease which infects both animals and humans. It is caused by bacteria called Leptospira. There are over 200 different strains of Leptospira found worldwide, with infections being most prominent in areas that have a hot and humid climate. Leptospirosis is considered an occupational hazard for many people who work outdoors or with cattle, for example farmers, veterinarians, abattoir workers, sewer workers etc. [1,2]

Leptospirosis is a disease caused by beactria (germs) that can be found in all mammals. The bacteria are spread through the urine of infected animals or people, and can live in polluted water. Some people may get it from touching or swallowing water that has these bacteria. People can also get this disease through direct or indirect contact with the infected urine of people or dogs. The bacteria can get into a person's body through eating or drinking food or water with these bacteria, through a cut in the skin, or through mucous membranes (eyes, nose, mouth, or anusoglobinuria (blood/hemoglobin in urine), jau. Leptospirosis is a bacterial disease that affects farm animals, wildlife and humans. There are many different strains or serovars, carried by rodents and many other wild animals including rabbits, skunks and birds. Cattle, pigs and dogs are the main domestic animal carriers of leptospirosis. Leptospirosis in cattle is generally caused by one of two strains: Leptospira hardjo or Leptospira Pomona. These two bacteria infect the kidney and genital tract of cattle. [2]

The disease was first described by Adolf Weil in 1886 when he reported an "acute infectious disease with enlargement of spleen, jaundice, and nephritis." *Leptospira* was first observed in 1907 from a post mortem renal tissue slice. In 1908, Inada and Ito first identified it as the causative organism and in 1916 noted its presence in rats. Leptospira bacteria have been found in all farm animals, rodents and wild animals. They colonize the kidneys of infected animals and, in females, they also colonise the reproductive tract. Infected animals can carry the bacteria for long periods, shedding them in urine and at birth or abortion, thus contaminating the animals' environment. [3, 4, 5, 6]

- Leptospirosis is also spread in contaminated water supplies, food, pastures and soil.
- Many infected animals do not display any illness. These apparently healthy carriers are the main source of infection for other cattle as well as for humans.
- The bacteria can live for a long time in surface fresh water, damp soil, vegetation and mud, but are very quickly killed on dry soil or by sunlight.
- Flooding after heavy rainfall can spread the bacteria to previously uninfected farms. Outbreaks of leptospirosis

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infection are therefore more common in wet years. Even closed herds are not completely safe, as water from other properties could carry Leptospira organisms onto the farm.

- The bacteria may infect animals and humans through damaged skin or through the membranes lining the nose, eyes or mouth.

Signs of the Disease in Cattle [4]

Although many infections may pass unnoticed, severe outbreaks do occur. The most severe outbreaks are usually due to the introduction of an infected animal to a previously unexposed and unvaccinated herd.

Signs of disease in adult cattle differ, depending on the infecting strain.

Infection with L. hardjobovis

The most characteristic signs of L. hardjobovis infection are one or more of the following:-

- In both beef and dairy herds-a 'storm' of abortion in cows more than 5 months pregnant. The abortions may often occur several weeks after exposure to leptospirosis. In dairy herds-a sharp drop in milk production; and/or
- There could be changes in the milk and udder of diseased animals, these symptoms being indicative of mastitis. The milk may become thick and yellow and may contain clots but there is no swelling or extra heat in the udder.

Infection with L. Pomona

The other strain, L. Pomona, is carried by pigs, including feral pigs, and is often introduced to cattle herds following the animals' exposure to effluent from a piggery or the introduction of infected pigs onto the property. Infection with L. pomona can cause:

- Abortion in cows which are more than 5 months pregnant;
- In calves, high fever, jaundice and reddish-brown discoloration of urine, hence the name 'red water' for the disease.

Immune response to leptospirosis infection

Animals exposed to leptospirosis will develop immunity (even if they do not show signs of the disease) but only to the particular strain to which they have been exposed; that is, animals immune to L. hardjobovis will still be susceptible to L. Pomona, and vice versa. As the disease spreads through an unvaccinated herd, the immunity of the herd increases and the incidence of disease decrease. Once most animals are immune, exposure decreases and therefore immunity will start to wane (unless the herd is vaccinated). This allows cattle to become infected again, either by carriers or by some other fresh exposure to infection. In herds where leptospirosis is endemic, this cycle will continue to repeat itself. Calves reared by previously infected or vaccinated cows are protected by colostral antibodies for up to 6 months before becoming susceptible to the infection again.[5-6] Transmission of leptospira often involves direct contact with infected urine, placenta or milk. It can be transmitted venereally or transplacentally. The most common transmission is through direct or indirect contact with infected urine. Dairies commonly have leptospira contaminations in their environment. Dairy feeder calves are probably the largest carriers of leptospira in commercial feed yards. Dairy calves commonly suckle the sheaths and scrotums of other calves in the pen. This would be a direct contamination of infected urine from carriers by this suckling habit. Leptospira can also survive in the environment. Leptospira favors moist environments and moderately warm temperatures. Leptospira can survive for extended periods in stagnant water. Survival of leptospiral is brief in dry soil, cold temperatures or very hot temperatures. Therefore leptospira outbreaks are most common in dairy calves in the fall and spring.[4]Pathogenesis Leptospira enter the body through exposed mucous membranes in the mouth, eyes, skin abrasions or gastrointestinal tract. The incubation period for leptospirosis is 4 to 20 days. The leptospires circulate in the blood for 7 days. The leptospires replicate in the liver, kidneys, lungs, genital tract and central nervous system. The bacteria remain in the kidneys and may be shed in the urine for a few weeks to many months after infection. People at higher risk of getting leptospirosis include veterinarians, sewer workers, and farmers People with dogs that have or might have leptospirosis should protect themselves.[3]

Etiology and Pathogenesis

There are at least eight serovars or strains of the species that are of significant importance for dogs and cats. The most commonly diagnosed serovars in canine leptospirosis have been canicola, icterohaemorrhagiae, grippotyphosa, Pomona, and bratislava. Serovars are maintained in nature by numerous sub clinically or asymptomatic infected wild and domestic animal reservoirs that serve as potential sources of infection and illness for humans and other incidental animal hosts. Incidental hosts may develop severe clinical signs and can shed the organism. Examples of incidental hosts include, companion animals as well as livestock like cattle, pigs and horses. According to statistical and epidemiological studies, host types can be dynamic with time and can change with geographic locations of the world. Transmission of leptospirosis occurs by direct or indirect contact. Direct transmission occurs via oro nasal exposure with infected urine, venereal or placental transfer, bite wounds, or ingestion of infected tissues. Leptospire contact with mucous membranes and abraded skin can also be a method of transmission. Indirect (fomites) transmission, a very common form of transmission, occurs via exposure to contaminated sources of water, for example ponds, rivers and water catchment tanks, as well as soil, food or bedding. Spirochetes (organisms) optimally survive for weeks in the environment with conditions such as stagnant or slow-moving warm water and in soil with a neutral or slightly alkaline pH. These organisms do not survive in freezing conditions. The significance of disease transmission is unknown in association with invertebrates and insects. However, there is evidence of spirochetes surviving within these animals. Transmission to humans can occur directly or indirectly as described previously, but can also occur from recovered dogs that have experienced leptospirosis. The reasoning behind this is that recovered dogs excrete the organism in urine intermittently for months after infection. [7]

Leptospires enter the incidental host's system by penetrating abraded skin lesions or mucous membranes found within the nose, mouth, eyes and genitalia. These leptospires rapidly multiply while entering the vascular system. Further replication and spread occurs in the kidney, liver, spleen, central nervous system or neurologic system, eyes and reproductive tract. Increases in serum antibodies and immunity will clear the spirochetes from most organ systems; however, the spirochetes may persist within the kidney and be shed in the urine for weeks to months. Host susceptibility and the virulence of the organism will determine the extent of damage to internal organs

Causative Agent

Leptospirosis is caused by spirochete bacteria belonging to the genus Leptospira. 21 species of Leptospira have been identified. 13 species cause disease or have been detected in human cases. Leptospira are also classified based on their serovar. About 250 pathogenic serovars of Leptospira are recognized. The diverse sugar composition of the lip polysaccharide on the surface of the spirochete is responsible for the antigenic difference between serovars. Antigenically related serovars are grouped into 24 serogroups, which are identified using the microscopic agglutination test (MAT). A given serogroups is often found in more than one species, suggesting that the LPS genes that determine the serovar are exchanged between species. The traditional serologic system currently seems more useful from a diagnostic and epidemiologic standpoint-but this may change with further development and spread of technologies like polymerase chain reaction (PCR). It can lead to potentially fatal infections of the kidney, liver, brain, lung or heart.

There are two common ways to develop leptospirosis:

- Drinking or contact with water (such as by swimming, rafting or kayaking) or soil that has been contaminated by urine or body fluids of infected animals.
- Exposure to the urine or body fluids of infected animals.

The symptoms of leptospirosis

- Symptoms of leptospirosis can develop anywhere from 2 days to 4 weeks after being exposed to the bacteria.
- Common symptoms of leptospirosis include: Fever, Chills, Headache, Muscle Aches, Vomiting, Diarrhea, Abdominal Pain, Jaundice (yellowing of the skin and eyes), Skin Rash, Red Eyes.

Animals spread leptospirosis to people

Many animals can spread leptospirosis, including pets (such as dogs), farm animals, or wildlife. The animals that commonly develop or spread leptospirosis include: Rodents, Raccoons, Opossums, Cattle, Swine, Dogs, Horses, Buffaloes, Sheep, Goats.

Risk

There is always a risk of infection for people who have contact with infected animals or soil/water where the bacteria are present. People who work outdoors or with animals may be at increased risk for infection, such as: Farmers, Mine Workers, Sewer Workers, Slaughterhouse Workers, Veterinarians/ Animal Caretakers, Fishermen and people who work with fish, Dairy Farmers, Military Personnel.

Leptospirosis treated

If you have symptoms of leptospirosis, contact a doctor who can test for the disease. If an infection is confirmed, it will likely be treated with antibiotics (medicine that can cure the disease). Treatment is most effective when started as soon as possible.

Leptospirosis is prevented

There are several steps you can take to help prevent getting leptospirosis. These include:

- See a veterinarian to get vaccines for your pets that can protect against this disease.
- Avoid contact with animal urine or body fluids, especially if there are any cuts or abrasion of the skin.
- Do not swim in, walk in, or swallow water that may contain animal urine.
- Wear protective clothing or footwear near soil or water that may be contaminated with animal urine.

Symptoms

Symptoms of infection with leptospira may range from no symptoms to fatal disease. The illness often occurs in 2 phases.

Phase-I

The first phase, which usually last 5-7 days, begins suddenly with symptoms including:

High fever, Vomiting, Diarrhoea, Red eye, Muscle aches, Rash, Chills, Headache

Phase-II

A 2-Phase of illness may follow 1-2 weeks later, with symptoms such as:

Jaundice, Kidney failure, Irregular heartbeat, Lung problems, Meningitis, Red eyes

Leptospiral infection in humans causes a range of symptoms, and some infected persons may have no symptoms at all. Leptospirosis is a biphasic disease that begins suddenly with fever accompanied by chills, intense headache, severe myalgia (muscle ache), abdominal pain, conjunctival suffusion (red eye), and occasionally a skin rash. The symptoms appear after an incubation period of 7-12 days. The first phase (acute or septic phase) ends after 3-7 days of illness. The disappearance of symptoms coincides with the appearance of antibodies against Leptospira and the disappearance of all the bacteria from the bloodstream. The patient is asymptomatic for 3-4 days until the second phase begins with another episode of fever. The hallmark of the second phase is meningitis (inflammation of the membranes covering the brain). Ninety percent of cases of the disease are mild Leptospirosis. The rest experience severe disease, which develops during the second stage or occurs as a single progressive illness. The classic form of severe leptospirosis is known as Weil's disease, which is characterized by liver damage (causing jaundice), kidney failure, and bleeding. Additionally, the heart and brain can be affected, meningitis of

the outer layer of the brain, encephalitis of brain tissue with same signs and symptoms; and lung affected as the most serious and life-threatening of all leptospirosis complications. The infection is often incorrectly diagnosed due to the nonspecific symptoms[8] severe manifestations include extreme fatigue, hearing loss, respiratory distress, and azotemia.

Symptoms of severe disease may include

- jaundice (yellow eyes or skin from liver damage),renal failure, hemorrhage
- encephalitis and meningitis (inflammation of the brain and spinal cord)
- pneumonitis (inflammation of lung tissue)
- haemodynamic collapse (collapse of the cardiovascular system)
- Miscarriage.

Severe cases can result in permanent complications, most commonly kidney (renal) failure. Some patients suffer long-lasting, recurring symptoms, such as depression or muscle pains, and may have repeat hospital admissions over a period of years. In some cases, uveitis (inflammation of the eye) develops up to 18 months after the original acute infection.[9]

Detection Test [10,11]

On infection the microorganism can be found in blood and cerebrospinal fluid (CSF) for the first 7 to 10 days (invoking serologically identifiable reactions) and then moving to the kidneys. After 7 to 10 days the microorganism can be found in fresh urine. Hence, early diagnostic efforts include testing a serum or blood sample serologically with a panel of different strains. Kidney function tests (blood urea nitrogen and creatinine) as well as blood tests for liver functions are performed. The latter reveal a moderate elevation of transaminases. Brief elevations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (GGT) levels are relatively mild. These levels may be normal, even in children with jaundice.

Dark-field microscopy

Leptospires are too thin to be visible under the light microscope, but are visible under dark-field microscopy and by silver impregnation techniques. In dark-field microscopy, Leptospires are seen as silvery threads against a dark background. There is a high risk of false positive results because serum protein, fibrin strands and cellular debris in blood resemble leptospires. The concentration of leptospires in urine is too low to be detected by this method. Dark-field microscopy is used to examine leptospires in culture and to detect agglutination in the microscopic agglutination test (MAT).

Serological tests

After infection, sero conversion usually occurs in 10 days, but the duration may be variable. IgM antibodies appear earlier than IgG antibodies and remain detectable at low titres for months or even years. Detection of IgG antibodies is even more variable. Genus-specific, serovar-specific and serogroup-specific antibodies produced by the host's immune system react with leptospiral antigens, when patient's blood is brought in contact with antigens in the serological test kits. Some tests use live leptospires as antigens, while others employ extracts of leptospires.

Several serological methods are used for the detection of IgM and IgG antibodies. Some are used as screening tests for leptospirosis. Enzyme-linked Immunosorbent Assay (ELISA), Micro-Agglutination Test (MAT), Indirect Hemagglutination Assay (IHA), Micro Capsule Agglutination Test (MCAT), and Lepto Dipstick are commercially available. To make a reliable diagnosis, it is essential to use multiple techniques together or in succession. The antibody titre gradually increases during the course of illness, peaks and decreases after recovery Diagnosis of leptospirosis is confirmed by any one of the following criteria-

- Detection of leptospires in blood, cerebrospinal fluid, or urine,
- Suggestive clinical symptoms associated with either–[a] four-fold increase in initial titres by Micro-Agglutination Test (MAT) or a single MAT titre ≥ 400, or [b] detection of specific IgM antibodies by Dot ELISA or Dipstick ELISA.

Macroscopic slide agglutination test (MSAT)

This test is rapid and reliable for screening purposes. A fixed quantity of concentrated killed antigen is mixed with a fixed quantity of patient's serum sample on a slide. Presence of agglutination is observed with the naked eye. Agglutination (formation of clumps) indicates presence of genus-specific Leptospira antibodies in the serum sample (i.e. positive test). The antigen is stable for six months at 4 ° Celsius. In the early stage of the disease, it is more sensitive than MAT. When the antigen is colored with a drop of Gentian violet, the visual reading of the result is improved. The frequency of false negative results (due to auto agglutination of antigen when old cultures are used) is low.

Enzyme-linked immunosorbent assay (ELISA)

ELISA is a rapid, sensitive, and specific test and can be designed to detect IgM antibodies. Several techniques of ELISA are available, depending on the type of antigens and reagents used. Conventional ELISA techniques involve the use of antigen-coated micro wells and a sonicated preparation of different antigens.

Dot ELISA

Minute quantities of the antigen are dotted on nitrocellulose discs and the sera are reacted with chromogenic substrate that can be precipitated. The test is rapid (about two hours), economizes on quantity of antigen used, and can be performed in field settings due to its portability.

Dipstick ELISA

The Dipstick assay is easy to perform quickly and it does not require electricity or special equipment. An additional advantage is that the dipstick and the staining reagent can be stored for prolonged periods at tropical temperatures. ELISA is used as a screening test for leptospirosis [3]. Generally, an antigen derived from serovar hard jo of *Leptospira interrogans* is used with horseradish peroxidase. An anti-species antibody conjugated to an enzyme is added. The activity of the enzyme

is determined by adding a specific chromogenic substrate. Within a certain range of concentration, intensity of colour reaction is proportional to quantity of antibody present in the serum sample. IgM titre of 1:80 to 1:100 is considered suggestive of leptospiral infection and the diagnosis is confirmed by MAT.

Sandwich ELISA

Two-tip nitrocellulose dipstick (after loading with conjugate and incubating at room temperature for 45 minutes) is incubated in substrate solution for 3-5 minutes till a colored dot appears at the upper tip of the dipstick. Development of colored dots in both upper and lower tips of the dipstick indicates a positive result. The test is negative if only the upper tip of the dipstick shows a colored dot.

Lepto lateral flow

Lepto Lateral Flow (Royal Tropical Institute, Amsterdam, The Netherlands) is a rapid diagnostic test based on the binding of leptospira-specific IgM antibodies to the broadly reactive heat-extracted antigen prepared from non-pathogenic Patoc 1 strain. These bound antibodies are detected with an anti-human IgM gold conjugate contained within the test devices .This test uses stabilized components and is performed by adding serum and sample fluid to the sample well of the assay device. The assay is read after ten minutes and staining of the test line indicates positive result. The assay can be also performed at the bedside of the patient, using a drop of whole blood obtained by finger prick. The test kit and sample solution do not require any special storage. Hence this test is suitable for use in peripheral health centres and in field settings.

Indirect Hemagglutination assay (IHA)

The Indirect Hemagglutination Assay (IHA) uses a soluble antigen from serotype Patoc to sensitize sheep erythrocytes, which are then fixed with glutaraldehyde. The assay is easy to perform, and does not require specialized equipment or highly skilled personnel. The sensitized fixed erythrocytes may be stored for at least one year. The sensitivity and specificity IHA, as reported by two studies are outlined in the Table. The sensitivity of IHA was found to be substantially lower in a study from Hawaii, as compared to that reported in previous studies, particularly in the early phase of illness.

Micro capsule agglutination test (MCAT)

Micro Capsule Agglutination Test (MCAT) employs chemically stable microcapsules instead of sheep erythrocytes. Sonically disrupted antigens of leptospira are sensitized to microcapsules treated with glutaraldehyde. The sensitized microcapsule antigens are stable for at least one year. When coupled with mixed antigens, the microcapsules can be used as a screening test for infections caused by several serovars of leptospira.

Other serological tests for Leptospirosis

- In the Complement fixation test (CFT), standardization of reagents is a technically complex procedure. Its other limitations include short shelf life of reagents, and anti-complement activity of sera.
- Indirect fluorescent antibody test (IFAT) requires fluorescent microscope (expensive) and is not used in routine diagnostic laboratories.
- Counter Immuno electrophoresis (CIEP) is not commercially available.

Choice of serological test

The available serological tests are genus-specific and sero-group/serovar-specific. Genus-specific tests are more sensitive, less specific, and rapid. The sero-group/serovar-specific tests are useful most other bacteria, leptospires do not use external sources of pyrimidine bases for incorporation into their DNA or RNA. Being resistant to antimicrobial action of 5-fluorouracil (a pyrimidine analogue), this drug is used in selective media to isolate leptospires from contaminated clinical samples.

Culture provides definite proof of leptospiral infection. Isolated leptospires can be sero-typed to identify locally pathogenic serovars and to detect new serovars (useful as tool for surveillance in public health). Culture is a useful for post mortem diagnosis of infection in patients who died in early phase of infection, before antibodies could be detected.

Disadvantages

Leptospires grow slowly with a maximum doubling time of 6-8 hours. Optimal temperature (28-30 ° Celsius) has to be maintained. By the time diagnosis is made, antibodies are already detectable by serological techniques. Thus, it is not useful as a diagnostic tool for treating patients.

Sero-surveillance

Microscopic Slide Agglutination Test (MSAT) and Indirect Hemagglutination Assay (IHA) are screening tests for serological surveillance of leptospirosis. Since Lepto Dipstick and IgM ELISA have higher positive predictive value (PPV) during all stages of illness, these are also useful as screening tests. For these screening tests, samples of capillary blood are aseptically collected by finger prick on filter paper and are allowed to dry at room temperature [10]

Treatment [12,14]

Effective antibiotics include penicillin G, ampicillin, amoxicillin and Doxycycline. In more severe cases cefotaxime or ceftriaxone should be preferred. Glucose and salt solution infusions may be administered; dialysis is used in serious cases. Elevations of serum potassium are common and if the potassium level gets too high special measures must be taken. Serum phosphorus levels may likewise increase to unacceptable levels due to kidney failure. Treatment for hyperphosphatemia consists of treating the underlying disease, dialysis where appropriate, or oral administration of calcium carbonate, but not without first checking the serum calcium levels (these two levels are related). Administration of corticosteroids in gradually reduced doses (e.g., prednisolone) for 7-10 days is recommended by some specialists in cases of severe hemorrhagic effects. Organ-specific care and treatment are essential in cases of kidney, liver, or heart involvement.

Doxycycline

It is an antibiotic that is used in the treatment of a number of types of infections caused by bacteria and protozoa. It is useful for bacterial pneumonia, acne, Chlamydia infections, early Lyme disease, cholera and syphilis. It is also useful for the treatment of malaria when used with quinine and for the prevention of malaria. Doxycycline can be used either by mouth or intravenously. Doxycycline is a broad-spectrum antibiotic of the tetracycline class. Like other agents of this class it kills bacteria and protozoa by inhibiting protein production. [31]

Ceftriaxone

It is sold under the trade name Rocephin, is an antibiotic useful for the treatment of a number of bacterial infections. This includes middle ear infections, endocarditis, meningitis, pneumonia, bone and joint infections, intra-abdominal infections, skin infections, urinary tract infections, gonorrhea, and pelvic inflammatory disease. It is also sometimes used before surgery and following a bite wound to try to prevent infection. Ceftriaxone can be given by injection into a vein or into a muscle.

Cefotaxime

It is an antibiotic used to treat a number of bacterial infections. Specifically it is used to treat joint infections, pelvic inflammatory disease, meningitis, pneumonia, urinary tract infections, sepsis, gonorrhea, and cellulitis. It is given either by injection into a vein or muscle. It is not recommended in people who have had previous anaphylaxis to a penicillin. [.31]

Benzylpenicillin

It also known as penicillin G, is an antibiotic used to treat a number of bacterial infections. This includes pneumonia, strep throat, syphilis, necrotizing enterocolitis, diphtheria, gas gangrene, leptospirosis, cellulitis, and tetanus. It is not a first-line agent for pneumococcal meningitis. Benzylpenicillin is given by injection into a vein or muscle. Two long acting forms benzathine benzylpenicillin and procaine benzylpenicillin are available for use by injection into a muscle. It is not recommended in those with a history of penicillin allergy.[31]

Ampicillin

Ampicillin is a second-line agent or for patients younger than 8 years of age, in whom doxycycline is contraindicated. This agent interferes with synthesis of cell-wall mucopeptides during active multiplication, resulting in bactericidal activity. Excretion is primarily renal, although some ampicillin is metabolized by the liver[31]

Erythromycin ethylsuccinate

Erythromycin inhibits bacterial growth, possibly by blocking dissociation of peptidyl tRNA from ribosomes, causing RNA-dependent protein synthesis to arrest. In pregnant patients who are allergic to penicillin, erythromycin is the therapy of choice[31.]

Amoxicillin

Amoxicillin is a second-line agent or for patients younger than 8 years of age, in whom doxycycline is contraindicated. This agent interferes with synthesis of cell wall mucopeptides during active multiplication, resulting in bactericidal activity against susceptible bacteria[31.]

Immunization

- Vaccines are, in principle, suspensions of killed leptospires.
- Protection is largely serovar-specific.
- Potective antibodies are produced only against the serovars present in the particular vaccine used.
- Protection is of relatively short duration, and boosting at regular intervals is necessary to maintain protective titres of antibodies.

Vaccination

Almost all cases of human leptospirosis originate from unvaccinated stock. About 90% of dairy farmers vaccinate their breeding stocks, mainly to protect themselves and farm workers from infection. Farmers should work with their veterinarian to carry out a risk analysis, and then decide whether to vaccinate or not. Shedding is almost zero when calves are vaccinated before three months old and less likely on farms where calves are first vaccinated before six months old [21]. All other dairy cattle should be vaccinated according to veterinary advice. Vaccination is a long-term strategy – it will take time for an infected herd first starting on a vaccination programme to reduce or eliminate the risk, and stopping vaccination will result in herds that are more susceptible to infection and outbreaks.

Prevention

Rodent control can be important, particularly in urban areas. Other protective measures include avoiding contact with potentially contaminated water (e.g., lakes), and protecting food from contamination. Improvements in sanitation reduce the risk of leptospirosis in urban slums. Environmental modifications such as draining wet areas may decrease the incidence of disease, but are not always feasible or desirable. Personal hygiene and protective clothing are important preventive measures in high risk occupations. Gloves and protective clothing should be used when working with infected animals or tissues, with the addition of face shields or protective eyewear and face masks when the organisms might be aerosolized. Rubber boots decrease the risk of leptospirosis when wading in urine-contaminated water. Doxycycline has been used for short term prophylaxis. Human vaccines are available in a limited number of countries. Immunization protects only against the serovar in the vaccine or closely related serovars, and regular boosting is required. The currently available vaccines generally consist of organisms killed by phenol or formaldehyde, and can have side effects including painful swelling.[14]

Awareness

1. Ensure employees are aware of the cause and symptoms of leptospirosis, and ways of reducing risk. Use a poster checklist in the cowshed or a similar place to remind employees about risks, protection and first aid for exposure.
2. Use a similar system to make sure anyone else who will be in close contact with animals is aware of the risks.

3. Run an induction programme for new and casual employees, including a leptospirosis briefing.
4. Ensure people involved in seasonal work, e.g. lambing, drenching, shearing, tailing and dagging, are aware that they may be at risk of infection.
5. Display control/clean-up information procedures if major splashes occur.
6. Ensure the vaccination status of animals is known and clearly documented.
7. Keep children away from potential sources of infection.

Hygiene

Personal hygiene is good additional protection.

1. Wash hands regularly, using water, soap, and disinfectant.
2. Use disposable towels only.
3. Don't scrub hands harshly as it may cause breaks in the skin.
4. Always wash your hands after using the toilet or handling animals, and before eating, drinking, smoking, or taking a break. Wash your face if you have facial hair.
5. Do not touch your eyes, nose or mouth before washing your hands.
6. Cover cuts, scratches, blisters and skin breaks with waterproof, sterilising coverings, and change coverings regularly.
7. Ensure deeper wounds are fully healed before doing close work like shearing or crutching.
8. Do not smoke, drink or eat when handling livestock, as this can introduce bacteria into the mouth. Keep coffee mugs away from the work area.
9. Wash your clothes after handling stock.
10. Keep toilets and hand-washing facilities clean.

Personal protective equipment

The aim of PPE is to prevent urine, contaminated water and fluids from getting through cuts in the skin or the mucous membranes of the eyes, nose or mouth. Provide and maintain PPE, and demonstrate how it should be worn. PPE may include:

1. Goggles.
2. Face shields that protect the eyes, nose and mouth, particularly during activities that pose a risk of urine splash on the face, eg milking.
3. Milking sleeves, and clean aprons and gumboots in the milking shed.
4. plastic aprons and gloves when assisting with animal birth, handling afterbirth and aborted fetuses, and kidneys or bladder (gloves are particularly important when scanning animals for pregnancy using rectal probes, as this requires holding the animal's tail which is often contaminated with urine).
5. Solid and sealed footwear so water doesn't get in from the top – wet boots and gloves should be changed before water softens the skin and allows bacteria in.[34]

CONCLUSION

Human Leptospirosis is a rare disease caused by bacteria Leptospira. In this disease vaccination are given to the animal neither the human beings. Clinicians must be more aware of Leptospirosis. Nonspecific clinical presentation. Laboratory diagnosis is difficult. Consider Leptospirosis as a differential diagnosis for any undifferentiated febrile illness. Early detection leads to early treatment with antibiotics, steroids and other supportive measures.

Future scope

Human leptospirosis having great scope for further research. Mechanism of action of drugs used in leptospirosis is not exactly known and specific drug for leptospirosis is not invented yet so having scope in the future for newer drugs which can be used on leptospirosis.

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