Acta vet. scand. 1961, 2, 85—101.

From the departments of medicine for non-ruminants and clinical biochemistry, Royal Veterinary College, Stockholm.

ELECTROCARDIOGRAPHIC CHANGES IN DOGS WITH URAEMIA

By

F. Persson, S. Persson and *Å. Åsheim*

Electrocardiographic studies on dogs have been made by *Lannek* (1949) who from a large material reports normal values and findings typical of certain diseases, including uraemia. Similarly to Lannek *Salutini* (1956) found prolongation of the QT interval, depression and a characteristic configuration of the T waves. Salutini points out that these changes are probably caused by disturbances of the serum-electrolyte balance. No determinations of serum-electrolytes are reported.

More is known about the influence of serum-calcium and serum-potassium concentration on the function of the heart in man, notably by electrocardiographic studies (*Levine et al.*, 1951; *Surawicz & Lepeschkin,* 1953; *Goldman,* 1956). These studies show that in hyperkalaemia tall "tented" T waves, and prolonged and depressed P waves are first obtained. Higher degrees of hyperkalaemia produce depression of the ST segment, auricular standstill and ventricular fibrillation. In hypocalcaemia the most important change is prolongation of the QT interval. This prolongation is the result of a prolongation of the ST segment.

MATERIAL AND METHODS

Electrocardiograms were taken of 14 dogs of the cocker-spaniel breed, all of which died from uraemia as a result of renal cortical hypoplasia at the age of 8—18 months. Repeated recordings were made in some of these cases, and in three cases the dogs were followed from birth by clinical investigations, including E.C.G. and serum-electrolyte determinations. In addition, four one-year-old mongrels were used for experimental production of

hyperkalaemia and hypocalcaemia, respectively, in order to study the electrocardiographic changes that occur in these conditions.

The E.C.G.s were recorded with a direct writing, single-channel electrocardiograph (Mingograf 11). At the end of the experimental series a direct writing, four-channel electrocardiograph (Mingograf Cardirex 42 B) was also used. The speed of the paper was for both 50 mm per second. The apparatus was adjusted so that 1 millivolt corresponded to an amplitude of 5 mm. For examination of the E.C.G.s as well as for the choice of leads, methods described by *Lannek (1949)* were used. Leads I, II and III are bipolar leads, which correspond to the usual extremity leads in man. Thus, the left fore-leg corresponds to the left arm, the right fore-leg to the right arm and the left hind-leg to the left leg. The fourth lead, by *Lannek* designated as the transthoracic lead IV, was not recorded. Three unipolar leads were also registered. The indifferent electrode was in all cases connected with the right fore-leg. The exploring electrode was connected with the lower part of the fifth intercostal space on the right side (lead CR_5), the lower part of the sixth left intercostal space (lead CR_{6L}), and at the level of the joints of the ribs in the sixth intercostal space on the left side (lead CR_{6U}). Serum-electrolytes were determined by the following methods: Potassium was estimated by means of flame photometry ("EEL"), calcium by *Clark & Collip*'s (1925) modification of *Kramer & Tisdall*'s method (1921), and phosphorus by the method of *Tausky & Shorr* (1953).

RESULTS

The parts of the electrocardiograms studied in particular were the duration of the QRS complex, the duration of the QT interval, the amplitude of the T wave, the amplitude of the R wave and the amplitude of the ST segment and the ST junction. Detailed examinations of these features have shown that the most important changes are to be found in the duration of the QT interval and the amplitude of the T wave. In the statistical analysis of these values comparisons were made with the normal values reported by *Lannek*.[1]) Table 1 records *Lannek*'s values and the

[1]) The evaluation of the electrocardiograms and the statistical analysis was done after discussion with Professor N. Lannek, to whom we are greatly indebted.

Table 1.

The duration of the QT-interval in seconds in E.C.G. of dogs with renal cortical hypoplasia.
Normal values reported by Lannek are given in parantheses.

Lead	II	CR_{6L}
Number	13 (229)	13 (63)
Mean	0.222 (0.176)	0.230 (0.192)
Standard deviation	0.027 (0.018)	0.027 (0.021)
Standard error of mean	0.007 (0.001)	0.007 (0.003)

values for the QT duration from the dogs with renal cortical hypoplasia. Since the QT duration does not deviate markedly between the different leads, only leads II and CR_{6L} are included and considered to be representative. At comparisons between normal values and values from the hypoplastic dogs with respect to the duration of the QT interval, Student's t-test shows that the values differ significantly ($P < 0.001$) in both leads. The heart-rate was throughout within the normal range for dogs.

Since the amplitudes of the T wave are alternately negative and positive classical analysis of mean values and comparisons between these and normal values, using the t-test, cannot be done. Therefore the deviating E.C.G. values are listed in full in Table 2 with a summary. Besides the prolongation of the QT interval discussed in the foregoing, it will be clearly seen from Table 2 that the amplitudes of the T wave in the hypoplastic dogs are markedly changed. Table 3 shows *Lannek*'s normal values, on which the assessment of the pathological E.C.G.s was based. In estimating serum-electrolytes a comparison was made with normal values reported elsewhere as follows (all values given as mg per 100 ml):

Potassium:	16.3	with	standard	deviation	2.0
Calcium:	10.1	„	„	„	1.2
Phosphorus:	4.7	„	„	„	0.8

The values for serum-electrolytes listed in Table 2 were considered to be probably pathological if they fell outside the limits of the mean value $\pm 2\ \delta$, and significantly pathological if they fell outside the limits of the mean value $\pm 3\ \delta$.

Table 4 and adjoining diagrams show the correlation between serum-calcium concentration, serum-phosphorus concentration and duration of the QT interval. It will be seen that there is a

Table 2.

Features of the E.C.G. deviating from the normal. Amplitudes are given in mm, durations in seconds. Electrolytes are expressed in mg/100 ml.
Values with the designation *** are significantly pathological ($P < 0.003$).
Values with the designation * are probably pathological ($0.05 > P > 0.01$).

Dog	Date of taking specimen	I	II	III	CR_5	CR_{6L}	CR_{6U}	Ca	K	P
286/55	7/4	QT 0.24*** T +3.2*	QT 0.24***	QT 0.24*** ST —1.5*** T —6.3***	QT 0.24* ST —1.0*** ST_J —1.0*	QT 0.25* T +23.2*** ST_J —1.5***	QT 0.25* T +25.2*** ST_J —1.7***			
888/56	24/10	QT 0.24***	QT 0.24***	QT 0.23*	QT 0.24*	QT 0.24*	QT 0.28*** T +10.2*** ST_J —2***	11.4	25.3***	24.0***
920/56	30/10	QT 0.28*** T +3.2***	QT 0.28*** T +6.0***	QT 0.27*** T +3.7*	QT 0.28*** T +28.2***	QT 0.27*** T +21.2*** ST_J —2.0***	QT 0.30*** T +22.2*** ST_J —2.0***	6.2***	33.5***	49.0***
1040/56	5/12	T +1.2*	QT 0.22* ST_J —1.0***	T —4.0***	QT 0.26***	QT 0.24*		6.3***	10.5***	11.4***
316/57	28/3	QT 0.22* T —3.2***	QT 0.22* T —3.5*	QT 0.23* R 23*	QT 0.23*	QT 0.24*		4.3***	15.3	63.6***
381/57	13/4		QRS 0.06* QT 0.22* T —3.0*	QT 0.23*	QRS 0.06***	T +14.2***		7.1***		—
1109/57	13/11	QT 0.24*** T +1.2*	QT 0.25*** T —7.0***	QT 0.23* T —7.0***	QT 0.23* T —8.0***	QT 0.24* T —8.0***	T —8.0***	6.8***	16.6	37.3***
313/58	11/4			T —2.5*	QRS 0.056*	T +9.2*		10.9		11.4***
160/60	26/2	T +1.7*	QT 0.24*** T —3.5*	QT 0.22* T —4.0***	QT 0.26***	QT 0.26*** T +11.2* ST_J —1.5***	QT 0.26***	7.3***	17.6	16.6***

E 60	4/3	T —2.0*	T —9.1*** R 29* ST —2.2*** ST_J —2.1***	T —6.2*** R 24* ST —2.0*** ST_J —1.0*	ST —0.5*		T —6.7***	11.3	17.6	25.6***
N 49	24/3	QT 0.21*	QT 0.22* ST_J —1.0*** T —3.0*	T —3.5*** ST_J —1*	QT 0.23*	QT 0.24*		7.9***	17.6	21.2***
	19/4		T —3.0* ST_J —1.0***	T —3.5***				10	23.0***	16.0***
I : 1	9/11 1956							(7.7***)	18.0	
	23/1 1957							9.9	13.5*	5.5
	5/9 1957	R 14***								
	12/9 1957	T —2.0*	T —3.0* ST_J —1.0***	ST_J —1.0*				8.6***	13.5*	33.5***
	21/10 1957	T +2.0*** R 19***	ST_J —1.5***	ST —1.2* ST_J —1.7***	QRS 0.06***		ST —1.7* ST_J —2.0***	7.9***	12.1***	25.5***
II : 4	9/11 1956	T +2.0***						9.6	14.7	8.0***
	27/5 1957	QT 0.21*			QT 0.23* QRS 0.05*	QT 0.25* ST —1.0*	QT 0.24*	10.4	14.8	27.3***
	28/5 1957	T —2.0* R 13*	T —3.0*					6.1***	14.6	51.0***
V : 7	16/4 1958									
	4/8 1958									

Summary of Table 2

The following deviations were observed in electrocardiograms of 13 hypoplastic dogs:

I. QT duration in 10 dogs:
   Significant prolongation in 6 cases
   Probable „ „ 4 „
II. The amplitude of the T wave in 13 dogs:
   Significant elevation in 6 cases
   Probable „ „ 4 „
   Significant depression „ 7 „
   Probable „ „ 4 „
III. Significant depression of ST junction in 8 cases
   „ „ „ ST segment „ 2 „
   Probable „ „ ST segment „ 1 case
IV. Significant prolongation of the QRS complex in 1 case
   Probable „ „ „ QRS „ „ 2 cases
V. Significant elevation of the amplitude of the R wave in 1 case
   Probable „ „ „ „ „ „ R „ „ 3 cases

correlation between prolongation of the QT interval and hypocalcaemia, while there is no correlation between QT prolongation and hyperphosphataemia. In order to throw further light on the correlation between prolongation of the QT interval and hypocalcaemia together with hyperphosphataemia, the following experiment was carried out in a dog. Under anaesthesia induced with pentobarbitone the dog was given 8 % sodium-phosphate solution intravenously by continuous infusion. This was calculated to produce a lowering of the serum-calcium level according to the same principle as in chronic renal damage. In the latter condition the reduced renal excretion of phosphate results in a hyperphosphataemia, which in turn, according to Guldberg-Waage's law, results in hypocalcaemia (*Albright & Reifenstein,* 1948). E.C.G.s were recorded continuously at the same time as blood specimens for examination of phosphorus and calcium were taken both before and during the experiment. The result is shown in Figs. 1 and 2. It will be seen from the figures that a very distinct prolongation of the QT interval was produced during the experiment. Complete reversal of the QT interval to normal duration did not occur, however, after injection of calcium, although this gave rise to hypercalcaemia instead of the previous hypocalcaemia. With increasing hypercalcaemia the E.C.G. showed a characteristic configuration of the ST segment, which formed a curve with the convexity upward (Fig. 2).

Table 3.

The normal values given by Lannek, on which the assessment of the pathological E.C.G.s in Table 2 was based.

		Mean	95.5 % range	99.7 % range
QRS duration				
seconds	I	0.035	0.021—0.056	0.017—0.063
	II	0.041	0.025—0.057	0.017—0.065
	III	0.041	0.025—0.057	0.017—0.065
	CR_5	0.038	0.024—0.052	0.017—0.059
	CR_{6L}	0.045	0.031—0.059	0.024—0.066
	CR_{6U}	0.047	0.029—0.065	0.020—0.074
QT duration				
seconds	I	0.167	0.131—0.203	0.113—0.221
	II	0.176	0.140—0.212	0.122—0.230
	III	0.177	0.141—0.213	0.123—0.231
	CR_5	0.191	0.153—0.229	0.134—0.248
	CR_{6L}	0.192	0.150—0.234	0.129—0.255
	CR_{6U}	0.194	0.150—0.238	0.128—0.260
T amplitude				
mm	I	—0.36	(—1.76)—(+1.04)	(—2.46)—(+1.74)
	II	+0.24	(—2.60)—(+3.08)	(—4.02)—(+4.50)
	III	+0.56	(—2.04)—(+3.16)	(—3.34)—(+4.46)
	CR_5	+3.62	(—1.18)—(+10.82)	(—2.38)—(+13.22)
	CR_{6L}	+2.94	(—2.76)—(+8.64)	(—5.61)—(+11.49)
	CR_{6U}	+1.85	(—3.69)—(+7.39)	(—6.46)—(+10.16)
R amplitude				
mm	I	3.89	(0)—(+11.09)	(0)—(+13.49)
	II	12.03	(+3.27)—(+25.17)	(+1.08)—(+29.55)
	III	9.45	(+1.85)—(+20.85)	(0)—(+24.65)
	CR_5	12.99	(+0.93)—(+25.05)	(0)—(+31.08)
	CR_{6L}	23.83	(0)—(+33.94)	(0)—(+37.31)
	CR_{6U}	21.23	(+6.85)—(+35.61)	(0)—(+42.80)
Amplitude of ST segment				
mm	I	—0.19	(—0.54)—(+0.21)	(—0.69)—(+0.29)
	II	—0.29	(—1.31)—(+0.39)	(—1.65)—(+0.56)
	III	—0.17	(—1.04)—(+0.41)	(—1.33)—(+0.56)
	CR_5	+0.72	(—0.36)—(+2.34)	(—0.63)—(+2.88)
	CR_{6L}	+0.48	(—0.88)—(+1.84)	(—1.56)—(+2.52)
	CR_{6U}	+0.06	(—1.14)—(+1.26)	(—1.74)—(+1.86)
Amplitude of				
ST_J mm	I	+0.08	(—0.19)—(+0.80)	(—0.28)—(+0.98)
	II	—0.18	(—0.70)—(+0.34)	(—0.96)—(+0.60)
	III	—0.18	(—0.90)—(+0.30)	(—1.14)—(+0.42)
	CR_5	+0.03	(—0.83)—(+1.32)	(—1.05)—(+1.75)
	CR_{6L}	—0.11	(—1.19)—(+1.51)	(—1.46)—(+2.05)
	CR_{6U}	—0.31	(—1.23)—(+0.61)	(—1.69)—(+1.07)

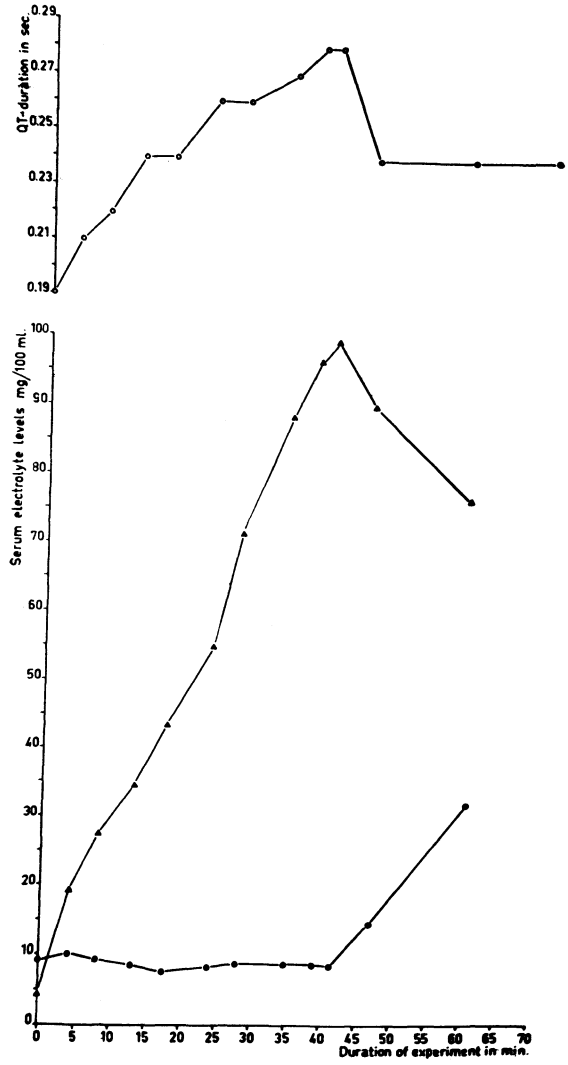
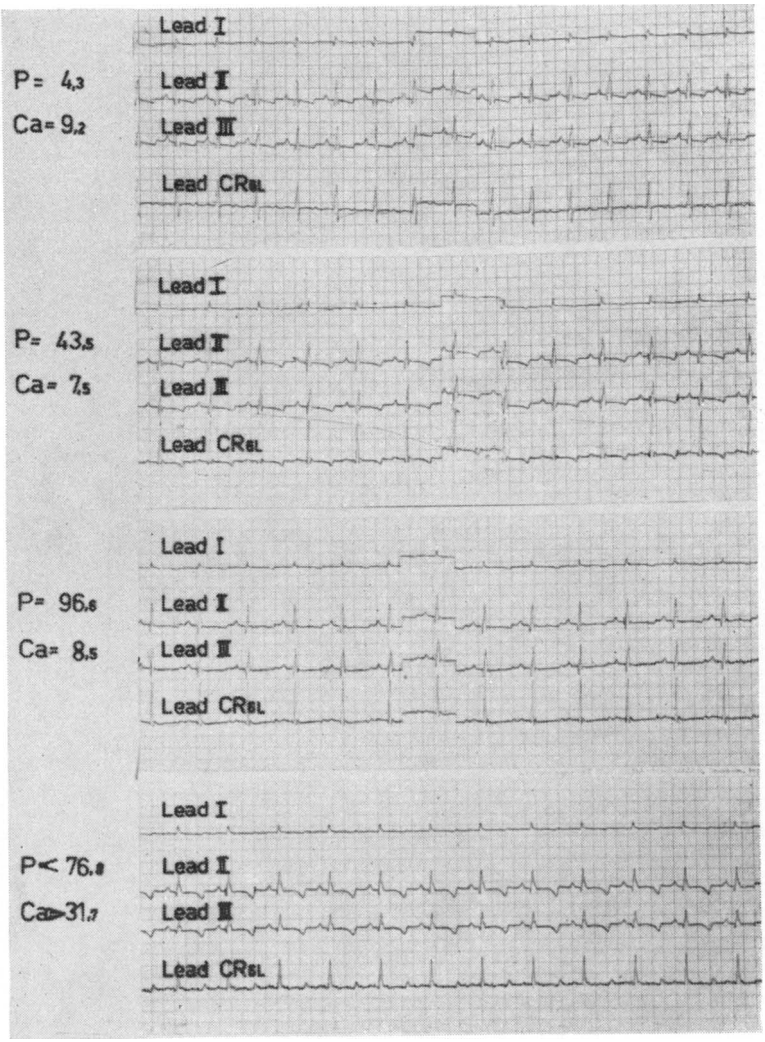


Fig. 1. QT duration in relation to serum level of calcium and phosphorus, respectively.

○ = QT duration — ▲ = serum-phosphorus level — ● = serum-calcium level



F i g. 2. E.C.G. during intravenous infusion of 8 % sodium-phosphate solution and after injection of calcium glyconate (bottom picture). Concentrations given in mg per 100 ml.

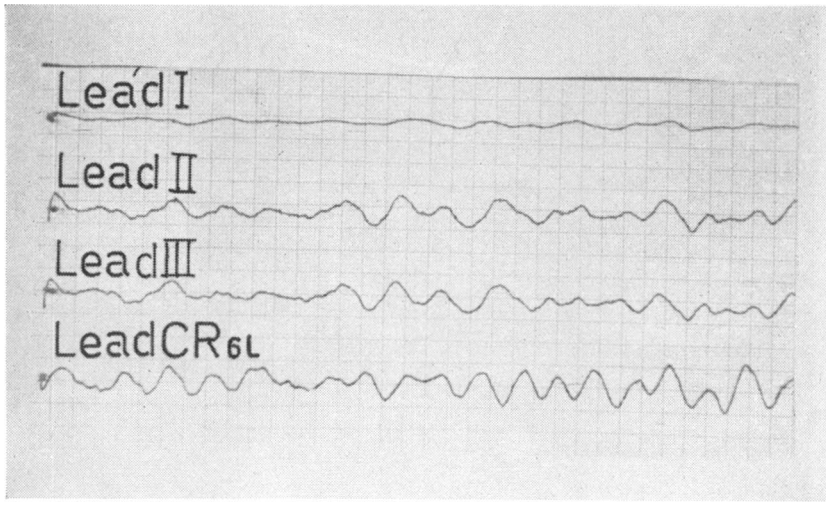


Fig. 3. E.C.G. showing ventricular fibrillation immediately before death.

Table 4.

Correlation between serum-calcium concentration, serum-phosphorus concentration and duration of the QT interval. An asterisk denotes a value for Ca below the normal mean value —2 δ (10.1—2.4) and for P exceeding the normal mean value +2 δ (4.7+1.6).

P mg/100 ml	Ca mg/100 ml	Prolongation of QT interval
24.0*	11.4	+
49.0*	6.2*	+
11.4*	6.3*	+
63.6*	4.3*	+
—	7.1*	+
37.3*	6.8*	+
11.4*	10.9	—
16.6*	7.3*	+
25.6*	11.3	—
21.2*	7.9	+
16.0*	10.0	—
5.5	9.9	—
33.5*	8.6	—
25.5*	7.9	—
8.0*	9.6	—
27.3*	10.4	+
51.0*	6.1*	—
5.8	10.5	—

		Phosphorus concentration		
		normal	hyperphosphataemia	
QT duration	normal	2	7	9
	prolonged	0	8	8
		2	15	

		Calcium concentration		
		normal	hypocalcaemia	
QT duration	normal	8	1	9
	prolonged	3	6	9
		11	7	

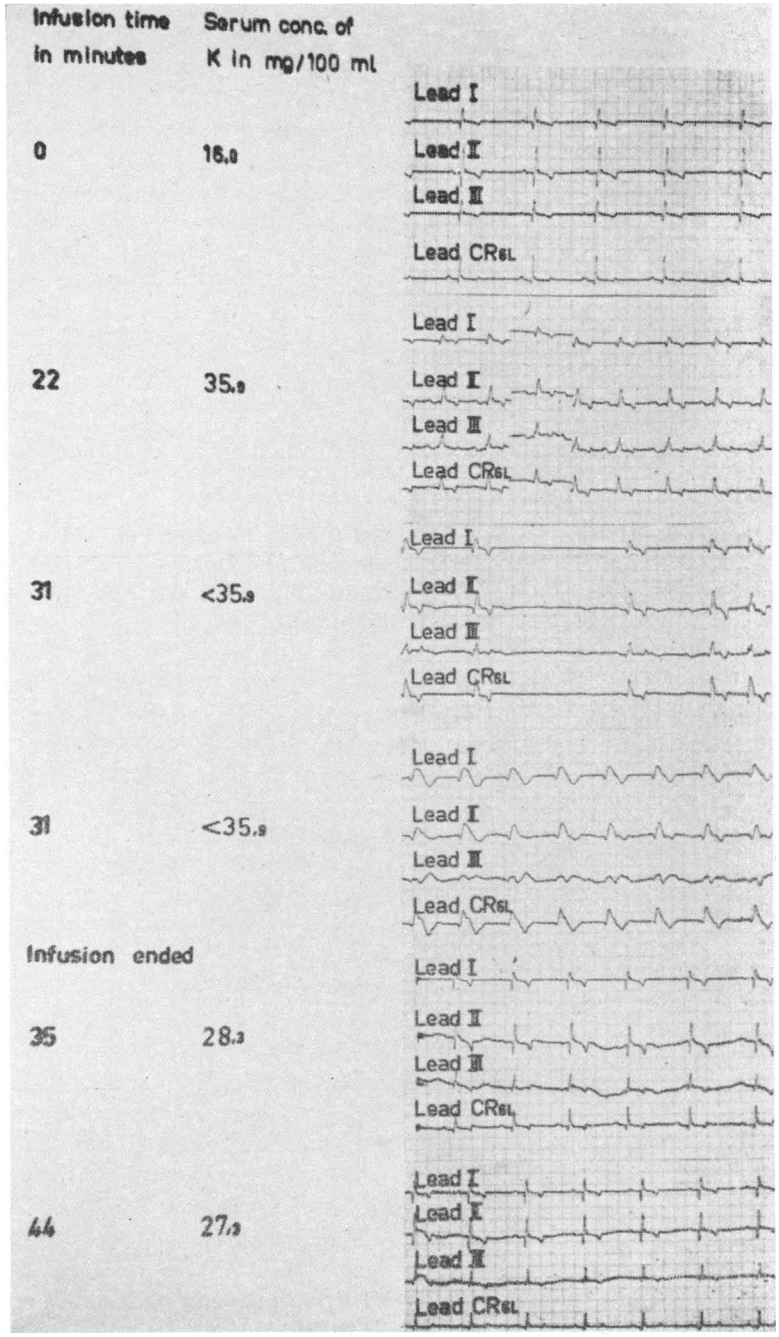


Fig. 4. E.C.G. during intravenous infusion of 1-molar potassium-chloride solution. Dog no. 1.

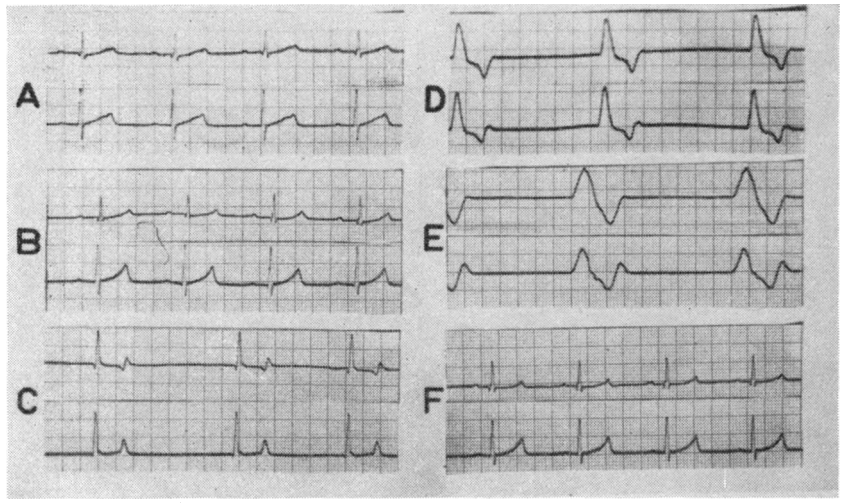


Fig. 5. Leads II and CR_{6L} recorded during intravenous infusion of 1-molar potassium-chloride solution. Dog no. 2.
A = 17.6 mg, B = 25.0 mg, C = 42.9 mg, D = 46.4 mg, E = 47.6 mg, F = 26.9 mg of potassium per 100 ml.

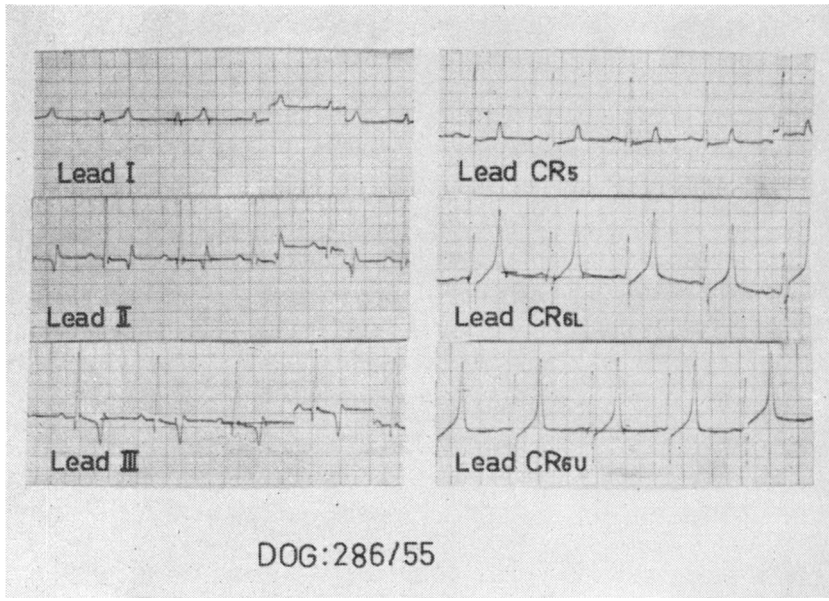


Fig. 6. E.C.G. strongly suggestive of hyperkalaemia with tall slender T waves in leads CR_{6L} and CR_{6U}.

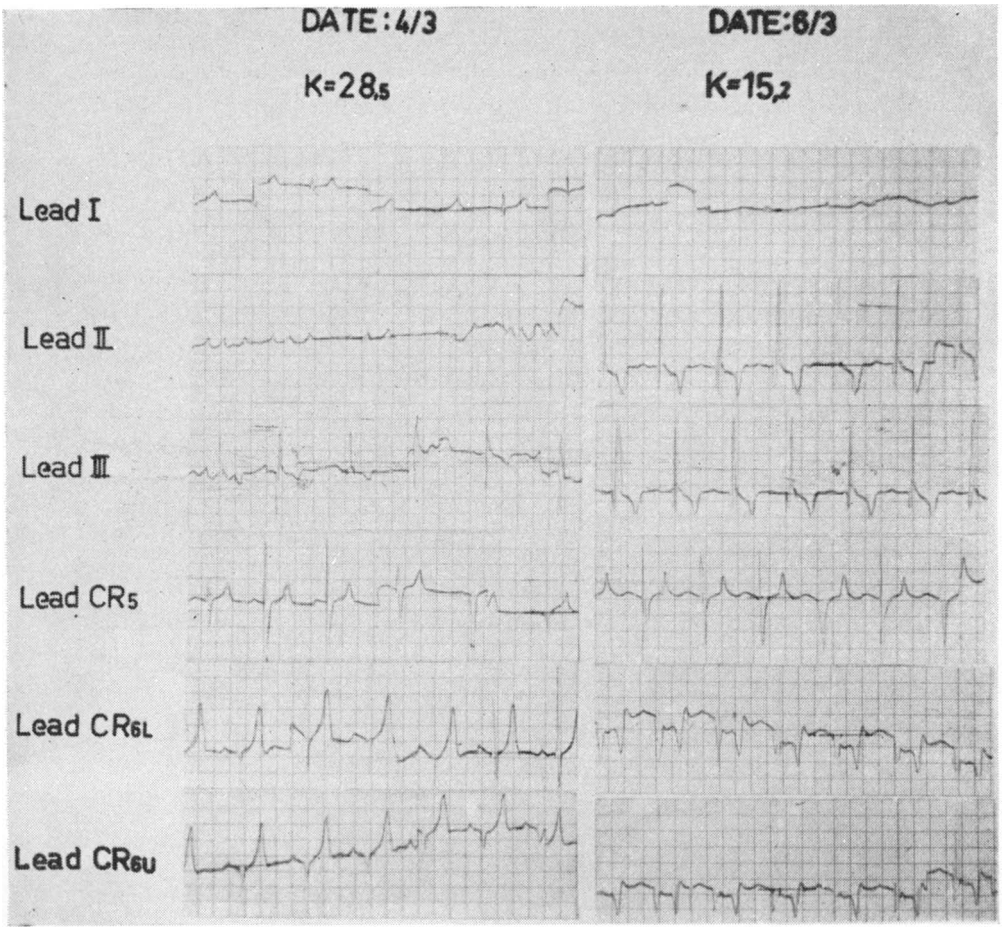


Fig. 7. E.C.G. of a dog in which the serum-potassium level had fallen markedly in 2 days. Concentrations given in mg per 100 ml.

In three dogs an experimental study was carried out to investigate the influence of the hyperkalaemia on the E.C.G. 1-molar potassium chloride solution was injected intravenously. By continuous recording of E.C.G.s and taking of repeated blood specimens a correlation between the concentration of potassium in blood serum and the electrocardiographic changes was obtained. The first dog was given potassium chloride in large single doses, after which E.C.G. were recorded and blood samples taken as shown in Table 5. This method was too unreliable. The E.C.G.

remained normal until quite suddenly ventricular fibrillation and death occurred. The E.C.G. at this stage is shown in Fig. 3. In the other two dogs potassium chloride was given by continuous infusion from an electrically driven infusion apparatus. The result is shown in Table 6 and Figs. 4 and 5.

DISCUSSION

The most important electrocardiographic changes in the hypoplastic dogs are prolongation of the QT duration and elevation or depression of the amplitude of the T wave. A comparison between these findings and the concentration of calcium in blood serum shows a definite correlation between the presence of hypocalcaemia and prolongation of the QT interval. In the case of experimentally produced hyperphosphataemia the secondary lowering of the serum-calcium level was not significant. In spite of this the QT interval was markedly prolonged. The correlation between the hyperphosphataemia and the QT prolongation is, thus, more distinct than that between the hypocalcaemia and the QT prolongation. That the QT prolongation should be due to the hyperphosphataemia is not very probable, as is also seen from the investigations of the clinical series. Further studies are needed to elucidate this question.

It will be seen from Table 2 that a significant hyperkalaemia was present in a large number of cases. The highest value, 33.5 mg per 100 ml, was found in dog 920/56. The E.C.G. changes were in this case striking, consisting of marked prolongation of the QT interval and elevated T waves. There was great conformity between the tracings from this dog and those from dog 286/55. Since it was phototechnically more readily reproducible, the E.C.G. of the latter dog is published (Fig. 6). Unfortunately, determinations of electrolytes are lacking in this case.

The E.C.G. findings in the experimentally produced hyperkalaemia agree well with those observed in man (*Levine et al.*, 1951; *Goldman*, 1956). Elevated T waves, as reported by *Winkler et al.* (1938), were not seen, however (Figs. 4 and 5). Elevated T waves in moderate hyperkalaemia are demonstrated in Fig. 7 from a young cocker spaniel with uraemia (necrotising nephrosis), in which a fall in serum-potassium from 28.5 to 15.2 mg per 100 ml occurred two days later. At the same time the character of the E.C.G. changed. The high positive T waves became

Table 5.

Result of intravenous injection of a large single dose of 1-molar KCl solution in a dog. See Fig. 2.

Amount injected	Serum concentration K mg/100 ml	E. C. G.
0	17.6	normal
5	22.6	„
10	24.4	„
18	39.0	„
10	Ventricular fibrillation and death	

Table 6.

Result of intravenous injection of 1-molar KCl solution.

Injection rate ml/min	Time in min	K concentration mg/100 ml	E. C. G.
		Dog no. 1	
0	0	16.8	Normal
1.5	5	24.4	„
1.5	13	28.3	Depressed or disappeared P waves.
2.5	22	35.9	Intraventricular block. Depressed ST segments.
4.5	31	> 35.9	Sinus block. Beginning ventricular
Infusion discontinued			fibrillation.
	35	28.3	
	44	27.3	Returning to normal.
		Dog no. 2	
0	0	17.6	Normal
1.5	5	25.0	„
1.5	10	28.9	„
2.5	17	36.3	„
2.5	21	42.9	Disappeared P waves.
2.5	23	46.4	Intraventricular block. Depressed ST segments.
2.5	25	47.6	Changes more marked.
Infusion interrupted	30	31.6	Returning to normal.
2.5	35	45.6	Recurrent changes.
Infusion stopped	42.5	34.3	Returning to normal.
0	45	32.4	„
0	60	31.6	„
0	75	28.9	„
0	85	26.9	Reappearance of P waves.

depressed and negative simultaneously with a depression of the ST segments. Autopsy of this case revealed acute myocarditis, which explains the depressed ST segments. Thus, our investigations show that the E.C.G. picture varies greatly with changes in the serum-potassium level.

REFERENCES

Albright, F. and *Reifenstein, E. C., Jr.:* Parathyroid glands and metabolic bone diesease. Baltimore, 1948.

Clark, E. P. and *Collip, J. B.:* J. biol. Chem. 1925, *63*, 461.

Goldman, M. J.: Principles of clinical electrocardigraphy. Los Altos, California, 1956.

Kramer, B. and *Tisdall, F. F.:* J. biol. Chem. 1921, *47*, 475.

Lannek, N.: A clinical and experimental study on the electrocardiogram in dogs. Ivan Häggströms Boktryckeri AB, Stockholm 1949.

Levine, H. D., Merrill, J. P. and *Somerville, W.:* Circulation, 1951, *3*, 6.

Salutini, E.: Ann. Fac. Med. vet. Pisa, 1956, *9*, 332.

Suravicz, B. and *Lepeschkin, E.:* Circulation, 1953, *8*, 801.

Taussky, H. H. and *Shorr, E.:* J. biol. Chem. 1953, *202*, 675.

Winkler, A. W., Hoff, H. E. and *Smith, P. K.:* Amer. J. Physiol. 1938, *124*, 478.

SUMMARY

Electrocardiographic studies have been made in 14 dogs of the cocker spaniel breed, which had uraemia as a result of renal cortical hypoplasia. The predominating E.C.G. changes were increased duration of the QT interval, elevation or depression of the T waves, and, in exceptional cases, increased duration of the QRS complexes and depression of the amplitude of the ST segment and the ST junction. Determinations of serum-electrolytes in the examined cases showed a correlation between increased duration of the QT interval and hypocalcaemia. A correlation was also demonstrated between hyperkalaemia and elevation or depression of the T waves. The electrocardiograms of dogs in which the hypocalcaemia or the hyperkalaemia had been induced were also examined.

ZUSAMMENFASSUNG

Elektrokardiographische Veränderungen bei Hunden mit Urämie.

Vierzehn Hunde der Cockerspanielrasse die infolge einer Nierenrindenhypoplasie an Urämie erkrankten, wurden elektrokardiographisch untersucht. Die Verlängerung des QT-Intervalles, die Erhöhung bzw. Senkung der T-Zacken, ausnahmsweise Verlängerung des QRS-Komplexes und die Senkung der ST- und ST_J-Amplituden, sind die Hauptveränderungen im EKG-Bild gewesen. Gleichzeitig unternommene Bestimmungen der Elektrolyten im Serum zeigten einen Zusammen-

hang zwischen der Verlängerung des QT-Intervalles und der Hypokalzämie. Auch eine Korrelation zwischen der Hyperkaliämie und der Erhöhung bzw. Senkung von T-Zacken wurde bewiesen. Abschliessend wurden die EKG von Hunden untersucht bei denen mann eine Hypokalzämie bzw. Hyperkaliämie experimentell hervorgerufen hat.

SAMMANFATTNING

Elektrokardiografiska förändringar hos hundar med urämi.

Elektrokardiografiska undersökningar har företagits på 14 hundar av cocker-spaniel-ras, som led av urämi till följd av njurbarkshypoplasi. De förändringar som dominerade EKG-bilden var ökad duration av QT-intervallet, höjda respektive sänkta T-vågor samt i undantagsfall ökad duration av QRS-komplexen samt sänkta ST-amplituder och ST_J-amplituder. Samtidigt företagna serumelektrolytbestämningar visade samband mellan ökad QT-duration och hypocalcämi. Även en korrelation mellan hyperkaliämi och höjning respektive sänkning av T-vågorna påvisades. Slutligen undersöktes EKG från hundar, hos vilka hypocalcämin respektive hyperkaliämin experimentellt framkallats.

(Received November 15. 1960).