OSCILLATIONS OF DIASTOLIC TENSION AS A POSSIBLE FACTOR IN MYOCARDIAL INSUFFICIENCY

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Oscillations of diastolic tension, known as "postcontractions" and unaccompanied by action potential development, have been recorded in isolated preparations of the myocardium of warm-blooded animals and man [1, 7, 8, 10]. Oscillations usually arise during overloading of the myocardial cells by Ca^{2+} ions [1, 10]. It has been suggested that the oscillations arise as a result of recirculation of Ca^{2+} ions between the sarcoplasmic reticulum and the myofibrils [1, 7, 8]. The amplitude of the oscillations usually increases in the presence of myocardial hypertrophy [4, 9], combined with a decrease in the ability of the reticulum to take up Ca^{2+} [11] and by slowing of relaxation [5, 6]. However, the question of the link between the appearance of oscillations and slowing of relaxation has not been studied.

In the investigation described below this problem was studied in experiments on the isovolumic guinea pig heart. In experiments on the atrial trabeculae of patients with heart diseases the frequency and amplitude of spontaneous oscillations were compared with parameters reflecting the degree of the pathological changes.

EXPERIMENTAL METHOD

Isolated guinea pig hearts were perfused through the aorta with Krebs' solution saturated with carbogen (96% O_2 + 4% CO_2) by means of a peristaltic pump with an output of 10 ml/min/g. A small balloon filled with fluid was introduced into the chamber of the left ventricle through an incision in the wall of the left atrium. The pressure in it was measured by means of a Gould Statham P 23DB transducer. The signal from the transducer, its first derivative, and also the ECG from the subendocardial layer of the apex of the heart were recorded on a Gould Brush 2200 recorder. The relaxation index [6] was calculated by dividing the maximal rate of fall of pressure by the maximal pressure developed, and the relaxation constant [5] was calculated by analysis of the dynamics of the whole phase of decline during relaxation. Substances inducing postcontractions, namely isoproterenol and K_2PdCl_4, were injected into the aorta by means of an infusion pump.

Altogether 25 preparations of the auricles of the right atrium from patients with rheumatic and congenital heart diseases were investigated [2]. Trabeculae 3-5 mm long and not more than 1 mm thick were isolated from the auricle. The trabeculae were placed in a working chamber through which flowed Tyrode solution saturated with carbogen at 32-34°C. One end of the trabecula was attached to a stationary rod fixed to the floor of the chamber, the other end was attached to the rod of a 6MKh1S mechanotron. The preparation was stretched by a load of 200-500 mg and stimulated by square pulses of above threshold strength, with a frequency of 0.5 Hz and a duration of 10-20 msec. The signal from the output of the mechanotron was led to the input of an S1-18 oscilloscope or Mingograph-81 instrument.

EXPERIMENTAL RESULTS

Postcontractions of the heart during hypothermia (24°C) appeared 3-4 min after the be-

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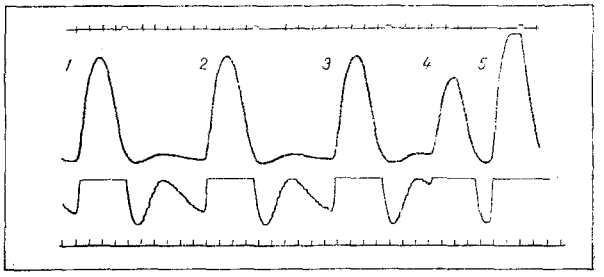

Fig. 1

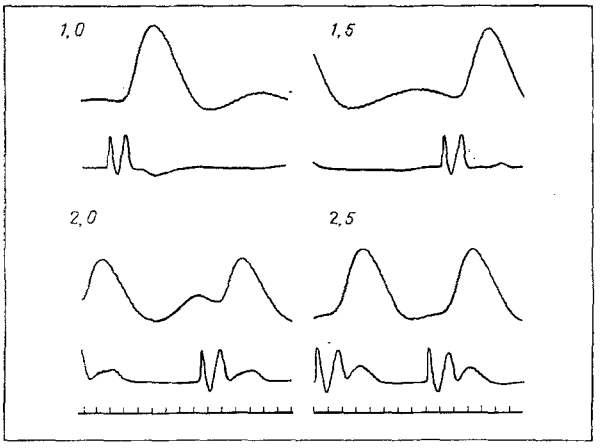

Fig. 2

Fig. 1. Oscillations (postcontractions) in isovolumic guinea pig hear during hypothermia (24°C) and the action of isoproterenol (1.10^{-7} to $5 \cdot 10^{-7}$ M). Numbers denote successive contractions. Top trace shows contractions during low-sensitivity recording, bottom trace — during high-sensitivity recording.

Fig. 2. Effect of frequency of stimulation on contractions and postcontractions of isovolumic guinea pig heart. Top traces show contractions, bottom traces show ECG. Frequency of stimulation (in Hz) indicated in top left corner of each frame.

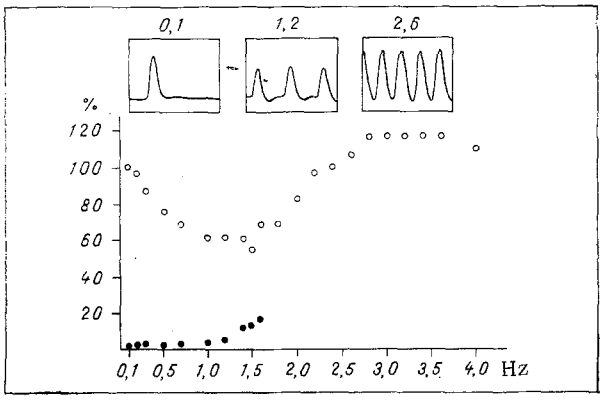

Fig. 3. Frequency—force curve in atrial trabecula of patient with rheumatic heart disease. Open circles — amplitude of contractions (amplitude during stimulation with frequency of 0.1 Hz taken as 100%), filled circles — amplitude of postcontractions. Insets: original traces of contractions and postcontractions during stimulation with frequencies of 0.1, 1.2, and 2.6 Hz respectively. Abscissa, frequency of stimulation (in Hz); ordinate, amplitude of contractions and postcontractions (in %).

ginning of injection of isoproterenol ($1 \cdot 10^{-7}$ to $5 \cdot 10^{-7}$ M) into the coronary circulation of the guinea pig hearts. Their appearance was preceded by arrhythmia and elevation of the diastolic pressure. The pressure developed by the isovolumic ventricle was found to depend on the end-diastolic pressure. A similar dependence of the force of contraction on the diastolic tension was observed in the course of development of oscillations in isolated papillary muscles previously [1, 7, 8]. It will be clear from Fig. 1 that when systole occurred at the peak of the oscillation (contraction No. 4) its amplitude was lower than in cases when systole developed before (contraction No. 5) or after the oscillations (contractions Nos. 1

TABLE 1. Clinical and Experimental Indices of Human Cardiac Pathology

No.	Clinical data			Experimental data		
	patient's age, years	cardiothoracic index (normal 0.4-0.45)	heart rate, beats/min	type of frequency—force curve	amplitude of oscillations	frequency of stimulation, Hz
			Acquired defects			
1	32	0,67	48—60	1	0,54	2,0
2	50	0,72	60—100	1	0,41	1,4
3	23	0,52	75	1	0,25	2,0
4	30	0,70	40—66	1	0,61	1,6
5	26		57—109	1	0,24	1,0
6	45	0,57	60—75	2	0,30	1,2
7	39	0,67	40—80	2	0,42	1,0
8	43	0,70	48—86	2	0,28	1,6
9	26	0,84	57—80	2	0,12	0,7
10	27		75—109	2	0,23	1,5
11	17	0,40	66—75	2	0,28	1,5
12	23		50—80	2	0,24	1,5
13	39	0,64	57—109	2	0,22	1,5
14	33	0,76	48—73	2		
15	28	0,62	57—80	3	0,54	1,6
16	38	0,64	60	3		
			Congenital defects			
1	13	0,40	67	2	—	—
2	24	0,45	67	3	—	—
3	11	0,46	100	3	—	—
4	17	0,46	63	3	0,36	1,0
5	44	0,62	74	3	0,26	1,5
6	6	0,57	60	3—4	—	—
7	7	0,45	80	4	—	—
8	7	0,43	100	4	—	—
9	14	0,41	109	4	—	—

and 2). Both the relaxation index and the relaxation constant were higher in contractions developing at the peak of the oscillations than in other contractions by as much as 19%. Conversely, the high-amplitude contraction (No. 5) had relaxation parameters 10% lower in magnitude.

In another series of experiments conducted at a temperature of 37°C an oscillation of end-diastolic pressure developed after injection of 0.1 mM K_2PdCl_4 into the coronary circulation. Spontaneous cardiac activity ceased but excitability was preserved. Electrical stimulation evoked contractions, followed by oscillations unaccompanied by any changes in electrical activity (Fig. 2). The steepness of rise of the oscillations and their amplitude increased with an increase in the frequency of stimulation. As the main contraction came closer to the peak of the oscillations a marked decrease in amplitude of the main contraction was observed (Fig. 2, frequencies 1.5 and 2 Hz). The amplitude of the contractions was largely restored if the frequency was increased even more, when systole occurred in the rising phase of the oscillation (Fig. 2, frequency 2.5 Hz). Contractions which coincided with the peak of the oscillations were characterized in this series also by increased values of the relaxation index and relaxation constant.

During repetitive stimulation of myocardial trabeculae from patients with acquired and congenital heart diseases oscillations of tension occurred in 70% of cases. Previously four types of dependence of the force of contractions of the trabeculae on the frequency of stimulation were distinguished [2]. Type 1 was characterized by a negative "staircase" and was observed in the most seriously ill patients with raised cardiothoracic index, whereas type 4, characterized by a positive "staircase," corresponded to patients with the mildest disease. In the series under discussion this criterion was compared with the frequency of onset of oscillations and their amplitude (Table 1). Postcontractions were found to arise in all five myocardial preparations with a type 1 frequency — force curve, and the mean amplitude of the oscillations with 41% of the amplitude of the main contraction. In preparations of type 2-3 oscillations appeared in 11 of 16 experiments and they had a mean amplitude of 20%. No oscillations whatever appeared in four experiments with a type 4 curve (Table 1).

The severity of the disease thus correlated with the frequency of onset of the oscillations and their amplitude.

During the study of the frequency—force curve the appearance of oscillations was coupled with a decrease in the force of contraction (Fig. 3), possibly because under these circum-

stances contractions appeared almost at the peak of the oscillations (Fig. 3, frequency 1.2 Hz). The amplitude of contractions increased considerably during stimulation with a high frequency, when contractions developed before the onset of oscillations (Fig. 3, frequency 2.6 Hz).

The decrease in amplitude of the contractions at the peak of the oscillations in the isovolumic guinea pig heart and in myocardial preparations from patients with heart diseases is thus identical and arises most probably on account of a decrease in the Ca^{2+} inflow into the cells [1]. If oscillations of diastolic tension develop in the patients' heart *in vivo*, they may reduce the stroke volume in cases of arrhythmia when premature contraction arises at the peak of oscillation. This may be the reason why a decrease in cardiac output is observed in patients with rheumatic heart disease and atrial fibrillation during physical function tests [3].

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STUDY OF SPASTIC REACTIONS OF THE SMOOTH MUSCLE OF THE LUNGS TO SOLUBLE IMMUNE COMPLEXES WITH MICROBIAL ANTIGENS

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Many authorities are of the opinion that soluble immune complexes (SIC), formed in some cases by autoantibodies and antigens (AG) of lung tissue [1, 4], and in other cases by soluble microbial AG and antibodies (AB) of nonreagin nature [2], participate in the pathogenesis of infectious-allergic bronchial asthma. It is considered that SIC induce an inflammatory reaction of Arthüs type in the lungs. It has also been shown experimentally that SIC may have a spasmogenic action [6, 8]. The mechanism of this phenomenon is largely unexplained. In the modern view the aggressive manifestations of SIC in the lungs are effected through a complement system [5]. The view is held that SIC act directly on smooth muscle [3]. The question of the different classes of immunoglobulins (Ig) to which the specific AB forming aggressive SIC belong likewise remains unclear.

The aim of the present investigation was to study the mechanism of the spasmogenic action of

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