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The origin of mean arterial and jugular venous blood pressures in giraffes

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Summary

Using a mechanical model of the giraffe neck and head circulation consisting of a rigid, ascending, 'carotid' limb, a 'cranial' circulation that could be rigid or collapsible, and a descending, 'jugular' limb that also could be rigid or collapsible, we have analyzed the origin of the high arterial and venous pressures in giraffe, and whether blood flow is assisted by a siphon. When the tubes were rigid and the 'jugular' limb exit was lower than the 'carotid' limb entrance a siphon operated, 'carotid' hydrostatic pressures became more negative, and flow was 3.3 l min^{-1} but ceased when the 'cranial' and 'jugular' limbs were collapsible or when the 'jugular' limb was opened to the atmosphere. Pumping water through the model produced positive pressures in the 'carotid' limb similar to those found in giraffe. Applying an external 'tissue' pressure to the 'jugular' tube during pump flow produced the typical pressures found in the jugular vein in giraffe. Constriction of the lowest, 'jugular cuff', portion of the 'jugular' limb showed that the cuff may augment the orthostatic reflex during head raising. Except when all tubes were rigid, pressures were unaffected by a siphon.

We conclude that mean arterial blood pressure in giraffes is a consequence of the hydrostatic pressure generated by the column of blood in the neck, that tissue pressure around the collapsible jugular vein produces the known jugular pressures, and that a siphon does not assist flow through the cranial circulation.

Key words: giraffe, siphon, cranial circulation.

Introduction

Three substantial studies have been done to measure giraffe blood pressures directly, by Goetz (Goetz, 1955; Goetz and Budtz-Olsen, 1955; Goetz and Keen, 1957; Goetz et al., 1960), Van Citters (Van Citters et al., 1966; Van Citters et al., 1969), and most recently by Hargens (Hargens et al., 1987). These studies have shown that the cranial circulation of giraffes is unique and characterized by high carotid artery pressures (~200 mmHg at the heart compared to ~100 mmHg in humans; 1 mmHg=0.33 kPa), and positive jugular vein pressures. The origin of these pressures is controversial. The controversy has been reviewed at least six times (Badeer, 1986; Seymour and Johansen, 1987; Pedley, 1987; Badeer, 1988; Badeer and Hicks, 1992; Seymour et al., 1993) and evaluated empirically five times using mechanical models (Holt, 1959; Hicks and Badeer, 1989; Pedley et al., 1996; Badeer, 1997; Seymour, 2000).

From these reviews and experiments two main mechanisms have been suggested for the origin of giraffe arterial blood pressure. The conventional, hydrostatic, mechanism predicts that the principal determinants of blood pressure at the level of the heart will be the required perfusion pressure plus the hydrostatic pressure generated by the length of the neck. Mean arterial pressure at the head, calculated from all pressures that have been measured at the head in giraffes, is 100.3±20.9 mmHg (systolic 128.3±20.2 mmHg; diastolic 78.3±20.2 mmHg) (Mitchell and Skinner, 1993). For a head 2 m above the heart, as it often is in giraffe, the hydrostatic pressure generated by the column of blood in the carotid artery is 2000 mm×1.055 (density of blood)/13.6 (density of mercury), which is 155 mmHg. Thus the pressure generated by the heart should be 255 mmHg. However, in the same animals from which average cranial arterial pressure was calculated, heart pressure was calculated to be on average 185±41.6 mmHg (systolic 211.1±37.6 mmHg; diastolic 151.4±32.6 mmHg) (Mitchell and Skinner, 1993). This lower than predicted average pressure may be because some of the animals were anaesthetized at the time of measurement, or were holding their heads at an average angle less than vertical, or did not have two meter long necks, but it is also possible that mechanisms exist that reduce the work of the heart.

Thus, Badeer (Badeer, 1986; Badeer, 1988; Badeer, 1997) and Hicks and Badeer (Hicks and Badeer, 1989) have suggested that as the giraffe cranial circulation can be regarded as an inverted U-tube that functions as a siphon, gravitational effects are neutralized and the high pressure results from high

peripheral resistance. Badeer (Badeer, 1997) further suggested that high peripheral resistance is a consequence of arteries with small lumens plus high sympathetic nervous system-mediated vasoconstriction, the latter resulting from the absence of a functional baroreceptor-mediated depressor mechanism.

There is also a third possibility. Giraffe may be hypertensive and have high blood pressure as a result of the mechanisms causing hypertension in humans. This possibility has not been considered seriously but it has also not been eliminated.

In addition to the controversy about the origin of giraffe arterial pressures, there is controversy about whether gravitational (hydrostatic) pressure can be neutralized (for example by a siphon) in the cranial circulation of any animal that stands upright. Hill and Bernard decided that '*the principle of the siphon is not applicable to the vascular system in which the arteries on the one hand and the veins on the other are of so very different in distensibility and elasticity*' (Hill and Bernard, 1897), and more recently other workers (Dawson et al., 2004; Gisolf et al., 2005) concluded that a siphon does not operate in the cranial circulation of standing humans. Holt wrote: '*... freely collapsible veins running from a part above heart level, such as the head, back to the heart can exert no siphoning effect on the flow of blood to the part*' (Holt, 1959), the reason being that if the tubes in a siphon system are collapsible (as in the giraffe jugular vein) the potential energy is lost as frictional heat (Seymour and Johansen, 1987; Seymour et al., 1993). Moreover, if the jugular vein acted as a siphon, the pressure gradient down the jugular vein would be negative, but, at least in giraffes, it is the opposite: pressure at the top of their jugular vein is far higher than it is at the bottom (Hargens et al., 1987; Mitchell and Skinner, 1993) (see Fig. 1).

In giraffe, however, following Burton's work (Burton, 1972), it was suggested (Badeer, 1986; Badeer, 1988; Hicks and Badeer, 1987; Hicks and Munis, 2005) that the gravitational pressure of blood in the jugular veins can counterbalance the gravitational pressure in the carotid arteries as long as sufficient flow exists to establish a continuous column of fluid. This idea was confirmed (Badeer, 1997) by using a collapsible tube as the siphon tube in the descending limb of a model. Flow through the system was greater than if there was no descending limb ('free fall' flow). He also concluded that high blood pressure '*is simply to minimize the collapse of the vessels in the head and neck*', thus allowing a siphon effect to exist (Badeer, 1997), and that its functional advantage was to reduce the work of the heart (Hicks and Badeer, 1987). When a pump was used to drive fluid through a vertical U-tube system, a siphon reduced 'heart' work by 12–15% (Hicks and Badeer, 1989), although Seymour et al. could not repeat this result and concluded that this finding was an artefact (Seymour et al., 1993).

To contribute to these debates we report here some results we have obtained from another mechanical model of the giraffe cranial circulation. The principle of the model was that gravitational and viscous flow pressures could be added or subtracted by various manipulations including creating or breaking a siphon system. The main purposes of the study were to measure and record pressures in both the ascending and descending limbs of the model simultaneously, and to establish the factors that contribute to the known giraffe arterial and jugular venous pressure profiles, which are summarized in Fig. 2. We show that a siphon does not assist cranial flow, and that the origin of the arterial and venous blood pressures in the giraffe cranial circulation is complex.

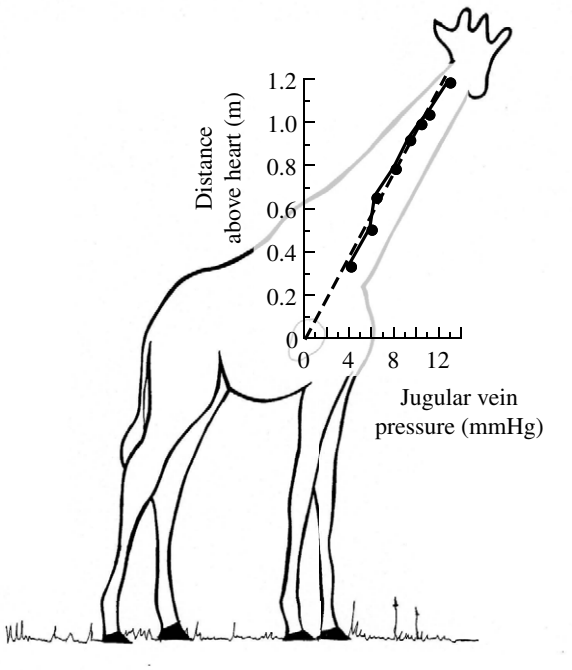

Fig. 1. Giraffe jugular venous pressures (JVP) as measured by Hargens et al. (Hargens et al., 1987) (circles and solid line) and a linear regression line calculated from the data (broken line). The relationship between height in meters and JVP in mmHg is JVP=0.093×height–0.022 (r=0.987). The linear regression predicts that right atrial pressure will be 0 mmHg, which is the measured value.

Materials and methods

The model

The model was designed to recreate the basic anatomy of the giraffe (*Giraffa camelopardalis* L.) cranial circulation, that is, a rigid 'carotid' tube, a flexible 'jugular' tube and a section between the two representing the microcirculation of the head and neck.

The main elements of the model, shown in Fig. 3, are listed below.

(1) A large water bath with a capacity of 175 l, in which the water level was kept constant by a constant inflow of water regulated by a float valve. The water was at room temperature throughout (~20°C).

(2) A submersible pump (Model 3E.12N, Little Giant Pump Co, Oklahoma City, OK, USA) able to deliver precisely regulated flow (F-400 flow meter, Blue White Industries, Hurlington Beach, CA, USA) of water at least 10 liters min^{-1}

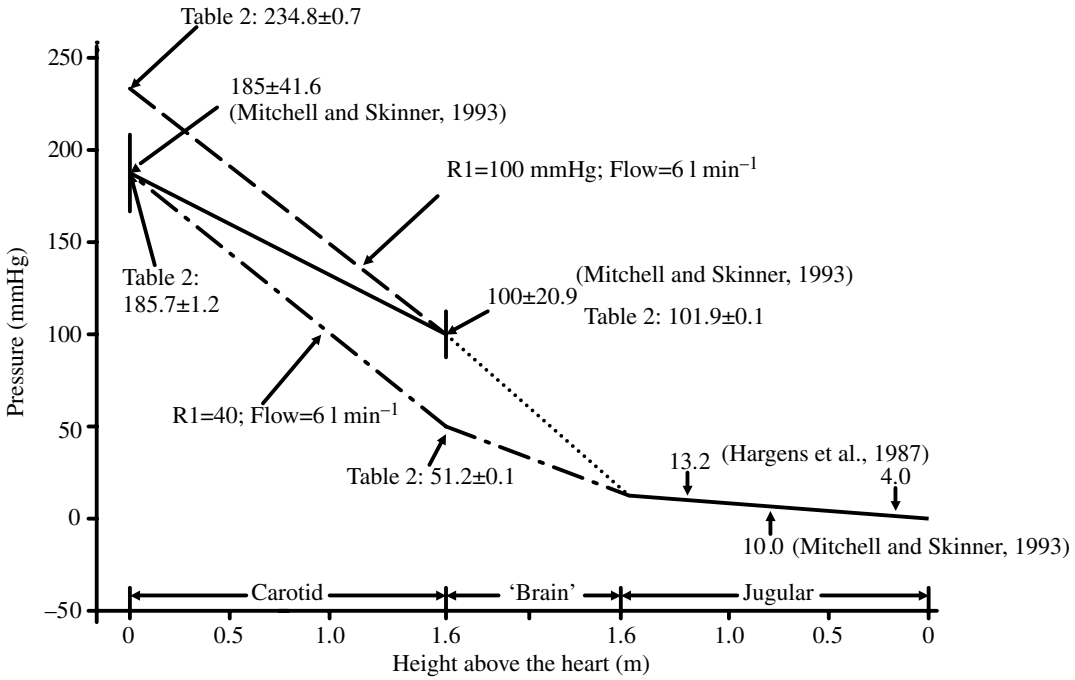

Fig. 2. Profile of giraffe cranial pressures. Solid lines show known pressures using published data (Mitchell and Skinner, 1993; Hargens et al., 1987). Broken lines show pressures generated by the model, and are given in more detail in Table 2. Note that the model can replicate known giraffe jugular pressures, can replicate separately mean arterial pressure and mean cranial pressure, but cannot replicate all typical giraffe carotid and jugular pressures simultaneously.

at a height of 2 m, irrespective of changes in resistance. Volume flow was regulated in two ways. First by altering the power input using a rheostat ('Powerstat' L116C; variable autotransformer, input 120 V at 50–60 Hz, output 0–140 V at 10 A; Superior Electric Company, Bristol, CT, USA). The power required to produce a given flow allowed an accurate measurement of the work of the pump, and by analogy, by how much heart work might be reduced by a siphon. Secondly, with the rheostat fixed at a specific power output (1000 W), flow was adjusted by altering the resistance in the pump's inflow pipe. Of the two methods, the second produced more stable flows, and was the method used when pump work was not being assessed.

(3) A rigid 'carotid' tube of 1660 mm in length (~2 cm longer than the 'jugular' tube to facilitate removal of air bubbles, see below) made of PVC tubing with an o.d. of 17.1 mm and an i.d. of 12.0 mm. These dimensions correspond to those of a carotid artery in a (medium sized) giraffe. The hydrostatic pressure generated by the column of fluid in a tube of this length is 122 mmHg (1660/13.6). The resistance to fluid flow (viscous flow resistance) offered by this tube was 31.8±0.5 mmHg l^{-1} min^{-1}, which is within the range of 26.6–38.6 mmHg l^{-1} min^{-1} calculated from known pressures and blood flows in giraffe: pressure gradient=ΔP=85 mmHg; $\dot{Q}$=2.2–3.2 liters min^{-1} (Mitchell and Skinner, 1993).

(4) A 'jugular' tube of 1638 mm in length that also could be made rigid (using PVC tubing) or collapsible (using rubber, 'flat-style', Gooch tubing cat. no. 75-1000-82, PGC Scientifics, Frederick, MD, USA). This Gooch tubing had a flat width of 31 mm and a round diameter of 25 mm, dimensions that are similar to those of a giraffe jugular vein. The hydrostatic pressure at the bottom of a stationary column of water in this tube, compared to the top, would be 120 mmHg. The resistance offered to fluid flow was 0.2–1.2 mmHg l^{-1} min^{-1}, whereas in giraffe it is 5–7 mmHg l^{-1} min^{-1} [ΔP=16 mmHg; $\dot{Q}$=2.2–3.2 liters min^{-1} (Hargens et al., 1987; Mitchell and Skinner, 1993)]. A valve was placed at the top of the 'jugular' tube so that the tube could be opened or closed to the atmosphere. With the valve opened to the atmosphere any siphon effect being produced in the descending 'jugular' limb of the model could be broken.

(5) A 'cranial' circulation that could be made rigid (using the same PVC tubing used to make the 'carotid' tube) or collapsible by replacing the PVC tube with the 'flat-style' Gooch tubing.

(6) Six pressure transducers (PX 143, Omega Engineering, Inc., Stanford, CT, USA) measuring pressures between –258 and +258 mmHg at 0.1 mmHg intervals. Three were placed in the 'carotid' limb (P1, P2, P3; Fig. 3) and three in the 'jugular' limb (P4, P5, P6; Fig. 3).

The collapsible 'brain' tube (between P3 and P4) and each collapsible section of the 'jugular' tube (between P4 and P5, P5 and P6, P6 and the exit) were enclosed in clear PVC tube with an o.d. of ~60 mm, and an i.d. of ~50 mm (i.e. much greater than the diameter of the Gooch tubing), such that it formed an airtight container around each section. Each of these containers was attached to a mercury sphygmomanometer so that a precise external pressure (mmHg) could be applied to

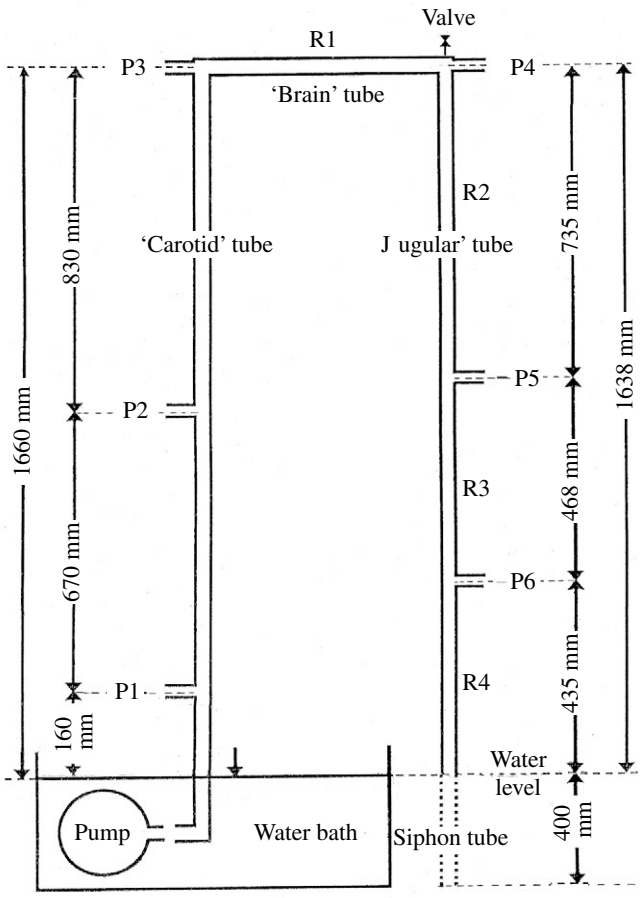

Fig. 3. A diagram of the model of the giraffe cranial circulation used. P1, P2, P3, P4, P5, P6 were sites of pressure measurement. R1, R2, R3 and R4 were sites where external pressure could be applied using a sphygmomanometer. A submerged pump and/or jugular limb extension tube was used to generate flow through the system. The jugular tube terminated outside the bath to allow for siphon operation, and bath water level was maintained with a valve-controlled constant inflow.

them to create a transmural pressure equivalent to the capillary hydrostatic pressure necessary to maintain filtration pressure, or positive pressures generated by cerebrospinal fluid, or to increase ascending limb hydrostatic pressure so simulating a longer neck ('brain' tube), or tissue pressure, or venoconstriction ('jugular' tube).

Experimental design

We made the assumption that functions of the giraffe cranial circulation could be addressed as if it consisted of a single afferent tube to the head and a single efferent tube. We also assumed that a giraffe carotid artery containing blood at a pressure of between 100 and 200 mmHg is for all practical purposes rigid even though its mix of elastic and collagen fibers (Franklin and Haynes, 1927; Goetz and Keen, 1957; Kimani and Opole, 1991) produces a *windkessel* effect. We also assumed that flow throughout the length of a carotid artery or a jugular vein is constant. It is not. Flow in the carotid artery decreases as it loses blood to tissues *via* tributaries and flow in the jugular vein increases as it gets nearer to the heart as it collects blood from tributaries.

Unlike other mechanical models of the giraffe cranial circulation (Seymour and Johansen, 1987; Hicks and Badeer, 1989; Pedley et al., 1996; Badeer, 1997) but like Seymour's model (Seymour, 2000), our model contained a 'brain' circulation that could be made rigid to simulate Goetz's 'deep, non-collapsible venous channels' (Goetz et al., 1960) or the effects of positive or negative cerebrospinal fluid pressure, or collapsible to represent a physiological microcirculation in which an internal pressure for achieving filtration exists, but which is subject to collapse if transmural pressure falls towards zero. Similarly the 'jugular' limb could be rigid to represent a jugular vein supported by extravascular connective tissue or filled by a high volume flow of blood, or one that was collapsible to represent its normal, observed, physiological state. The model does not take into account the possibility of two parallel, simultaneously operating, venous drainage systems – one rigid (venous plexuses) and one collapsible (jugular vein) as did Seymour's (Seymour, 2000).

The model allowed for the following. (1) Four different tube configurations: (i) all rigid; (ii) carotid and brain rigid, jugular collapsible; (iii) carotid and jugular rigid, brain collapsible; (iv) carotid rigid, brain and jugular collapsible, the combination presumed to occur in giraffe. (2) Three flow states: (i) 'siphon', or (ii) 'pump-driven', and (iii) a combination of these. (3) Many combinations of flows, pressures and resistances, all in the physiological range of giraffe.

The purpose of the experiment was threefold. First, we wanted to establish the pressures and flows that could be generated by a siphon. Secondly, we wanted to establish what pump-driven pressures in the ascending carotid and descending jugular limbs of the model were, whether these pressures were affected by a siphon, what effect collapsible tubes representing the head and neck microcirculations and jugular vein had on 'carotid' pressures, and what effect different fluid flow rates and external pressures had on 'carotid' and 'jugular' pressures. Thirdly, we wanted to try and replicate the combination of flows, and resistances to flow, that produce the pressures that are known to exist in the giraffe cranial circulation in order to understand the factors that may contribute to them.

The system was calibrated by using the rigid tube configuration and filling the tubes with water, with no siphon tube attached, and no flow. Gravitational pressures measured by pressure transducers at each height above water level were adjusted to predicted values. Predicted values were P1=–11.8 mmHg, P2=–61.1 mmHg, P3=–122.1 mmHg, P4=–120.4 mmHg, P5=–66.4 mmHg, P6=–32 mmHg.

At least three measurements of pressures were made during steady state flow rate or test procedure over a period of a few minutes. Statistical analyses were done using Students *t*-test. *P* values of less than 0.05 were regarded as significant.

Results

Siphon flow

Rigid tube configuration

A first experiment was to establish if typical giraffe cranial blood flow (2.2–3.2 liters min^{-1}) (Mitchell and Skinner, 1993), could be produced through the model by a passive system such as a siphon alone, i.e. in the absence of pump driven flow. Preliminary experiments were done using the 'all rigid' configuration, in which the jugular tube was either the same length as the carotid tube, or lengthened by up to 400 mm below water level by attaching lengths of rigid PVC tubing to its exit. When the two tubes were the same length there was no flow. With a rigid extension tube attached to the jugular tube exit the flow rate increased from 0.32 liters min^{-1} (at 5 mm length) to 3.3 liters min^{-1} (at 400 mm length, which equals a siphon pressure head of 29.4 mmHg). These data confirm a ubiquitous finding about which there is no controversy, namely that a siphon can generate large flow. In all subsequent experiments a 400 mm rigid extension tube attached to the bottom of the jugular tube was used to establish the siphon effect.

These experiments also showed that in the absence of a jugular tube extension, all pressures were negative and reflected gravitational pressure. Attachment of a jugular tube extension generated more negative pressures especially in the jugular tube, and produced the high flow rate mentioned above (Fig. 4A).

Collapsible tube configurations

There was no flow when any part of the model contained a collapsible tube, and 'carotid' pressures were not altered by a jugular extension. In the collapsible jugular tube, pressures were always negative, and became more so when the extension tube was attached (Fig. 4B–D), but when the valve at P4 was opened all pressures in it reverted to atmospheric pressure (not shown).

We conclude that a siphon has no effect on 'carotid' pressures and cannot produce flow if any part of the system is collapsible. Zero flow confirms previous conclusions that resistance in collapsed tubes is high, and that collapse prevents a siphon effect (Holt, 1959; Seymour et al., 1993; Seymour, 2000).

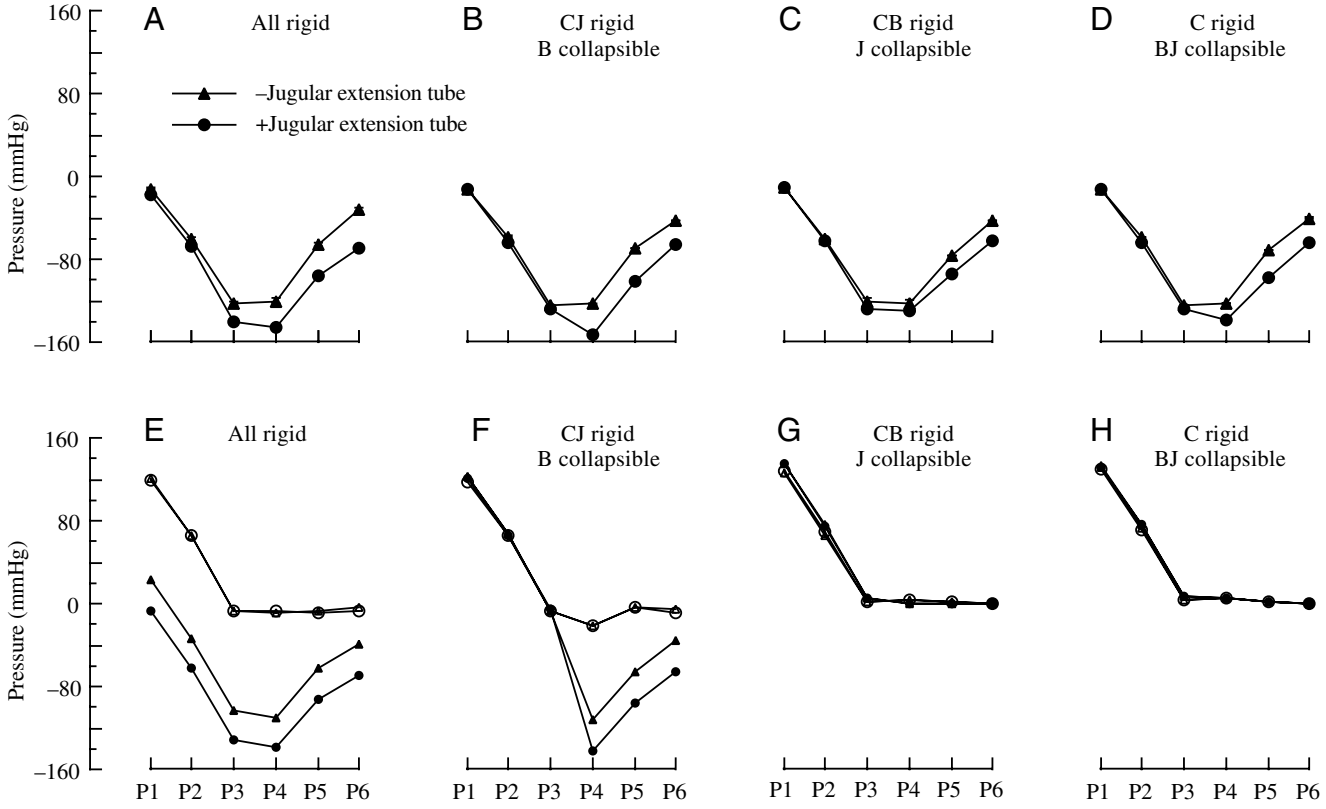

Fig. 4. (A–D) Pressures when there was siphon-driven flow, and the valve at P4 was closed. Closed triangles show pressures when the jugular limb extension tube was not attached, and closed circles when it was attached. Note that in A, P1–P3 (carotid) pressures were reduced by the extension tube. In B–D, the extension tube had no effect on carotid pressure. In all cases the extension tube reduced jugular tube pressures by the expected 30 mmHg. (E–H) Pressures when there was pump-driven flow of 4 l min^{-1} through the model. Circles show pressures when the extension tube was attached and triangles when it was not. Open circles and open triangles show pressures with the valve at P4 open. Note that in E and F opening the valve, and thereby removing the effect of the siphon in the rigid jugular tube, resulted in pressures identical to those in tube configurations (G and H) where the jugular tube was collapsible. In G and H the pressures were not affected by a siphon or by the position of the valve, because of the presence of the collapsible jugular tube. B, brain; C, carotid tube; J, jugular tube.

Pump flow

Rigid tube configuration

When all the tubes were rigid, pump flow rate at 4 l min^{-1}, and the valve at P4 closed, it was obvious that a siphon can assist flow, can significantly reduce pressures throughout the system by the amount of the siphon pressure head (approximately 30 mmHg), and can reduce the work of the pump, as suggested by Hicks and Badeer (Hicks and Badeer, 1989) (Table 1; Fig. 4E). For example at the 'heart' level (P1), in the absence of a jugular extension the pressure at P1 was +22.8±0.5 mmHg. When an extension tube was attached, P1 decreased to the predictable –7.2±0.4 mmHg. The power needed to generate 4 l min^{-1} flow in the absence of the extension tube was 645 W. With the extension tube in place the power needed was only 465 W (i.e. about a 30% decrease).

Fig. 4E also shows that if the siphon effect was broken by opening the valve at the top of the rigid jugular tube (P4) to the atmosphere, then the pressures in the jugular limb became atmospheric, those in the carotid limb became equivalent to the height of the water column, and the power consumption of the pump required to maintain a flow of 4 l min^{-1} increased to 900 W (Table 1).

In all these experiments viscous resistance ($\Delta P/\dot{Q}$) in the carotid arm did not change: it was 31.8±0.5 mmHg l^{-1} min^{-1} (ΔP=127.3±2.2; $\dot{Q}$=4 liters min^{-1}). Thus the decrease in 'carotid' pressure and reduction in the work of the pump when the jugular extension was present and a siphon was operating, can be attributed to the subtraction of the effect of gravity and not to a change in viscous resistance.

Table 1. *The effect of a siphon on the work of the pump*

Tube combinations	Siphon tube	Position of siphon valve	Power (W)
C,B,J rigid	–	C	645
	–	O	900
	+	C	465
	+	O	890
C,J rigid, B collapsed	–	C	910
	–	O	890
	+	C	885
	+	O	890
C,B rigid, J collapsed	–	C	880
	–	O	880
	+	C	895
	+	O	880
C rigid, B,J collapsed	–	C	900
	–	O	880
	+	C	880
	+	O	880

B brain; C, carotid; J, jugular tube.

Note that when all parts of the model were rigid but with no extension tube attached, the work of the pump is reduced by about 30% from 890 W to 645 W. When the extension tube was attached, the work of the pump was reduced by another 30% from 645 to 465 V. In all other cases (i.e. when any part of the system is collapsible), whether the valve at P4 is open (O) or closed (C) or whether there was an extension tube attached (+) or not (–), the work of the pump was high and constant at around 900 W.

Collapsible tube configurations

In contrast to the all rigid configuration, if either the cranial or jugular tube, or both, was a collapsible tube then the jugular extension had no effect on the 'carotid' pressures generated by the pump. With a jugular extension tube attached, carotid limb pressure at P1 was between 121.7 and 134.7 mmHg. In the absence of a siphon effect 'carotid' pressure was between 123.4 and 135.9 mmHg, with the latter values not significantly different from those recorded when the jugular extension tube was attached (Fig. 4F–H). In the collapsible jugular tube, pressures were always close to atmospheric, but the pressure measured at its top (P4) was usually slightly positive and greater than it was at the bottom (P6), as in giraffe (Hargens et al., 1987) (Fig. 2), whether the extension tube was attached or not.

We conclude that a collapsible tube establishes an isolated column of fluid in the ascending limb that exerts a gravitational, hydrostatic pressure that determines 'carotid' pressures. Confirmation of this conclusion is that the work of the pump was unaltered by the presence of an extension tube: power output to maintain flow was approximately 900 W in all cases (Table 1). Further confirmation of these conclusions is that breaking the siphon had no effect on 'carotid' pressures or the work of the pump (Fig. 4F–H; Table 1).

The effect of 'jugular' cuff constriction

A muscular cuff is present in the wall of the anterior vena cava of giraffe at the point just proximal to its entry into the right atrium (Goetz and Keen, 1957). Its function is unknown but its morphology suggests that it can constrict. One consequence of constriction could be generation of the typical giraffe jugular pressure profile. Fig. 5 shows changes in pressures when an external, 'tissue' pressure of 120 mmHg was applied to the lowest part of the model's jugular tube (R4, Fig. 3), to simulate constriction. A typical jugular pressure profile did not result. All pressures in the system increased with 'carotid' pressures increasing less than did 'jugular' pressures. The 'jugular' pressure gradient was reversed: pressures at the top of the 'jugular' tube (P4) were less than those in the middle (P5) or at the bottom (P6).

The elevated 'jugular' pressures did reveal an interesting consequence of the constriction, however. Resistance as calculated from $\Delta P/\dot{Q}$ across the 'brain' circulation fell from 6 to 2 mmHg l^{-1} min^{-1}, because the pressure gradient between P3 and P4 decreased from 24 mmHg to 7 mmHg while flow remained the same.

The effect of 'cranial' circulation resistance on 'carotid' limb pressures

Blood needs to be delivered to the head at a pressure that will support microcirculation hemodynamics. The requirement for a filtration pressure can be simulated in our model by

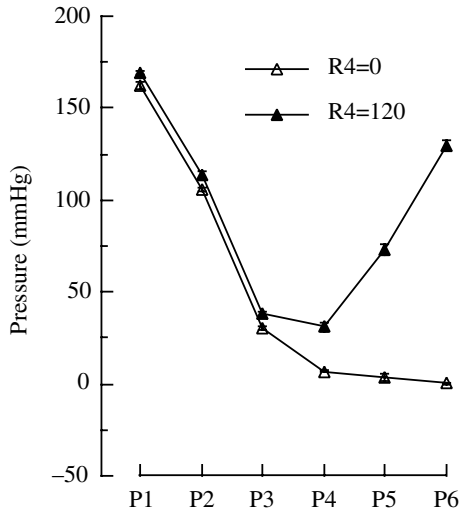

Fig. 5. The effects of constriction of the lowermost 'jugular cuff' (R4) region of the jugular tube. Constriction of the 'jugular cuff' area of the jugular tube (R4) does not produce typical giraffe jugular pressures.

applying an external pressure to the 'brain' collapsible tube. Adding an external pressure at R1 (Fig. 3) reduces the diameter of the tube and so is the equivalent of increasing cranial resistance.

When we increased cranial resistance, 'carotid' pressures increased in proportion to the increase in external pressure at R1 (Fig. 6A,B); to overcome the resistance an increase in hydrostatic pressure was required.

The effect of flow rate on 'carotid' and 'jugular' pressures

When both the carotid and jugular tubes were rigid (Fig. 6C) and the brain tube collapsible, doubling flow rate from 1 liter min^{-1} to 2 liters min^{-1} increased carotid pressures by 40–50 mmHg. When flow rate was doubled again from 2 to 4 liters min^{-1} 'carotid' limb pressures increased by another 40 mmHg. When both the brain and jugular tubes were collapsible (Fig. 6D) the effect on 'carotid' pressures was less. Pressure at P1 increased by only 10 mmHg (from 122±0.1 to 132.9±0.7) when flow increased from 1 to 4 liters min^{-1}. These data confirm that flow rate has a minor effect on pressures when most parts of the system are collapsible, and by extrapolation, changes in flow probably contribute little to giraffe carotid artery pressures.

Replicating giraffe cranial pressures

We tried to replicate the known giraffe pressure profile, using combinations of flows and external resistances in the 'giraffe' tube configuration. The external pressure around each segment of the jugular tube was adjusted so that 'jugular' pressures corresponded to the known pressures (shown in Fig. 1) in the jugular vein, namely approximately 14 mmHg at P4, 10 mmHg at P5 and 7 mmHg at P6. At the same time, flow rates of 4–6 liters min^{-1} were produced, 'brain' circulation external pressure was maintained at 40 mmHg (a value assumed to be physiological), and pressures in both the carotid and jugular limbs were measured.

The calculated mean giraffe 'heart' pressure of 185 mmHg (Mitchell and Skinner, 1993) was established when brain resistance was 40 mmHg, and flow rate was 6 liters min^{-1} (Table 2; Fig. 2). The calculated cranial pressure of approximately 100 mmHg at P3 (Mitchell and Skinner, 1993) was established when the external pressure at R1 was 80–100 mmHg (not shown). Known jugular pressures (Hargens et al., 1987) were reproduced by 'tissue' pressures equivalent to 2–4 mmHg. These pressures are close to the 1 mmHg found by Hargens et al. (Hargens et al., 1987), the general tissue pressure of 1 mmHg estimated by Guyton (Pedley et al., 1996), and those obtained by Seymour from his model (Seymour, 2000).

Overall these data reveal that the giraffe cranial pressure profile depends on a complex interaction between hydrostatic pressure, fluid flow rate, vessel wall (viscous) resistance and tissue pressure, which cannot be replicated by the model with a single common combination of these factors.

Discussion

In all discussions concerning the craniovascular physiology of giraffe, the idea of a siphon mechanism neutralizing gravity or assisting flow is raised, and if a siphon is operative then there must be another origin for their arterial pressures. The idea of a siphon in giraffe seems to have originated from a brief report (Patterson and Warren, 1952), and has been supported, mainly by Badeer and colleagues, in several articles (Badeer, 1986; Badeer, 1988; Hicks and Badeer, 1989; Badeer and Hicks, 1992; Badeer, 1997). Goetz (Goetz, 1955), who in 1955 was the first to study giraffe blood pressures, encapsulated the idea by asking '*whether the left ventricle does provide the moving force unaided or whether it is assisted in its task by other mechanisms such as a peristaltic wave along the carotid artery or a siphon effect of the venous blood carrying down the jugular vein helping to 'elevate' the blood in the carotid artery*' (Goetz and Budtz-Olsen, 1955). After making measurements of giraffe blood pressure Goetz and Keen concluded that the giraffe cranial circulation proceeded unassisted by siphons or peristalsis although it was '*doubtless aided by subatmospheric pressures at the brain level*' (Goetz and Keen, 1957). Goetz and colleagues (Patterson et al., 1957; Warren et al., 1957) later concluded, however, that there was no '*necessity for any important contribution to cerebral perfusion pressure from negative venous pressure at brain level*' (Patterson et al., 1965).

If a siphon does exist then the origin of arterial blood pressure suggested by Badeer (e.g. Badeer, 1997) is high peripheral resistance caused by small vessel lumens, and excess sympathetic tone, itself the product of an ineffective baroreceptor mechanism. However, the giraffe has a highly functional baroreceptor system (Kimani and Mungai, 1983; Millard et al., 1986; Mitchell and Skinner, 1993), so excess

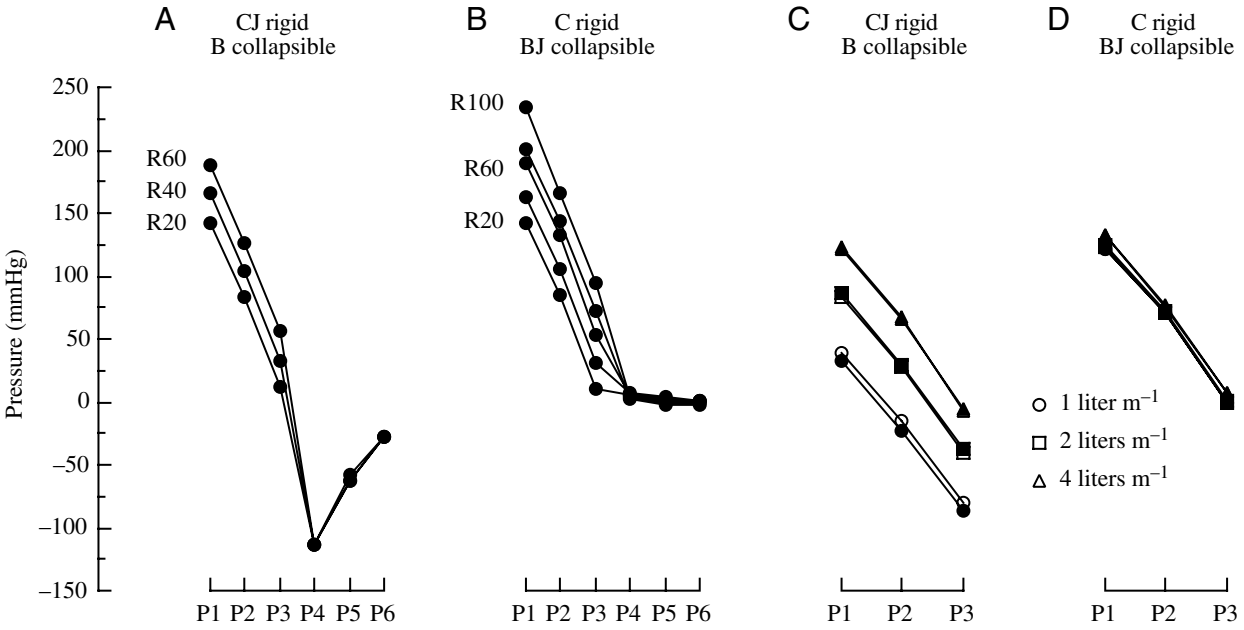

Fig. 6. The effect of adding brain vascular resistance, or changing flow, on pressures. (A,B) Pressures at all sites when brain (A) or brain and jugular (B) tubes were collapsible and resistance was added to the brain tube (magnitude indicated by R20, R40 etc beside traces). In A and B adding external pressure to the collapsible 'brain' tube increased carotid pressures in proportion to the increase in external pressure. Pressures in the jugular tube follow previous findings and were unaffected by external pressure on the brain tube. (C,D) The effect of changes in flow generated by the pump (flow magnitude indicated by legend between panels) on pressures generated in the 'carotid' when the brain (C) or brain and jugular (D) tubes were collapsible. Open symbols show pressures when the extension tube was not attached and closed symbols when it was attached. When the jugular tube was rigid (C), increasing the flow increased carotid pressures. When the jugular tube was collapsible (D) increasing flow had no effect on carotid pressures. B, brain; C, carotid tube; J, jugular tube.

sympathetic tone arising from its absence is unlikely. Furthermore the density of sympathetic innervation of arteries is inversely related to vessel wall thickness and with height, so peripheral constriction is at best likely to be poor (Nilsson et al., 1988). Calculated peripheral resistance in giraffes is 2 mmHg l^{-1} min^{-1}, which is one-tenth that in humans, and this value supports the view that their peripheral resistance is not the source of high arterial pressure. In addition, the data we report here were obtained from a model in which there was no peripheral resistance component other than that in the model itself, and no sympathetic nervous system, and yet the pressures produced in it are very similar to those found in giraffe.

There is also little anatomical or physiological evidence that a siphon mechanism exists in the cranial circulation of giraffe. The arterial and venous arms of the cranial circulation are not known to be connected by anastomotic channels and they are not similar to an inverted U-tube. They are separated by extensive intracranial and extracranial capillary beds consisting of highly permeable vessels. For these capillary beds to function, capillary pressure must be greater than colloid osmotic pressure. Colloid osmotic pressure of giraffe blood is

Table 2. *Simulating the giraffe cranial pressures profile by applying external pressure*

	Pressure (mmHg)									
Flow	Applied				Measured					
(liters min^{-1})	R1	R2	R3	R4	P1	P2	P3	P4	P5	P6
4	40	5	3	3	+164.6±1.0	+106.8±1.0	+35.7±0.1	+14.9±0.3	+11.9±0.2	+5.7±0.3
5	40	3	1	1	+176.4±1.0	+119.6±0.1	+46.5±0.1	+12.7±0.4	+7.5±0.1	+7.2±0.1
6	40	3	1	1	+185.7±1.2	+126.4±0.4	+51.2±0.1	+14.1±0.3	+11.1±0.8	+7.7±0.3
Mean		+3.7±1.1	+1.7±1.1	+1.7±1.1	+177.1±8.3	+119.1±7.6	+46.1±5.4	+13.9±1.1	+10.2±2.3	+6.9±1.0

R1–4, sites where pressure was applied; P1–6, sites of pressure measurement.

Pressure was applied to the brain tube (R1) and to three parts of the jugular tube (J: R2, top; R3, middle; and R4, bottom: see also Figs 2 and 3), using the tube combination of carotid rigid, brain and jugular collapsible, as exists in giraffe. Pressures shown were generated in the absence of an extension tube and with pump-driven flow.

about 25 mmHg (Hargens et al., 1987; Mitchell and Hattingh, 1993) the same as it is in other mammals. Thus capillary hydrostatic pressure must be greater than 25 mmHg. Textbook values for microcirculation pressures are, at the arterial-end, 35 mmHg with mean capillary hydrostatic pressure about 20 mmHg, which are not compatible with siphon-assisted flow. Therefore, the heart must generate a pressure that overcomes hydrostatic pressure generated by the column of blood in the carotid artery, the peripheral resistance of the cranial microcirculation, and that delivers blood to the cranial tissues at a pressure sufficient to ensure filtration.

This conclusion is supported by calculations of expected hydrostatic pressure. Calculated values fit exactly with the known dimensions of giraffe cranial vessels and with their measured arterial pressures (e.g. Goetz and Budtz-Olson, 1955). It is also supported by the data we report here and that collected by Seymour (Seymour, 2000). We have shown here that adding or subtracting gravity by various manipulations, or breaking the siphon in the jugular limb by allowing air to enter the water column, does not alter carotid tube pressures, except when all the tubes are rigid. When they are rigid, breaking the siphon results in carotid pressures identical to those measured in it when the tubes are collapsible. These results show, therefore, that gravity accounts for most of arterial pressure.

The lack of a siphon effect is in one sense a pity. If a siphon did exist it would, as our data show (Table 1), and as first proposed by Hicks and Badeer (Hicks and Badeer, 1989), produce a significant decrease in heart work. When the pump was producing flow through rigid tubes in our model, a siphon reduced the work of the pump by half. When Hicks and Badeer introduced collapsible tubes they found that a siphon decreased heart work by 12–15% (Hicks and Badeer, 1989), but we could not replicate this result (Table 1).

Assessing the contribution of viscous resistance

Giraffe cranial resistance is known to double when they raise their heads and we suspect this is the consequence of extracranial blood vessel constriction (Mitchell and Skinner, 1993). Data from our model show that reducing the radius of the tubes by applying external pressure, increases resistance and increases 'carotid' pressures significantly. Changes in flow rate have a less marked effect on 'carotid' pressures. Reducing the radius of the jugular tube had no effect on 'carotid' pressures.

There was, however, an interesting effect of constriction of the lowermost resistance in the jugular tube (R4, Fig. 3). This manipulation simulated contraction of the muscular cuff in the anterior vena cava (Goetz and Keen, 1957). The function of the cuff is unknown, but there are at least three potential functions. One function is that it might reduce the flow of blood into the right atrium during head-raising. The amount of extra blood that collects in the jugular veins when a giraffe is drinking can be calculated to be about 20 liters. The heart would be unable to accommodate this volume if it emptied into the right atrium when the animal lifts its head. If the cuff constricts as part of the head raising reflex then flow into the atrium would be less impetuous. A second possibility is that it constricts when a giraffe lowers its head so reducing regurgitation of blood from the inferior vena cava and right atrium into the jugular vein. A third possibility is that it provides jugular resistance and thus contributes to the counter-gravitational pressures in the vein that are unique to giraffe. Our model showed that simulation of cuff constriction did not result in counter-gravitational pressures, but it did show that cranial resistance was lowered when this part of the jugular tube was constricted (Fig. 5B). It is conceivable therefore that if the jugular cuff constricted during head-raising, when extracranial constriction is counterbalanced by diversion of blood to the brain *via* the occipitovertebral anastomosis (Mitchell and Skinner, 1993), then a lowering of cranial resistance could promote cerebral perfusion and contribute to the prevention of fainting in a very elegant orthostatic reflex.

Reconstructing giraffe cranial pressures

The giraffe cranial circulation is continuously exposed to changes in gravitational pressure and to changes in blood flow. To simulate this variety of circumstances we changed flow rate and external resistances in the model to establish what combination of flows and pressures best replicates the known pressure profile in giraffe. As might be expected no particular combination recreates the profile. What is difficult to replicate is a pressure at the head of 100 mmHg, and at the same time typical heart pressures of 185 mmHg. This difficulty suggests that the factors that contribute to cranial resistance are too complex to replicate in a model.

Venous pressures

Apart from establishing the origin of arterial pressures, the data generated by our model also support the conclusion that the origin of giraffe positive and inverted jugular pressures is tissue pressure. Holt (Holt, 1959) predicted that jugular pressures should be zero. For the pressures to be positive viscous resistance must be greater than the force of gravity. Seymour and colleagues (Seymour et al., 1993; Seymour, 2000) concluded that tissue pressure was responsible and that the linearity of decrease could be attributed to a similar decline in tissue pressure. Our model showed that the amount of tissue pressure needed was small, similar to that measured by Hargens et al. (Hargens et al., 1987), was fairly constant throughout the length of the 'neck', and decreased at high flow rates when the tube itself offered resistance to flow.

Pedley et al. concluded that three factors in addition to tissue pressure were also important (Pedley et al., 1996). These were the degree of collapse of the vein, wall compliance and flow rate. They also suggested that the origin of tissue pressure lay in the thickness of giraffe skin (15 mm). An analysis of this last possibility found that the average thickness of head and neck skin from six different sites in a giraffe was uniform, 5.7±0.1 mm, and not different to its thickness in the legs (4.7±1.2 mm). The thickest skin was over the trunk (9.2±1.8 mm) (Mitchell and Skinner, 2004). However, giraffe skin is completely collagenous (Mitchell and Skinner, 2004) and can be assumed to be very inflexible.

We think that in order to account for the lower resistance in our model's jugular tube (1 mmHg l^{-1} min^{-1}) compared to that in a giraffe's jugular vein (6 mmHg l^{-1} min^{-1}) another factor is important. This factor is the viscosity of blood. Blood is four times more viscous than water and, therefore, from Poiseuille's equation, will offer higher resistance to flow. Thus tissue pressure, perhaps arising from inflexible skin, in addition to blood viscosity, are the most probable sources of jugular resistance in giraffe and are sufficient to create the inverse positive pressures found in them.

In summary our data combined with those from other studies have established that giraffe mean arterial (heart) pressure is a consequence of a baroreceptor-regulated mechanism that results in the generation of sufficient hydrostatic pressure to overcome gravitational effects, and to supply the head with blood at a pressure of ~100 mmHg. No siphon effect is needed. The counter-gravitational, positive, jugular venous pressures found in giraffes are a consequence of viscous resistance resulting from a combination of blood viscosity and tissue pressure.

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