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BLOOD-PRESSURE IN DOGS WITH RENAL CORTICAL HYPOPLASIA

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In earlier reports on renal cortical hypoplasia in dogs accounts have been given of the clinical picture of the disease, with special reference to the uraemia and the secondary hyperparathyreoidism and to electrocardiographic changes in the uraemia due to renal cortical hypoplasia. In his works on the pathology of renal cortical hypoplasia in the dog *Krook* (1957) points out that some of the non-renal changes in this disease are caused by hypertension. It has long been known that some chronic renal disorders in man are attended by a raised blood-pressure. The occurrence of spontaneous renal hypertension in the dog has been much debated. The strongest supporting evidence for the occurrence of renal hypertension is considered to be the hypertrophy of the left side of the heart often seen at autopsy of uraemic cases (*Nieberle* and *Cohrs,* 1954). In the study presented here results of blood-pressure determinations in dogs with renal cortical hypoplasia will be reported. Normal values from blood-pressure measurements will also be reported.

MATERIAL AND METHODS

The studies concerned partly dogs admitted to the medical clinic of the Veterinary College over the years 1955—1960, and partly experimental dogs. All were cocker-spaniels with recognized renal cortical hypoplasia. The first group comprised 7 dogs, 5 males and 2 females. Their ages ranged from 8 to 18 months. Six of the seven dogs were subjected to autopsy, at which the diagnosis was verified. The experimental dogs were obtained from parents that had earlier born puppies with renal cortical hypoplasia. In this group, which consisted of 21 dogs from 5

litters, the disease manifested itself in 3 dogs, all females. These three died at the age of 10, 16½ and 17½ months, respectively. All the dogs in the experimental group were subjected to continuous clinical investigations, including blood-pressure measurements. The blood-pressure values for the healthy dogs were treated statistically and regarded as a normal material.

The blood-pressure was measured by a direct method, using a polyethylene catheter inserted into the femoral artery and connected with a mercurial manometer. The mean arterial pressure was thus obtained. In most of the dogs the blood-pressure recordings were done on the same occasion as renal clearance determinations were performed under anaesthesia with "Mebumal".[1]) In some cases of the clinical material the blood-pressure was recorded in non-anaesthetized dogs. The dogs did not show any unfavourable responses that might be thought to have influenced blood-pressure.

RESULTS

From the continuous blood-pressure measurements in the 16 healthy experimental dogs one value from each dog, taken at the age of approximately 12 months, was selected for statistical analysis. The result of the latter is presented in Table 1, in which the values both for the normal and for the hypoplastic dogs are given.

Table 1.

Blood-pressure in normal dogs and in dogs with renal cortical hypoplasia. The values are given as mm Hg.

	Number of dogs	Range	Mean	Standard deviation	Standard error of mean
Normal dogs	16	130—160	148	8.7	2.2
Dogs with renal cortical hypoplasia	10	105—165	137	17.5	5.5

[1]) The formula of "Mebumal" is as follows:

5-ethyl-5(1-methylbutyl)-malonylcarbamide (pentobarbitone)	1.8 g
Pentobarbitone sodium	4.0 g
Urethane	25.0 g
Spir. conc.	15.0 g
Glycerin	12.5 g
Aq. steril.	ad 100 ml

In the comparison of the values given in Table 1 Student's t-test was used for determining the degree of significance. No significant difference in blood-pressure was found between healthy and hypoplastic dogs ($P > 0.05$). Table 2 shows in detail the results of the different blood-pressure recordings as well as the state of the heart at autopsy.

Table 2.

Blood-picture, mean arterial pressure, and state of heart at autopsy in dogs with renal cortical hypoplasia.

Dog	Clinically observable anaemia (+)	Red-cell count 1000000 /c. mm	Haemo-globin mg/ 100 ml	Date of death	Date of blood-pressure measure-ment	Mean arterial pressure mm Hg	State of heart at autopsy
888/56 ♀	+	2.4	5.9	25/10	24/10	155	Eccentric hypertrophy Chronic myocarditis
1040/56 ♂	+	5.2	12.5	5/12	5/12	145	Eccentric hypertrophy
1109/57 ♀	+	4.2	11.0	17/11	14/11	120	Eccentric hypertrophy Acute focal myocarditis
313/58 ♂	—	5.2	13.9	15/4	11/4 15/4	165 100	Autopsy not performed
160/60 ♂	+	4.0	9.2	2/3	26/2	140	Eccentric hypertrophy
E 60 ♂	+		13.2	5/3	4/3	105	Eccentric hypertrophy Fatty degeneration of myocardium
N 49 ♂	+	2.8	7.1	15/6	24/3 6/5 14/6	130 130 130	Eccentric hypertrophy
I : 1 ♀	+	4.6	7.4	22/10	1/2 15/5 9/9 13/9 21/10	150 170 137 140 105	Eccentric hypertrophy
II : 4 ♀	—	7.2	16.8	29/5	27/5	125	Chronic focal myo-carditis
V : 7 ♀	—	5.9	15.7	19/1-59	12/12-57 29/1 -58 11/4 -58 12/6 -58	130 155 140 145	Dilatation of right ventricle

DISCUSSION

The normal blood-pressure values recorded in Table 1 agree well with values reported earlier (*Hamilton et al.*, 1939; *Katz et al.*, 1939; *Wakerlin*, 1943; *McCubbin* and *Corcoran*, 1953; *Romagnoli*, 1953; *Katz, Skom* and *Wakerlin*, 1957; *Schulze*, 1958).

Among the non-renal changes which occur in uraemia and which are considered to be due to the renal hypertension, the eccentric cardiac hypertrophy and the arteriosclerotic changes are the most important ones. As early as 1827 *Bright* reported that he had observed co-existing renal lesions and heart disease in man. *Goldblatt*'s experiment in 1934, in which he was able to produce hypertension in dogs by closure of the renal artery, has become classical. Numerous authors have since then demonstrated the important role of renal lesions in the development of hypertension in man. *Floyer* (1957), in a recent work, mentions the occurrence of two different phases in renal hypertension: 1) an early phase in which a renal pressor substance is secreted from the kidney, and 2) a late phase in which the high blood-pressure is maintained by an extrarenal mechanism. In a previous work (*Helander, Persson* and *Åsheim*, 1958) we showed that a constriction of the renal artery on one side produces a corresponding change in the function of the other kidney. The same phenomenon has been observed by *Floyer*, who presumes that it is due to secretion of a humoral substance and that this would possibly be identical with the above-mentioned pressor substance.

The question whether raised blood-pressure occurs in dogs is a subject of controversy. Experimental renal hypertension in dogs on the model of Goldblatt's experiment has been induced by many workers (*Katz et al., Stamler, Katz* and *Rodbard*, 1949; *Stamler, Rodbard* and *Katz*, 1950; *Campbell*, 1954; *Floyer*). Others (*Morehead* and *Little*, 1945; *McIntyre* and *Montgomery*, 1952; *Platt*, 1952; *Baur*, 1955; *Dahme*, 1956; *Dahme*, 1957; *Krook*, 1957) have taken the autopsy findings in uraemic cases, notably the eccentric hypertrophy of the heart, as evidence supporting the presence of renal hypertension. It is only in recent years that the intra-arterial blood-pressure in normal dogs has been measured on such a large scale that normal values have been obtained. Occasional cases of spontaneous hypertension in asso-

ciation with renal disorders have been reported (*Wakerlin,*
McCubbin and *Corcoran, Katz, Skom* and *Wakerlin*).

More systematic blood-pressure studies by a direct method
in dogs with renal disease have been done by *Robin* (1948) and
Schulze. Robin does not believe that renal hypertension occurs
in dogs and considers that the hypertension and the hypertrophy
of the left side of the heart have a common renal cause. *Schulze*
reports that out of 56 dogs with renal disease 4 dogs with chronic
interstitial nephritis had raised blood-pressure. It should be
noted, however, that he has fixed the upper limit for normal
pressure at 150 mm Hg for the mean arterial pressure. *Gärtner*
(1956), without mentioning the technique used at the blood-
pressure measurement, reports hypertension in 5 cases of glo-
merulonephritis and states that together with haematuria, ascites
and oedema, hypertension would be the cardinal symptom in
cases of acute glomerulonephritis. *Hamilton et al.* also observed
hypertension in cases of glomerulonephritis.

It will be seen from Tables 1 and 2 that in 10 dogs with renal
cortical hypoplasia, in which the blood-pressure was measured,
no significantly raised pressure was recorded. Only on one occa-
sion in dog no. I : 1 did the blood-pressure reach the borderline
value of 170 mm Hg. In all the dogs, excepting no:s 160/60, E : 60
and N 49, light anaesthesia was induced with "Mebumal". *Hamil-
ton et al.* state that surgical anaesthesia with barbiturates has
the effect of lowering blood-pressure in the hypertensive dogs.
As has also been pointed out in earlier publications (*Helander,*
Persson and *Åsheim, Åsheim, Helander* and *Persson,* 1958), we
have made repeated experiments with continuous recording of
blood-pressure before and during the induction of anaesthesia
and during anaesthesia. A slight rise of blood-pressure, about
10—15 mm Hg, occurred during injection of "Mebumal", but
after a minute or two the pressure returned to normal. In one
experiment the dog was allowed to wake up during the blood-
pressure recording. On awakening he went into a state of exci-
tation, which caused a rise in blood-pressure. After about 25
minutes, when the dog had calmed down, the blood-pressure had
fallen to the same level as before and during the anaesthesia. In
the three dogs that were not anaesthetized the blood-pressure
was consistent with that of the others.

In a not yet published study on blood-pressure measurements
in dogs with renal disease the blood-pressure was recorded with-

out anaesthesia. The values for that material will apparently agree with the values for the hypoplastic dogs.

Since our investigations thus show that raised blood-pressure in the dog is not at all so common as has been asserted in earlier reports, in which the assumption of a raised blood-pressure was mainly based on the autopsy findings, it is of interest to study Table 2. It will be seen from the table that eccentric cardiac hypertrophy or other pathological changes of the heart were present in all the autopsy cases. Accordingly, these observations indicate that eccentric cardiac hypertrophy occurs in the absence of hypertension. Therefore, an essential cause of the hypertrophy must be some factor other than hypertension. From this study, and from what has been shown earlier, it is quite clear that there is a very close relationship between renal disorders and hypertrophy of the heart. It is therefore probable that by some secondary mechanism other than hypertension renal lesions would give rise to cardiac hypertrophy. In man the anaemia (*Spühler* and *Zollinger,* 1953) is considered to be a very important symptom and one of the first to appear in renal diseases. Some authors (*Hare,* 1934; *Hogg,* 1948; *Niemand,* 1954; *Nielsen* and *McSherry,* 1954; *Paplanus, Zbar* and *Hays,* 1958) have also reported the presence of anaemia in dogs. The tendency to anaemia in hypoplastic dogs is evident in Table 2. Elsewhere we have shown that there is a significant difference between healthy and hypoplastic dogs with respect to both the red-cell count and the haemoglobin concentration. Among our 10 cases anaemic mucous membranes were also seen clinically in 7. More recent studies (*Forssell,* 1958; *Naetz,* 1958) have shown that the cause of anaemia in cases of chronic uraemia is the lack of erythro-poietin, a substance which is formed in the kidneys and whose function is to stimulate bone-marrow activity. The production of erythropoietin is stimulated by different forms of anoxia. Since it can be considered established that the nephrogenic anaemias are of greater importance than has earlier been appreciated, it may be hypothesized that the eccentric cardiac hypertrophy would arise as a result of the increased stroke volume with which the heart must work in anaemia. *Paplanus et al.,* in experiments on dogs, have demonstrated that anaemia induced by repeated venesection gives rise to hypertrophy and dilatation of the heart.

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SUMMARY

The blood-pressure in young dogs of the cocker spaniel breed was measured by a direct method. The mean arterial pressure in healthy dogs was 148 mm Hg with a standard deviation of 8.7. Among 10 dogs with renal cortical hypoplasia a raised blood-pressure was not recorded in any case. The hypertrophy of the left side of the heart observed at autopsy is hypothetically explained by the anaemia.

ZUSAMMENFASSUNG

Der Blutdruck bei Hunden mit Nierenrindehypoplasie.

Bei jungen Hunden der Cockerspanielrasse wurden Blutdruck-bestimmungen mittels direkter Methode durchgeführt. Der arterielle Druck betrug im Durchschnitt 148 mit einer Standardabweichung von 8,7. Bei zehn Hunden mit Hypoplasie der Nierenrinde, wurde keine Blutdruckerhöhung festgestellt. Die bei der Sektion bemerkte Hyper-trophie der linken Herzhälfte wird hypothetischerweise durch das Vorkommen einer Anämie erklärt.

SAMMANFATTNING

Blodtrycket hos hundar med njurbarkshypoplasi.

Blodtrycksbestämningar hos unga hundar av cockerspaniel-ras har utförts med direkt metod. Medelartärtrycket för friska hundar var 148 med stand. dev. 8,7. Hos 10 hundar med njurbarkshypoplasi kunde förhöjt blodtryck ej registreras i något fall. Den vid sektion iakttagna vänstersidiga hjärthypertrofin förklaras hypotetiskt av den förekom-mande anämin.