TABLE IV. Inhibition of Hemadsorption to Infected Tissue Sections by Pretreatment with Antiserum.

Serum and dilution used to pretreat tissue		Hemadsorption after serum pretreatment A. Vaccinia-infected chick embryo liver	B. NDV-infected chick embryo liver
Normal rabbit	1:10	++	++
Anti-vaccinia	1:10	—	++
	1:20	—	++
	1:40	—	++
	1:80	++	ND*
	1:160	++	ND
Anti-NDV	1:10	++	—
	1:20	++	—
	1:40	++	—
	1:80	ND	—
	1:160	ND	++

* Not done.

cinia(4) and measles(5). To our knowledge, this principle has not previously been applied to the demonstration of viruses in microtome sections of infected tissues. This development of the test has certain advantages. A simple method is made available to test tissues for the presence of viruses. Furthermore, the opening of infected cells by the microtome knife may reveal intracellular viruses and thus allow any hemagglutinating virus to be detected, in contrast to hemadsorption on cell cultures which apparently reveal only those viruses which form hemagglutinin on the cell surface.

Summary. Frozen tissues infected with vaccinia, NDV and influenza were sectioned. The sections were incubated in a slide-chamber with 1% suspensions of RBC derived from various species. Hemadsorption to infected tissue sections occurred with RBC agglutinable in the test tube by the infecting virus. Other RBC did not hemadsorb. The phenomenon could be specifically inhibited by using anti-virus sera. It was shown that the described procedure can be used as a reliable tool for detecting viral infection.

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Effect of Quinidine on Plasma Potassium and Glucose in the Intact Dog.* (29594)

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Interest in potassium dynamics and its relationship to quinidine therapy has followed the initial observations by Huggins and Chapman(1) on decreases in plasma potassium as caused by intravenous quinidine lactate. Gertler *et al*(2) found a significant increase in canine intracellular ventricular K with the alkaloid and Armitage(3) and Holland(4) have reported on similar findings in isolated rabbit atrial preparations. During recent studies on the acute reduction of plasma potassium concentration in dogs by vivodialysis it was observed that the electrocardiographic changes seen in this type of hypokalemia were similar to those produced by quinidine. The study reported here was undertaken to ascertain if similarly low potassium levels could be obtained with quinidine sulfate and if such could be related to electrocardiographic changes in the intact dog.

Methods. Experiments were conducted in animals of 8-14 kg in weight which were allowed to fast for 24-36 hours and then

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anesthetized by intravenous administration of an initial dose of 20 mg/kg of sodium pentobarbital and further doses of 5 mg/kg as needed. In a series of 11 dogs, 7 experimental animals were given doses of 30 mg/kg of quinidine sulfate intramuscularly as a 20% solution in propylene glycol at one-hour intervals for 4 hours. The 4 controls were similarly given equal doses of propylene glycol only. All animals were given 10 mg plus 0.2 mg/kg of heparin initially and 0.2 mg/kg every half hour. Blood samples were simultaneously drawn from ipsilateral femoral artery and vein of one control and 3 experimental animals. Only femoral venous blood was obtained in the rest of these experiments at similar sampling intervals. Urine specimens were also obtained simultaneously to blood sampling. All samples were analyzed for potassium and sodium by flame photometry following the internal standard principle (5). Standard lead II ECG tracings were obtained during sampling in all dogs. In 6 animals (3 controls and 3 tests) venous blood glucose levels were obtained in an effort to determine whether K changes could be associated with a glucose "shift." The glucostat colorimetric technique(6) was used in these determinations.

The second series of experiments consisted of a comparative study on the effect of quinidine in fasting and non-fasting animals. Four dogs were studied in each group following the same procedures used in the first series and utilizing femoral venous sampling.

Results. Quinidine effected a statistically significant lowering in plasma potassium of all the experimental animals of the first series, with a mean decrease of 42% of the control value. Fig. 1 summarizes this effect as compared to the control animals. A "t" test performed on the difference between the first and subsequent samples for the experimental animals showed a statistically significant lowering in plasma potassium for each of the experimental animals at a level of confidence of <0.001.

Fig. 2 shows the arterio-venous differences in plasma potassium in the hind leg of typical control and experimental animals. An

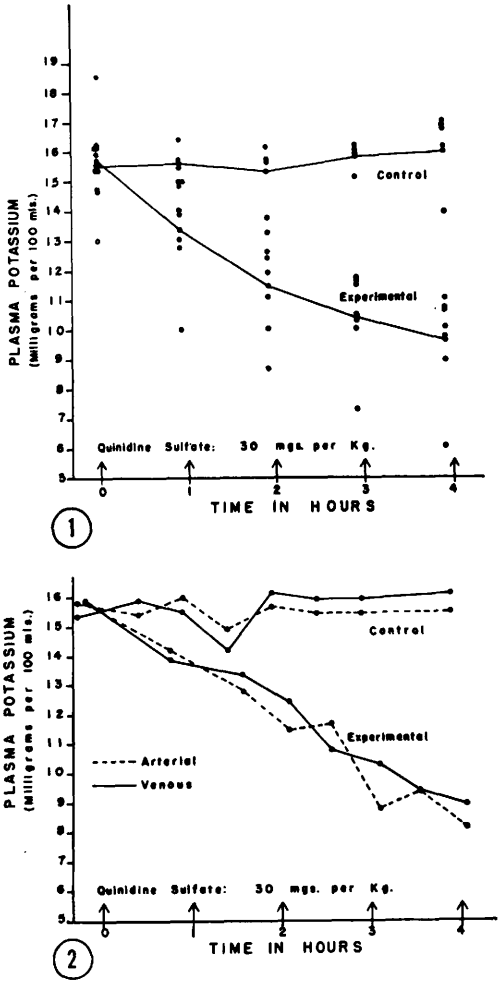


FIG. 1. Mean venous plasma potassium changes in intact dogs under the effect of intramuscular quinidine sulfate.

FIG. 2. Arterio-venous plasma potassium differences in control and quinidine treated dogs.

analysis of variance of the results in all animals where arterial and venous samples were drawn revealed a non-significant difference between arterial and venous plasma potassium values, and a highly significant difference between control and experimental animals. Analysis for plasma sodium values revealed a non-significant variation. Urine specimens could not be uniformly obtained in all experiments, but in those where analysis was possible (5 exp.) there was no significant change in urinary sodium or potassium. The electrocardiographic changes are similar to those previously described in the literature

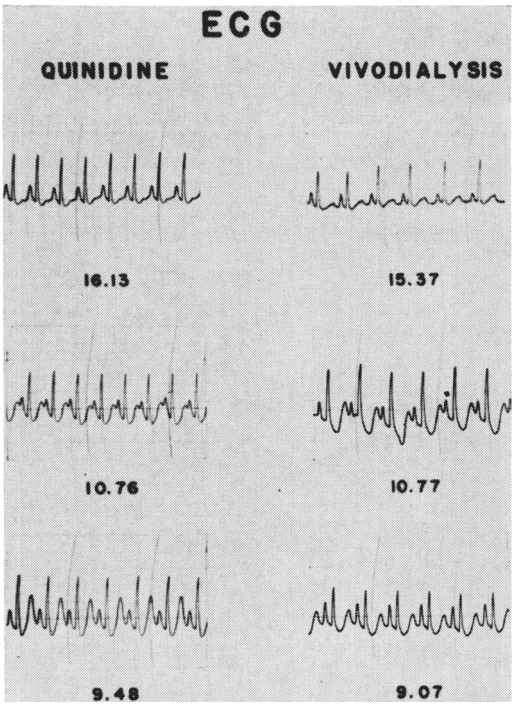
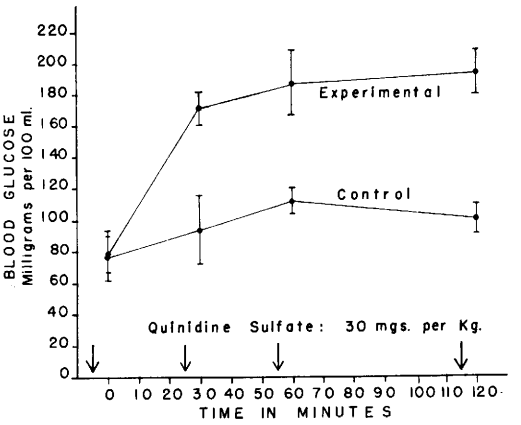


FIG. 3. ECG changes observed in quinidine treated animals at plasma potassium levels similar to those observed in dialyzed animals. (Numbers indicate plasma potassium in mg %.)

for hypokalemic dogs and for hypopotassemia in humans consisting mainly of widening of the QRS complex, T wave inversion, heart block at different levels and prolonged time of repolarization. Dogs rendered hypokalemic with quinidine show a striking similarity in electrocardiographic changes to those rendered hypokalemic by vivodialysis (Fig. 3). Fig. 4 shows the effect of quinidine on blood glucose resulting in a sustained increase in the latter significant to the 0.001 level. In the second group of experiments, a significant lowering of plasma potassium was observed in both fasting and non-fasting animals, but more so in the non-fasting group. Statistical analysis by the Student's "t" test revealed a P = 5% in the fasting dogs as compared to a P = 0.1% in the non-fasting animals.

Discussion. These results indicate that quinidine definitely evokes a significant lowering of plasma potassium without affecting plasma sodium, urinary sodium, or urinary potassium. Considering the hypotensive(7,8) effect of quinidine which would result in a net decrease in flow at the muscle level, the evidence herein indicates that the drug does not alter the normal efflux or influx of potassium in the somatic muscle of the intact anesthetized dog. Since it does not alter urinary potassium excretion, it seems that quinidine effects an accumulation of this cation in some other tissue to account for the hypopotassemia observed. This idea is supported by the results obtained by Huggins and Chapman(1). Feldman and Sherrod(9) and Conn and Wood(10) have established an increase in intracellular potassium in the dog's heart under the effect of quinidine which in part may explain the hypopotassemia produced by quinidine.

The marked increase in blood glucose of quinidine treated animals has not been reported previously. It is known that quinidine will inhibit glucose utilization in incubated rat heart slices(11), impair glucose utilization in humans, who tend to show an abnormal glucose-tolerance test when ingesting the drug (12), and will inhibit both glucose and fructose uptake in the rat diaphragm abolishing also the stimulation of glycolysis by these two



d. f.	5	5	5	5
$\bar{x}_e - \bar{x}_c$	1.6	78.6	75.4	93.7
S. E.	10.0	12.3	12.5	9.0
t	0.16	6.39	6.03	10.41
P	>0.20	0.01-0.001	0.01-0.001	<0.001

FIG. 4. Effect of quinidine on blood glucose of intact fasting dogs. (d.f. represents degrees of freedom, $\bar{x}_e$-$\bar{x}_c$ represents the difference between experimental and control values, S. E. is standard error of difference between the two means; and t represents Student's "t".)

sugars(13). Yet, the marked increase in blood glucose of fasting (30 hrs) animals, significantly above the control changes (probably due to experimental stress) and maintained for a relatively long period of time, suggests that some mechanism for glucose release may be triggered by quinidine. Studies on the effect of quinidine on isolated perfused livers have been initiated.

The differences observed between the fasting and non-fasting animals tend to indicate an inhibitory effect of quinidine on potassium transport at the gut level. At present, this aspect needs further investigation.

The electrocardiographic evidence suggests the possibility that the action of quinidine upon the heart may be mediated via its effect on the K ion, since dogs rendered hypokalemic either by quinidine, vivodialysis or vomiting associated with intestinal obstruction(14) show a striking similarity in cardiac changes.

Summary. Evidence is presented to demonstrate that quinidine, when administered as described here, produces a significant and progressive hypopotassemia; with a non-significant variation in the arteriovenous potassium concentration, denoting that the drug does not alter the normal efflux or influx of the potassium ion at the somatic muscle cell level. The drug also effects a marked hyperglycemia and an apparent inhibition of K transport at the gut level. The electrocardiographic evidence suggests the possibility that the mechanism of action of quinidine may be directly related to the latter's effect on the potassium ion.

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Influence of 5-Fluorodeoxyuridine on Growth Characteristics of Rubella Virus.* (29595)

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The action of 5-Fluorodeoxyuridine (5-FUDR) on DNA synthesis by its inhibitory effect on thymidine synthetase has been the subject of many reports(1,2,3). Salzman (4) first demonstrated that 5-FUDR inhibits DNA, but not RNA viruses, and proposed that the use of 5-FUDR might provide a method for typing the nucleic acid moiety of

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