this changing fluid pattern may be suggested in outline. That there may be endocrine factors at work, such as an antidiuretic substance not effectively inactivated by a poorly functioning liver has been indicated.[4] The role of the pituitary in this mechanism has been suggested,[18,19] and requires further elucidation. Recent data, however, disclose a significant elevation in the level of excretion of biologically active estrogen in the urine during acute infectious hepatitis which attains normal values during late convalescence.[20] It is conceivable that movements in body fluid may follow these alterations in active estrogen and be mediated through a central agency such as the pituitary.

Summary. Interstitial fluid volume (thiocyanate space), total blood volume and plasma volume were measured at frequent intervals in 14 young adult males with acute infectious hepatitis. In each patient, the body fluid movement pattern was similar. Detailed data presented in one typical case disclose an increase in the interstitial fluid compartment during the preconvalescent period and a tendency to store ingested water as measured by a water tolerance test. Diminished plasma and urinary chloride values are also found during this period, probably because of chloride storage in the increased interstitial fluid compartment. With convalescence and the restitution of liver function, the interstitial fluid and its retained chloride are mobilized and the interstitial fluid volume falls to lower values. There is an accompanying fall in body weight and frequently a diuresis follows. Less tendency to store ingested fluid is also observed at this time. Plasma chlorides are now restored and urinary chlorides appear in normal amounts. A slight drop in plasma volume and total blood volume accompany these changes and appear to be independent of alterations in the plasma proteins.

It is suggested that these movements in the body fluids may have an endocrine basis.

18 Gilman, A., and Goodman, L., *J. Physiol.*, 1937, **90**, 113.

19 Ingram, W. R., Ladd, L., and Benbow, J. T., *Am. J. Physiol.*, 1939, **127**, 544.

20 Gilder, H., and Hoagland, C. L., PROC. SOC. EXP. BIOL. AND MED., 1946, **61**, 62.

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Recovery Curves of Intraventricular Conduction; QRS Aberration.

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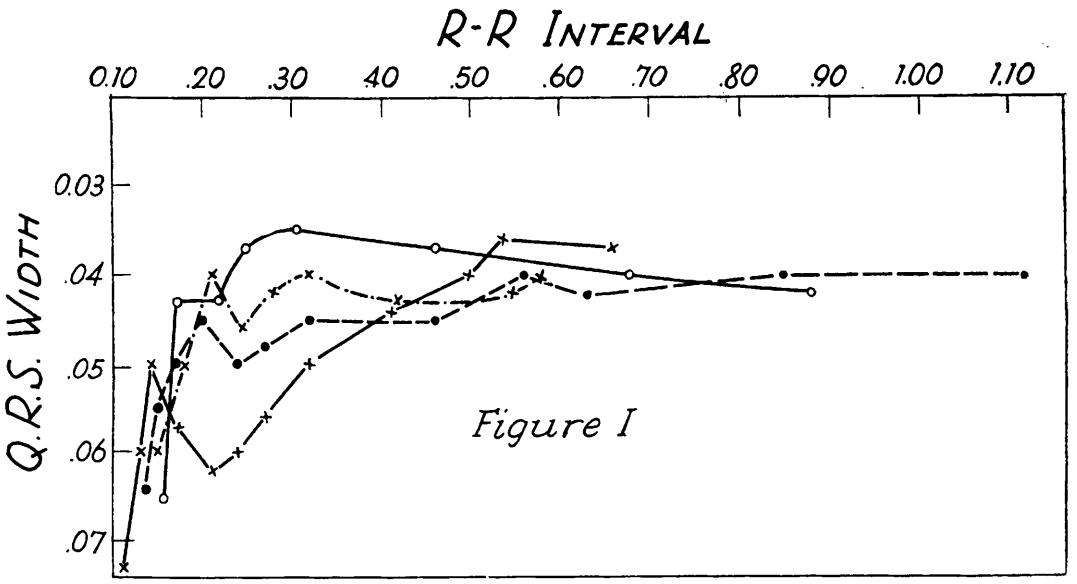
Aberrant intraventricular conduction, with change in form and duration of the QRS complex, is commonly encountered in paroxysmal tachycardia of supraventricular origin, and in premature beats from similarly located foci. Such aberration is regarded as being due to fatigue, or to inadequate recovery, of the conducting tissues. The recovery curves of A-V conduction have been carefully studied;[1] similar studies have been made of ventricular muscle strips, but no analogous data are available for the intact mammalian ventricle.

Method. We have used the isolated rabbit heart, perfused through its coronary vessels by a cannula tied into the aorta. The perfusion fluid was prepared according to the formula of Krebs and Henseleit;[2] it was kept at 37°C, and through it was bubbled oxygen containing 5% CO_2. The atria were cut off, and stimulating electrodes were pushed through the upper part of the I-V septum. The electrodes were activated by an electronic stimulator devised, and made for us, by Dr. S. A. Peoples.[3] This device permits variation in the strength of the stimulus, as well as wide

1 Decherd, G. M., and Ruskin, A., *Brit. Heart J.*, 1946, **8**, 6.

2 Krebs, H. A., and Henseleit, K., *Z. f. Physiol. Chem.*, 1932, **210**, 33.

3 Peoples, S. A., in press.



Four recovery curves of intraventricular conduction in the isolated rabbit heart.

variation in the rate. The overflow of the perfusate ran into a beaker, kept at a constant level by suction, and was returned to the reservoir. Electrodes for the electrocardiographic records were placed in this beaker. Stimuli were delivered to the ventricle at a rate first approximating the idioventricular rate; they were increased by stages up to about 400 per minute, or until some were blocked, or until transient paroxysmal ventricular tachycardia developed.

The QRS width was measured with the Cambridge Record Measuring Instrument. This was plotted against the time interval between stimuli, which was taken as an index of recovery time. Satisfactory preparations beat well for several hours; the experimental data were usually obtained within 60 minutes. Effects of fatigue were further excluded by repetition of both control and drug measurements at various intervals.

Results. Effect of varying rates. Several typical examples of the curves obtained are shown in Fig. 1. Some recovery curves show, in the range of slow rates, gradual shortening of the QRS with increasing rates; more common, however, is gradual prolongation with more rapid rates. A consistent observation is improvement in intraventricular conduction over a short range of rapid rates, causing a notch in the descending limb of the curve where the RR intervals are shortest. Immediately following the notch, however, with increasing rates, QRS widening becomes most marked.

A transient increase in aberration was usually noted in the second, third, and sometimes the fourth complexes of groups produced by sudden increases in rate; rapid shortening of relative refractoriness, as the rapid rate persisted, led to decrease in QRS width and distortion, with the maintenance of a constant QRS form and time for that rate. Similar findings have been made by Scherf[4] in experimental A-V block, and may be seen in patients who have paroxysmal tachycardia with partial A-V block.[5]

Effect of Strophanthin. Strophanthin-K (Strophosid, Sandoz)* was injected into the rubber connection of the cannula in a dose averaging 0.006 mg/kilo of weight of the intact rabbit. This caused a prolongation of the intraventricular conduction time (Fig. 2), which was greater with larger doses of the drug. This effect disappeared in approximately 15-30 minutes, with a return to the control values.

Effect of Quinidine. Quinidine sulphate was injected in a dose of 0.15 mg/kilo. Pro-

[4] Scherf, D., *Wien. Arch. inn. Med.*, 1929, **18**, 403.

[5] Decherd, G. M., Herrmann, G. R., and Schwab, E. H., *Am. Heart J.*, 1943, **26**, 446.

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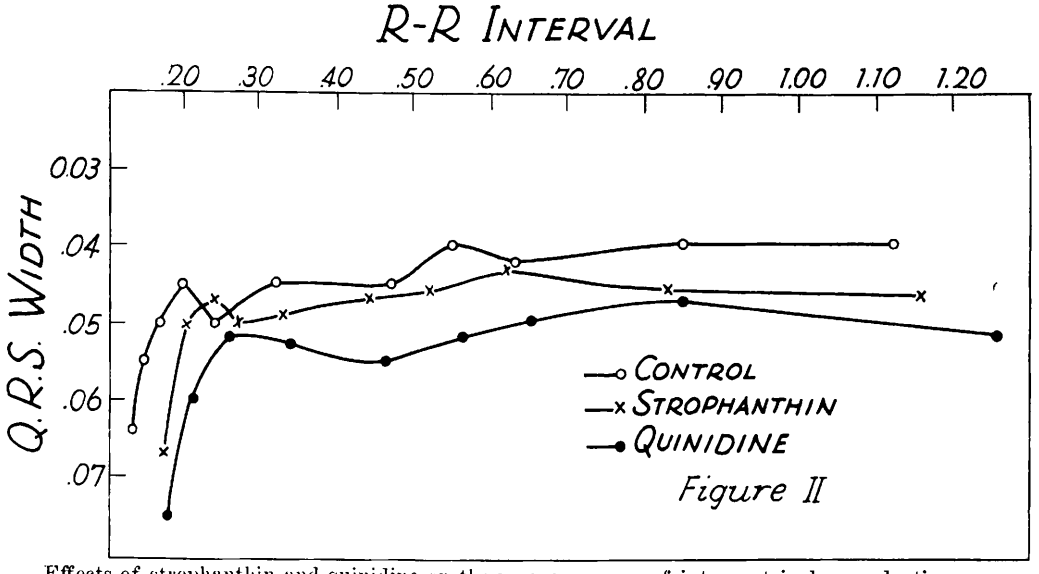

Effects of strophanthin and quinidine on the recovery curve of intraventricular conduction.

longation of conduction times, and of refractoriness, was uniformly produced.

Comment. With shortened periods of recovery the intraventricular conduction time is prolonged. This parallels the well-established recovery curve for A-V conduction. There is, however, one exception: at rapid rates there is a narrow range within which I-V conduction is temporarily improved. This phenomenon has not been noted in recovery curves of A-V conduction, unless it is analogous to the period of supernormal conduction sometimes found at the end of the period of relative refractoriness. Another possible explanation lies in the manner in which these values were determined. Recovery curves of A-V conduction are usually drawn from PR intervals of single complexes of varying degrees of prematurity, with a constant basic rhythm. Our own unpublished data, as well as Lewis and Master's,[6] show shortening of refractoriness and improvement of conduction with increasing rates. We have not measured, for the curves shown in the figures, the first few more aberrant complexes following rapid stimulation, but have utilized measurements made in complexes which represented a steady state of relative refractoriness at a given rate. The present data thus correspond to those which might be obtained from paroxysmal supraventricular tachycardia, rather than from single premature beats.

Aberrant wide QRS complexes are often seen after quinidine administration; the effect of digitalis is variable,[7] but aberration may occur. The effect of these drugs on conduction in the ventricle is, therefore, similar to their effect on the A-V conduction tissues. This impairment in conduction is probably effective throughout the myocardium, and cannot be assumed to pertain to clinical or experimental bundle branch block, where there is thought to be a localized region of defective conduction.

Rapid rates of stimulation of the ventricle, usually in the neighborhood of 350-400 per minute, fairly constant in the same, but varying in different hearts, often led to the persistence of ventricular tachycardia after cessation of the stimuli. The duration varied from a few seconds to a few minutes. In this preparation, and under the conditions thus far employed, we have been unable to note any effect of strophanthin in facilitating, or of quinidine in preventing or terminating, these paroxysms.

Summary. Data have been obtained from the isolated rabbit ventricle, from which have been drawn recovery curves of intraventricular conduction. Similar curves have been drawn after the injection of strophanthin and of quinidine.

[6] Lewis, T., and Master, A. M., *Heart*, 1925, **12**, 209.

[7] Berliner, K., *Am. Heart J.*, 1931, **7**, 189.