

## VENOUS RETURN AND CARDIAC FILLING IN VARANID LIZARDS

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### SUMMARY

1. The duration of ventricular diastole relative to the cardiac cycle length is much shorter (46 %) in varanids than in mammals (>70 %).

2. Atrial systolic pressures were high (15–20 cmH<sub>2</sub>O), and atrial contraction was apparent in pressure waveforms from the ventricular cavum arteriosum and cavum pulmonale. Atrial contraction coincides with the short period of ventricular diastole and represents the filling agent for the ventricular cava.

3. Increased central venous flow coincides with ventricular contraction, which by reducing the intrapericardial pressure will promote the expansion and filling of the atria and central veins, implying a suctional element of cardiac filling.

4. Inspiration during spontaneous breathing will reduce central venous pressure, steepen the pressure gradient towards the heart and aid flow towards central veins. There is a positive correlation between the systolic level of central venous pressure and cardiac cycle duration.

### INTRODUCTION

The end-diastolic volume of the cardiac ventricular lumen is the most direct determinant of ventricular power output (Starling, 1920). This volume in turn depends on the central venous pressures, atrial contraction, and on venous and cardiac compliance. In mammals, the atria are relegated to a relatively minor role in ventricular filling, at least when cardiac output is low. The mammalian atria typically provide channels for venous blood to enter the ventricle during diastole more than being actual filling pumps for the ventricles. Their contraction contributes only 30 % or less of ventricular end-diastolic volume in resting mammals (Brecher, 1956).

There have been very few studies of the haemodynamics of central venous return to the heart in tetrapods other than birds and mammals. Examination of angiograms and ciné films of dipnoan, amphibian and reptilian hearts (Johansen & Hol, 1968; Johansen, 1963; Shelton & Jones, 1965) suggests that ventricular filling in ectotherm

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vertebrates is entirely due to atrial contraction. The anatomical basis for the greater importance of the atria in ventricular filling of infra-homeotherm vertebrates appears to be based on the presence of sinu-atrial valves on the right atrial side and on a valving effect where the main pulmonary vein empties into the left atrium (Meinertz, 1952, 1966).

Varanid lizards, unlike most other reptiles or the amphibians, may well place unusual demands on mechanisms responsible for ventricular filling, since cardiac output, heart rate and systemic arterial pressures are all high compared to values obtained from other non-homeothermic vertebrates (Wood, Johansen & Gatz, 1977; Burggren & Johansen, 1982; Heisler, Neumann & Maloiy, 1983).

The objective of the present study was to test the hypothesis that atrial contraction is the main filling agent for the ventricle and that central venous return is influenced by *vis tergo* as well as *vis a fronte* mechanisms. To this end, we have measured intracardiac, intrapericardial, central venous blood pressures and central venous flow in varanid lizards.

#### MATERIALS AND METHODS

Experiments were performed on six savannah monitor lizards, *Varanus exanthematicus* Bosc, and one desert or yellow monitor, *Varanus griseus* Daudin, weighing between 1.67 and 5.68 kg. The lizards were maintained in animal cages providing a range of ambient temperatures from 30–40 °C. The lizards were fed mice daily. All animals had been in captivity and in good health for over 1 year. This study has involved experiments on both anaesthetized, open-chest preparations and on non-anaesthetized, spontaneously breathing lizards not subjected to major surgical intervention.

##### *Intracardiac and central venous pressures*

Anaesthetic and surgical procedures for haemodynamic studies have been described in detail elsewhere (Burggren & Johansen, 1982). Briefly, lizards anaesthetized with 1.5% halothane (Fluothane) in air were artificially ventilated at physiological tidal volumes and frequencies. Body temperature was maintained at 34–36 °C.

The sternum was split to expose the heart and central vessels. Central arteries and veins were non-occlusively cannulated in an upstream direction using 55–60 cm lengths of PE 60 (0.76 mm bore) or PE 50 (0.58 mm bore) polythene cannulae. Great care was taken to avoid producing any obstruction to blood flow. In some experiments, a cannula was carefully inserted into the pericardial chamber and tied into place, and in most animals varying combinations of the ventricular compartments, the cavum pulmonale, cavum arteriosum and the left and right atrium were cannulated without losing pericardial fluid or destroying the integrity of the pericardium (see Burggren & Johansen, 1982). The location of the tip of each cannula was confirmed by *post mortem* dissection. All cannulae were filled with heparinized saline, and approximately 200 i.u. kg<sup>-1</sup> body weight of sodium heparin was injected into the lizard at the beginning of the experiment.

Catheters were connected to Statham 23 Db or 23 V fluid pressure transducers, which were attached to a Gould Brush 260 six-channel amplifier/recorder system. The

entire pressure recording system with PE 60 catheters had a resonant frequency of 30 Hz with 11 % critical damping, while with PE 50 catheters the resonant frequency was 29 Hz with 28 % critical damping. Heart rate was about 1 Hz, so both pressure recording systems were assumed to be adequate to record blood pressure transients without significant phase lag or amplitude error. Pressure calibrations and zero levels were frequently applied to each transducer during the course of the experiments.

Measurement of blood flow in the right or left aorta, pulmonary artery or right cranial vena cava was made with Statham SP 2202 blood flow meters with electrical, non-occlusive zero function. Periarterial flow probes with lumen diameters of 1.5–4.0 mm were used. Occlusive zero flow readings obtained by squeezing the blood vessel with blunt forceps as well as non-occlusive zeros were determined, where possible. All flow probes were calibrated *in vitro* using heparinized blood delivered from an elevated reservoir through an excised portion of vessel. Each probe was calibrated with blood drawn from the same animal in which the probe was implanted.

In some animals electrocardiograms were recorded using standard bipolar leads.

#### *Central venous pressures in spontaneously breathing, awake lizards*

The right jugular vein of two anaesthetized animals was exposed in the neck, and a PE 50 cannula introduced into the vein and advanced towards the heart until its tip lay within the right cranial vena cava. The cannula was tied into the right jugular vein (occlusive cannulation), and the incision closed with interrupted sutures. The lizards, otherwise intact, were allowed to recover from anaesthesia, and central systemic venous pressure was recorded during spontaneous ventilation, postural changes and movement.

#### *Anatomy*

The heart of *Varanus*, like that of other squamate and chelonian reptiles, consists of separate right and left atria, and three ventricular cava in anatomical connection – the cavum arteriosum, cavum venosum and cavum pulmonale. However, in *Varanus* the cavum venosum is reduced and the cavum arteriosum enlarged compared with conditions in other reptiles. As a consequence of these and other morphological specializations, the ventricle during systole becomes functionally divided into a high pressure pump (resulting primarily from contraction of the cavum arteriosum) perfusing the systemic arteries and a low pressure pump (cavum pulmonale) perfusing the pulmonary arteries. Details of ventricular pressures and ejection into the central arteries in *Varanus exanthematicus* have been given elsewhere (Burggren & Johansen, 1982; Heisler, Neumann & Maloij, 1983). Another noteworthy feature of the cardiac anatomy of *Varanus* is the enclosure of the heart and proximal regions of the great veins and arteries in a comparatively firm and non-compliant pericardium (Meinertz, 1952; Burggren & Johansen, 1982).

### RESULTS

#### *Central venous pressure and flow and atrial filling*

Blood pressure and flow recorded from the right cranial vena cava were distinctly pulsatile (Figs 1, 2, 3). While the highest venous pressure (up to 10 cmH<sub>2</sub>O) occurred immediately before and during atrial systole, and much higher systolic atrial pressure

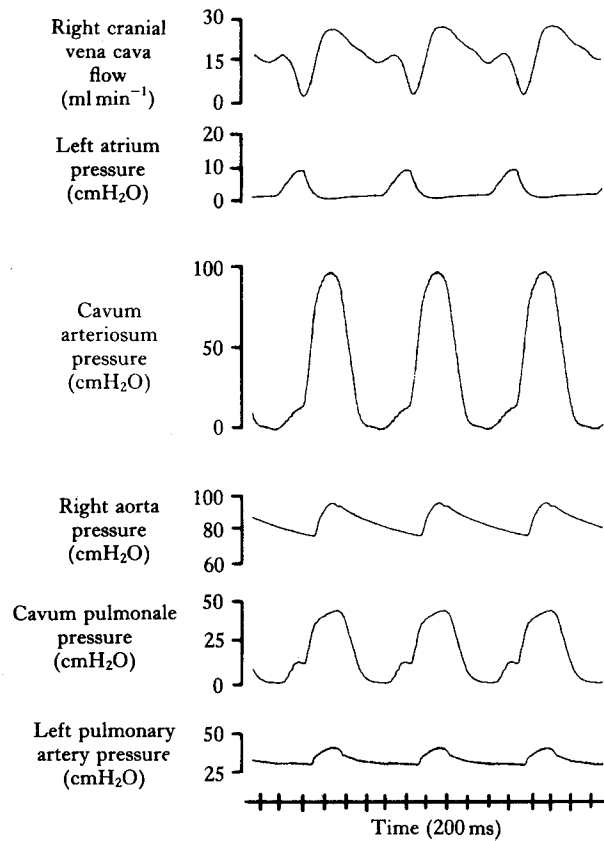


Fig. 1. Left atrial, ventricular (cavum arteriosum, cavum pulmonale) and arterial blood pressures (right aorta, left pulmonary artery) and blood flow in the right cranial vena cava in an anaesthetized *Varanus exanthematicus*.

was never evident as an increase in the recorded venous pressure but rather as a downstroke.

Arterial pressure pulses (Fig. 2, note right aorta tracing) do not appear to transmit to the venous side, since the highest venous pressures appear when the right aortic pressure is at its lowest.

Central venous systemic flow showed in most cases a biphasic pattern with maximum flows of approximately  $8\text{--}12\text{ ml kg}^{-1}\text{ min}^{-1}$  in the right cranial vena cava. This flow pulse typically peaked during early atrial diastole, coinciding with ventricular systole (Fig. 1). At this time the lowest vena cava pressures were also recorded, suggesting that when the sinu-atrial valves open at the beginning of the atrial diastole there is little impedance to central venous blood flow and that an aspirating effect of ventricular contraction occurs. Fig. 1, showing vena cava pressure and flow, and Fig. 3, showing vena cava flow and atrial pressures, indicate that during atrial filling in early diastole the pressure gradient from vena cava to the right atrium is approximately  $5\text{ cmH}_2\text{O}$ . At the very end of diastole and beginning of atrial systole, venous pressure again rises while vena cava flow declines to its minimum values.

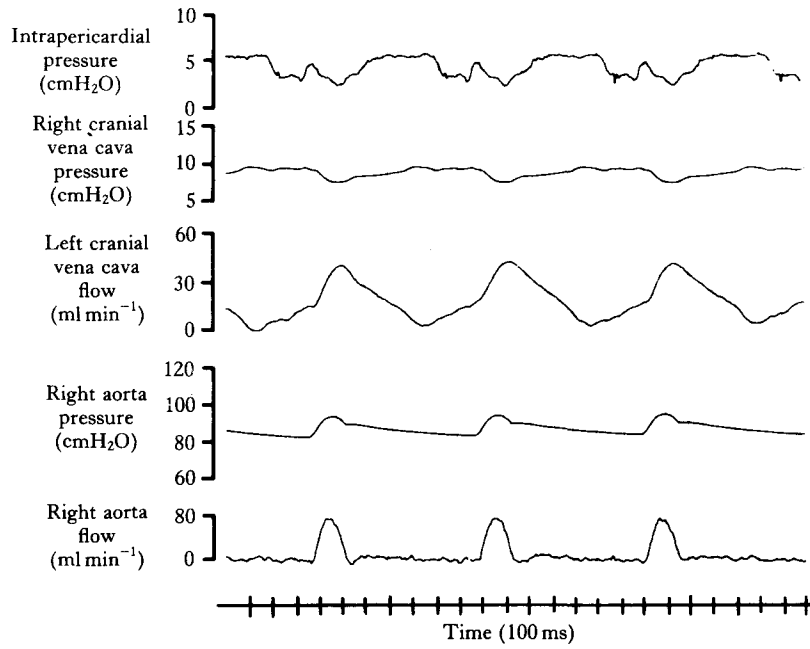


Fig. 2. Pressures in the pericardial cavity, right cranial vena cava, and right aorta and blood flow in the left cranial vena cava and right aorta of an anaesthetized *Varanus exanthematicus*.

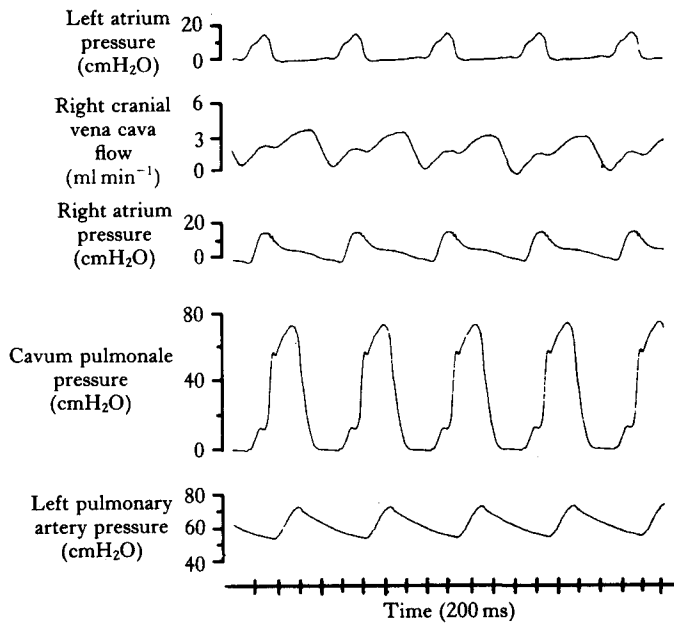


Fig. 3. Left and right atrial, cavum pulmonale, and left pulmonary arterial pressures and right cranial vena cava flow in an anaesthetized *Varanus exanthematicus*. In this figure venous, atrial and ventricular pressures and incoming venous flow, all through the right side of the heart, are presented.

Notably, vena cava flow only very briefly approaches zero when the sinu-atrial valves have closed. This suggests a very high compliance of the central veins, which apparently allows some central venous flow towards the atria even during atrial systole when atrial inflow has ceased.

#### *Atrial contraction and ventricular filling*

Fig. 3 shows that diastolic pressure in both atria was close to zero, and certainly well below central venous pressures (right cranial cava) of 7–10 cmH<sub>2</sub>O (Fig. 2). Systolic atrial pressures were quite high, averaging 15–20 cmH<sub>2</sub>O, and in a few lizards exceeded 25 cmH<sub>2</sub>O. Such high pressures could not develop if reflux into the large central veins had occurred. The rise in left and right atrial pressure during atrial systole was clearly visible in the pressure waveforms recorded in the ventricular cavum arteriosum and cavum pulmonale, respectively (Fig. 1), but not in the right cranial vena cava.

Several lines of evidence suggest that ventricular filling occurs rapidly as a result of contraction of the distended atrial chambers, rather than more slowly throughout the entire diastolic period. Electrocardiographic information in combination with concurrently recorded haemodynamic events have shed further light on interrelations between atrial contraction and ventricular filling. Fig. 4 shows that atrial diastole and filling is a prolonged event in the cardiac cycle, while conversely the ventricular filling is very short and restricted to the time of atrial contraction.

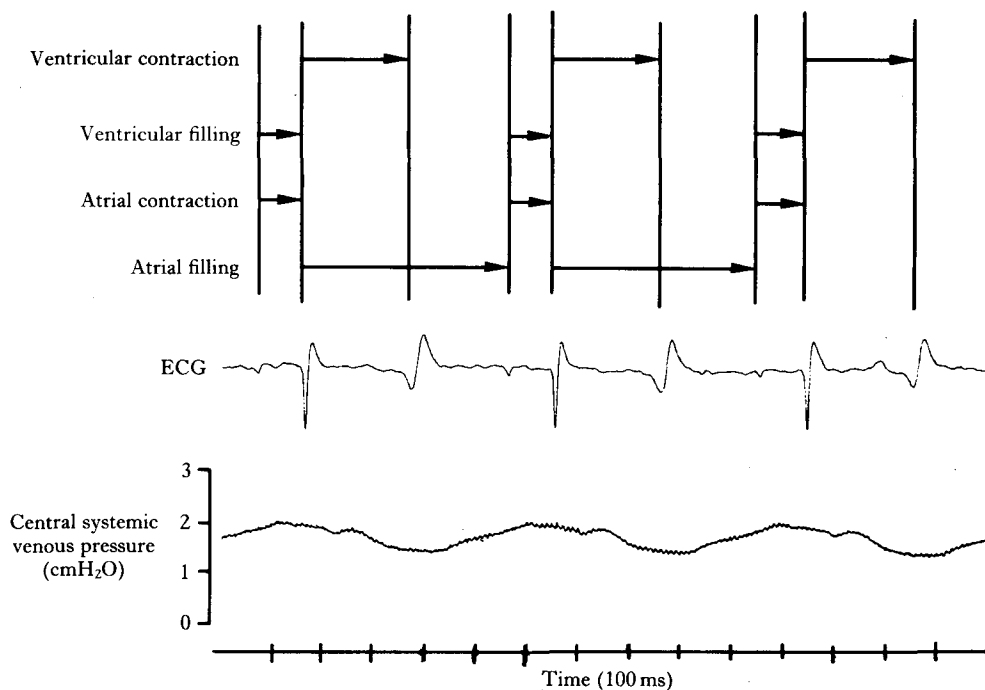


Fig. 4. Electrocardiogram and central venous pressure recorded from a cannula introduced into the right jugular vein and advanced into the right cranial vena cava of an artificially ventilated, anaesthetized *Varanus exanthematicus*. Also indicated are estimated durations of atrial and ventricular filling and emptying.

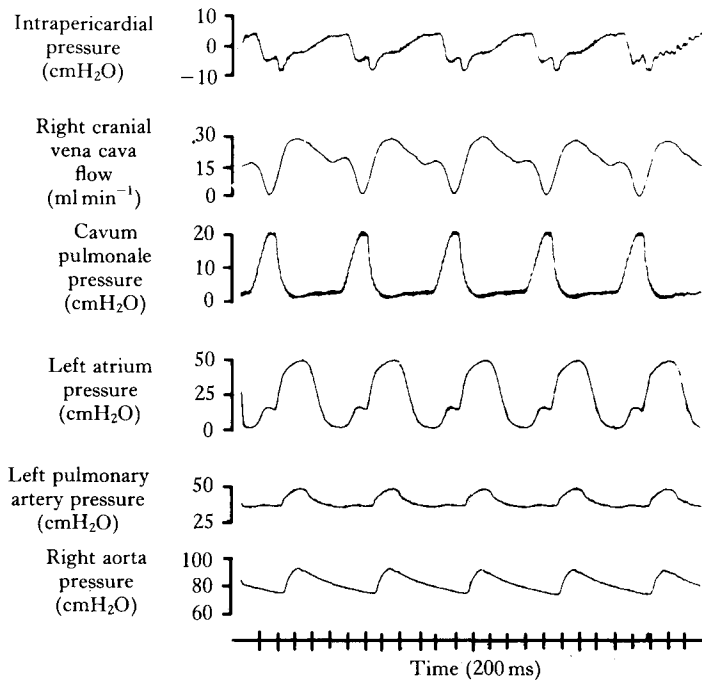


Fig. 5. Pressures in the pericardial cavity, left atrium, cavum pulmonale, left pulmonary artery and right aorta, together with blood flow in the right cranial vena cava in an anaesthetized *Varanus exanthematicus*.

#### *Intrapericardial pressure during the cardiac cycle*

Pressure changes correlated with both atrial and ventricular contractions were recorded in the pericardial space. Both atrial and ventricular contraction caused a reduction in intrapericardial pressure to levels below those in all cardiac chambers. A transient increase in pressure sometimes occurred between peak atrial and ventricular contraction, resulting in a complex waveform (Fig. 5).

#### *Central venous pressure in intact animals*

An intact, closed chest wall and spontaneous aspiratory breathing are known to influence greatly central venous pressure in mammals. Therefore, experiments were performed on unanaesthetized varanids involving recording of central right cranial vena cava pressure during spontaneous breathing.

Fig. 6 shows right cranial vena cava pressure (bottom tracing) in a spontaneously breathing, unanaesthetized *Varanus griseus*. The top panel shows beat-to-beat variations in systolic central venous systemic pressure and the middle panel plots cardiac cycle duration. There is a clear positive correlation between the systolic level of central venous pressure and the duration of the cardiac cycle. Towards the end of the recorded time lapse, a spontaneously occurring breath was accompanied by a lowered central venous pressure and a decrease in cardiac cycle duration (rise in heart rate).

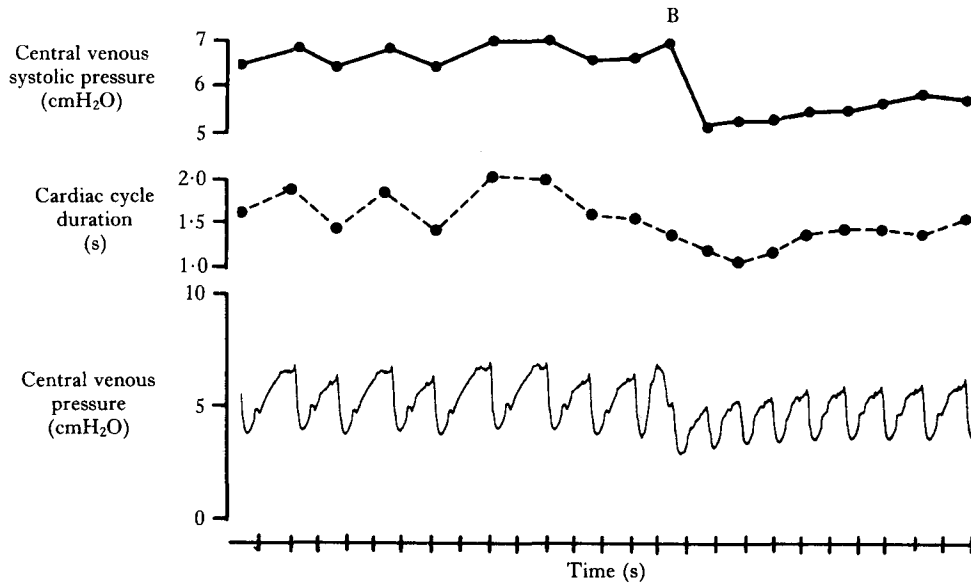


Fig. 6. Systemic venous pressure in an unanaesthetized, spontaneously breathing *Varanus griseus* recorded *via* a cannula introduced under anaesthesia into the right jugular vein and advanced into the right cranial vena cava. Also indicated are cardiac cycle duration and systolic systemic venous pressure derived from the pressure record. Note the positive correlation between cycle duration and venous pressure. B marks a spontaneous breath.

#### DISCUSSION

A primary consideration when discussing the dynamics of cardiac filling is the length of the diastolic period relative to the entire cardiac cycle, for only during diastole will a pressure gradient exist to drive blood from the central veins into the atria and ventricle(s). Table 1 presents data on the duration of mechanical ventricular diastole based on our examination of published blood pressure profiles recorded directly from the ventricle of several different vertebrates. Since the duration of diastole varies greatly with heart rate, interspecific comparison is facilitated by only including data derived from blood pressure measurements at relatively similar heart rates (about 50–80 beats  $\text{min}^{-1}$ ). The table reveals that when the duration of ventricular diastole is expressed as a percentage of the cardiac cycle length the ectothermic tetrapods have values between 37% and 47% compared to values exceeding 70% for the mammals. A comparison with birds is difficult because of the lack of data on heart rates as low as those listed in Table 1. At a higher heart rate of 150 beats  $\text{min}^{-1}$  ventricular diastole in a domestic duck occupies 67% of the cardiac cycle length (Butler & Jones, 1971). A lower heart rate would mainly prolong the diastolic period and thus further increase the duration of ventricular diastole relative to cardiac cycle length.

During most of ventricular diastole, mammals show a positive pressure gradient from the central veins, through the atria to the ventricles. Ventricular filling will thus initially proceed by passive filling from the central veins. When the relatively small



Table 1. Duration times for ventricular events in the cardiac cycle of amphibians, reptiles and mammals

Species	Heart rate (beats min <sup>-1</sup> )	Duration of cardiac cycle (s)	Duration of ventricular diastole (s)	Ventricular diastole as a % of cardiac cycle	References
Bullfrog	68	0.88	0.38	43	Langille & Jones (1977)
Grass frog	45	1.33	0.55	41	Shelton & Jones (1965)
Garter snake	79	0.76	0.28 (CV)	37	Burggren (1977)
Savannah monitor lizard	67 67	0.90 0.90	0.41 (CA) 0.44 (CP)	46 47	Burggren & Johansen (1982)
Water snake	67	0.90	0.42 ('V')	47	Johansen (1959)
Dog	50	1.20	0.95 (LV)	79	Kumada <i>et al.</i> (1979)
Man	70 61	0.86 0.99	0.61 (LV) 0.75 (RV)	71 76	Detweiler (1979) Cournand (1950)

CV = cavum venosum; CA = cavum arteriosum; CP = cavum pulmonale; 'V' = 'ventricle'; LV = left ventricle; RV = right ventricle.

atria start contracting, ventricular volumes have already increased to two-thirds or more of their end-diastolic value (Burton, 1965). The atria are thus not important as filling pumps for the ventricles. Also, the lack of valves at the atrial inflow orifices precludes development of high atrial systolic pressures. In lower vertebrates, on the other hand, mechanical systole is a prolonged event, and consequently the duration of ventricular diastole occupies less than one-half that of the cardiac cycle length (Table 1, Fig. 4). The short duration of ventricular diastole has important consequences for cardiac filling, since it implies that passive filling of the ventricle by a central venous pressure head does not occur or is insignificant.

The evidence for this is firstly that changes in central venous and/or atrial pressure were never reflected in intraventricular pressures during early diastole, suggesting functional ventricular isolation during this period. Additionally, ventricular diastolic pressures were declining towards zero until atrial contraction began. An increase in ventricular diastolic pressure might have been expected if the ventricular chambers were passively filling through 'open' atria during diastole. Secondly, the most striking visual observation to be made of the intact, beating heart of *Varanus* is the progressive engorgement of both atrial chambers in diastole, during which time the ventricle still remains in its end-systolic volume. With atrial contraction, the ventricle is seen to increase rapidly in size and then immediately diminish as ventricular contraction and ejection into the arteries develop.

The important distinctions between the varanid lizards and the homeothermic vertebrates in regard to cardiac filling have also been documented in lungfish based on intracardiac pressure recordings (Johansen, Lenfant & Hanson, 1968) and from angiocardigraphic evidence (Johansen & Hol, 1968). Similarly a long duration of ventricular systole relative to cardiac cycle length occurs in anuran (Shelton & Jones, 1965) and urodele amphibians (Johansen, 1963) as well as in snakes (Burggren, 1977).

The presence in varanids of a suctional attraction for venous blood, set up by ventricular contraction mediated through the corresponding pressure changes in the semi-rigid pericardium and transmitted to the central veins, was clearly apparent from the pressure and flow recordings obtained (Figs 1, 5). The intrapericardial pressure changes will directly affect the transmural pressures between all heart chambers and regions of the vessels enclosed in the pericardium. This influence will be greatest on the atria and greater veins, which are presumably more compliant than the more thick-walled ventricle and central arteries. In the veins and atria, low intrapericardial pressures will promote their expansion and thus filling, implying a *vis a fronte* element of cardiac filling.

A *vis a fronte* or suctional attraction phase of cardiac filling is a trait apparently shared among all infra-amniotic vertebrates and has also been suggested to be important in mammals (Hamilton, 1930): it has been demonstrated in sharks (Sudak, 1965; Johansen, 1965), lungfish (Johansen *et al.* 1968) and urodele amphibians (Johansen, 1963).

The relationship between breathing and central venous pressure in varanid lizards is not resolved fully from our experiments. A spontaneous breath cycle always starts with an active expiration, which as a compression of the chest wall will increase body cavity pressure and will be apparent as a pressure rise in the central veins. If this pressure rise coincides with the atrial filling period it will obviously steepen the pressure gradient towards the atrium and promote its filling. During inspiration, which is also an active process, the expansion of the chest wall causes a central venous pressure downstroke. This downstroke will steepen the pressure gradient between the more peripheral and the central veins and possibly aid venous inflow to the more central veins.

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