Leptospirosis: yesterday and today...

Leptospirosis was described first in 1852 in dogs. Because of its appearance at a dog show in Stuttgart it was long time known under the term „Stuttgarter Hundeseuche“. The physician Adolf Weil described the disease roughly 30 years later for the first time in humans (Weill disease or “field fever”).

Today, we know that in addition to the clinical disease we even have a high percentage of sub-clinical infected animals, which excrete leptospires. These can be of potential risk for transmission to humans.

Aetiology
Leptospires are gram-negative bacteria belonging to the group of spirochetes. They are very thin flexible helicoid bacteria with a spiky end. Leptospires are actively moving. Within the genus *Leptospira interrogans sensu lato* we find different pathogenic and saprophytic types. Differentiation cannot be made morphologically, but only serologically or genetically. Since 1989, over 250 serovars are described. Currently 24 serogroups are distinguished.

Epidemiology
The transmission takes place directly through urine or blood of infected animals or indirectly through vectors such as contaminated water sources, food and bedding or living vectors like rodents. Leptospires survive best in a moist environment at temperatures of 0-25 °C. In studies there is a significant correlation between the average rainfall recorded three months prior to diagnosis and the number of cases identified. A recrudescence of leptospirosis cases can be expected after intense rainfall and/or floods, especially in the warm season.

Dogs four to ten years of age seem to be more affected than juveniles under one year. A rural environment and animals that have contact with livestock as well as hunting dogs are at a greater risk of developing leptospirosis than dogs mainly staying in homes.

Pathogenesis
Leptospires infect their host by through skin lesions or the intact mucosa of the digestive or genital tract. The incubation period is described as roundabout seven days depending on the virulence or the immune response of the affected animal.

Clinic features
The clinical picture of leptospirosis is expressed initially by anorexia, vomiting, dehydration and fever. In the ongoing disease process the animals appear apathic and often show a forced breathing.

Quite often the mucous membranes show icteric coloration. Animals show anaemia with haemoglobinuria and in some cases complication such as DIC may occur. Toxic by-products lead to a hemorrhagic diathesis and necrosis.

As a consequence, there may develop an acute nephritis with azotaemia. In some cases a severe and acute hepatitis occurs.

Laboratory Diagnostics
Laboratory diagnostic work most frequently shows increased levels of urea, creatinine, phosphate and bilirubin. AST, ALT, AP and LDH values usually are elevated as well. Amazingly in some serovars, like *L. canicola*, *bra tišlava* and *grippotyphosa* renal dysfunction dominate over liver involvement, while *L. icterohaemorrhagiae* and *L. pomona* seem to primarily cause hepatopathy. In young animals, there seems to be a tropism for liver tissue, while in peracute cases renal dysfunction is the major sign.

This means that in some cases "only" an increase of one or the other group of laboratory parameters is seen. These aspects should be taken into account in judging differential diagnosis. Leukocytosis together with a left shift is observed almost always. In almost all cases there will be a significant proteinuria and haematuria.
Serological evidence of infection is found via micro agglutination (MA). Positive antibodies (≥ 1:100) initially only confirm contact with the pathogen. Many animals are seropositive without clinical signs. Recently published studies showed a 25% prevalence of antibodies in clinically healthy dogs without vaccination history with MA titres of 1:200 and higher against up to six serovars. This correlates with investigations of samples received at LABOKLIN, which show that dogs show immunological reactions against various serovars. Generally titres of ≥ 1:400 or a three-fold titre increase in a confirmatory test is the diagnosis preferred. Since a bundle of serovars usually are tested in case of questionable infection antibodies due to vaccination usually don’t hamper the interpretation of the serologic result.

One problem, however, is a “diagnostic gap” between incubation period and the immune response of the body. Severe and especially peracute diseased animals show only low or even negative antibody titres. Treating animals already in an early phase of infection with antibiotics may not develop high titres or show a titre increase. Diagnostic test of choice in these cases is the PCR (see below).

In recent years a shift in the types of serovars taken responsible for infection is observed. Own investigations from the year 2002 (n = 1440) and 2007 (n = 2638) in the dog showed following distribution:

Antibodies were classified on a basis of 1:400 and higher as positive. Lower titres were not included in these statistics. This should ensure that the titres confirm infections and are not considered to be titres due to vaccination. The results show a significant increase in the prevalence of serovars of L. grippotyphosa, bratislava and canicola. All three serovars have represented approximately 20% of positive samples. The serovars L. saxkoebing, autumnalis and pomona showed only minimal shifts. A particularly significant change was the emergence of serovar L. icterohaemorrhagiae in 2002 still 46.7% of the samples were positive as today only 6.3%.

A diagnosis bases on PCR using urine as sample material is the method of first choice especially in acutely infected and pre-treated animals, since bacterial growth can be impaired, and/or antibodies are not yet detectable. Healthy dogs can excrete leptospires over a period of months, so this detection method is an interesting tool for multi-dog-households/ breeders or animal shelters especially under zoonotic aspects. A “disadvantage” of PCR is that it is not possible to distinguish between serovars using routine test designs. This is reserved to more elaborate molecular biological methods. However, the PCR method has a higher sensitivity and is therefore by far preferable over formerly used dark field microscopy.

**Treatment and Prognosis**

In addition to the symptomatic therapy with antiemetics and infusion, the aim is to reassure a sufficient urine production. Urine output should be ≥ 2ml/kg/h. An antibiotic therapy should take place in two stages:

1st critical stage: Ampicillin or Amoxicillin 20-25 mg / kg i.v. bid
2nd stage: Doxycyclin 10 mg / kg sid/bid for at least three weeks to prevent urinary excretion
(Source: F. Gaschen WSAVA 2008)

The prognosis varies according to different studies by 50-90% recovery after about 10 days. Oliguric / anuric renal failure is a strong negative prognostic factor.

**Prevention**

The most important aspect of prevention is regular vaccination. It is unfortunately not clear to what extent a cross-protective immunity between the serovar of L. canicola / grippotyphosa and other serovar exists. During humid and warm weather the owners should prevent that the dogs drinks from ponds or standing puddles.
Leptospirosis in other species

Leptospirosis is also seen in other domestic and farm animals. Leptospirosis of ruminants can lead to economic losses and is a notifiable animal disease. Of 130 cattle samples received in our lab 11 samples / 8.46% had detectable leptospires antibodies > 1:400. Serovars prevalent here were L. icterohaemorrhagiae (44.4%), saxkoebing (38.9%) and bratislava (16.7%). The emerging serovar L. hardjo was not detected.

Even in horses infection occurs more often now. There were 1,649 samples analyzed and in 4.73% of these submitted samples a titre of > 1:400 could be detected. Prevalent serovars were:

<table>
<thead>
<tr>
<th>Serovar</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>L. grippotyphosa</td>
<td>24.8%</td>
</tr>
<tr>
<td>L. bratislava</td>
<td>23.9%</td>
</tr>
<tr>
<td>L. saxkoebing</td>
<td>16.5%</td>
</tr>
<tr>
<td>L. canicola</td>
<td>11.9%</td>
</tr>
<tr>
<td>L. australis</td>
<td>7.3%</td>
</tr>
<tr>
<td>L. icterohaemorrhagiae</td>
<td>6.4%</td>
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<tr>
<td>L. sejroe</td>
<td>5.5%</td>
</tr>
<tr>
<td>L. autumnalis</td>
<td>3.7%</td>
</tr>
</tbody>
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Zoonotic potential

Leptospirosis is a notifiable disease in many European countries. People get infected during agricultural work but also in leisure activities or water sports. People at higher risk such as e.g. veterinarians and owners of infected animals should take care of specific hygiene as well as wear gloves during manipulation. This applies equally, because of risk of asymptomatic shedding, to larger canine facilities.