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Paired-pulse stimulation of an electric-hydraulic pump used to replace the mammalian heart

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PAIRED electric stimuli (the first stimulus initiating, the second stimulus augmenting, systole) in experiments by Katz,[1] were observed to have several specific effects on the activity of the mammalian heart. There is an optimal time interval between the two stimuli, for which a maximal potentiation of the ventricular activity is observed. This positive inotropic effect is easily reproducible in the laboratory. In addition, paired or coupled stimulation has been used not only to enhance myocardial activity, but also to reduce undesirably high heart rates.[2]

There is general agreement that in a normal human heart, paired stimulation increases the peak systolic pressure in the ventricle, the time of ascent of this pressure's wave and the myocardial oxygen consumption, while it does not affect the cardiac output. In a failing heart, according to recent studies,[2-4] the effect is different: the stroke volume is increased, but the oxygen consumption also is increased. Generally, Fisher and associates[5] found paired stimulation capable of inducing maximal or nearly maximal contractility of the ventricular muscle at any specific ventricular volume, and of causing a 64 percent increase of pressure-time index (dP/dt) above maximal control values. The mechanism of these effects is not known.

An analogous observation was made while experimentally driving a compressed-air pump designed to maintain the circulation. Paired stimulation of this device increased considerably the stroke volume. This observation is reported here since it offers an example of potentiation through coupled stimulation in an exclusively electric-hydraulic system, uncomplicated by factors other than purely mechanical ones. The study was made

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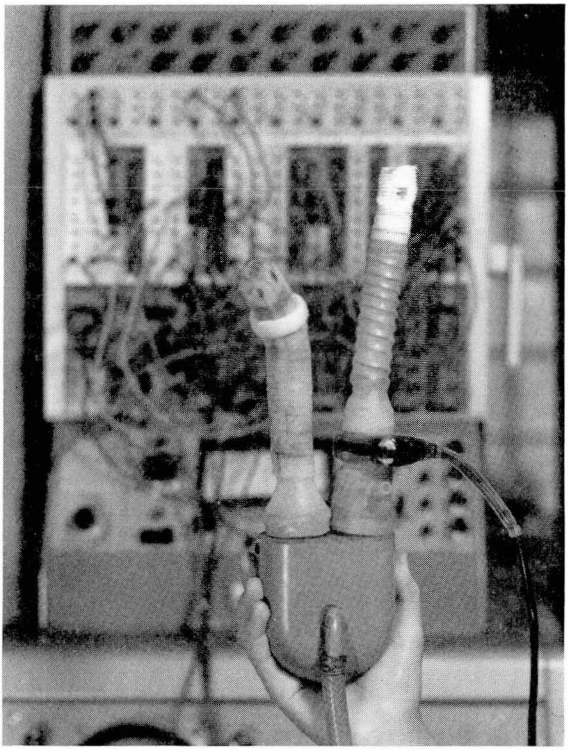

Fig. 1. Photograph of driving equipment and pump used.

in a mock circulation, excluding all physiologic regulating feedbacks, as well as in living calves and sheep.

MATERIALS AND METHODS

A pump (designed to replace the mammalian heart)[6] driven by compressed air was used. It consists of a metal case over a chamber made of Silastic (*Fig. 1*). Air forced between the metal case and the plastic inner chamber drives the pump. The inner chamber contains the fluid to be pumped and is provided with one inlet valve and one outlet valve; Silastic-ball valves and leaflet valves were used.

A 10-foot long, ¼-inch inner diameter Tygon tube connects this pump to an air valve.* Compressed air and suction are alternately applied to the air valve and to the pump through the valve.

The valve is operated by an electric signal, the magnitude, duration, rate, and shape, of which are regulated by a special system, constructed at

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the NASA Lewis Research Center, Cleveland. It is a modification of a prior servosystem.[7] Fifty potentiometers, mounted on a matrix, may be used to form any desired wave at any part of one cycle. The electric function is then transformed into an air-pressure wave of the same shape.

The in vitro tests were done in the usual simple mock circulatory system. The pump operates against a resistance of a vertical water column in a Tygon tube, ¾ inch in diameter and 80 cm in length, ending in an open reservoir. A second inlet reservoir, with a free level 10 cm above the pump input, is used to fill the pump. A rotameter in the circuit indicates the pump mean output per minute. A debubbling device is placed between the first reservoir and the rotameter.

The air valve was driven with a pair of pulses at a rate of 83 per minute. The duration of the first pulse was fixed at 216 msec, while the tested lengths of the second pulse ranged from 144 to 216 msec. Both pulses had the same 1- or 2-v amplitude. The time interval between the end of the first pulse, and the beginning of the second pulse ranged from zero to 360 msec, and it was increased by 36 msec each time[7] (the time controlled by one potentiometer, when 20 potentiometers are used in a cycle of 720 msec at the above rate).

The in vivo tests were performed in calves and sheep. The heart of the animal was excised under extracorporeal blood circulation and oxygenation[6] and two of the pumps described were connected, one between the right atrium and pulmonary artery, and the other between the left atrium and the aorta. Paired pulsing of the pump in the position of the left ventricle was tried, with the same pulse characteristics as in the in vitro test. The pump output was measured with an electromagnetic flowmeter* placed at the connection of the outlet of the pump to the aorta.

The test was repeated while a feedback[8] loop was closed between the left atrial pressure and the air valve. This loop is fed through a TR-10 computer that changes the performance of the valve so as to maintain a constant atrial pressure. It is a part of the NASA system already mentioned.

During both the in vitro and in vivo tests a recording† was made of the pump output, the electric signal, the air-valve pressure, the intraventricular pressure, and the pressure at the outlet of the pump.

RESULTS

The in vitro test demonstrated that a double pulse produced an increase in the pump output over that achieved by a single pulse, of a duration not exceeding that of the two pulses together (*Fig. 2*). The increase over the single pulse value ranged from 3 to 120 percent, depending mainly on the

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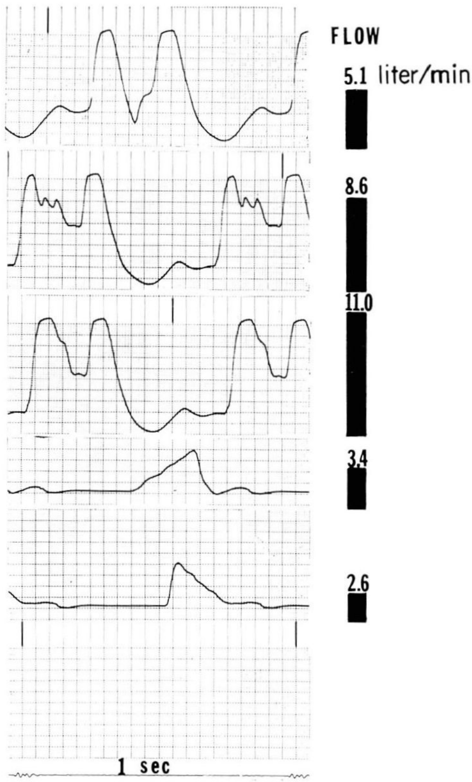

Fig. 2. In vitro test. The pump output increased with paired pulses.

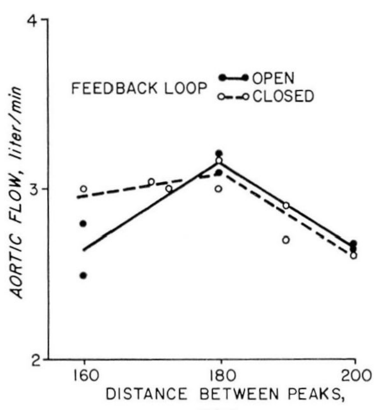

Fig. 3. In vivo test. The aortic flow was increased when the distance between the two peaks in the pumping chamber pressure wave was 180 msec.

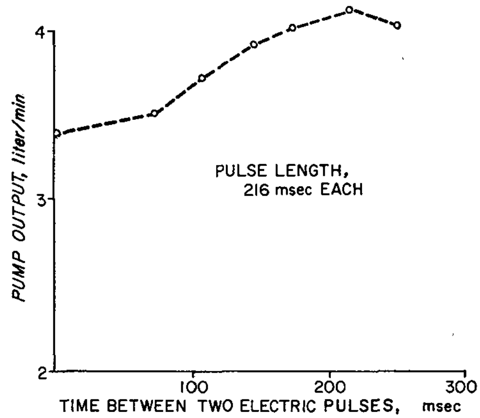

Fig. 4. In vivo test. Changes in aortic flow correlated with changes in the time intervals between two paired pulses driving the air valve, and hence the pump is in the place of the left ventricle.

distance between the two pulses. The increase in output for a time interval of from 200 to 250 msec between the two pulses was greater than that obtained for higher or lower time intervals.

The results in vivo indicated an increase in aortic flow when paired pulses were used. The time interval was measured (in msec) between the two peaks appearing in the pressure tracing which was obtained from the air-pressure line just beyond the servovalve. An interval of 180 msec was observed in several instances to produce the optimal increase in flow. The same observation was made when the air valve was regulated by the feedback of the atrial pressure changes to the computer. (*Fig. 3 and 4.*)

Discussion

To facilitate understanding of the mechanism of paired pulsing of the mammalian heart in situ, a higher pump output, obtained in vitro and in vivo, with the help of paired pulsing of a pump, was related to the performance characteristics of the system. The paired pulses possibly could affect the following characteristics. (1) *The performance of the electric air valve.* The servovalve used has a high-frequency response and closely follows the electric signal. The same value can be used for the paired-pulses performance.

(2) *The performance of the pump itself.* The heart (or the moving plastic chamber) and the fluid pumped, each has an inertia that must be overcome before motion starts or stops. This is shown in the pressure waves of the air chamber. Although the electric signal consists of two distinct pulses, the pressure wave, recorded distal to the air valve, shows a single pulse with

a dip in the middle. The depth and the duration of the dip depend on the time interval between the two pulses. Therefore, the second electric pulse starts the second pressure wave before the first pressure wave has returned to the base line. Thus, the second pressure wave starts building up on a higher base line and may be more effective in pumping out a part or all of the residual volume, left over from the first pulse.

This increase in pump output is similar to the physiologic increase in contractility of the myocardium, when paired stimulation is applied independently of the ventricular volume.[2] In spite of the great differences between the pumping system used here and the living heart, one cannot help but notice that the optimal time interval for a maximal increase in output (180 msec) is almost the same in the two systems.

(3) *The input impedance of the system.* The input impedance should not be affected by coupled stimuli pumping, since the pressure in the pumping chamber does not have time to fall, after the first pulse, so as to allow the inlet valve to open. Hence, the pump is working only on the initial filling volume.

(4) *The output impedance of the system.* The first pulse opens the outlet valve and sets in motion the fluid in the aorta (in vivo test) or in the Tygon tube (in vitro test). The second pulse, when arriving at a proper time for the frequency response of the pumping mechanism and/or the outflow system, may enhance the flow and increase the output of the pump, as long as a residual volume is available. Consequently, synchronization phenomena should also be considered in the understanding of the effect of the paired pulses.

SUMMARY

Paired electric stimulation of a pump, designed for experimental replacement of the mammalian heart and driven by a servosystem, has been tested in vitro and in vivo. A significant increase in the pump output has been observed in both instances, and is optimal for a certain time interval between the two pulses. The operation of the second pulse at a different state of performance of the pumping mechanism (produced by the first pulse), and synchronization phenomena are considered in the discussion of the observations.

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