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PRESSURE AND VOLUME RELATIONSHIPS IN THE VENTRICLE, CONUS AND ARTERIAL ARCHES OF THE FROG HEART

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INTRODUCTION

In the amphibian heart the pattern of blood flow from the auricles through to the arterial arches is not fully understood (de Graaf, 1957; Simons, 1959; Johansen, 1963; Foxon, 1964*a*). The action of the single-chambered ventricle and the imperfectly divided conus arteriosus, together with the details of their relationships to one another and to the arterial system, still constitute major problems. The conus is developed from the bulbus cordis (following Goodrich, 1930) seen during embryonic development in all vertebrates but persisting as a functional and contractile chamber of the heart only in amphibia and some fish. The amphibian conus, situated as it is between the divided truncus arteriosus and the undivided ventricle, must have considerable effect on blood distribution and flow pattern from the heart into the major arteries.

In a recent monograph on the cardiovascular dynamics of *Amphiuma*, Johansen (1963) expressed views on the second of these two functions of the conus which were later criticized by Foxon (1964*b*). Both workers accepted that the blood pressure and flow of blood in the major arteries during different parts of the cardiac cycle were greatly modified because of conus action. Johansen suggested that the conus had a depulsating and distributing effect on the ventricular output which was so effective that outflow was maintained from the heart throughout the whole cardiac cycle. This opinion was not shared by Foxon who cited direct observations of intermittent flow in anurans made by himself (1947) and Vandervael (1933). The aortic pressure measurements made by Simons (1957) in which an incisura early in the falling phase of the pulse was interpreted to indicate closure of the synangial valves also supported Foxon's view. However, de Graaf (1957) and Shelton & Jones (1965) placed a different interpretation on the inflexion which Simons called the incisura, suggesting that it separated ventricle and conus pressure components as recorded in the aortic arches.

Some features of the pattern of flow through the heart can be decided if the blood pressures within the ventricle, conus, and aortic arches are known. Since inertia may cause continued flow in the face of small but reversed pressure gradients (Spencer & Greiss, 1962) it is also desirable to know whether the valves at the proximal (pylangium) or distal (synangium) ends of the conus are opened or closed. Sánchez-Casco & Foxon (1963) recorded pressures in the conus of frogs but without determining them elsewhere. Johansen (1963) recorded pressures simultaneously in the ventricle, conus and aorta of the urodele *Amphiuma*. He showed that the pressure due to ventricular contraction was very much reduced in the conus and was followed by a

second component, which was of the same or greater size, produced by contraction of the conus itself. In the aorta this relationship was reversed with the peak pressure clearly associated with ventricular contraction and exceeding that recorded in the conus. The pressure due to conus contraction was not usually obvious in the falling phase of the pressure wave recorded in the aorta. It is not easy to reconcile these features of the pulse records with the anatomy of this region of the vascular system.

Pressure measurements alone are insufficient to allow complete understanding of a system in which interactions between the contractile chambers must occur. It is important to know the extent of the volume changes occurring in different regions of the heart and whether the cardiac muscle in these regions is activated or relaxed. The latter can be determined relatively easily from the electrocardiogram (e.c.g.), but the former presents certain difficulties. A cardiometer has been used to determine ventricular output (Shelton & Jones, 1965), but the extra inertial and resistive load placed on the heart by such a device is undesirable, particularly if a moment-to-moment analysis is required. Other transducer systems (e.g. Rushmer, 1961) also impose varying degrees of extra load on the heart. Net output can be measured by an electromagnetic blood-flowmeter (Johansen, 1963), but the flow cannot be related quantitatively to contraction of the ventricle or the conus. Ciné films of the heart have the advantage of imposing no extra load on the system and have been used previously in work on amphibia to give information about the duration of parts of the cardiac cycle (Davies & Francis, 1941) and the distribution of blood from the heart (Simons, 1959; de Graaf, 1957). In the present study they have been used to estimate volume changes in ventricle, conus, and truncus during the time that pressure measurements were made in these chambers.

METHODS

The experiments were carried out on *Rana pipiens* varying in weight from 20 to 30 g. The frog was anaesthetized by immersion in Sandoz MS 222 solution (300 mg./l.) and the heart was exposed by removing the sternum. With its ventral side uppermost the animal was then fastened to a wax block and allowed to recover to a lightly anaesthetized state in which normal breathing was resumed. The frogs were kept, and the experiments were performed, at room temperature (18–21° C).

The blood pressures were measured with two Hansen capacitance manometers and recorded by means of a Tektronix oscilloscope and camera or an A.E.I. four-channel pen recorder. Wide-bore copper tubes connected the manometers to no. 20 or no. 26 hypodermic needles and these were inserted into the heart or blood vessels with the openings pointing downstream. The manometers and needles were filled with saline containing 10 i.u. Heparin per ml. Further details of blood pressure determinations are given in an earlier paper (Shelton & Jones, 1965).

The movements of the heart were photographed on 16 mm. film using either a Bolex or a Vinten ciné camera running at a nominal 24 frames per second. The region of the heart was evenly illuminated using four stereomicroscope lamps fitted with heat filters. The reflexion of highlights was avoided by running Ringer solution into the tank in which the frog was held so that the heart was just submerged. This was done before each record was taken and the level of Ringer was so arranged that the

front of the animal's head remained in air and breathing went on normally. A rotating disk with two easily distinguishable sectors was included in the camera field. The disk rotated once every second and was connected to contacts which acted as a switch for a neon in the oscilloscope recording system. This provided both a time calibration and a means of precisely synchronizing the ciné films and the pressure records.

Only the ventral view of the heart and arterial arches was photographed and to calculate volumes from the measurements certain approximations were necessary. The truncus and conus were treated as cylinders, the mean diameter and length being

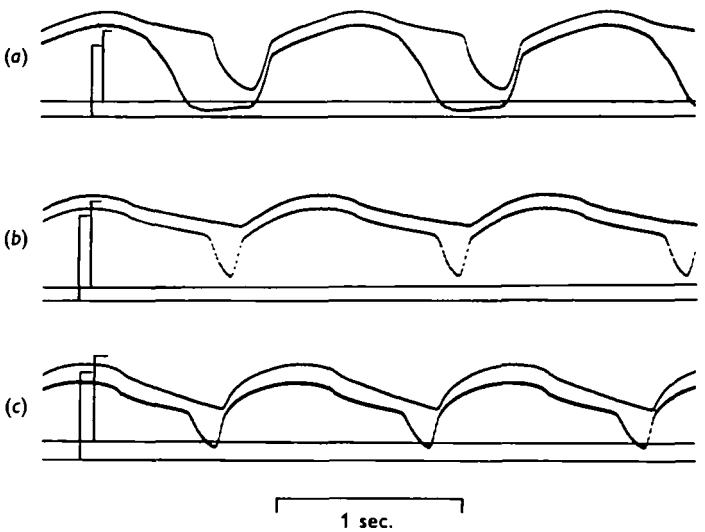

Fig. 1. Blood pressures in the heart and arterial arches of *Rana pipiens*.
(*a*) Upper trace—conus arteriosus; lower trace—ventricle.
(*b*) Upper trace—left systemic arch; lower trace—conus arteriosus.
(*c*) Upper trace—left pulmocutaneous arch; lower trace—conus arteriosus. Pressure calibration 30 mm. Hg above zero line in all cases.

measured on the photographs. It was assumed that the ventricle was circular in cross-section and the volume was calculated exactly on this basis at the extremes of the range. To make the measurement and calculation less time-consuming these figures were then used to produce a factor which would convert the area enclosed by the ventricular outline to volume. The area was measured by means of a planimeter.

RESULTS

A. *Blood pressures in the ventricle, conus and arterial arches*

The blood pressure recorded within the ventricle during systole showed an extensive swing from close to zero to approximately 30–40 mm. Hg. The initial pressure change to 20–25 mm. Hg was accomplished very rapidly, after which the pressure continued to rise more slowly to the maximum level. The subsequent ventricular relaxation caused a fairly rapid decline to the minimum value (Figs. 1 *a* and 2). The ventricular muscle was contracting actively for two-thirds of a complete cardiac cycle

and during almost the whole of this time blood was leaving the chamber to the conus and arterial arches. At the beginning of the cycle the rapidly rising ventricular pressure soon exceeded that recorded from the conus, after which the pylangial valves opened and the two pressures followed the same course, with that in the ventricle being higher by about 1 mm. Hg. Continued contraction of the conus after ventricular relaxation ultimately reversed the pressure relationship and at this point (neglecting possible inertial effects) the pylangial valves between ventricle and conus must

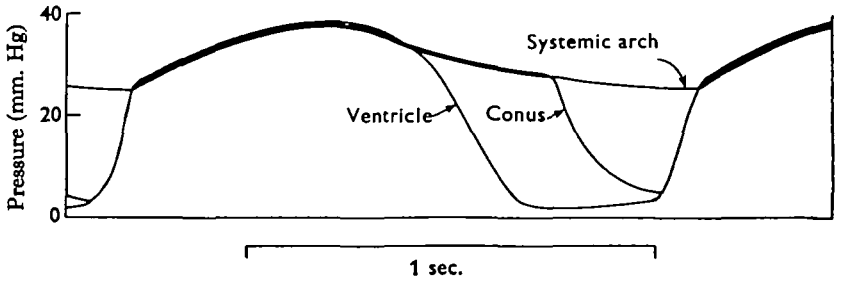

Fig. 2. Superimposed records of pressures from the ventricle, conus arteriosus, and systemic arch of *Rana pipiens*.

have closed. The pressure in the conus then decreased slowly until the muscle of the conus itself relaxed and the pressure fell rapidly towards zero. In a heart that was beating at a normal rate (30–50/min.) the pressure level in the conus never fell as low as that measured in the relaxed ventricle. Direct application of acetyl choline to the beating ventricle caused a rapid fall in heart rate and during the prolonged diastolic pause the pressures in conus and ventricle eventually reached the same level (Fig. 3*a*). Acetyl choline also caused a considerable fall in the systolic pressure, a change in the shape of the ventricular pulse curve, and an increase in the relative size of the conus-pressure component. Adrenaline was applied to the ventricle in two experiments and in neither case was there a change in heart rate. The diastolic pressure in the conus fell very slightly even though there was a considerable increase in the systolic and pulse pressures in both ventricle and conus (Fig. 3*b*). The relative size of the pulses measured in ventricle and conus varied considerably, therefore, heart rate being an important but not the only factor in the relationship. However, the size of the conus pulse was never less than 70% of the size of the ventricular pulse.

During the rapid pressure rise in the early stages of ventricular systole there was a short period of time (up to 0·1 sec.) when blood was entering the conus, but the pressure level in the arterial arches had not been reached and the synangial valves were closed. After this period the ventricular and conus pressures slightly exceeded those in the arches and blood flowed out of the heart into the arterial system. The pressure in the conus was greater than that in the systemic arch, usually until the time that the conus muscle relaxed and the synangial valves closed once more. The synangial valves were open and blood was leaving the heart for about four-fifths of the complete cardiac cycle. Despite apparent differences in the anatomy of the distal ends of the two systemic arches (Foxon, 1964*a*), the pressures recorded from them were identical. The size of the pulse in the systemic arch was approximately 35% of

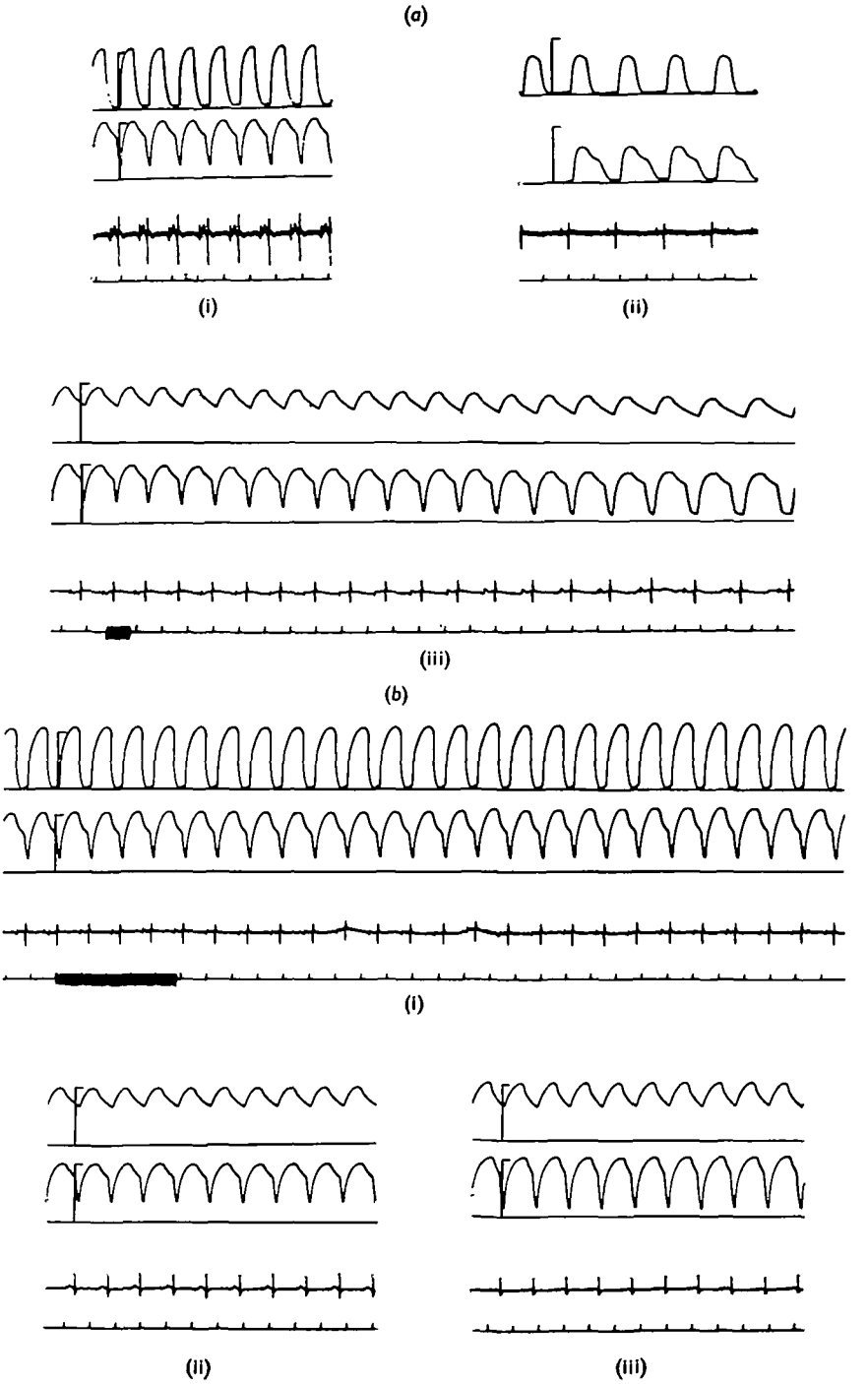

Fig. 3. The effects of acetyl choline and adrenaline on central blood pressures in *Rana pipiens*. (*a*) Acetyl choline. (i) and (ii) Pressures in the ventricle (trace 1) and conus arteriosus (trace 2) before and 40 seconds after the direct application of 5 μg of acetyl choline to the ventricle. (iii) Continuous record of pressures in systemic arch (trace 1) and conus arteriosus (trace 2) after application of 5 μg acetyl choline at time shown by event marker (trace 4). (*b*) Adrenaline. (i) Continuous record of pressures in ventricle (trace 1) and conus arteriosus (trace 2) after application of 5 μg adrenaline at time shown by event marker (trace 4). (ii) and (iii) Pressures in the systemic arch (trace 1) and conus arteriosus (trace 2) before and 120 sec. after application of 5 μg of adrenaline. Trace 3 shows electrocardiogram and trace 4 time (sec.) in all cases. Pressure calibration 30 mm. Hg above zero line.

that in the ventricle, though again this relationship varied under different conditions, particularly after the application of acetyl choline (Fig. 3*a*). As the heart rate decreased the systemic arch pulse showed a longer run off and so became larger in relation to the ventricular pulse. Even after the application of acetyl choline the size of the pulse in the systemic arch was always less than 45% of that in the ventricle in hearts that were beating rhythmically.

Relaxation of the ventricle produced an inflexion in the systemic and conus pressure curves, and subsequent slight changes of slope in the declining pulse were due to continued conus contraction as suggested by de Graaf (1957) and Shelton & Jones (1965). The contribution made by conus contraction in the final stage of ejection of blood must have been quite small in an animal which was in good condition and had not lost any blood because it was usually quite difficult to see any effect of conus

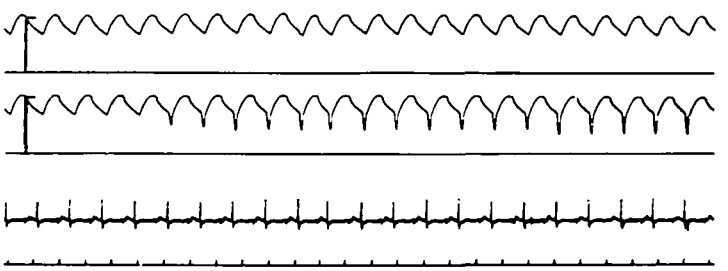

Fig. 4. Pressures above and below the synangial valves in *Rana pipiens*. Trace 1—pressures from systemic arch. Trace 2—pressures recorded using a needle inserted through the conus wall and manœuvred past the valves into the systemic arch. As the record proceeds the needle is slowly pulled back into the conus. Trace 3—electrocardiogram. Trace 4—time (sec.). Pressure calibration 30 mm.Hg above zero line

relaxation on the pressure curve in the systemic arch (Fig. 1*b*). A clear inflexion at the point of synangial valve closure, such as that seen on ventricular relaxation, cannot be seen. There can be no doubt that it is the closure of the synangial valves which sustains the considerable pressure difference between the aortic arches and the relaxed conus. If the recording needle was pushed through these valves from the conus into the truncus, then a pulse characteristic of the systemic arch was recorded. When the needle was pulled back into the conus the pattern gradually assumed the characteristics of the conus as the needle passed through the valves (Fig. 4). In some cases it is just possible that the synangial valves may have closed shortly before conus relaxation occurred. This could happen if in the final stages of activation the tension produced by the muscles of the conus was less than that of the elastic arterial walls.

In a previous paper (Shelton & Jones, 1965) differences were noted in the pressure pulses recorded from systemic and pulmocutaneous arches. The main point of difference was seen in the falling pressure phase after the inflexion, with the pulmocutaneous pressure showing a much steeper slope and dropping to a lower diastolic level. Since blood is still leaving the conus after the inflexion, this suggests that there may be a difference in pressure on the two sides of the spiral valve. The cavity on the body circuit side of the valve was the one from which the records were usually taken. This is located on the ventral side of the conus over a substantial part of its length, particularly at the anterior end. As a result we found that needles inserted

into the conus in a downstream direction were almost invariably situated in the body circuit side. It was relatively easy to record pressures in this part of the conus and to compare them with similar pressures from the systemic artery (Fig. 1*b*) and dissimilar ones from the pulmocutaneous artery (Fig. 1*c*). By carefully manœuvring the hypodermic needle at the posterior end of the conus it was possible to record similar falling-phase slopes in both conus and pulmocutaneous arch. We were unable to record the different pressure curves directly from the two sides of the spiral valve; presumably two needles in the conus interfered substantially with its normal function.

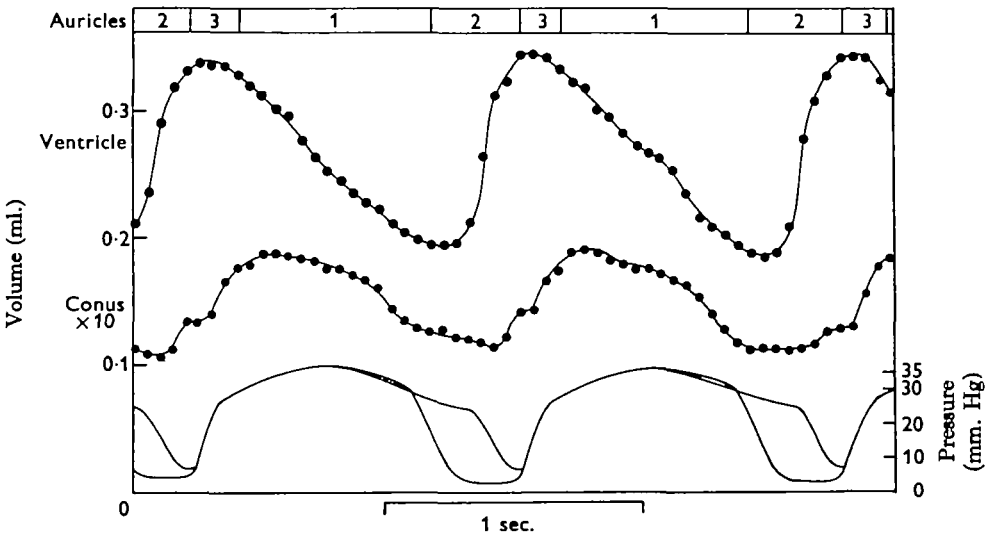

Fig. 5. Pressure and volume changes in the ventricle and conus arteriosus. The conus volume is multiplied by 10. Each point represents a ciné frame. The cycle of activity in the auricles is shown in three phases: 1—expanding; 2—contracting; 3—fully contracted.

B. *Volume changes in ventricle, conus and truncus*

The volume changes of the ventricle were large and the analysis easy and accurate. A decrease in volume began immediately after the QRS complex of the e.c.g., the rate being low at first but gradually increasing to reach a maximum about the time of maximum systolic pressure. Thereafter the rate decreased slowly until the ventricle relaxed and the pressure fell towards zero (Fig. 5). Usually ventricular filling was due entirely to contraction of the auricles (Fig. 5), but in some cases when the heart rate was low filling began before the auricle contracted.

Both the volume and the volume changes in the conus were an order of magnitude smaller than in the ventricle and analysis was more difficult. The conus began to contract about one-fifth of a cycle after the ventricle. This delay was variable, but contraction always started after the appearance of the pulse wave in the arterial arches and before this had reached the maximum systolic level. The time of appearance of the conus component of the e.c.g. was also variable over this part of the cardiac cycle. The conus volume had always decreased appreciably before the ventricle relaxed; suggestions made previously (Shelton & Jones, 1965) that the early stages of conus contraction were isometric were not substantiated. Relatively little decrease

in the volume of the contracting conus occurred after the ventricle relaxed. The major part of conus filling was accomplished during the initial stages of ventricular contraction. During the filling phase blood passed through the conus into the arterial arches because, by the time the conus was full, the ventricle had already decreased in volume by an amount several times greater than the volume of the conus. This could be accounted for by elastic and viscous elements in the conus wall preventing rapid filling of the relaxed conus. In all the animals examined, the conus showed some increase in volume before contraction of the ventricle began, during a time

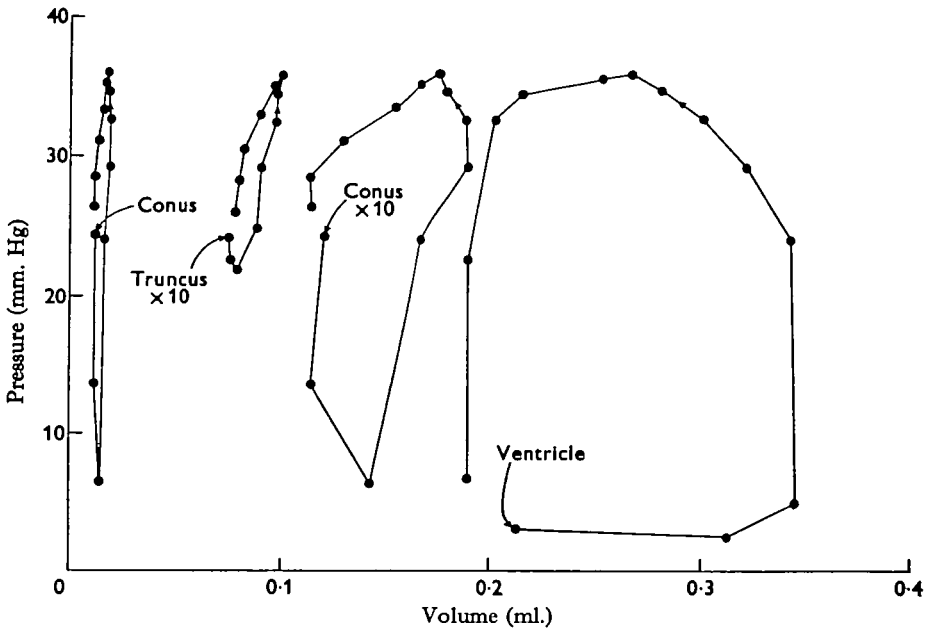

Fig. 6. Pressure and volume relationships in the ventricle, conus and truncus arteriosus. The ventricle and conus are shown at actual volumes and the conus and truncus are shown at 10 times actual volume. The loops all start and end at the same point in time and cycle in an anticlockwise direction. The points are $\frac{1}{10}$ sec. apart.

when the pressure gradient between conus and ventricle would have opposed blood flow. The increase in volume may be apparent rather than real; it may be that the conus was changing shape after relaxation and this was measured as a change in volume. Alternatively, the valves between the conus and arterial arches may have been imperfect so that the conus was partially filled from in front after relaxation.

When the pressure is plotted against volume for a complete cardiac cycle, a closed loop is described in the cases of both ventricle and conus (Fig. 6). Time advances in an anticlockwise direction round the loop. Both the conus and the ventricle are doing work, the amount being proportional to the area enclosed by the loop. It was found that the ventricle was doing 20 to 40 times the work done by the conus. Four phases of activity, isometric contraction, ejection, isometric relaxation and filling, were fairly clearly defined in the ventricle, though, as in the mammal, they merged into one another. In the conus filling began during the falling pressure phase and was completed when the pressure increased steeply, so that isometric relaxation, filling and isometric contraction did not exist as distinct phases.

The pressure–volume relationship for the truncus is also shown in Fig. 6. In this particular case a narrow anticlockwise loop was produced, but in other cases narrow clockwise loops have been seen. In the truncus the volume changes are small and approximately proportional to the pressure changes. This part of the system appears to be almost entirely elastic. The loops which have been seen may be produced by inaccuracies in the volume determinations at this level. However, the anticlockwise loops can be explained as being due to the presence of a little cardiac muscle at the posterior end of the truncus and the clockwise loops to viscous components in the artery wall. Both of these are present and the overall effect would depend on the balance of the two factors.

DISCUSSION

The experiments show that, in anurans at least, the ventricle is the chamber of major importance in the ejection of blood from the heart into the arterial arches. Contraction of the ventricular muscle causes the pressure to rise simultaneously in the ventricle, conus and arterial arches and blood to leave to both the conus and major arteries. The pressures in the ventricle, conus and arterial arches all approximate to the same value during systole. A pressure gradient does exist, but since the connexions between these central parts of the circulatory system are of relatively large diameter (and therefore low resistance), this gradient is small and amounts only to one or two mm. Hg. Large pressure differentials between ventricle and conus such as those described by Johansen (1963) imply high-resistance connexions between the two chambers, and this must result in considerable loss of efficiency in the circulation as a whole.

The conus is filled early in ventricular systole by a small proportion (5–10%) of the total ventricular output. During the later stages of conus filling a substantial volume of blood passes through the chamber to the arterial arches while it is still increasing in volume. The increase in volume continues until the conus muscle is activated, after which the volume immediately begins to go down. Ejection of blood from the heart cannot be regarded as a strictly sequential series of events with ventricular contraction filling the conus and producing an initial pressure peak, which is followed by conus contraction discharging blood to the arteries and producing a second pressure peak (Foxon, 1964*b*). When the conus begins to contract the ventricular muscle is itself still active and the ventricle decreasing in volume. The blood pressure continues to rise in all parts of the system for a short while after conus activation. It seems very doubtful whether the conus is effective in depulsation in the sense of reducing the peak systolic pressure. This pressure seems to be almost entirely a function of ventricular activity, being reached when the ventricle is contracting most rapidly. At this time the conus too is decreasing in volume, and, if anything, increasing the systolic level. It was hoped that the muscular activity of the conus could be eliminated by tying off the coronary artery which supplies it, leaving a chamber with elastic and viscous properties only. Unfortunately the conus went on beating normally for long periods under these conditions and we were unable to evaluate the contribution to blood pressure made by its active contraction.

The conus continues to contract after the ventricle has relaxed and so prolongs the flow of blood out of the heart. However, the change in volume during these

later stages is so small that flow must be negligible, and this is borne out by the fact that relaxation of the conus does not produce an inflexion in the arterial pulse curve. At this stage the purely elastic recoil of the arterial wall is just as effective in maintaining blood pressure and flow as the active contraction of conus muscle.

Compared with the ventricle, the conus in the frog plays a very small part in the work of pumping blood from the heart. Nor does it have a major influence in reducing systolic or maintaining diastolic pressures. In anurans the conus probably has a much more significant role in the separation of two blood streams flowing from the ventricle. In urodeles the balance between the various chambers of the heart seems to be different and it seems likely that the conus has a more important role in depulsation and is less relevant in regulating blood distribution.

SUMMARY

1. Peak systolic pressures in the ventricle, conus and arterial arches differ by 1 or 2 mm. Hg only, and are reached at the same time. Pulse pressures are largest in the ventricle and smallest in the arterial arches, though their relationship to one another is variable and depends partly on heart rate.

2. The conus continues to contract after relaxation of the ventricle. Blood flow from the heart occurs during four-fifths of the cardiac cycle and stops with the closure of the valves at the top of the conus.

3. Volume changes in the conus are 5–10% of those seen in the ventricle. The conus is filled early in ventricular systole before the peak pressure is reached. The ventricle does 20 to 40 times more work than the conus in ejecting blood from the heart.

4. The conus does not serve a depulsating function or make a major contribution to blood outflow from the heart in anurans.

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