vs. 85 mm^2 and 128 mm^2 vs. 58 mm^2, while the latter showed 109 mm^2 vs. 36 mm^2 and 75 mm^2 vs. 35 mm^2 (Table II).

The inflammatory lesions produced by the staphylococci cultivated in presence of potassium hyaluronate showed no significant differences in comparison with the control lesions produced by staphylococci cultivated in normal media. Neither potassium hyaluronate nor its split products induced any appreciable lesion in the 2 rabbits inoculated as controls.

No definite statement can be made about the mechanism with which hyaluronic acid, and in lesser degree its split products, caused the remarkable spreading of inflammation processes. We assume that the mucopolysaccharide, by causing alterations of the tissue where it was inoculated together with the staphylococci, possibly originated interactions between these microorganisms and the tissue, thus favoring the development of the lesions.

Summary. Intradermal inoculation of a mixture of K hyaluronate and staphylococci constantly produces larger lesions than by staphylococci alone. A similar but slighter increase in lesions is also observed after inoculation of a solution containing staphylococci and K hyaluronate split products.

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A New Method for Direct Recording of Cardiac Output.* (21134)

GERHARD A. BRECHER AND CHARLES A. HUBAY. (Introduced by George Sayers.)
From the Departments of Physiology and Surgery, Western Reserve University School of Medicine, Cleveland, Ohio.

No simple method is available to measure under physiological conditions directly and accurately total blood flow in the main pulmonary artery. It is the purpose of this communication to report a method for the determination of cardiac output which makes it possible to measure directly in experimental animals main pulmonary artery flow and its fluctuations from one heartbeat to the next. This has been accomplished with the aid of a bristle flowmeter(1-3) which is suitably modified for use in the pulmonary artery trunk.

Method. Fig. 1 shows a diagram of the flowmeter cannula. The device consists of 3 brass parts (A,B,C) which are assembled by threaded joints. The tip of part A is inserted into the vessel wall by slipping the lip D through a "button hole" opening in the artery wall using a technic similar to that employed with the non-suture aortic shunt developed in this laboratory(4,5). The lip D is secured firmly to the intima by the pressure of plate E on the outside of the wall. Plate E is held in place by the screw F. In the shaft of part A lies a snugly fitting stainless steel cylinder G, which can be pushed forward or retracted by means of a cable release H, suitably attached to the outside of the cylinder. When the cylinder G is in the retracted position as shown in Fig. 1, the bristle I, protruding into the lumen of the pulmonary artery, can be

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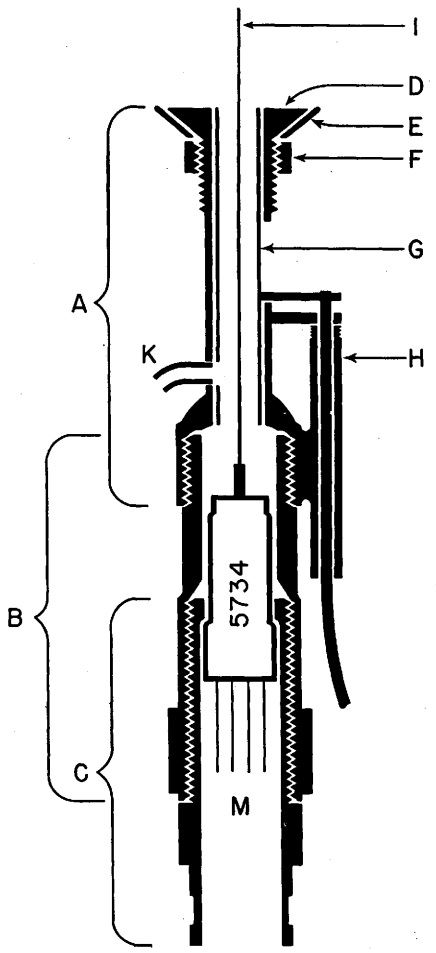

FIG. 1. Diagram of "bristle-flowmeter" modified for use in the pulmonary artery trunk for cardiac output determination. Total length of cannula, 75 mm. Description in text.

deviated by the blood stream. When the cylinder G is pushed forward it advances one mm beyond the tip of the bristle I and protects the bristle from deviation by the blood current. This device for producing "zero flow" makes it possible to check on electronic zero drift at frequent intervals. The small diameter of the cylinder (4 mm) precludes any significant obstruction to blood flow during the zeroing maneuver. Since the cable release H is 20 cm in length, the zeroing device can be operated from the outside of the animal after chest closure. A stainless steel tube K (13 gauge hypodermic needle) is attached at the side of part A for obtaining pulmonary artery pressures and for removal of air bubbles. Part B is a long-threaded shaft, into which part C can be advanced by turning. Part C serves as a socket for the RCA 5734 vacuum tube mechano-electrical transducer. Deviation of the bristle I results in an electrical signal which is transmitted by the electrical leads M to a recording instrument(1-3).

The placement of the flowmeter in the pulmonary artery trunk is illustrated in Fig. 2. The chest was entered at the fourth left intercostal space and the pericardium incised for a distance of 4 cm over the pulmonary artery trunk, leaving the heart in the pericardial sac. A string was passed around the main pulmonary artery. About one-quarter of the anterior pulmonary artery wall was gently clamped in a longitudinal direction with a modified Potts clamp, thus creating a dry field for a button hole incision of the wall. The clamping interfered only slightly with the maintenance of pulmonary flow judging from the aortic blood pressures. The bristle had

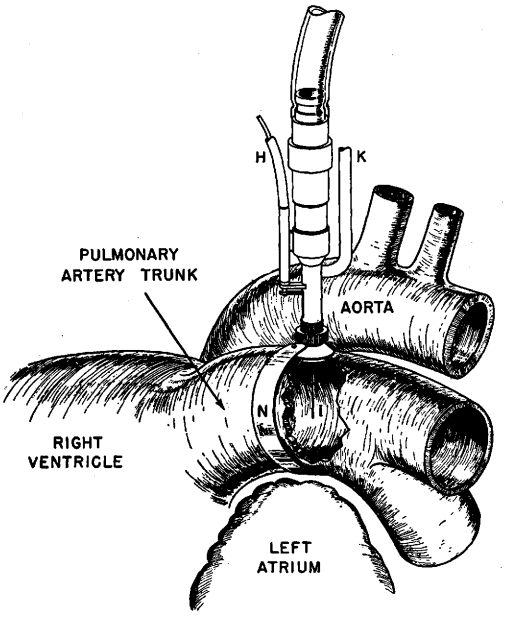

FIG. 2. Diagram of the "bristle-flowmeter" illustrating its position in the pulmonary artery. H = Cable release, K = Pressure recording tube, I = Bristle, N = Metal band, which fixes the circumference of the pulmonary artery trunk by passing around the vessel. The zeroing cylinder is not visible because it is retracted.

to be protected from damage during the insertion. This was accomplished by turning part C in the threads of part B until the tip of the bristle was retracted behind the lip D of part A (Fig. 1). Then lip D was slipped into a button hole incision in the clamped anterior wall of pulmonary artery without blood loss. Slipping of the lip from the vessel wall was prevented by closing the incision around the cannula tip with 5-0 silk suture, although this is not essential. Then plate E was pressed on the adventitia. After releasing the Potts clamp the tip of the bristle was advanced 1 cm into the lumen of the pulmonary artery trunk by turning part C in the threads of part B. A 4 mm wide stainless steel metal band N was drawn around the pulmonary trunk with the aid of the previously placed string and then securely fastened with 2 snaps to plate E (Fig. 2). This metal band stabilized the vessel diameter, which was indispensable for volume flow measurements. The length of the band was chosen according to the vessel's diameter; it fitted snugly to the outer wall during diastole without restricting flow. In several experiments the chest was closed after the flowmeter insertion and normal intrathoracic pressures were reestablished. The flowmeter was calibrated *in situ* with the animal's own blood after each experiment. For calibration, blood entered the pulmonary artery from a cannula, which was tied into the pulmonary conus, and was allowed to leave through another cannula ligated into the bifurcation of the right and left pulmonary arteries.

Ten experiments were performed in heparinized dogs weighing from 17 to 28 kg. The animals were anesthetized with 3 mg/kg of morphine sulfate subcutaneously and 30 mg/kg sodium pentobarbital intravenously. Simultaneously with pulmonary artery flow, optical records were taken of aortic, right atrial, and main pulmonary arterial pressures. The pressures were recorded with modified Gregg manometers using established methods of this laboratory(2).

Results. Fig. 3 shows a segment of an original record illustrating the phasic flow changes in the pulmonary artery during the heart cycle. Ejection from the right heart occurred almost simultaneously with the rise of aortic pressure and terminated at the time the incisura was reached. The flow rate at the peak of ejection was 5300 cc/min. Ejection was followed by a brief period of backflow marked X which reached a rate of 1500 cc/min. Backflow was a consistent finding in all experiments. The backflow is presumably caused by the backward movement of blood into the proximal portion of the pulmonary artery trunk when the semilunar valves bulged into the right ventricle during their closure. It is possible that some of the backflow reached the right ventricle during the process of valve closure. A slight forward movement of blood occurred during the early part of diastole. This is borne out in the record of Fig. 3 by the slight forward flow during early diastole, marked y. Flow then came essentially to a halt until the next ejection.

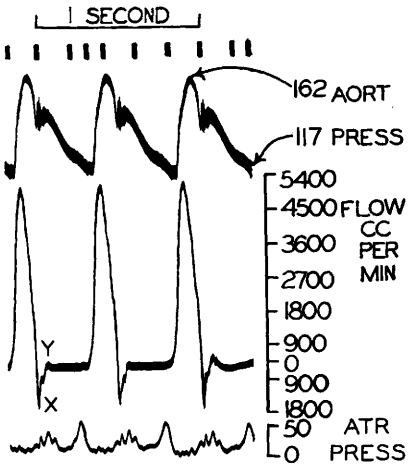

FIG. 3. Cardiac output phasically recorded with the bristle flowmeter illustrated in Fig. 1 and 2. (Dog, 18 kg weight, heart rate 120, cardiac output 862 cc.) Tracings from top to bottom: Time, aortic pressure in mm Hg. Flow in pulmonary artery trunk in cc/min., right atrial pressure in mm H_2O. (⅓ of original.)

The stroke volume can be calculated by measuring the area under the flow curve. Table I shows the values of forward and backward flow during each of the 3 cardiac cycles depicted in Fig. 3. Cardiac output calculated from these values amounted to 862 cc. To obtain correct values, backward flow must be deducted from forward flow. It is

TABLE I. Stroke Volume in cc Calculated from the 3 Heartbeats Shown in Fig. 3. (Heart rate 120.)

Heartbeat No.	1	2	3
Forward flow during cardiac ejection	8.67	7.67	7.86
Backward flow following ejection, marked x	.68	.64	.71
Forward flow during diastole, marked y	.02	.01	.13

noted that backflow amounted to 9% of the stroke volume. In the other experiments this value was smaller. The tracing in Fig. 3, which exhibits large backflows, was primarily selected in order to illustrate the suitability of the flowmeter to record backflow.

Fig. 4 shows a segment of an original record illustrating the action of the "zeroing" device. This record was taken from an experiment in which the chest was closed and zero flow was obtained by actuating the zeroing cylinder (G in Fig. 1) through the cable release from the outside of the animal. Pulmonary artery flow during the first cardiac cycle showed a pattern similar to that described in Fig. 3. However, it is to be noted that during atrial systole (marked AS) flow in the pulmonary artery was briefly accelerated and decelerated. This is obviously due to an impact from the neighboring atria on the proximal region of the pulmonary artery, which caused the forward and backward movement of the fluid column. The impact of atrial systole is also seen in the pulmonary artery pressure tracing and to a mild degree even in the aortic pressure pulse contour. Atrial impacts on arterial pressure curves have often been described; however, those on flow have not. One must be cautious, therefore, in assuming that blood does not flow in the pulmonary artery trunk during diastole. Baxter and Pearse(6) based the determination of "zero flow" in the pulmonary artery on this assumption.

During late systolic ejection of the second heart beat (marked x in Fig. 4) the zeroing cylinder was pushed forward. This maneuver took 80 milliseconds, judged from the duration of the impact during late systole on the pulmonary artery pressure tracing (marked y). The absence of turbulence or oscillations in the flowtracing during the cylinder movement at the end of the ejection period should be noted. From then on, the flow record is practically a straight line. The backflow after the ejection did not register, nor did the forward flow during the next ejection. However, there was slight bristle movement during the ejection, which was presumably caused by some turbulence of the blood rushing past the cylinder opening. The pressure tracings in the third heart cycle remained, of course, unaffected by the zeroing cylinder. From these findings it must be concluded that the cylinder affords an effective means of protecting the bristle from the streaming blood and thus for establishing zero flow during the experiment without interfering with the major blood flow in the vessel.

One of the important conditions for all measurements of volume flow is the constancy of the vessel's cross-sectional area. This is usually accomplished by cannulating the vessel with a cannula of fixed diameter. Since in these experiments the cross-sectional area of the pulmonary artery was kept constant by an external metal band it was felt that the flow pattern should be checked against that of a

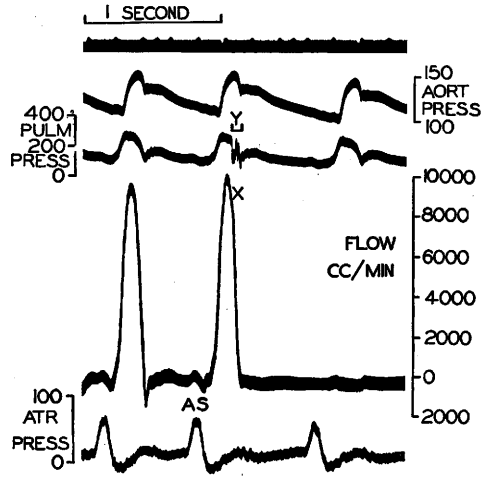

FIG. 4. Cardiac output phasically recorded with the bristle flowmeter illustrated in Fig. 1 and 2, showing effect of zeroing cylinder on flowtracing. (Dog, 28 kg weight, heart rate 98, cardiac output 2156 cc.) Tracings from top to bottom: Time, aortic pressure in mm Hg, pulmonary artery pressure in mm H_2O. Flow in pulmonary artery trunk in cc/min., right atrial pressure in mm H_2O. (¼ of original.)

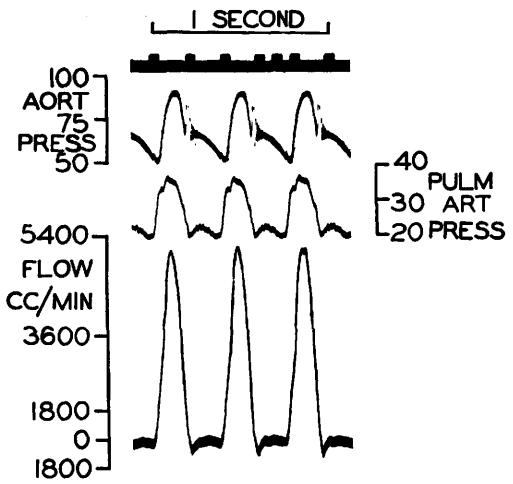

FIG. 5. Cardiac output phasically recorded with conventional bristle flowmeter(1-3) which fixes the cross-sectional area of the pulmonary artery trunk by the insertion of a ring-like cannula head into lumen of vessel. (Cannula internal diam. 12 mm, heart rate 155, dog 15 kg weight, cardiac output 1240 cc.) Tracings from top to bottom: time, aortic pressure in mm Hg, pulmonary artery pressure in mm Hg, flow in pulmonary artery in cc/min. (⅓ of original.)

flowmeter of conventional design. Therefore, in addition to the 10 experiments, 3 others were undertaken in smaller dogs in which the ring-like head of a standard bristle flowmeter (1-3) was quickly inserted through a small incision into the pulmonary artery trunk. This was done without occlusion of the artery but with loss of a considerable amount of blood. Fig. 5 shows a segment of a record illustrating the pulmonary artery flow pattern when the blood passed through the cannula head of the flowmeter, which fixed the inside diameter of the vessel. It is noted that the profile of the flow curve is very similar to those shown in Fig. 3 and 4.

Discussion. The modification of the bristle flowmeter described here has been successfully employed in our laboratory for one year for various cardiac output studies. Its application is not limited to right heart output measurements, since the device can be easily inserted into other major vessels such as the aorta. Its use is particularly indicated in all investigations where accurate knowledge of phasic changes of right heart outflow is indispensable, where stroke for stroke changes occur and where the existence of an "unsteady state" does not permit the application of indirect methods such as the Fick determination.

The advantages of the new method are the following: 1. The flowmeter can be inserted at leisure into the pulmonary trunk without blood loss and without interrupting flow. 2. The resistance to blood flow introduced by the flowmeter is negligible. 3. Accurate zero flow can be determined at any time during the recordings without vessel occlusion or interference with the circulation. 4. Changes in forward and backward flow can be faithfully recorded owing to the high fidelity of the flowmeter (125 cycles/sec.). 5. Mean cardiac output can be recorded through electrical integration by merely turning a dial at the amplifier. 6. Since the "electrical mean" averages all actual forward and backward flow at the site of the flowmeter it records what is conventionally defined as "cardiac output." 7. The sensitivity of the instrument is very high: 20 mm deflection of the galvanometer 50 cm in front of the camera for a flow of 20 cc per second when the electrical signal is amplified only 50 times. 8. The insertion of the cannula induces a negligible amount of trauma and furthermore the animals remain in good condition for many hours.

Baxter and Pearse(6) reported recently a differential pressure method with which they recorded pulmonary artery flow in anesthetized cats. Their method suffered, however, from the following shortcomings which were avoided in the new method described here. 1. The pulmonary artery trunk must be briefly occluded for the insertion of the flowmeter, which damages the right myocardium by overdistention in normovolemic animals. 2. The device introduced into the artery offers resistance to flow, and this may distort the pattern of phasic flow(7). 3. The determination of zero flow, upon which the accuracy of all flow measurements depends, is unreliable. It is accomplished by setting automatically an electronic "zero" at flow during diastole. According to Baxter and Pearse, this is done: "under the assumption that diastolic flow in the trunk of the pulmonary artery is negligible, but occasionally there was evidence of slight flow at the beginning of diastole. This

slow changing forward flow tended to upset the tuning of the circuit and the measurement of subsequent beat outputs." 4. The automatic zeroing precludes the recording of backflow and analysis of flow changes during the cardiac cycle, particularly with valvular lesions. 5. The low sensitivity of 1 mm deflection for 3.6 cc per second limits the accuracy of the flow determinations.

Summary. A modification of a bristle flowmeter is described which permits direct recording of cardiac output and its fluctuations from one heartbeat to another. The device is inserted into the trunk of the pulmonary artery of anesthetized, heparinized dogs without blood loss and without interrupting blood flow. Zero flow can be established by mechanical means without occluding the vessel. Phasic changes during the cardiac cycle consist of a marked forward flow during cardiac ejection and a brief period of backflow following ejection. Mean cardiac output can be directly recorded by electrically averaging the phasic flows.

The authors wish to thank Mr. Willard Stires for the cannula construction, Dr. Julius Praglin for his help in electronic designs and Dr. F. L. Clement and Mr. Clyde Bratton for their assistance.

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Effect of a Mercurial Diuretic on Thyroid Uptake and Renal Clearance of Radioiodine.* (21135)

SIDNEY N. SPIES. (Introduced by R. L. Libby.)

From the Radioisotope Unit, Wadsworth General Hospital, Veterans Administration Center, Los Angeles, Calif.

This study was undertaken to determine what effect, if any, the administration of a mercurial diuretic exerted on the validity of the radioiodine uptake procedure as a measure of thyroid function. It has been demonstrated by Meyers(1) that the analytic procedure for the determination of serum protein-precipitable iodine is rendered non-valid by the recent administration of meralluride sodium. Because of the competition between the thyroid and the kidney for the available supply of inorganic iodide, it would also appear that should mercurial diuresis significantly alter renal iodide excretion, this might adversely influence the validity of thyroid radioiodine uptake studies. The effect on other halogens is better known: the production of a chloride diuresis is one of the early effects of mercurial diuretics; a similar effect has been found in the experimental animal for the bromide ion(2). In man, the renal clearance of iodide, unlike that of bromide, has been stated to appear independent of variations in chloride intake and excretion(3); in the dog, however, the renal clearance of iodide, like bromide, is largely determined by the rate of chloride excretion(4).

Method. In this study, thyroid radioiodine uptakes were initially determined at 6 and 24 hour periods on 8 euthyroid patients, 3 of whom had congestive heart failure. Uptakes were repeated 2 weeks later, at which time the intramuscular administration of 2 ml

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