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SIMULTANEOUS MEASUREMENT OF PULMONARY ARTERIAL FLOW AND PRESSURE USING CONDENSER MANOMETERS

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Variations in pulmonary arterial pressure, in response to changing intrathoracic pressures and various stimuli, have been frequently recorded in intact animals. The significance of these pressure variations is difficult to assess unless the concomitant fluctuations in pulmonary arterial flow are known. This report describes the construction and use of an apparatus designed by one of us (I. G. B.) for the simultaneous measurement of pressure and flow in the pulmonary artery. The method employs the pressure-drop principle to register the velocity of blood flowing past a Pitot tube through a portion of the vessel of fixed diameter. Capacitance manometers were chosen to provide an adequate frequency response and stable calibration, and electrical correction of the square law relating flow to differential pressure has obviated a tedious stage in the analysis of records. The results of the combined measurement have been used primarily to derive an index of changes in pulmonary vasomotor activity, but the method also provides a measure of right heart output.

There appears to have been no previous measurement of pulsatile flow in the pulmonary artery, and only a method whose calibration is not influenced by environmental changes may be applied to this vessel. However, the use of the pressure-drop principle with differential manometric recording to measure the volume flow in vessels is not new. Cybulski (1885) and Frank (1899) described Pitot tubes used for the measurement of blood-stream velocity in various great arteries. Later Fleisch (1920) utilized the pressure drop across a tube of uniform narrow bore to measure the volume flow of blood in the perfused hind-limb of small animals. Daly (1926) described a differential manometer, with a method for converting pressure excursions to voltage variations, for the recording of the volume flow through a Venturi or Pitot tube incorporated into a vascular system. Wagoner & Livingston (1928) constructed a glass Venturi tube and a differential saline manometer to measure volume flow in the rabbit aorta. Then Frank (1928) applied his differential membrane optical manometer to the simultaneous measurement of stream velocity and pressure in the aorta with the Pitot tubes he had previously designed. An ingenious modification reported by Broemser (1928*a*, *b*) was a differential sphygmograph used to estimate the blood-stream velocity in unopened vessels. Lauber (1928) applied a pressure-drop device to measure volume flow in the aorta, and a modified Venturi tube was used for the same purpose by Reissinger (1928). He pointed out incidentally that the aorta itself is a form of pressure-drop device, as there is a pressure difference,

dependent on stream velocity, between its concave and convex sides. Fasold & Hartl (1928) estimated coronary arterial flow by subtracting values of blood flow in the ascending aorta, determined with a Venturi tube, from those obtained for heart output by the direct Fick method. These workers estimated the random error of the differential manometer method, but did not establish the correspondence between the two methods in measuring the same blood flow. Finally, Gregg & Green (1940) described a flowmeter incorporating a differential membrane manometer which measures the pressure drop across a small orifice included in the course of an artery. These authors and their associates have investigated flow patterns in systemic arteries, and changes in these flow curves resulting from alterations in vasomotor activity.

In the study of vasomotor activity changes, the simultaneous measurement of pressure and flow in an artery can yield information about the resistance of its vascular bed. For a given moment in a perfused system a quantitative expression of the total peripheral resistance can be obtained by dividing the pressure value by the concomitant flow value. This expression of resistance will not necessarily remain constant if the flow or pressure varies, even if the vasomotor activity be unchanged. In fact, as has been emphasized by previous workers, a change in resistance may be expected to follow an increase in flow, for example, and will be due to a passive increase in total cross-sectional area of the vessels and to reduction in the effective viscosity of the blood. The increase in cross-sectional area will depend on the volume elasticity characteristics of the vascular bed, and these may be altered by the increase in flow rate. The passive 'capacity' effects, and the variations in effective viscosity, may be largely eliminated if the flow to the vascular bed is kept constant. In such a preparation large changes in resistance, following various stimuli, may be attributed to alterations in vasomotor tone. Individual readings of pressure/flow, with the changing flows usually found in the intact animal, are obviously not comparable as expressions of degree of vasomotor activity. However, over a small flow range, a series of pressure readings plotted against corresponding flow values will give a roughly linear plot. If the vasomotor activity increases and the flow range stays constant, a similar series of points should fall on a line with a greater average pressure co-ordinate value and probably an increased slope, although any slight deviation from linearity will remain. Results from perfused limb preparations used by Green, Lewis, Nicherson & Heller (1944) yielded a roughly parabolic relationship between pressure and flow. Following changes in vasomotor activity there was a shift of the plotted curve in the expected direction. They concluded that the straight lines published by other workers, which did not extrapolate through zero, had been derived from data chosen from the end of the parabola. These investigators showed that, at similar perfusion flow rates, comparisons of the positions of these curves (or of *ranges* of quantitative resistance units) gave indices of changes of vasomotor activity; less consistent results were obtained comparing similar perfusion pressures instead. The principle of this method was used in the analysis of results to be described.

The application of the above reasoning, based on steady flow experiments on systemic vessel preparations, to the study of pulsating flow in the pulmonary vascular system, requires justification. There is some evidence that the physical characteristics of the vessel walls of the systemic and pulmonary vascular systems are not grossly different. Values for pulmonary arterial pressure in perfused lungs of the dog (Daly, 1938) and of the rabbit (Wagner, 1928), plotted against a wide range of steady flow-rate values, have been shown to fall on a line which resembles a parabola. It is probable that, over the range of medium flow values seen in the intact animal, the derived portion of the line would be roughly linear. However, the capacity of the pulmonary vascular bed is largely made up of capillaries (Daly, 1938), and the capacity is constantly changing with respiration as an effect of lung expansion and changing intrapleural pressure. Thus some points on a graph relating pressure to flow during a respiration would not be expected to lie on a pressure-flow curve derived from observations on perfused stationary lungs. But since the major change in pulmonary vascular capacity as a result of lung expansion occurs beyond the arterioles (Macklin, 1946), and as changes in pulmonary arterial pressure for a given rate of inflow can be accepted as an expression of effects on pulmonary arterioles (Daly, 1938), pressure-flow curves derived from measurements taken on the arterial side can still be expected to show small displacement as a result of respiration. It was on this last assumption that the interpretation of records was to be based, as well as on the hope that the pressure-flow curve for the cat lung would prove to be roughly linear over the flow range in the intact animal.

In altering the pulmonary vasomotor tone, histamine was used as a constrictor and amyl nitrite as a dilator. There appears to be little information about the action of the latter drug in the cat, but histamine has been shown by Dirken & Heemstra (1948) to cause constriction of pulmonary vessels in perfused rabbit lungs when given as an aerosol. The drug has also been shown to constrict pulmonary vessels in whole perfused dogs, and the larger part of the effect was proved independent of the associated bronchoconstriction (Alcock, Berry, Daly, & Narayana, 1936). Woodbury & Hamilton (1941) obtained a marked increase in pressure gradient from pulmonary artery to veins of anaesthetized cats following intravenous histamine. This pulmonary arterial constriction was accompanied by a fall in systemic pressure.

METHODS

The flowmeter comprises three main assemblies. A *cannula* incorporating a Pitot head is inserted into the pulmonary artery for obtaining a differential pressure proportional to the volume flow rate squared. The tubes from the Pitot head are connected to a *differential condenser manometer* which converts fluctuations of pressure into changes of electrical capacity. These in turn are

transformed into voltage changes by an *electrical circuit* that also corrects for the pressure/flow square law. The output voltage, proportional to flow rate, is displayed on a cathode-ray tube for photographic recording.

Cannula

The cannula is based on the general pattern of one previously used for recording pulmonary arterial pressures. In principle, it consists of a small Pitot head of which the forward end, with its front and side orifices, is surrounded by a ring to form an annulus of fixed area through which the blood must stream when the cannula is inserted. By-pass flow is prevented by apposing the vessel wall to the ring with an extravascular thin metal band.

A ring and Pitot head were chosen for the metering section in preference to a Venturi tube or similar device because it enabled this part to be kept very short, simplifying insertion and suiting the limited section of artery available, which is curved and seldom exceeds 12 mm. between valves and point of bifurcation. Previous attempts to design a Venturi tube which fulfilled these requirements met with failure, since the small exit angle necessary was incompatible with a short length. Furthermore, the obstruction to flow is small, and because the pressure points are in mid-stream there is less likelihood of trouble from eddies or changes in direction of the artery in the vicinity of the cannula.

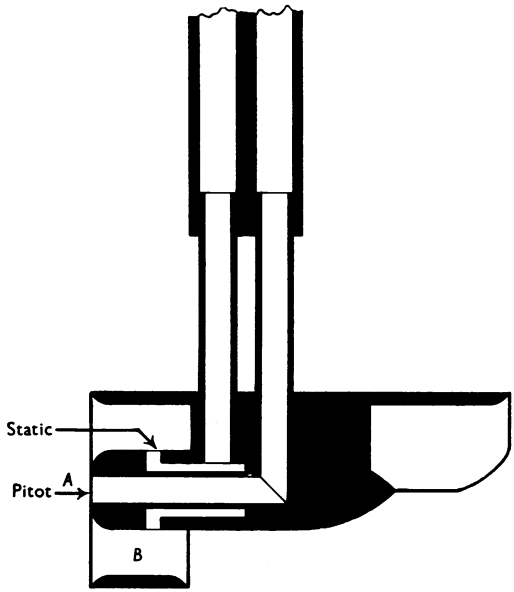

Fig. 1. Vertical section of Pitot head, shield, and metering ring, showing connexion between orifices and tubes. (Magnification, 4 ×.)

In Fig. 1, let p_1 be the pressure and v_1 the stream velocity at point A where the flow cross-sectional area is a_1. At B the corresponding values of these quantities are p_2, v_2 and a_2 respectively. If the fluid density is ρ, then according to Bernouilli's theorem,

$$p_1 + \tfrac{1}{2}\rho v_1^2 = p_2 + \tfrac{1}{2}\rho v_2^2.$$

The forward facing orifice at A registers the total arterial pressure $p_1 + \frac{1}{2}\rho v_1^2$, whereas the lateral facing ones at B only pick up p_2. The difference in pressure is, therefore, $\frac{1}{2}\rho v_2^2$. That is

$$\begin{aligned}\triangle p &= \tfrac{1}{2}\rho v_2^2 \\ &= \tfrac{1}{2}\rho(Q/a_2)^2,\end{aligned}$$

where Q is the volume flow rate.

A photograph of the complete cannula was given in a preliminary report (Baxter & Pearce, 1951), and the external appearance is illustrated again in Figs. 2 and 4, while the structure of the ring and Pitot head is shown in Fig. 1. To seal the insertion slit in the artery, the vessel wall is sandwiched locally between an internal shield and an external saddle carried by a sleeve on the connecting tubes. The saddle may be forced in place by tightening a clamping nut which bears on

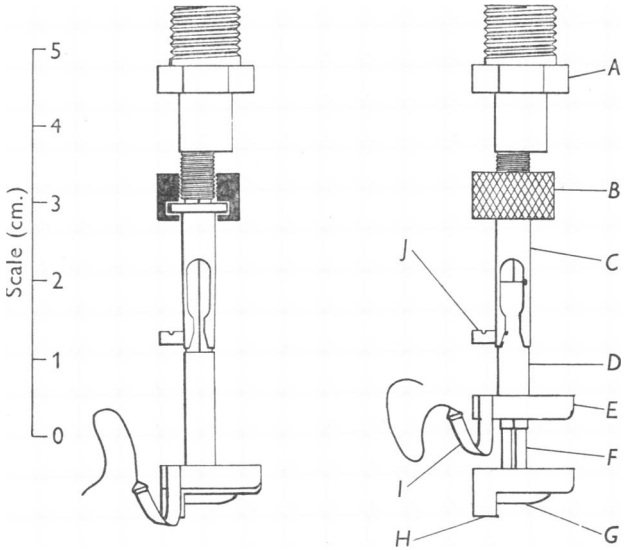

Fig. 2. Cannula. *Right*: saddle retracted; *left*: saddle extended. *A*, union; *B*, clamping nut (sectioned in left-hand view); *C*, split sleeve; *D*, saddle sleeve; *E*, saddle; *F*, tubes from Pitot head; *G*, Pitot head; *H*, ring; *I*, band and thread; *J*, cleat.

a split sleeve abutting against the saddle sleeve. Prior to insertion, the saddle sleeve is retracted within its split companion, the springy halves of which click inwards behind the saddle sleeve when this is lowered. The vessel is held against the metering ring by a brass foil band fixed to one side of the saddle and passed around to the other side where it is pulled taut by a thread anchored to

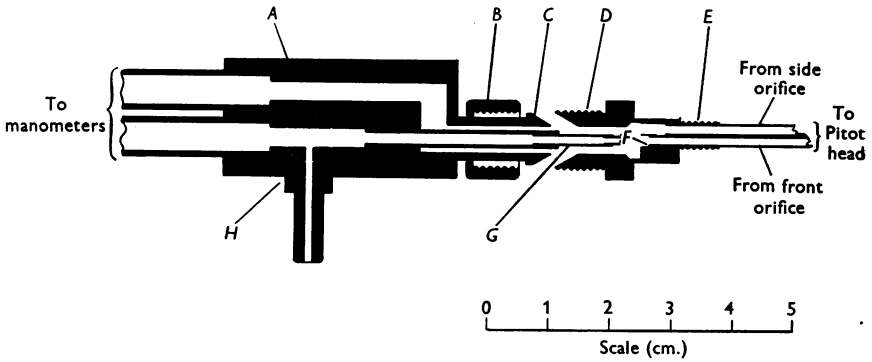

Fig. 3. Junction of cannula to manometers, shown for clarity partly disconnected. *A*, union block; *B*, union nut; *C*, union cone; *D*, union socket; *E*, screw thread for clamping nut; *F*, seating for inner stem; *G*, inner stem; *H*, three-way cock and side connexion.

a cleat on the cannula tubing. The Pitot head is coupled to the manometer by a single union (Fig. 3) having an inner hollow stem which fits into a seating of its own when the main cone joint is engaged. At the union one pressure is transmitted within the central stem and the other via the annular space between the stem and the union body.

The insertion of the cannula into the exposed and occluded pulmonary artery must be carried out as quickly as possible. A longitudinal slit, slightly shorter than the diameter of the ring, is made in the wall of the artery at a point just distal to the centre of the portion of the vessel exposed. The tail end of the cannula head is slipped into the lumen of the artery and the slit is

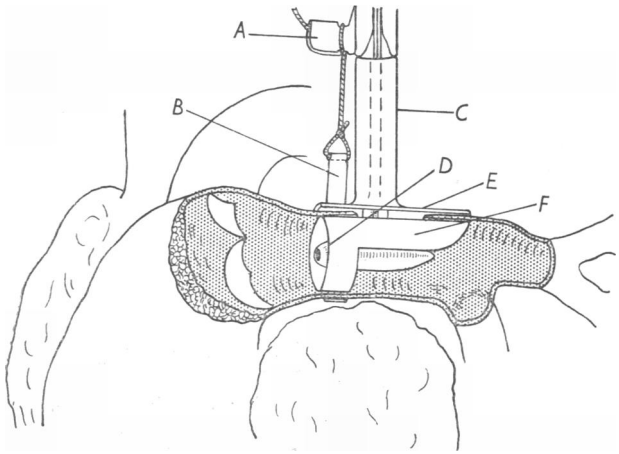

Fig. 4. Sketch of cannula inserted into the pulmonary artery. *A*, cleat; *B*, band; *C*, saddle sleeve; *D*, Pitot head; *E*, saddle in section; *F*, shield.

worked over the ring. The head is shifted proximally, bringing the slit over the rear end of the shield, and the saddle is then lowered into place, thus closing the slit. It is essential to avoid catching the auricle or the phrenic nerve under the saddle. Once the absence of bleeding is confirmed, the saddle is secured with the clamping nut and the ligature about the vessel is released. The brass band attached to the saddle is now drawn around the artery by means of a thread which was passed through earlier with the occlusion ligature. This thread is pulled up and fixed to the cleat.

Manometers

The differential manometer consists essentially of a thin metal diaphragm close to which an insulated electrode is rigidly mounted. Any difference between the pressures at each side of the diaphragm will cause it to bulge one way or the other and proportionately alter the electrical capacity between it and the electrode.

The complete manometer assembly with tubing is shown in Fig. 5, and the differential manometer in section in Fig. 6. To prevent earthing of the electrode by the saline solution which conveys pressure from the lateral Pitot orifices, the manometer body is filled with a light mineral oil which is retained by a thin-walled cylindrical polythene expansion chamber that allows pressures to be freely transmitted between the liquids it separates. To avoid rupture of the polythene chamber by thermal expansion of the oil, the filling hole is permanently submerged in a reservoir whichever way up the instrument may be; between experiments the filling hole stopper is loosened to allow free expansion of the oil.

On the manometer body are two cocks for each of the pressure leads to the diaphragm. The smaller ones control a supply of saline solution from a pressurized container to enable the tubing to be filled and flushed free of air bubbles. The larger ones are three-way cocks, each with a side

connexion used during pressure calibration. At the cannula union block there is another three-way cock for switching the forward Pitot orifice off from the manometer and on to the side connexion for pulmonary arterial blood sampling.

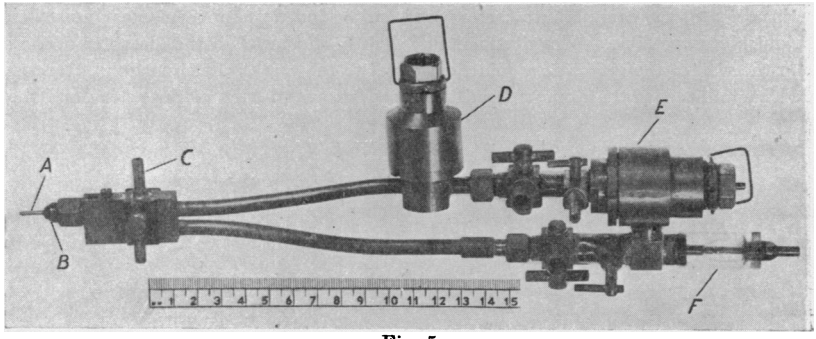

Fig. 5

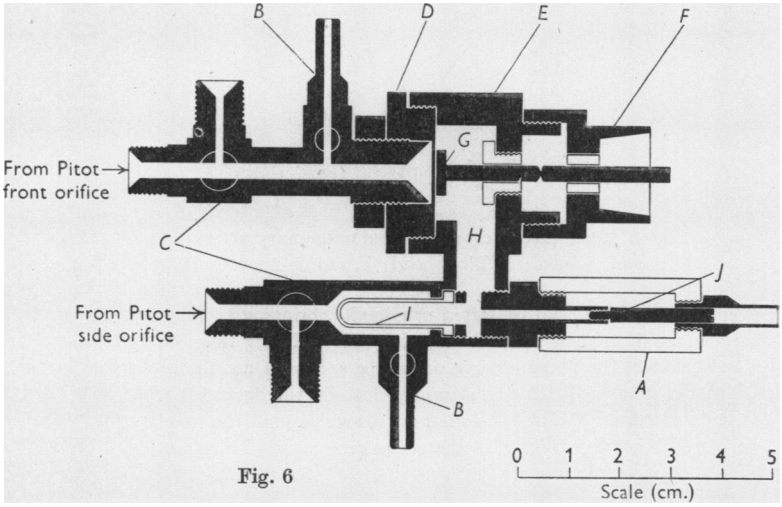

Fig. 6

Fig. 5. Photograph of manometers and union block for cannula. *A*, inner stem; *B*, cone joint for cannula; *C*, side connexion for withdrawal of blood from the pulmonary artery; *D*, ordinary condenser manometer; *E*, differential manometer; *F*, oil reservoir.

Fig. 6. Differential manometer, in section to scale. For clarity the electrode and electrical socket are depicted schematically, and the cocks and side connexions are shown lying in the plane of the diagram instead of normal to it. *A*, oil reservoir; *B*, cocks and connexions to saline reservoir; *C*, three-way cocks; *D*, diaphragm and mounting; *E*, main body; *F*, electrical socket; *G*, electrode; *H*, oil filling; *I*, expansion chamber; *J*, filling hole stopper. Plastic, □ ; metal, ■.

A plain condenser manometer is connected to the tube from the forward orifice for registering total arterial pressure.

In accordance with well-known principles the natural frequency of the recording system has to be high compared with the highest frequency component of the pressure wave-form. This demands stiff manometer diaphragms that have a volume elastic coefficient appropriate to the effective mass

of the liquid columns in the relatively narrow bore tubes in the cannula. In each manometer the diaphragm is about 13 mm. in diameter, and in the plain manometer is about 0·5 mm. thick, for which the estimated volume elastic coefficient is 10×10^9 dynes $\times$ cm.$^{-5}$; in the differential manometer these quantities are 0·4 mm. and 4×10^9 dynes $\times$ cm.$^{-5}$. The change of capacity with pressure is about $2{\cdot}5 \times 10^{-3}$ $\mu\mu$F./mm. Hg for each manometer. The natural frequency of the differential manometer when coupled to the cannula and filled with saline is 160 cyc./sec.

Each limb of the manometer is independently tested for bubbles in the liquid fillings by checking the natural frequencies with first one side of the diaphragm, and then the other, switched by its three-way cock into communication with the open side connexion instead of the normal pressure lead.

Coupling the manometer to the inserted cannula merely involves withdrawing the obturator, allowing a drop or two of blood to escape, and then connecting the union after establishing a very slow saline drip, subsequently turned off.

Electrical circuit

The circuit (Baxter, 1951) is shown schematically in Fig. 7, and comprises three main sections. The first one is a phase modulation system for converting capacity fluctuations linearly into voltage changes, which are then fed to a second stage which gives an output voltage proportional to the

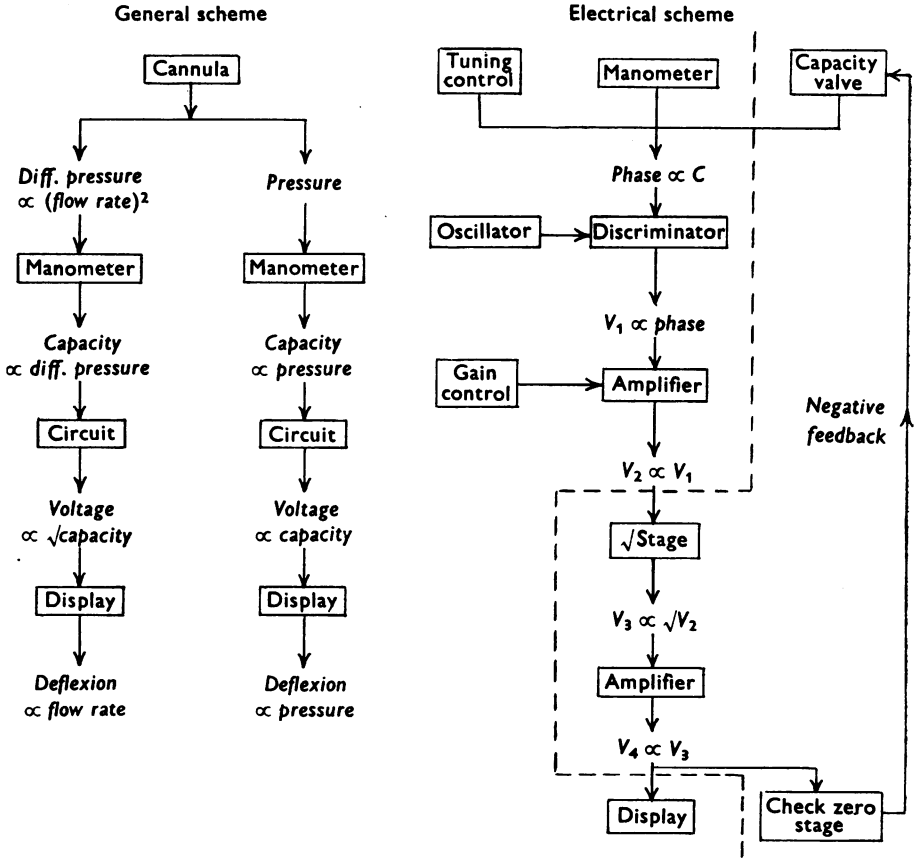

Fig. 7. At the left is a diagram to represent stages of the method described. At the right is a block diagram of the circuit used to measure flow; the circuit for measuring pressure utilizes only the portion to the left of the dashed line.

square root of its input. In this way the overall conversion from volume flow rate into output voltage is made linear. The third section is a negative feedback loop for compensating drift; capacity change with flow is so small that unavoidable extraneous capacity alterations can be of comparable magnitude and cause serious drift of the output voltage. Matters are aggravated by the square law effect, for a drift of one-tenth the total voltage excursion preceding the 'square rooting' section becomes a drift, at the beginning of the range, of about one-third the output voltage amplitude. Instead of dealing individually with the various sources of drift, negative feedback is provided which introduces an automatic capacity correction if the output voltage corresponding to no flow deviates for long from its correct value. This only becomes possible because there is negligible flow in the pulmonary artery at the point of measurement during diastole. Automatic drift correction renders the circuit useless for measuring steady flow, so the output is condenser coupled to the cathode-ray tube.

There are two control knobs. One adjusts the sensitivity to suit the flow range being measured, and the other trims the input capacity in conjunction with a 'magic eye' tuning indicator for showing the right setting.

Calibration of apparatus

The overall performance of the flowmeter was determined by combining the separate calibrations of the cannula, circuit and recording unit. Four flow calibrations of the cannula head fitted in a brass tube were carried out with water, and one with sheep's blood. It was also calibrated six times *in situ* with water admitted through a cannula tied into the right ventricle of the excised heart, and allowed to leave by the two main branches of the pulmonary artery which had been

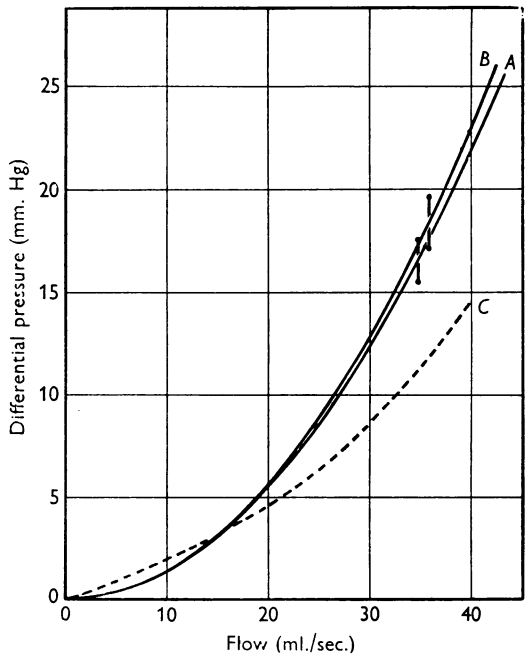

Fig. 8. Best parabolae derived from (*A*) nine *in situ* water calibrations (49 points) and (*B*) four brass tube water calibrations (33 points) of the Pitot head. The vertical bars represent the extent of the standard deviation of individual points from the derived curve. The best curve for a single brass tube blood calibration (16 points) lay between *A* and *B*. The curve *C* represents the pressure drop between positions in the brass tube just before and after the Pitot head, at various steady blood flow rates (8 points).

severed a few mm. from its bifurcation. Differential pressures were measured with a mercury manometer and the corresponding steady flow rates by collecting the outflow in a measuring cylinder during periods timed by a stop-watch. Results of these tests are shown in Fig. 8. The calibration of circuit and recording unit was calculated from section to section measurements, checking the final result by applying known step changes of pressure to the differential manometer and recording photographically, as with flows. In this way it was found that, at the sensitivity setting usually employed, 1 mm. deflexion on the record corresponded to 3·6 ml./sec. volume flow rate for blood.

Experimental procedure

Experiments have been carried out by J. W. P. on cats anaesthetized with chloralose (70–80 mg./kg.) following ethyl chloride and ether induction. Positive pressure ventilation was established and the chest opened through the fourth left intercostal space. The upper lobe of the left lung was collapsed and packed off, exposing the pulmonary artery. The pericardium over the artery was removed between the conus arteriosus and the phrenic nerve, and a thick ligature was then passed around the artery with a blunt aneurysm needle; at this stage the animal was heparinized. After occlusion of the artery by pulling up the ligature the cannula was inserted in the manner described. The lung was then reinflated and the chest closed in layers. After withdrawal of any air remaining in the intrapleural space, spontaneous respiration was usually resumed.

The electrocardiogram was recorded from Lead II, with the cannula serving as the earth lead. Amyl nitrite was administered by inhalation from a broken perle, and histamine was injected intravenously in doses of 20–50 μg.

The analysis of photographic records necessitated the measurement of small areas reduced further in size by the camera lens. Each flow wave-form chosen to be measured was projected on to a flat surface with an epidiascope, giving a linear enlargement of about 7 ×. The area of the image of the wave-form, or a tracing of it, was measured in two directions with a hatchet planimeter. By suitable calculation this area could be expressed as an absolute quantity of blood ejected during the beat. The mean output of all the beats occurring during a respiratory cycle was multiplied by the heart rate to give the right heart output per minute.

In plotting pressure against flow, the effective incisural pressure was used as the ordinate value and the corresponding beat output as the abscissa value. Although the pressure measured at almost any selected point on each of a series of pressure pulse curves showed about the same proportional variation in response to flow changes, it was believed that either diastolic or incisural pressures would represent more accurately the pressure variation in the vascular bed caused by an injection of blood. Since there is a pressure drop across the cannula head, the recorded systolic pressure does not represent the true pressure in the portion of the artery distal to the cannula. Furthermore, pressure recorded during the ejection of blood is partially dependent on the inertia effect of the blood column in the artery. Thus systolic pressure may be altered by a shorter ejection time (such as occurs after adrenaline administration), while the same quantity of blood, once 'accommodated', will produce the same diastolic pressure level if the capacity of the system is unchanged.

RESULTS

To check its performance, the instrument was used to measure an artificially produced intermittent blood flow. The cannula head was fitted in the brass calibration tube and human blood was passed through from a reservoir under pressure, the outflow being controlled by a cam actuated piston valve. Two differently shaped cams were used, one giving a flow pattern (Fig. 9, top) not unlike that in the pulmonary artery and the other giving a sharper rise and fall with a plateau in between (Fig. 9, bottom). Vibrations at the point of cut-off

were attributed to bounce in the rubber connecting tubes. The cams were driven at a frequency of about 3 cyc./sec. through gearing from an electric motor. In a succession of measurements with various pressures in the reservoir, the outflow was collected in a graduated cylinder for 10 sec. intervals, and the volume rate of flow found in this way was afterwards compared with that obtained by analysis of the flow record. Using the first cam, the mean discrepancy, regardless of sign, in seven readings ranging from 200 to 400 ml./min., was 3%; with the second cam it was 4·5%. In a test with water, using the two cams, the mean discrepancy in ten readings was 2·5%.

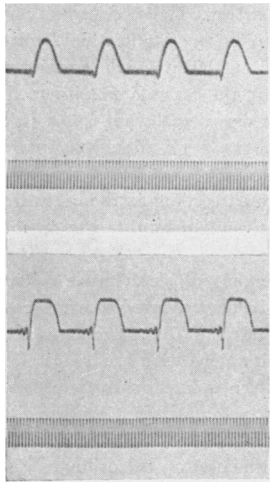

Fig. 9

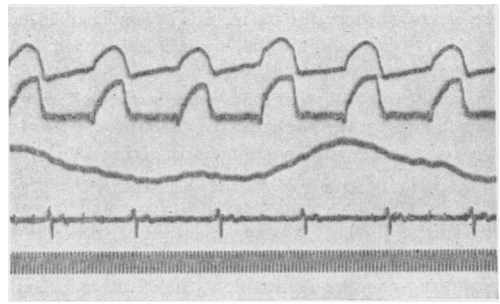

Fig. 10

Fig. 9. Record of two pulsating flow calibrations with blood; to be read from right to left. The time marker is 50 cyc./sec. The upper record showed an output of 372 ml./min., with an error of +3% from the measured volume delivered. The lower record gave a value of 486 ml./min., with an error of +1%.

Fig. 10. Record obtained from a cat; to be read from right to left. From above downwards are shown the pulmonary arterial pressure, the pulmonary arterial flow, the intrapleural pressure (inspiration upwards), the electrocardiogram, inverted and from Lead II, and 50 cyc./sec.

Respiratory variations

The portion of record shown in Fig. 10 illustrates the typical variations in pulmonary arterial volume flow during spontaneous respirations. In all records obtained in ten experiments, the right heart output per beat began to increase as soon as inspiration commenced, reaching a peak at the height of inspiration, or, more commonly, during expiration, and fell to its previous expiratory pause value within a beat or two after expiration. Combining records from each of the ten experiments, the average maximum change in beat output during respiration was about 50%, while the average output during the

combined inspiratory and expiratory phases was about 35% greater than the average output during the expiratory pause.

The changes in flow in the pulmonary artery produced by two respiratory manoeuvres, which cause large fluctuations in pressure in that vessel, have been investigated in connexion with the identification of pulmonary vascular fibres in the vagus nerve. The first manoeuvre was a sustained negative pressure deflation of the lungs, which caused a marked increase in beat to beat output

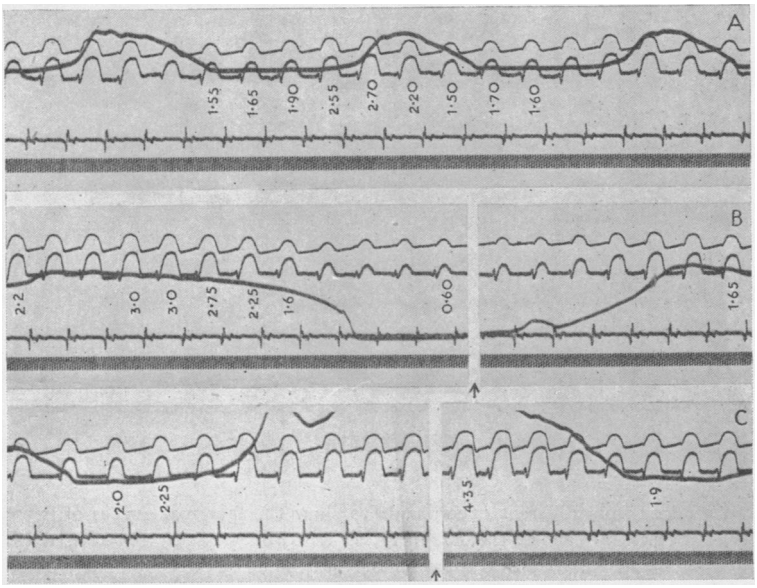

Fig. 11. Records obtained from a cat (weight 4·1 kg.). From above downwards the features registered are the same as in Fig. 10, and should be read from right to left. Section *A* shows spontaneous respirations, *B* shows the effect of a positive pressure inflation of the lungs, and *C* the effect of a negative pressure deflation. Short pieces of record have been omitted from sections *B* and *C* at the point indicated by the arrows. The numbers adjacent to each beat refer to its volume in ml. The heart output during this period of the experiment was 385 ml./min.

of the right heart. The increase itself sometimes as much as equalled the average beat output during a normal respiratory cycle, and the average increase observed was about 75%. The same effect, to a lesser extent, was seen during an obstructed inspiration.

The second one, a sustained positive pressure inflation of the lungs, gave an immediate marked decrease in beat output. Following the release of the inflation the volume of the second or third beat, was, as an average value, 25% greater than the mean beat output of any preceding respiratory cycle and usually greater than the maximum beat output during that period. These results are shown by the examples in Fig. 11.

Flow patterns

The flow patterns recorded could be assigned, purely with regard to shape, to one of four groups (Fig. 12), but variations between any two types were seen. The rounded (*Rd*) type was not observed as commonly as the round-triangular (*RdTr*) type, and each was only recorded early in an experiment when the heart output was highest. The triangular (*Tr*) type was associated with lower output

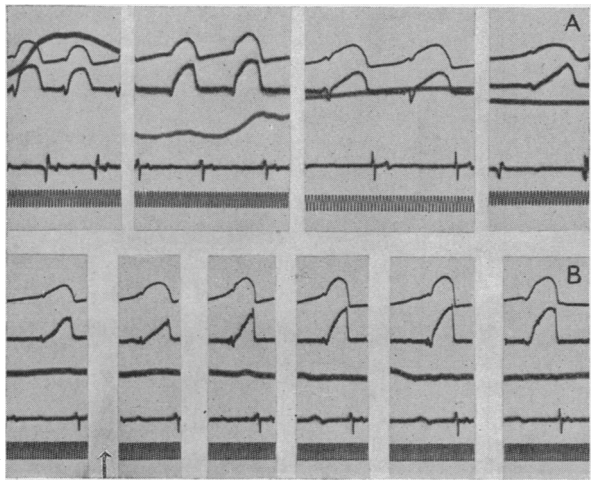

Fig. 12. *A*, sections from different experiments to show the four main types of flow patterns. From left to right are shown the *Rd*, *RdTr*, *Tr* and *Pk* types (see text). *B*, sections taken at intervals of several beats, at approximately the same respiratory phase, from a record obtained immediately before and after the administration of 50 μg. of adrenaline. The injection was made between the first and second sections at arrow. Values of beat outputs reading from left to right, were 2·25, 1·8, 2·4, 2·95, 3·75 and 4·95 ml. In both parts of the figure the individual sections read from right to left and the flow tracing is second from the top; the tracings are in the same order vertically as in Fig. 11.

values and was usually seen towards the end of an experiment. The peaked (*Pk*) type was recorded from animals with low outputs, but was also seen immediately following histamine and adrenaline injection. Adrenaline gave a more rapid increase in the speed of contraction, as evidenced by a steeper rising phase, but its administration was shortly followed by a rise in venous return which was indicated by rounding of the flow curve. Amyl nitrite inhalation, which was shown later to produce vasodilatation, caused the development of more rounded flow patterns, but again the change could be attributed to the almost immediate increase in beat output. In a series of twenty-four experiments the initial recorded wave-form was the *RdTr* type in sixteen animals, the *Rd* type in four, and the *Tr* type in a further four. During the course of any experiment, there was a gradual transition of the initial wave-

form to a more triangular or peaked type. This was caused by changes in venous return, in speed of cardiac contraction, and possibly in degree of vasomotor activity. Progressive integration of any type of flow pattern (Fig. 13) yielded a sigmoid curve relating intraventricular volume to time; the different volume curves varied principally in height and rate of rise.

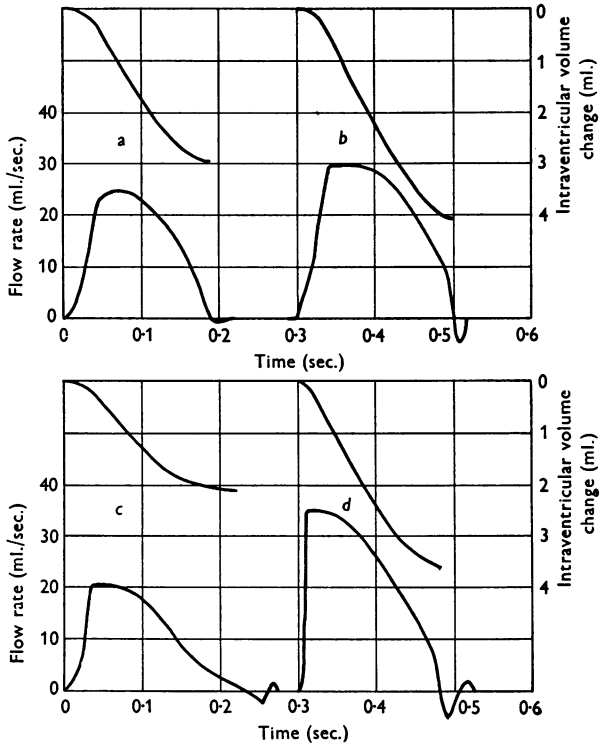

Fig. 13. Curves of intraventricular volume change derived by integration of flow tracings selected from Fig. 12. (*a*), a beat during an expiratory pause; (*b*) the preceding beat at the peak of inspiration; (*c*) later in the same experiment immediately prior to adrenaline administration; (*d*), shortly after the injection of the drug. Note more rapid increase in contraction rate following both the increased venous return, associated with inspiration, and the action of adrenaline. The latter was accompanied by more than doubling of the right heart output.

Immediately preceding closure of the pulmonary valves there was a small backward flow which was increased by a negative pressure deflation of the lungs and during inspiration. The instrument was not designed to give a quantitative measurement of reverse flow, so that in the record this portion of the curve was exaggerated in size, and represented, in fact, a very small quantity and velocity of blood flow. In most records there was a small fairly abrupt change in slope some way up the rising phase of each flow pattern, corresponding to an initial slower ejection velocity. When the change was marked it was

often also apparent in the pressure tracing. The pressure pulse itself frequently varied greatly in shape from the flow pattern. A well-rounded pressure curve was often produced by a *Tr* type flow pattern, and the peak stream velocity was almost always reached before the peak pressure was developed. Larger pulse pressures were associated with more rapid ejection, but the latter was usually accompanied by greater beat output.

The peak blood-stream velocity in the pulmonary artery could be estimated roughly. In records from ten experiments, peak volume flow rates varied from 12 to 30 ml./sec., giving a stream velocity through the Pitot ring of 60–150 cm./sec. The diameter of the artery was usually larger than that of the ring, and making an approximate correction for this difference gives a peak stream velocity range of 30–80 cm./sec. in the pulmonary artery of cats. The peak velocity seldom persisted for more than 60 msec.

Assessment of vasomotor activity changes

Incisural pressure values from suitable records were plotted against corresponding beat output values. The loci of groups of points thus obtained could be adequately represented by straight lines, but the scatter was sufficient to preclude assigning to these a precise slope value. The displacement of some

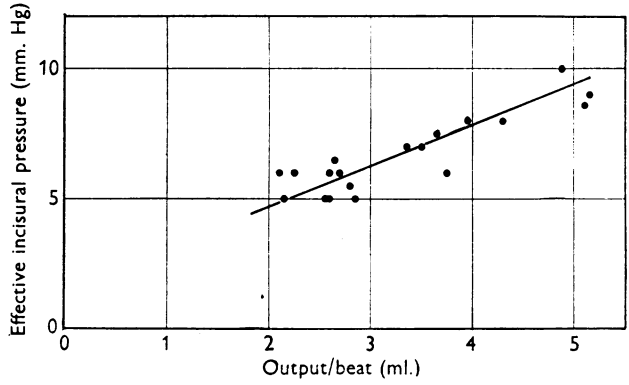

Fig. 14. Relationship between pressure and flow derived from records taken during a respiratory cycle and during positive pressure inflation and negative pressure deflation of the lungs. These manoeuvres produced a wide range of flow values and were assumed not to change the vasomotor activity.

points obtained during the active phases of respiration was considerable. The loci occasionally tended to flatten parallel to the flow axis at higher values of both measurements. The lines could never be extrapolated through the origin but always cut the pressure axis above it; there were never sufficiently low flow values to indicate the shape of the lower end of the curves. During a variety of respiratory manoeuvres, which were assumed not to influence the vasomotor activity, the position of the loci did not change, although points

corresponding to extremes of flow values often lay well off the line (Fig. 14). These manoeuvres were carried out consecutively, and resulted in a range of beat output values from 2 to 5 ml.

In a small number of experiments in which drugs were injected to alter vasomotor activity, marked changes in the position of the loci were observed. Immediately following the injection of adrenaline and histamine there was an upwards shift (in the direction of increased pressure) and following the ad-

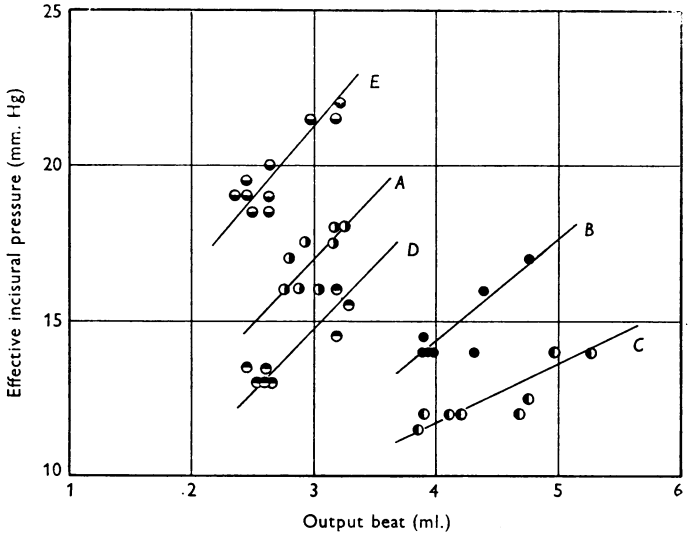

Fig. 15. Relationship between pressure and flow following the administration of drugs to alter the vasomotor activity. *A*, control series of beats; *B*, immediately after amyl nitrite inhalation; *C*, several seconds later after amyl nitrite; *D*, control series much later; *E*, several seconds after the intravenous injection of 20 μg. of histamine.

ministration of amyl nitrite there was a downwards shift. As both adrenaline and amyl nitrite produced large increases in output, giving lateral shift as well, these plots could not be used in assessing vasomotor activity changes. However, in a few experiments, the heart output before and after a drug effect remained almost constant. The plot from such an experiment is given in Fig. 15. Histamine produced the rise in pressure level and the greater slope of line *E*, although the flow rates corresponded closely to those of the control series *D*. This was accepted as evidence of active pulmonary vascular constriction. Following the administration of amyl nitrite the initial change in the position of the line from *A* to *B*, indicating a decrease in mean pressure and slope, was associated with a considerable increase in mean flow. However, the further series of points plotted at *C*, with a mean flow value almost equal to that of *B*, gave a further decrease in pressure level and slope, which was accepted as evidence of active vasodilatation.

DISCUSSION

During the development of the method it was feared that the different vessel configurations might cause the calibration of the Pitot head to differ from that previously arrived at in a brass tube, but this alteration did not occur to a significant degree, as is shown by the results plotted in Fig. 8. The natural frequency of the system was demonstrated, in all experimental records, to be of adequate value to register flow patterns faithfully, and the sensitivity ranges provided have proved appropriate to the flow values encountered in cats. The automatic zeroing device was included 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 slowly changing forward flow tended to upset the tuning of the circuit, and invalidated the measurement of subsequent beat outputs. However, it is felt that the method, with certain circuit modifications, is quite suitable for the measurement of flow in other vessels. In systemic vessels a Venturi tube could be substituted for the Pitot tube, as it possesses the advantage of offering a smaller resistance to flow. A useful addition, especially for heart output estimation, would be an electrical integration stage.

It is unlikely that perivascular nerves, probably predominantly efferent, travelling along the pulmonary artery would survive the application of the cannula band. The use of heparin makes gradual blood loss from the chest wound inevitable, and limits the period of usefulness of the experimental animal. The presence of the cannula in the pulmonary artery adds extra resistance to flow in the vessel, and it was determined (Fig. 8) that the resistance to *peak* flows was increased by as much as half by the insertion of the Pitot head. The relationship between pressure and flow for the latter is ascertained experimentally instead of using a calculated value, so that the question of any effect due to a radial velocity gradient in the neighbourhood of the head does not arise. In regard to factors unknown, it must be admitted that the flow patterns recorded from the artery may have been modified in some way by the mere presence of the metering device.

The observation of the changes in flow to the lungs during various respiratory manoeuvres requires little comment, but controversy about the influence of inspiration on right atrial flow persists (Opdyke, Van Noate & Brecher, 1950). There can scarcely be any doubt that, under the conditions of our experiments, inspiration does increase the output of the right heart. Since a linear relationship was shown to exist between pulmonary arterial incisural pressure and beat output during the respiratory manoeuvres, it is unlikely that they influence vasomotor activity. Considering the role of the heart, changes in venous return to the thorax must, then, be predominant in governing the pressure level in the artery during these manoeuvres and during any period of

constant vasomotor activity. But the exact contribution of alterations in flow to pressure changes, separated from the contribution of changing lung volume and intrapleural pressure to vascular capacity and thus to pressure changes, has not yet been completely investigated in the intact animal.

This work has been devoted mainly to developing a method of approach to some pulmonary vascular problems, but one implication follows from the observation of flow changes during the respiratory manoeuvres. Although the incisural pressure was selected as the best quantitative expression for relating arterial pressure to flow, the pulse pressure was also seen to follow closely the beat output. Since the activity in pulmonary vascular nerve fibres closely parallels the pulmonary arterial pulse pressure (Pearce & Whitteridge, 1951), so does the discharge in these fibres parallel the beat output. This is not inconsistent with the view that the site of the receptors is on the arterial side of the pulmonary vascular bed registering conditions proximal to the arterioles, but if they were situated beyond these vessels they might equally well be responding to flow changes. When conditions arise in which there is a change in pressure but not in flow—fibre discharge under such conditions has not been described—there may be response to one and not to the other, thus tending to place the site of the receptors before or beyond the arteriolar bed. Hence it would be informative to determine the effect of histamine administration on pulmonary vascular nerve fibre discharge, although variations in venous return would make simultaneous recording of flow and pressure advisable.

The use of the method to detect changes in vasomotor activity is shown to be justified, but conclusions can only be drawn when there is an almost constant heart output before and after the stimulus is applied to the vascular bed, or if the flow change is large and opposite in direction to the pressure change. As with adrenaline, so with histamine, the increase in venous return may occur so rapidly that the significance of a pressure rise cannot be exactly determined. Even with the required conditions of output, one cannot positively state in which part of the vascular tree vasomotor activity has changed, although, as mentioned earlier, the height of the pulmonary arterial pressure may be considered to depend chiefly on arterial rather than venous resistance. When using such a stimulus as histamine the effect of the drug on bronchiolar calibre has to be considered, but the considerable changes in pulmonary arterial pressure observed were unlikely to have been due to bronchomotor effects. It is hoped that the method will be applied to investigating further the possibility of reflex control of the pulmonary vascular system, with special reference to the effects on this system of pulmonary starch embolism.

SUMMARY

1. A method of measuring simultaneously the pulmonary arterial pressure and pulsatile volume flow in spontaneously breathing animals is described. It employs a Pitot head inserted into the pulmonary artery, a differential and a plain condenser manometer, and electronic-recording circuits.

2. The method records flow patterns with linear co-ordinates.

3. The mean error of the method is 4%, as tested with artificially pulsating blood flows.

4. Flow patterns in the pulmonary artery are described. The shape of the flow wave depends principally on the magnitude of the beat output and on the speed of cardiac contraction. The approximate range of peak stream velocity in the pulmonary artery of cats was found to be 50–80 cm./sec.

5. Variations in beat to beat volume flow in the pulmonary artery during respiration, and during positive pressure inflation and negative pressure deflation of the lungs, are described.

6. During periods of presumably constant vasomotor activity, the effective incisural pressure bears a roughly linear relationship to the beat volume flow in the artery.

7. A method is described of assessing changes in vasomotor activity in the pulmonary vascular bed, providing that experimental conditions do not involve more than slight changes in the right heart output.

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