BIOPHYSICS IN CARDIOVASCULAR DYNAMICS

FREDERICK OLMSTED
Division of Research

SINCE the first employment of the U-tube mercury manometer by Poiseuille, to measure blood pressure, nearly a century ago, almost all study of hemodynamics has been by observation of blood pressure alone. In the last few decades it has been possible to measure also mean cardiac output in momentary fragments by the indirect methods of oxygen consumption and dye dilution. We have been primarily concerned with continuous and instantaneous direct measurement of flow into the arterial system, and its relations to blood pressure and peripheral resistance. A second concern is that measurements in experimental animals should be made under natural conditions, or without surgical trauma and the disturbance of anesthesia.

To this end, special electronic and surgical technics were developed. *Figure 1* shows the position of an implanted electromagnetic flow transducer around a dog's ascending aorta, and a catheter for sensing blood pressure. Connections to the outside are made through skin buttons; the flowmeter plugs into one, and a strain gauge pressure transducer is connected to another. A third button communicates with a small intravenous catheter, used for infusion and injection of vasoactive substances. At operation, performed at least one week before experiments and measurements, pressed polyvinyl sponge is placed between the edges of the flow transducer and the aorta, to prevent rapid erosion of the blood vessel wall. The junction of the artery and pressure-sensing tube is reinforced with Dacron arterial graft material sutured to the vessel and tied around the catheter.

Several electromagnetic flowmeters were investigated for this chronic preparation. A "square wave" device[1] was found to be too large for implantation; a special small square wave unit became hot from overloaded coils. A plan using a gated sine wave that seemed suitable has recently been described.[2,3] This was constructed in our laboratory, but examination of its operation showed it was not possible to obtain a correct wave form of blood flow or to locate a zero flow point as had been described.[2] It became apparent that "electronic gating," or selective sampling of the sine wave signal from the flow transducer, at the frequency of the wave, to obtain an optimum, background-free flow curve, was impractical because the signal changed in phase, or was unstable in time, with change in blood flow.

Therefore, a circuit sensitive to phase change only,[4] and not to amplitude change, as in all other flowmeters, was designed and was found to be satisfactory. It has the advantage of the quietness and fidelity of phase-sensitive systems such as frequency modulation (FM), and the additional advantage that the flow signal arises from phase relationship of the transducer wave form components, and not their absolute amplitude. The magnetic field can be very small, and the sensor unit

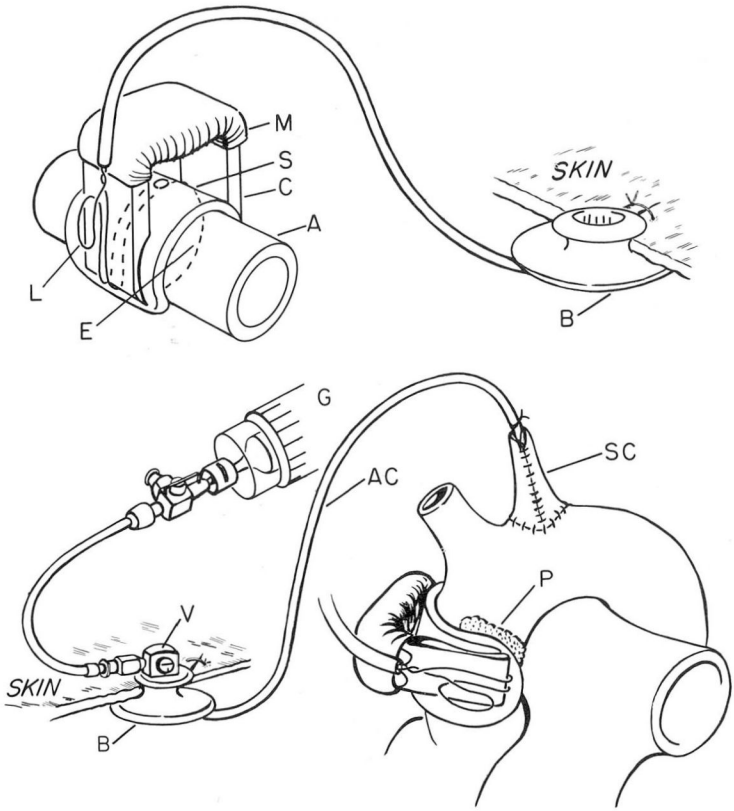

Fig. 1. Upper left shows the flow transducer. Magnet (M) creates a 400-cycle field at right angles to sleeve (S) and artery (A). Electrodes at right angles to both field and flow pick up potentials generated by moving blood, a conductor (1 per cent salt) cutting lines of force of the magnetic field as in an electric generator. C is a 12-gm. laminated core, L a balancing loop in the electrode lead (E). The external connecting skin button (B) is at top right. Below is the flow transducer in place around the ascending aorta. Reinforcing polyvinyl sponge (P), is placed between the sleeve and artery wherever mural erosion tends to occur. The arterial pressure catheter (AC) in the reinforced subclavian artery (SC) terminates in a skin button and small stopcock (V). The catheter is filled with 50 mg. per milliter of heparin to prevent clotting, and is connected to a pressure transducer (G) when recording. (Courtesy of Olmsted, F.; J. Appl. Physiol. **17:** 152-156, 1962.)

itself can be smaller and lighter than in other schemes, and still produce an accurate flow signal.

The dogs were allowed to become accustomed to the laboratory environment while connected to the electronic apparatus by a 35-foot cable (acting as a leash) on a sliding track. A few hours of training assured the animal that the laboratory procedure was innocuous. Relative freedom provided by the leash had the paradoxic effect, after time to explore the surroundings, of causing the dogs to lie down and often to go to sleep, in striking contrast to the tension seen in restrained, unanesthe-

tized animals. During the course of training the heart rate and cardiac output usually fell 30 to 40 per cent from the initially measured values. Blood pressure also was lowered, sometimes to 100/60 mm. of Hg, with a heart rate of 50 to 60 beats; such low values are not usually found in transient measurements by femoral artery puncture in normal dogs.

In addition to velocity of inflow to the arterial system, and arterial blood pressure, *Figure 2* shows the other functions recorded from the animals. Stroke volume,

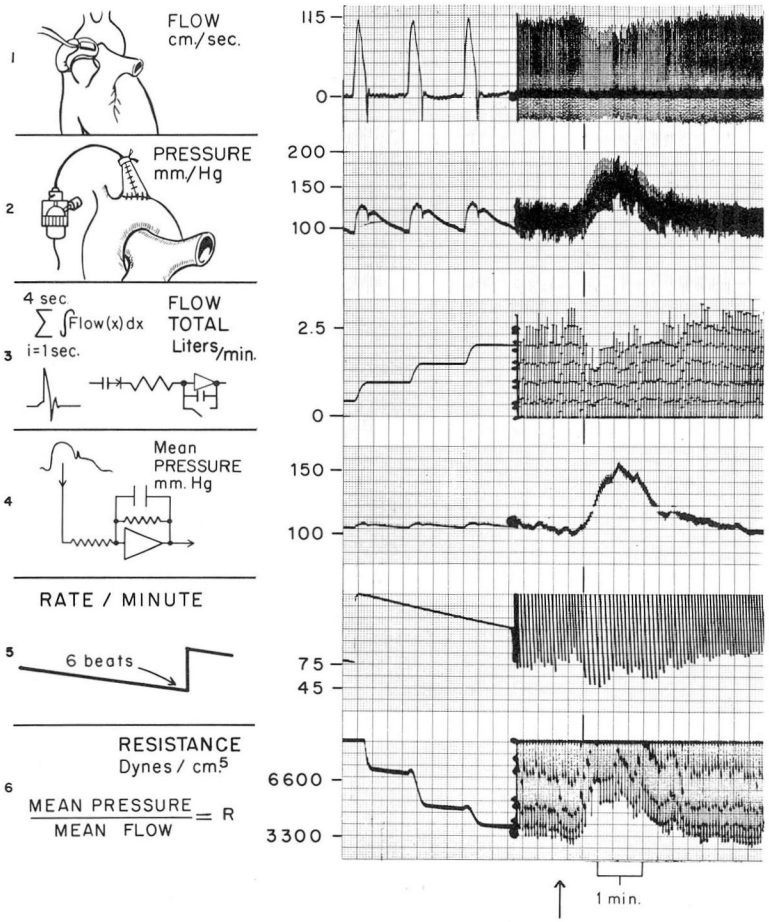

Fig. 2. From the top down: 1, Velocity of blood flow in the ascending aorta. 2, Pressure pulse in the aortic arch. 3, Stroke volume and cardiac output. The curve in 1 is integrated to form a voltage step equal to its area or flow volume, and these steps are added for 4 seconds to total cardiac output, and the process is then repeated. 4, Average (mean) pressure. 5, Heart rate by a constant slope recycled every six beats; the lower the end of the line, the slower the rate. 6, Mean pressure divided every 4 seconds to give peripheral resistance—the lower the tracing, the lower the resistance. At the arrow, 4 units of angiotensin was injected by intravenous catheter. (Courtesy of Olmsted, F.; J. Appl. Physiol. **17:** 152-156, 1962.)

cardiac output (less coronary artery flow), mean pressure, heart rate, and peripheral resistance are simultaneously derived from the electric flow and pressure curves by electronic analogue computing circuits.[5] In *Figure 2*, superimposed on the major change in cardiac output, are numerous smaller variations that are far too rapid to be distinguished by indirect methods, but that might readily, if they coincided with drawing of a blood sample for dye dilution or oxygen analysis, lead to erroneous results.

At present it is apparent that much previous work on cardiac output should be repeated with these new technics. Under way or completed[6] are studies of hemodynamic response in experimental hypertension, and of the normal response in the dog.

The dog's natural cardiovascular response in a basic resting state, to situations requiring increment in cardiovascular activity is increased cardiac output accompanied by a decrease in peripheral resistance, but no particular change in mean arterial pressure or stroke volume, although pulse pressure may increase and the ventricular ejection curve may change in contour. The "situations" employed in the laboratory include changes in posture, arousal, eating, startle. An exception to the lack of change in stroke volume was found in a field experiment, when a dog chased a station wagon for a half mile over rough terrain. The animal was connected to apparatus in the automobile by flexible cables carrying the flow and pressure signals. In this case stroke volume increased about 25 per cent, heart rate 100 per cent, and cardiac output 300 per cent; but again, there was no change in mean arterial pressure. *Figure 3* shows the variety of left ventricular flow pulses under various conditions.

If, as in *Figure 2*, which shows the decrease in cardiac output from a single injection of angiotensin, the experiment is continued for one hour with an infusion instead of an injection of the drug, the effect is not diminished—peripheral resistance remains elevated, as does pressure, with continued decrease of cardiac output, heart rate, and stroke volume. This is in contrast to results with a similar infusion of norepinephrine, where before the end of the hour, all functions tend to return toward control values,[6] the dog, however, is known to become refractory to norepinephrine. When the infusion of angiotensin is continued for a much longer time, there is a tendency for the development of tolerance in the dog, and in one case (28 days), a considerable increase in the infusion rate was necessary to maintain an elevated blood pressure. Heart rate and cardiac output, however, remained lowered during this long infusion.

Thus biophysical methods, applied to the study of hemodynamics in normal dogs, and dogs made hypertensive by experimental procedures, show differences between elevation of blood pressure by exogenous angiotensin and norepinephrine.[6]

Measurements are being made during the development of experimental renal hypertension brought about by partial constriction of one renal artery and contralateral nephrectomy. Another aspect of the circulation under study concerns a

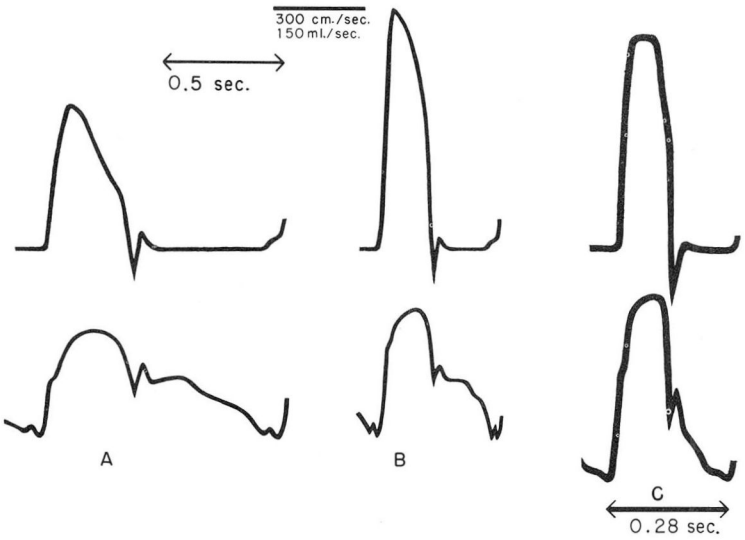

Fig. 3. Left ventricular ejection volume curves, and corresponding pressure curves below. A, Resting, quiet, reclining dog. B, Mild exercise or moderate excitement. C, Exceedingly vigorous, prolonged exercise. The volumes of A and B are almost identical, while C is 25 per cent larger.

more exact determination of resistance to blood flow in the large vessels, down to those 2 mm. in diameter. Peripheral resistance is now considered equivalent to a form of Ohm's law in a direct current (DC) system. In alternating current (AC) systems, resistance varies with wave form, frequency of the wave, and quality of transmission line. Except for the smallest vessels, the arterial system contains pulsating flow; a complex hydraulic impedance opposes the work of the heart. Energy at various points in the arterial circulation can be found from instantaneous flow and pressure at these points, and various energy levels are established for specific segments of the arterial circulation.

These experiments show the great amount of work to be done by biophysical study of the hemodynamics of the arterial system, and a suggestion of the wealth of material to be obtained.

References

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