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DISCUSSION ON CANINE JAUNDICE: WITH SPECIAL REFERENCE TO LEPTOSPIRAL INFECTION

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[*Reprinted from the* PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE, *1925, Vol. XVIII (Section of Comparative Medicine), pp. 17—21.*]

London
JOHN BALE, SONS & DANIELSSON, LTD.
OXFORD HOUSE
83-91, GREAT TITCHFIELD STREET, OXFORD STREET, W.1
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1925

DISCUSSION ON CANINE JAUNDICE: WITH SPECIAL REFERENCE TO LEPTOSPIRAL INFECTION.

Dr. C. C. OKELL: I do not propose to discuss in detail the work carried out by Dalling, Pugh and myself on this disease. In the *Veterinary Journal* of January, 1925, we have given a full account of our attempt to ascribe enzootic jaundice in dogs to leptospiral infection. In brief, our hypothesis was developed along the following lines: we compared enzootic jaundice clinically and anatomically with leptospiral infection in man and other animals.

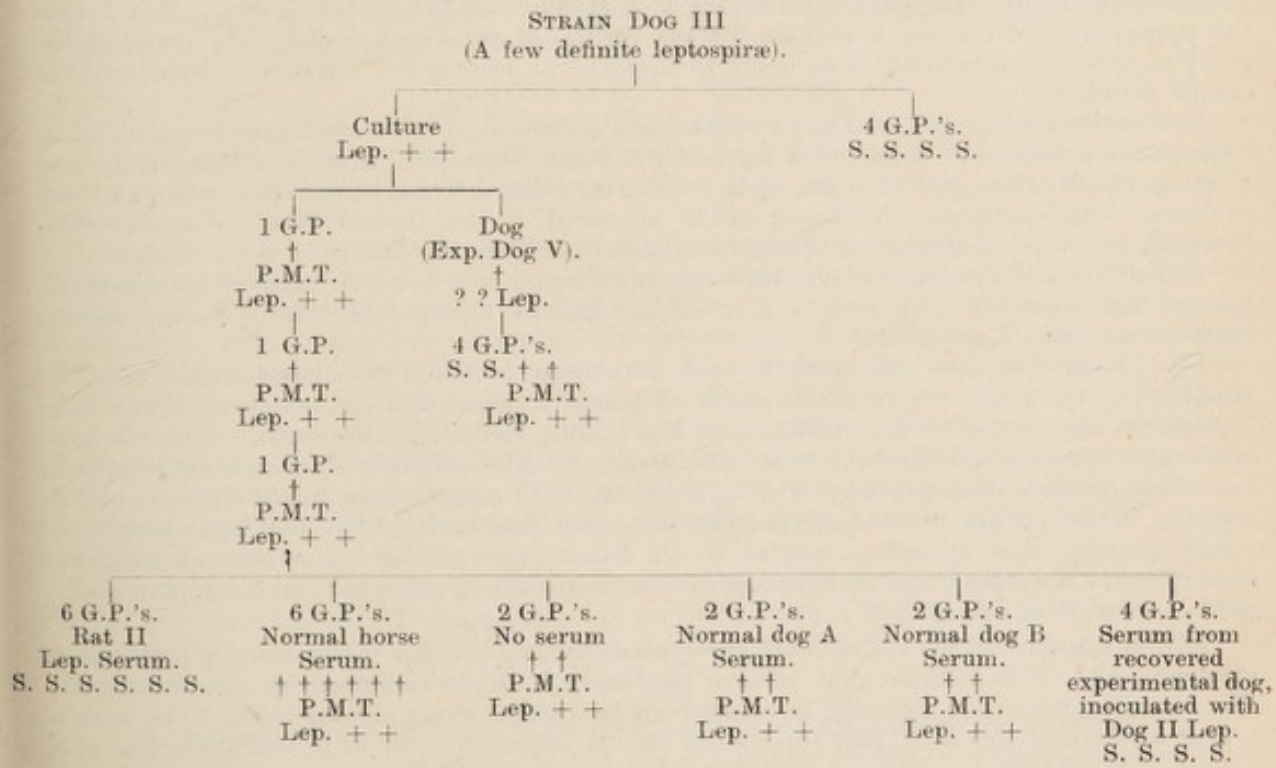
From the *clinical standpoint* we found in common such a characteristic group of symptoms as jaundice, hæmorrhages, albuminuria and a definite type of temperature curve. We found, moreover, such exceptional symptoms as acute muscular tenderness, hæmorrhages, herpes and keratitis, all of which occasionally occur in canine jaundice and are characteristic of leptospiral infections in general. From the standpoint of *morbid anatomy* we met with almost identical lesions in canine jaundice as in leptospiral infection in man and other animals—enteritis, nephritis, parenchymatous degeneration of the hepatic cells, and the hæmorrhagic condition of the lungs and other organs so typical of leptospiral infection.

To make a still closer comparison, we inoculated dogs with leptospiræ from the rat and reproduced a disease which, so far as we were able to see, was indistinguishable from the naturally occurring enzootic jaundice.

We examined in detail the material from ten dogs which had suffered from enzootic jaundice, and from the tissues of three of these we were able to isolate a leptospira and to submit it to further experimental study. In one further case we saw undoubted leptospiræ by dark-ground examination of ground-up liver, but we failed to isolate them.

The accompanying "passage tree" gives an account of the passages and cross-protection experiments with serum performed with one strain; similar experiments were done with the other two strains we isolated from dogs.

PASSAGE TREE OF STRAIN DOG III LEPTOSPIRA.



P.M.T. = Typical post-mortem appearances. † = Died. G.P. = Guinea-pig.
Lep. + + = Many leptospiræ present. S. = Animal survived with no symptoms.

With respect, then, to the three strains that we isolated, we have satisfied almost completely the postulates of ætiology usually demanded before ascribing a disease to a given micro-organism. We were able to show that the virus was living and could be propagated through many generations, that it was capable of producing the typical disease in dogs and other animals, and that pure cultures of the three strains were fully and characteristically pathogenic. All the strains are still being maintained in culture and in guinea-pig passage, and there is no evidence of any deterioration in their virulence. In all respects they seem identical with *Leptospira icterohæmorrhagiæ*.

We were less fortunate in satisfying Koch's important postulate, "that the parasitic micro-organisms are to be found in all cases of the disease." We met with, however, an almost equal difficulty in finding and isolating the leptospira in dogs we infected with massive doses of leptospiræ of canine and rat origin, which produced death with typical post-mortem lesions. A similar difficulty is, of course, met with in isolating leptospiræ from human beings suffering from Weil's disease, though nobody now seriously questions that the disease is due to leptospiral infection.

We had hoped to obtain confirmation of our hypothesis by finding leptospiræ constantly present in the tissues of affected dogs, and we made a full examination of the material by means of Dobell's modification of Levaditi's stain. In one dog only did we find characteristic leptospiræ in a hæmorrhagic lumbar gland. We found equal difficulty in finding leptospiræ in the tissues of dogs experimentally infected with massive doses of leptospiræ.

It is an interesting question, which I hope will receive attention in the subsequent discussion, as to why the leptospiræ, which can be found with comparative ease in infected guinea-pigs, should be so elusive in man and in the dog. A further important line of confirmation is the study of the immune properties of the serum of dogs which have recovered naturally from the disease. The serum of animals which have been experimentally infected with leptospiræ and subsequently recover, usually has marked protective properties. In our own experience untreated enzootic jaundice is so fatal that we have been unable to obtain much material of this kind.

We have obtained a small amount of serum from only one dog which had recovered from the natural disease, and that reached us in a contaminated condition. Two guinea-pigs were injected with 0·25 c.c. of this serum and afterwards with a virulent strain of leptospira, one of dog and one of rat origin. Both died prematurely from peritonitis, but without any trace of jaundice or other symptoms of leptospiral infection, while all the control animals inoculated with the same strain died typically of jaundice on the preceding day. May I take this opportunity of making a request for the serum of recovered dogs? The result of the study of a few such sera would do much to advance or destroy the leptospiral hypothesis of canine jaundice.[1]

It is an interesting question as to why human cases do not more often occur in association with canine enzootics of jaundice if the latter is due to leptospiral infection. Krumbein and Frieling, in 1916, reported an instance in which two officers, living in the same room as a dog suffering from jaundice, developed what appeared to be typical Weil's disease. The investigators were, of course, at that time unable to confirm the nature of the infection.

Uhlenhuth and Fromme (1919), while investigating an area in which cases of human Weil's disease had occurred, met with a case of jaundice in a dog which they proved almost conclusively was leptospiral.

Dr. Passey has also met with a case of human jaundice associated with a case of jaundice in the dog. A further case of associated human and canine jaundice has been brought to our notice by Dr. Stirling and Mr. Lornie, M.R.C.V.S., of Perth. These isolated cases are, however, all we have been able to trace. The problem is, of course, related to the other problem, namely, why is Weil's disease in human beings relatively rare in this country, while 20 per cent. to 30 per cent. of adult rats harbour virulent leptospiræ? It seems possible that sporadic cases of Weil's disease are not so uncommon as published accounts would suggest, and possibly some cases diagnosed as catarrhal jaundice are in reality mild cases of Weil's disease.

At the same time, the spirochætal group of organisms present many obscure problems of virulence, and it is possible that strains may vary in their virulence to certain animals. These are matters that can only be cleared up by further experimental work. The work of recent workers in this field, particularly the recent important study by Buchanan, has shed

[1] Since this was written the serum of another dog which had recovered from enzootic jaundice has been examined. 1 c.c. of this serum protected against certainly lethal doses of leptospiræ obtained from both the dog and the rat.

much light on the biology of the leptospiral group, but at the same time has shown how complicated are their activities in nature and in disease.

If enzootic jaundice in dogs is, indeed, a leptospiral infection, the main line of both prophylaxis and treatment is obvious.

In the enzootics we have investigated, we have found that the affected kennels have always been infested with rats. In the only three outbreaks in which we have been able to examine the rats from the kennels we have found that they harboured virulent leptospiræ. A source of infection by leptospiræ is therefore not far to seek, and we consider that anti-rat measures offer a most promising method of prophylaxis.

The use of anti-leptospiral serum in both prophylaxis and treatment has already been put to the test, and although our experience is small, we believe we have obtained significant results. We are also testing the value of leptospiral vaccines in the prevention of the disease.

In conclusion, I should like to take this opportunity of thanking my veterinary colleagues, Mr. Dalling and Mr. Pugh, for giving me the opportunity of co-operating with them in their work on this very interesting subject of what may be properly called comparative pathology.

Mr. L. P. PUGH: Clinically, canine jaundice caused by *Leptospira icterohæmorrhagiæ* can be classified as (1) the hyperacute type, (2) the icteric type.

Hyperacute Type.—This form is characterized by a rapid febrile course, extreme prostration, complete inappetence, and the passing of blood-stained mucus-coated fæces. Hæmorrhages from the lips, gums, nose, and occasionally from the eyes and face, are observed. Dyspnœa frequently occurs, accompanied by a short cough, and great thirst is often observed. Death may take place in a few hours or the dog may live for several days. Icteric symptoms are only occasionally met with.

Icteric Type.—This form is generally referred to as "yellows" by the lay public, because of the coloration of the various mucous membranes and tissues. The onset and course vary. Some dogs show icteric symptoms when first affected, whilst in others, the disease commences with general malaise, discharge from the eyes and nose, constipation and loss of appetite, the discoloration of the tissues appearing at a later stage. It is rare to find the initial temperature above 103° F., and it usually falls to normal or subnormal on the appearance of icterus. The buccal mucous membrane is at all times normal except for the yellow coloration. Vomiting is a constant symptom, the vomitus often being blood-stained. Constipation is usually marked in the early stages, and later gives place to diarrhœa with blood-stained stools. The urine is highly albuminous and dark-coloured. The death-rate is high—usually over 90 per cent., intussusception of the intestine being apparently an important contributory agent in the causation of death.

DIFFERENTIAL DIAGNOSIS.

Canine Piroplasmosis.—It is doubtful if this condition ever occurs under natural conditions in this country. We have examined many blood-smears from naturally occurring cases of infectious jaundice and on no occasion have we observed any evidence of an intracorpuscular parasite.

Moreover, we have treated many naturally occurring cases of infectious jaundice with trypan blue and have failed entirely to obtain the same gratifying results that are obtained abroad with this treatment. A perusal of the literature on canine piroplasmosis brings out considerable differences between it and the disease we are now considering, though in some points there is apparent agreement. In piroplasmosis, hyperæmia of the internal organs, especially the liver, kidney and bone-marrow, is common. There is marked enlargement of the spleen, and the gastro-intestinal tract is pale; in leptospiral jaundice these features are uncommon. In both diseases the mesenteric lymphatic glands are red and enlarged, and hæmorrhages may occur on the serous membranes. In these points there is agreement. Again, recovery is said to be common in piroplasmosis, while in jaundice there is death in at least 90 per cent. of affected cases.

Mr. T. DALLING: Dr. Okell and Mr. Pugh have discussed leptospiral jaundice from an experimental and a clinical standpoint. I propose to add a little to what has already been said, taking two points only: (1) a comparison between the naturally occurring and the experimentally produced disease; (2) prophylaxis.

COMPARISON BETWEEN THE NATURAL AND EXPERIMENTAL DISEASE.

As Mr. Pugh has pointed out we classify naturally occurring leptospiral jaundice as hyperacute, hæmorrhagic, and the icteric, i.e., the form in which dogs die early in the course of

the disease without showing yellow coloration of the mucous membranes and skin, and that in which the course is more insidious and the characteristic symptom is a general icterus. Of the ten naturally occurring cases we have examined, three were of the former type and seven of the latter. In no experimentally produced case of the disease have we seen the hyperacute hæmorrhagic type. Of the eighteen dogs used for experiment with dog-strain leptospira, sixteen developed marked jaundice symptoms, and all of the three dogs inoculated with the rat strain became typical clinical cases of the icteric type.

The points of resemblance between the natural and experimental disease during life are the following: (*a*) Constipation early in the course, giving place later to loose, clay-coloured stools, often blood-streaked and mucus-coated. (*b*) Vomiting; with the experimental dogs this does not occur till the third or fourth day after infection. It is not a constant feature of either disease to find blood in the vomitus, but it may be present. (*c*) An elevated temperature preceding the development of icterus with a fall to normal or subnormal immediately following the appearance of icterus and continuing to fall till the death of the dog. (*d*) The appearance of general icterus. The time that it takes for icterus to make its appearance after the first symptoms are observed in the naturally occurring cases is shorter than that needed for its development after inoculation of leptospiral material in the experimental dogs. This may be accounted for by the time taken for the onset of symptoms after infection, for we know that it is common for experimentally infected dogs to show nothing abnormal till jaundice appears, and yet death may occur the following day. (*e*) Depression and general malaise occur in both forms, and though they may not be marked early in the disease, they become very obvious as the disease progresses, and for hours the dog may lie as if dead before death actually occurs. Such symptoms as hæmorrhages of the gums, discharge from the nose, &c., are seen in both conditions, though they are not common in either form.

From the standpoint of morbid anatomy the natural and experimental diseases are identical, and while in neither form are constant gross lesions found, yet in both the essential lesions are present. These lesions can be grouped under the term hæmorrhage, for no matter in which tissue the lesion occurs it is essentially a hæmorrhage. The tissues most commonly involved are the lungs, intestine, lymphatic glands and serous membranes. The *lungs* exhibit hæmorrhages varying much in size. Cases have been seen in which the whole lung is involved, while on the other hand, we have observed other lungs where it was only after careful search that small lesions could be located. In the *intestine* the lesions may be confined to small areas or the whole tract may be involved. The hæmorrhages are subserous, and submucous. Any or all of the *lymphatic glands* may contain lesions, but in all cases, both natural and experimental, the mesenteric and bronchial gland lesions are constant. The gland may show minute hæmorrhagic points or it may be enlarged, congested and œdematous. The lumbar and hepatic lymphatic glands are usually but not constantly affected. Hæmorrhages occur on any or all of the serous membranes, and, as in the case of other tissues, the size and appearance of the lesion vary.

Prophylaxis.

The general lines upon which prophylactic measures should be undertaken have been pointed out, i.e., the use of anti-leptospiral serum and the eradication of rats from kennels. We have shown experimentally that anti-leptospiral serum has the power of protecting dogs from developing leptospiral jaundice even after infection has taken place. Eleven dogs were inoculated intraperitoneally with guinea-pig liver containing the parasite in doses which experience had shown were sufficient to produce death in five to six days. Twenty-four hours after inoculation two dogs received 10 c.c. of antileptospiral serum. Forty-eight hours after inoculation, two more received a similar inoculation. On the third day yet another two received such an injection, and on the fourth day four more were treated, one being left untreated. Those dogs inoculated with serum on the first, second and third day following infection, presented no abnormal characters at any time, while all the others, i.e., those inoculated on the fourth day, and the control dog, developed the typical icteric form of the disease and died. We have shown many times, under carefully controlled conditions, that the inoculation of antileptospiral serum at the same time as virulent leptospiral material into guinea-pigs, has given a complete protection. In the field we have also had proof that protection is afforded by the use of the above serum; hence it can be definitely laid down that an important prophylactic measure is the use of such serum. It may be necessary to repeat the inoculation of serum if the dogs are still believed to be exposed to infection.

The presence of leptospiræ in rats and the association of infected rats with disease-producing kennels induces us to believe that such rats play an important part in the transmission of the disease. Since publishing an account of our experiments we have received several communications from veterinary surgeons and others who have had experience of this condition. They draw attention to the association of jaundice with rats, and two state that the infected dogs had been bitten by rats before the appearance of symptoms. We are not in the position to say that the bite from an infected "carrier" rat may give rise to leptospiral jaundice, but we believe that the common means of transmission is food and bedding soiled by rat urine containing living leptospiræ. We have no evidence that lice or other arthropods play a part in transmission. Many, but not all, infected dogs harbour lice.

In dealing with prophylaxis the fact that one of our experimental dogs, which recovered after showing icteric symptoms, still harboured leptospiræ in the kidneys for some weeks, must be borne in mind. Recovered dogs, therefore, should be treated as "carriers" until it has been proved that they do not excrete leptospiræ in the urine.