is not valid to equate age with weight in spontaneously hypertensive and Wistar rats does not agree with my experience that spontaneously hypertensive rats and American Wistar rats do not differ in weight during the first 7-8 weeks of life. Other investigators agree with my experience on this point (Circ Res 24:85-91, 1969). After 8 weeks of age, the growth rate of the spontaneously hypertensive rat slows compared with that of the normal American Wistar rat. However, compared with the Kyoto-Wistar rate, the growth rate of the spontaneously hypertensive rat remains the same. Thus, in the age range of 3 to 7 weeks, weight matching is valid.

Third, I am confused by the conclusion of Dr. Campbell and Dr. Pettinger that serum renin activity does not change with age in unanesthetized rats, for their published data coupled with the data presented in the preceding letter (Table 2) seem to show that serum renin activity changes with age in both spontaneously hypertensive and normal Wistar rats. The latter conclusion is not supported by the observations of my group or the observations of others and raises a question about the validity of the method used to determine the serum renin activity in these experiments.

Regarding the method for determination of serum renin activity, I would like to make two comments: (1) these authors incubated serum for 16-24 hours without adding exogenous substrate and did not demonstrate that substrate remained in excess during that entire period, and (2) they did not use angiotensinase inhibitors during incubation.

Incidentally, De Jong et al. (Proc Soc Exp Biol Med 139:1213-1216, 1972) have also shown an increased plasma renin activity in unanesthetized, decapitated spontaneously hypertensive rats. I have no comments on Dr. Campbell's speculation that spontaneously hypertensive rats are more prone to release renin under anesthesia than are normotensive rats, since I have no data on unanesthetized rats. However, before accepting this theory, further experimentation is required.

Subha Sen
Research Division
Cleveland Clinic
Cleveland, Ohio 44106

Potassium Canrenoate and Digitalis Intoxication

Nielsen and Lucchesi showed in their paper (Circ Res 34:635-640, 1974) that the rate of the ouabain-induced ventricular tachycardia was 130 beats/min (Fig. 1B) and that the sinus rate after potassium canrenoate conversion of the ventricular tachycardia was also 130 beats/min (Fig. 1D). My associates and I have reservations as to whether the conversion of ventricular tachycardia by potassium canrenoate as described should be called "sinus overdrive." These authors also reported in the same paper that with a mean rate of 185 ± 10.3 beats/min for the ouabain-induced ventricular tachycardia in 12 dogs, it was possible to "overdrive suppress" the ventricular tachycardia with atrial pacing at a mean rate of 184.5 ± 7.9 beats/min. Their experience is quite different from ours. A few captured beats and even a temporary suppression of the ouabain-induced ventricular tachycardia in 12 dogs, it was possible to "overdrive suppress" the ventricular tachycardia with atrial pacing at rates just higher than the rate of the ventricular tachycardia. We do not know how such suppression could have been achieved in each and every one of their 12 dogs.

Lucchesi and his associates (Eur J Pharmacol 22:256-262, 1973; Circ Res 34:635-640, 1974) concluded that "any apparent restoration of sinus rhythm in response to potassium canrenoate is due to overdrive suppression of the ouabain-induced ventricular tachycardia" and that "potassium canrenoate fails to exert an antiarrhythmic effect against digitalis-induced arrhythmias." The observation of slight sinus speeding in some of our experiments as well as in their own experiments was greatly emphasized, leading to the broad conclusion that it formed the sole basis for the counteraction of "digitalis-induced arrhythmias." Unfortunately, their conclusion neglected the variety of other antiarrhythmic effects reported in digitalis intoxication (outlined earlier in this letter). Moreover, this conclusion was not directly tested.

To definitively test this conclusion, we have further investigated the antiarrhythmic activity of potassium canrenoate in ouabain-induced ventricular tachycardia in three pentobarbital-anesthetized dogs with complete heart block. In this setting, sinus overdrive cannot mask the effect of ouabain or canrenoate on underlying ventricular activity. Complete heart block was induced by injecting Formalin into the area of the atrioventricular node. In all three experiments, potassium canrenoate, 30 mg/kg (the same dose used by Lucchesi and his associates), suppressed the ventricular tachycardia due to ouabain intoxication. Figure 1 illustrates the fact that potassium canrenoate suppressed the ouabain-induced ventricular tachycardia in the absence of any conducted supraventricular impulses in vivo. These findings are consistent with our previously published data showing the reversal of ouabain-induced toxicity in isolated, superfused canine Purkinje fibers (Circ Res 32:501-508, 1973). We would encourage Dr. Lucchesi et al. to present more definitive evidence to support their contentions rather than restating their conclusions in essentially similar studies (Eur J Pharmacol 22:256-262, 1973; Circ Res 34:635-640, 1974).

Billy K. Yeh
Division of Clinical Investigations
Miami Heart Institute
Miami Beach, Florida 33140

REPLY TO THE ABOVE LETTER

I read with great interest Dr. Yeh's letter regarding my paper (Circ Res 34:635-640, 1974) dealing with the inability of potassium canrenoate to convert experimentally induced ouabain arrhythmias in the anesthetized dog. The results of these studies are in total agreement with previously reported observations from our laboratory (Eur J Pharmacol 22:256-262, 1973) as well as with the findings of Baskin et al. (Proc Soc Exp Biol Med 143:495-498, 1973). I welcome the opportunity, therefore, to respond in the hope that my comments will make my position clear.

It might be important to restate the criteria we have used for many years in the analysis of antiarrhythmic activity of a large number of drugs. One of the experimental arrhythmias we have used is that resulting from an excessive dose of ouabain given in a manner which will produce a ventricular arrhythmia, usually ventricular tachycardia, for a period in excess of 3 hours. The drug to be tested must cause reversion to normal sinus rhythm for a period of at least 30 minutes, and during the period of sinus rhythm stimulation of the distal end of the
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BILLY K. YEH

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