0.9% saline. The incubation mixture contained 1.0 ml of a pretreated angiotensinase-free plasma pool of nephrectomized animals without pressor or depressor activity. The angiotensinogen concentration in different charges was about 4000 ng angiotensin II-amid equivalent/ml. In the presence of 0.01 ml of 5% di-isopropylfluorophosphate (in isopropanol), 0.3 ml phosphate buffer (0.1 mol, pH 5.5), 0.65 ml 0.9% saline, 0.04 ml neomycin-sulfate 0.5 %and 0.25 to 0.5 ml plasma, the mixture was adjusted to ph 5.5 and incubated at 37 °C for 2 h. Following heat inactivation at ph 5.1, the clear supernatant was bioassayed by pressor response in the nephrectomized, vagotomized, pentolinium-blocked rat as described in details elsewhere[6].

Results. As to be expected, bilateral nephrectomy resulted in a complete disappearance of renin activity in the arterial and portal venous plasma within 2 to 24 h after operation. When these animals were subjected to hemorrhagic hypotension lasting from 60 to 165 min, reappearance of renin in the portal venous or arterial plasma could not be detected (Table). Under the same circumstances, 40 to 65 min after inducing hemorrhage, unnephrectomized animals revealed a threefold increase in the arterial plasma renin activity from 65 $\pm$ 21 ng/ml to 221 $\pm$ 48 ng/ml ($n = 5$) within a one-hour incubation time. According to our findings, the portal system of rats does not liberate renin. This contrasts with published results[7] in which a prevalent increase in renin activity in portal venous blood has been reported in dogs under similar conditions. Whether this difference is due to a species-specific binding of plasmatic renin located in the mesenteric vessel wall[8] which can be liberated by the hypoxic hypotensive state, remains to be established. In non-nephrectomized dogs, a significant increase but no measurable difference in the arterial and portal venous renin level after hemorrhage was reported[8]. So far renin synthetizing structures in the splanchnic area have not been described.

Zusammenfassung. An 2–24 h nephrektomierten männlichen und weiblichen Wistar-Ratten wurden Vergleichsbestimmungen der Renin-Aktivität im arteriellen und portalvenösen Plasma durchgeführt. Die Renin-Aktivität war in beiden Gefässystemen auf nicht messbare Werte abgefallen. Die infolge Blutentzug von 10–12 ml/kg erzielte hämorrhagische Hypotension führte im Zeitraum von 60–165 min nicht zu einem Renin-Aktivitätsanstieg. Die Versuchsresultate ergeben keine Bestätigung, dass Renin in der portalen Strombahn produziert oder freigesetzt wird.

H. WERNZE and A. SEKI

Medizinische Universitätsklinik der Universität, Josef-Schneider-Strasse 2, D-87 Würzburg (Germany), 29 November 1971.

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Stretch Sensitive Intrinsic Autoregulatory Mechanisms for Rhythmicity and Contractility of the Heart

While conducting experiments on isolated frog hearts, the author observed that change in the perfusion pressure consistently produced changes in heart rate. Extensive experiments conducted on various preparations of isolated frog hearts and its individual chamber (Pathak[1–4]) and on isolated dog hearts and isolated atria of dogs, rabbits, ginea-pigs and albino rats (Pathak[5]) demonstrated that distension of various chambers of frog hearts and distension of right atria of mammalian hearts by raising the intraluminal pressure resulted in cardioacceleration in a progressively linear fashion up to a certain critical pressure beyond which either no further acceleration occured or the heart rate started declining. In a given heart, depending upon initial stretch of the pacemaker due to prevalent right atrial pressure in relation to this critical degree of stretch, one could get either acceleration or deceleration or no change in the heart rate, on increasing the distending pressure.

The present communication is based upon further confirmation and extension of these findings using more refined electronic recordings.

Material and method. The activity of isolated frog hearts (*Rana temporaria*) perfused in situ with frog Ringer solution was recorded with a four-channel inkwriting recorder. The recorded parameters included perfusion (venous) pressure, heart rate, arterial pressures (systolic, diastolic and pulse pressure) developed by the isolated heart working against an artificial resistance and cardiac output. The effect of graded increase in venous pressure by raising the perfusion pressure and of graded increase in arterial pressure produced by increasing the artificial resistance, was investigated. Although pressure-tachycardia was observed in a large number of frogs used in various experiments, detailed analysis of this nature was undertaken in 18 hearts. The temperature of laboratory was thermostatically regulated.

Results. Graded increase in venous pressure in steps of 1 cm from 0 to 6 cm of Ringer produced graded increase in the heart rate up to 3 to 4 cm pressure. Further increases in pressure beyond this level either produced no further increase in the heart rate or the heart rate declined (Figure 1) below the plateau level. Graded increases in arterial pressure in steps of 10 mm Hg produced similar changes due to back pressure causing distension of the sinus venosus. The following additional observations were confirmed: 1. The pressure-acceleration response was reversible. 2. For each heart there was a critical pressure up to which both inotropic and chronotropic responses increased simultaneously with the degree of pressure-stretch. The frog hearts worked optimally at about 3 cm Ringer pressure. 3. Hypodynamic hearts could be reactivated and quiescent hearts could be restarted by increasing the distending pressure. Heart beat considerably slowed down or stopped altogether when the pressure was reduced to zero level. 4. Repeated testing with pressures

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greater than the critical pressure either stabilized the heart rate at a high level or produced arrhythmia. 5. Variation in temperature and ionic composition of Ringer fluid or pH did not produce a significant change in stretch-acceleration response.

Discussion. The electrophysiological studies were conducted to verify the origin and nature of pressure tachycardia, and it was observed that this was due to increased impulse generation at the pacemaker (Pathak[4]). In view of the experimental evidence referred to above, and in view of the fact that isolated frog hearts suspended in Ringers solution and mammalian hearts perfused through coronary artery are activated and stimulated when the pacemaking chamber is distended additionaly, it is concluded that stretch of pacemaker and muscular tissue produced by the venous return is the fundamental stimulus for intrinsic autoregulation of heart rate as well as force without involvement of the superimposed neurohumoral influences. The intimate mechanism of action of stretch itself could, however, be different in the pacemaker and in the contractile musculature. Mechanical stretch is, therefore, a basic biological stimulus for the rhythmicity and contractility of the heart and it links the venous circulatory load with cardiac output (work performance) in a positive feed-back manner. The importance of stretch as an intrinsic autoregulatory mechanism for the inotropic response implied in Frank Starling's law of heart and its application in the body is well recognized[8]. But because of the subtle nature of the action of stretch on the pacemaker, and because of the erroneaus concept of the 'Bainbridge reflex' (Pathak[6,7]), the role of stretch in the autoregulation of chronotropic response has not received due recognition. With this point in view, the relative role of stretch and superimposed neurohumoral influences is diagrammatically highlighted in Figure 2. The common property of stretch sensitiveness of chronotropic and inotropic responses makes the heart an unique autoregulating pump.

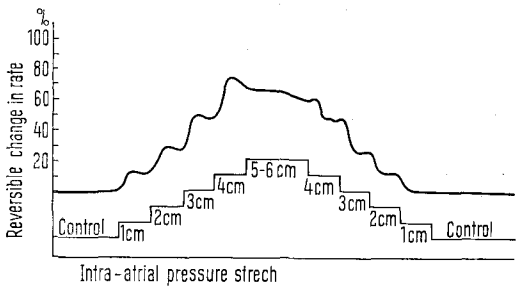

Fig. 1. Pattern of Stretch-acceleration response due to raised sinus or right atrial pressure. Note the sudden increase in the heart rate to a peak value followed by tendency to stabilization at a slightly lower level during the maintenance of each increment of pressure from below 1 cm up to 4 cm water pressure, at which level the heart rate tended to assume a plateau. The plateau was either maintained or the heart rate fell below the plateau level between 5 to 6 cm. Reversing the steps of pressure changes reversed the heart rate back to the initial control level.

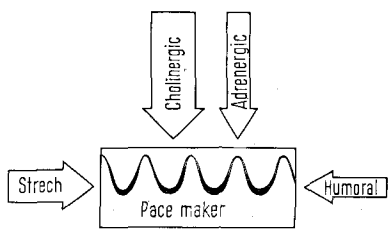

Fig. 2. Main physiological factors modulating pacemaker activity and their relative intensity as indicated by the thickness of arrows.

Résumé. L'étirement mécanique est une force motrice fondamentale pour l'autorégulation intrinsèque du rhythme du cœur en modifiant l'activité du «pacemaker» de la même manière que la distension du myocarde influe sur le réponse inotropique. L'étirement est un mécanisme biologique de base pour la rythmicité cardiaque et la contractilité et il met en interdépendance positive le retour veineux et le débit sanguin. La sensibilité à l'étirement est une propriété des réponses chronotropiques. Elle fait du cœur une pompe autorégulatrice unique en son genre.

C. L. Pathak

Department of Physiology, Medical College, Jodhpur (India), 9 June 1971.

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The Aorta Wall as a Storage Organ for Neurosecretory Material in Orthopteroid Insects

The corpora cardiaca and/or the aorta wall have been described as neurohaemal organs in insects. Three different conditions have been reported in previous accounts. Neurosecretory material may be stored both in the corpora cardiaca and the aorta wall, or only in the aorta wall, or only in the corpora cardiaca.

In the hemipterans *Iphita limbata*[1] and *Adelphocoris lineolatus*[2], it has been found that the A-material present in the aorta wall is released from the corpora cardiaca. Similarly in the dipteran *Calliphora erythrocephala*[3,4] neurosecretory material is stored partly in the aorta wall and partly in the corpora cardiaca. In the beetle *Aulacophora foveicollis*[5], the corpora cardiaca and the aorta wall are fused and neurosecretory material has been seen entering the latter from the former. Dogra[6], working on 5 species of Heteroptera, however, came to the conclusion

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