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The Remarkable Cardiovascular System of Giraffes

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Abstract

Gravity affects the physiology of many animals, and the effect is, for good reason, most pronounced in tall species. The physiology—in particular, cardiovascular function—of giraffes has therefore captivated the interest of physiologists for centuries. Several studies document high mean arterial blood pressure of giraffes of about 200 mm Hg. This appears necessary to establish a cerebral perfusion pressure on the order of 100 mm Hg at the cranial end of the carotid arteries. Here, we discuss the unique characteristics of blood vessels, the heart, and the kidney of giraffes and how these functional and structural adaptations are related to very high blood pressure. We also discuss how the cerebral circulation of giraffes is established and what we know about how the blood flow and arterial and venous pressures in giraffes change when they stop to drink and subsequently lift their heads 5–6 m in one sweeping movement.

INTRODUCTION

Gravity affects many physiological functions, most notably in the cardiovascular system. Tall animals face particular challenges in supplying the brain with sufficient cerebral perfusion pressures, while tissues and organs below the heart may suffer extensive fluid filtration and edema as a result of excessive pressures. The challenges imposed by gravity on the cardiovascular system are obviously directly dependent on the actual height differences as well as any changes in body stature, such as the transition from the supine to the upright position in humans, or when animals lower the head to drink or forage at ground level. In these cases, which are often associated with translocation of blood volumes between different parts of the body, regulation of cardiac function and tone on the blood vessels serves an important role in ameliorating the changes in perfusion pressures in the various organs. Given the erect (and unusual) posture of humans, it is no surprise that the influence of gravitational force on the cardiovascular system, and the adaptations to changes in body position, represents an important part of the curriculum for all students of human physiology. The influences of gravity on human cardiovascular function, however, are benign compared to those affecting a giraffe, as males may reach a height of 5–6 m.

The peculiar anatomy of giraffes attracted attention in antiquity, and while influential anatomists, such as Sir Richard Owen (1) and Edwards Crisp (2, 3), provided anatomical descriptions of giraffes during the nineteenth century, virtually no physiological studies were conducted until Robert H. Goetz moved to South Africa in the 1930s after refusing to join the Nazi party in his native Germany. In the 1950s, Goetz and numerous esteemed colleagues established that giraffes have high blood pressure, i.e., an arterial pressure near the heart of around 200 mm Hg (4–7) (**Figure 1**), an observation that was supported by subsequent giraffe studies by Robert Van Citters and collaborators in the 1960s (8–10). These studies also showed that the arterial pressure near the head is about 100 mm Hg (**Figure 1**), which is similar to other mammals, and the high mean arterial pressure is likely a necessity to perfuse the brain (11, 12). After the studies by Van Citters and collaborators, the influence of gravity was studied by Alan Hargens, Kjell Johansen, and coworkers (13–15) and most recently by Graham Mitchell, John Skinner, and others (16, 17), as well as ourselves, with a large number of collaborators, during several expeditions to South Africa. The many different efforts, stretching over the past century, have revealed a number of cardiovascular adaptations in the heart and blood vessels of the tallest extant animal on Earth. Nevertheless, as we emphasize in this review, there are many unanswered questions to be addressed in the future.

In this review, we summarize the current understanding of the cardiovascular physiology of giraffes, with an emphasis on four major hemodynamic challenges: What are the arterial and venous pressures in the lower leg of giraffes, and how is leg edema prevented? Is the giraffe heart large consequent to high blood pressure? How does the kidney adapt to accommodate a renal arterial pressure of approximately 200 mm Hg? How do hemodynamic parameters vary as a consequence of the position of the head; i.e., what happens when giraffes drink?

HOW ARE GIRAFFES PROTECTED AGAINST DEPENDENT EDEMA?

With a vertical distance from the heart to the hooves of around 2 m, the intravascular pressure near the hooves would be expected to be ~150 mm Hg higher than at heart level, i.e., 350 and 150 mm Hg on the arterial and venous sides, respectively. Arterial and venous pressures near the hooves of a standing giraffe were reported to be ~260 mm Hg and 150 mm Hg, respectively (14), which is somewhat less than expected from gravity on the arterial side, but consistent with a gravitational effect on the venous side. We measured pressure profiles in the forelegs of anaesthetized, hoisted giraffes (18) (**Figure 2**) and reported pressure increases of 60 mm Hg/m and 83 mm Hg/m for the

Figure 1

Illustration of the blood pressure and arterial pressures in the heads of giraffes in different positions. In particular, the arterial pressure in the head of a drinking giraffe is only reported for one animal (8) and needs confirmation. Note that information on aspects of water homeostasis of giraffes is also apparent from the figure.

arteries and veins, respectively. This is consistent with a gravitational effect (74 mm Hg/m). With such high intravascular pressures, it becomes of interest to understand how dependent edema is prevented.

Large Veins

The femoral/tibial veins have bicuspid valves approximately every 3 cm (18) (this may also be the case in the brachial/median veins, but this has not been quantified) that must protect the capillaries during walking or running. This is emphasized by the dramatic finding that venous pressure in the giraffe leg varies between −250 mm Hg and 240 mm Hg during walking (14).

Conduit Arteries

On the arterial side, a number of morphological features ameliorate high capillary pressures. Goetz & Keen (6) were the first to report that the tibial arteries and metatarsal arteries have very thick media and a pinpoint lumen compared to the carotid artery. This was confirmed by Hargens et al. (19) and by us (18). It would be tempting to assume that this thickening of the media and reduction of lumen of the conduit arteries develop gradually with the progressive rise in arterial pressure from the heart toward the hoof. However, Kimani et al. (20) reported a

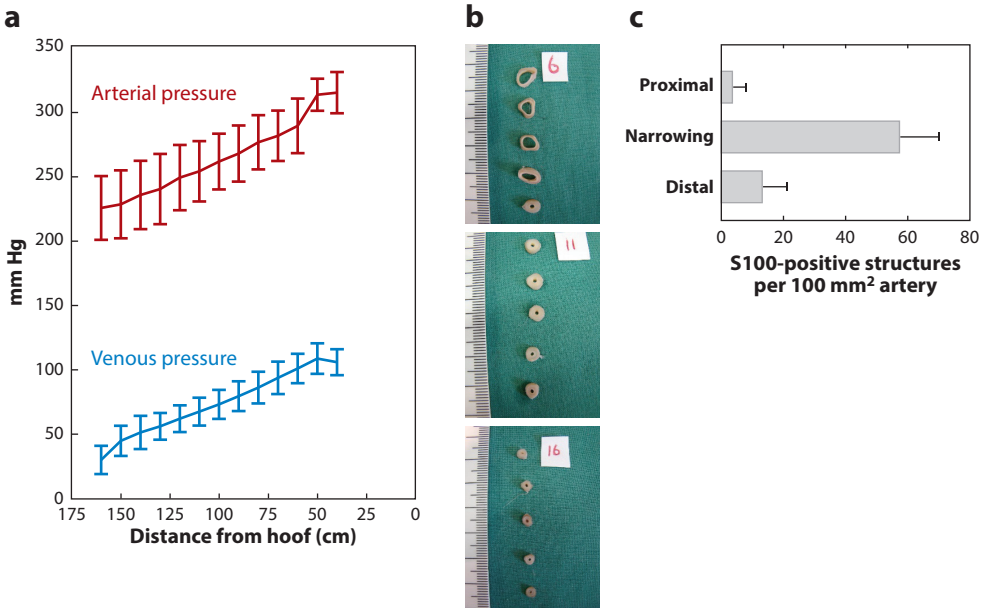

Figure 2

(*a*) The legs of the giraffe experience high arterial and venous pressures that may reach approximately 300 mm Hg and 130 mm Hg, respectively, close to the hooves. (*b*) Cross sections (2 cm between sections) of hindlimb arteries. The conduit arteries in the hind legs of giraffes exhibit an abrupt narrowing around the position of the knee where the lumen becomes very small within a few centimeters. The site of this narrowing is surrounded by smooth muscle and appears to function as a sphincter that provides viscous resistance to blood flow and establishes a pressure gradient. (*c*) The sphincter appears densely innervated by sympathetic nerves (stained with S100), and we propose that the pressure reduction in the large conduit arteries is regulated by the sympathetic nervous system. Figure based on data presented in Reference 18.

very abrupt transition from a typical conduit artery, with relatively thin media and large lumen, to an artery with thick media and small lumen in the tibial artery 2–4 cm below the knee. We confirmed this in the hind leg (18) and later in the median artery immediately below the elbow (21) (**Figure 2**). It was also shown that the first few centimeters of the thick-walled artery were more densely innervated by sympathetic fibers based on staining of Schwann cells with S100 (18, 20) or staining for tyrosine hydroxylase (21). The nerves were present near the media–adventitia border. However, some nerves penetrated into the media at the location of highest nerve density at the first part of the thick-walled artery. This could suggest that this section of the tibial and median arteries serves a sphincter-like function. A number of other features are associated with the transition (18). The thick media is consequent to an increased number of smooth muscle cells resulting in an increased number of smooth muscle cell layers, while the size of the individual smooth muscle cells is similar in the thick-walled and thin-walled conduit arteries. The density of vasa vasorum increases from the proximal part of the thick-walled artery to the distal part, and in the distal part the vasa vasorum penetrates into the media. Also, the volume fraction of elastin is substantially reduced from the femoral to the tibial artery, with the major reduction occurring in the transition between thin-walled and thick-walled artery.

The thick-walled artery provides dynamic hemodynamic resistance (21). In the anaesthetized, hoisted giraffe, viscous resistance provides a 10-mm Hg pressure decrease from the median artery

before the wall thickens to ~20 cm above the hooves. Under these conditions, an ultrasound recording of the artery revealed occasional spontaneous constrictions of the median artery, but the consequence for viscous pressure drop was unfortunately not recorded. Consistent with the sympathetic innervation, injection of norepinephrine in the proximal part of the median artery causes a constriction of the thick-walled part of the median artery. Sometimes only the first few centimeters constrict, consistent with the possibility that this segment functions as an arterial sphincter. In most cases, the whole median artery constricts with a 2- to 3-min delay after injection of norepinephrine. Immediately after injection of norepinephrine, before median constriction, the blood flow stops and, consequently, the viscous pressure drop of 10 mm Hg disappears. This most likely reflects a rapid constriction of the small arteries distal to the median artery and testifies to the substantial viscous resistance provided by these small arteries. After 2–3 min, flow reappears, and the median artery slowly (5–10 min) constricts. Associated with this, the viscous pressure drop between the proximal and distal part of the median artery slowly increases to ~30 mm Hg. This demonstrates the hemodynamic consequence of (sympathetically induced) constriction of the median artery. It would be of interest to know when this function of the "conduit" arteries in giraffe legs is important in free-ranging giraffes.

It could be hypothesized that the structural adaptation of the leg conduit arteries develops consequent to the high arterial pressure in the legs. This is most likely not the case, however, because the tibial arteries of both a neonate and 6-month-old calf had the sudden narrowing of the lumen and thickening of the wall as seen in adult giraffes (18), although in a second neonate the narrowing was not so obvious.

Small Arteries and Capillaries

The traditional resistance arteries with internal diameters of approximately 200 μm are also structurally modified. A comparison of muscular arteries from the lower leg, proximal neck, and distal neck revealed that the media became thicker and media thickness/lumen diameter increased the closer the small arteries were to the hooves (21). The isometric force produced by isolated segments of the small arteries from the lower leg would indicate that these arteries can constrict against a transmural pressure of ~500 mm Hg (21). Therefore, the large media thickness/lumen diameter of the small arteries in the lower leg undoubtedly contribute to the powerful constriction that may stop blood flow (as discussed above). In addition to the thick media of the small arteries in the legs, the basement membrane of capillaries in the leg is thick relative to the neck of giraffes (22), although this result is based on measurements in one giraffe. Presumably this may contribute to edema protection in the lower leg.

Osmotic Pressure and Tissue Compliance

High intravascular osmotic pressure would protect against edema. However, the osmotic pressure is ~25 mm Hg (14, 23), which is similar to the osmotic pressure of other mammals and cannot appreciably contribute to protection.

A low tissue compliance would also contribute to protection against edema. Hargens et al. (14) reported tissue pressure of 44 mm Hg in the lower leg, while tissue pressure in other parts of the giraffe was 1–6 mm Hg. We (21) later found similar values, which is consistent with a low tissue compliance. However, a more direct measure of tissue compliance is obtained by injection of a known fluid volume into the interstitium and measuring the resulting transient increase of tissue pressure. This pressure increase is approximately 5 times higher in the lower leg compared to the neck (21), strongly suggesting that there is a low tissue compliance in the lower leg, which contributes to the protection against dependent edema.

IS THE GIRAFFE HEART LARGE CONSEQUENT TO HIGH BLOOD PRESSURE?

Common knowledge holds that giraffes are endowed with extraordinarily large hearts to support their high blood pressure. This intuitive notion stems from the initial studies by Goetz & Keen (6) on a rather small cohort of animals. However, more recent studies show that this is not the case, and numerous independent measurements on a much larger number of specimens now agree that the giraffe heart constitutes approximately 0.5–0.6% of body mass (24–28). Ironically, and as pointed by Mitchell & Skinner (25), the "normal" cardiac mass of giraffes had actually been reported already in 1864 by Crisp (2, 3), and Cobbold (29) also remarked in 1854 that there was nothing unusual about the heart mass in a giraffe. Nonetheless, the fact that relative heart mass of giraffes resembles that of other mammals raises the interesting question of understanding how the giraffe heart generates the high blood pressure.

As emphasized by Seymour & Blaylock (30), wall stress in the left ventricle appears very similar among mammals of different body mass and can be evaluated using the principle of Laplace, such that the mechanical stress exerted on the ventricular wall is proportional to left ventricular pressure (PLV) and the radius (r) of the ventricular lumen, but inversely proportional to the thickness of the ventricular wall (Twall):

$$\text{wall stress} = (\text{PLV} \times \text{r})/(2 \times \text{Twall}).$$

On this basis, Mitchell & Skinner (25) proposed that the giraffe heart may have normal mammalian wall stress, despite very high pressures, if the giraffe heart is volumetrically small (i.e., a small radius of the ventricular cavity) and with proportionally thicker ventricular walls. Based on simultaneous measurements of intraventricular pressures by implanted catheters and visualizations of ventricular dimensions by ultrasound, Smerup et al. (26) demonstrated that this is indeed the case. Thus, the giraffe heart is characterized by a small left ventricular cavity, small ventricular radius, and a rather thick left ventricular wall that results in a wall stress resembling that of other mammals (26, 30). Smerup et al. also used the diffusion tensor imaging technique to track and visualize the orientation of the cardiomyocytes and found no evidence for exceptional adaptations in giraffes. The ability of the giraffe heart to maintain high blood pressure therefore seems to be explained by the thick myocardial wall and small left ventricular radius.

The ventricular anatomy of the giraffe heart resembles the cardiac remodeling of the human heart in response to hypertension, but it does not appear to be associated with myocardial fibrosis, and the rapid recovery of intraventricular pressures after each contraction indicates effective diastolic function (**Figure 3**). Consistent with this view, Smerup et al. (26) also reported a normal mammalian ejection fraction in the anaesthetized giraffes of 56%. The thick ventricular wall appears to develop as the giraffes grow, i.e., as the higher neck progressively increases arterial blood pressure (25). Smerup et al. therefore proposed the term concentric eutrophy as a suitable description for the giraffe heart.

While the concentric eutrophy of the giraffe heart leads to normal wall stress, the reduction in ventricular diameter and the normal ejection fraction mean that stroke volume is rather low in giraffes. This was indeed confirmed by ultrasonography and concurrent assessments of stroke volume from simultaneous measurements of cardiac output (by virtue of inert gas rebreathing) and heart rate. Given that giraffes do not appear to have higher heart rates than other similar-sized mammals (e.g., 8), cardiac output is relatively low. Apart from that by Smerup et al. (26), only two earlier studies provide measurements of cardiac output in giraffes. Using dilution of dye and the Fick method, Goetz et al. (7) measured a cardiac output of 48 and 78 mL kg^{-1} min^{-1} in

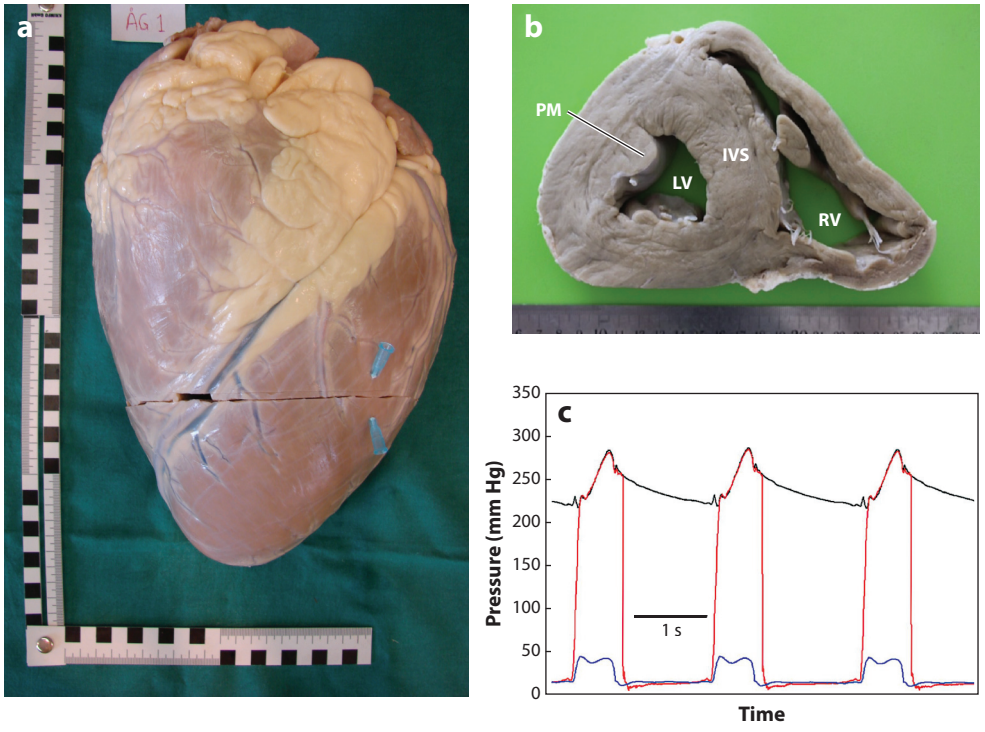

Figure 3

(*a*) The giraffe heart constitutes the same proportion of body mass (around 0.5%) as in other mammals but (*b*) has a thick ventricular wall and a small ventricular lumen. (*b*) A short-axis view through the giraffe heart at the level of the papillary muscles. (*c*) An original recording of aortic pressure (*black*), left ventricular pressure (*red*), and right ventricular pressure (*blue*) of an anaesthetized giraffe (pressure recordings from Reference 26). Abbreviations: IVS, intraventricular septum; LV, left ventricle; PM, papillary muscle; RV, right ventricle.

two individual giraffes. Linton et al. (31) estimated cardiac output in one giraffe using a lithium dilution technique and was surprised to find a low value of 25 mL kg^{-1} min^{-1}. This result, however, fits well with the value from our research (33 mL kg^{-1} min^{-1}) (26).

The low cardiac output imposes a potential limitation to systemic oxygen delivery and may mean that arterial-venous oxygen extraction is high and/or that oxygen demands of giraffes, i.e., both resting and maximal metabolic rates, are low. As an intriguing possibility, the long legs of giraffes may confer reduced costs of locomotion (32), and the low stroke volume due to concentric ventricular eutrophy needed to elevate blood pressure to perfuse the brain may in fact be possible due to the lower requirement for oxygen delivery given the long legs. This speculation needs to be investigated properly by measurements of field metabolic rate in freely moving giraffes, preferably in concert with measurements of cardiovascular responses to locomotion.

HOW CAN THE GIRAFFE KIDNEY WITHSTAND AN ARTERIAL PRESSURE OF APPROXIMATELY 200 mm Hg?

In humans, there is a close relationship between kidney function and blood pressure. Kidney disease can cause high blood pressure, and more importantly in connection with this review, high

blood pressure often damages the kidneys, although the mechanisms are not fully understood (33). Therefore, it is of interest to understand how giraffes have evolved mechanisms to protect the kidney. In the giraffe, the kidney is at the same horizontal level as the heart, and the pressure in the renal artery is therefore about 200 mm Hg. Such pressure would severely damage the human kidney.

Two studies have addressed the morphology of the giraffe kidney (34, 35) and merely found minor quantitative differences in comparison to other mammals. These differences include a relatively thin outer stripe and broad inner stripe of outer medulla and pelvic extensions that reach almost to the cortex. None of these morphological characteristics provide a clue about how the giraffe kidney is protected against the high arterial pressure.

High arterial pressure might contribute to an increased glomerular filtration rate (GFR), because the transmural pressure over the glomerular capillary wall is a key factor for GFR. We therefore determined GFR in anesthetized giraffes through measurements of the clearance of sinistrin. Surprisingly, GFR was low—about 40% lower than the predicted value from the scaling relationship—and less than 50% of that measured in horses of similar size (35). This would indicate that the hydrodynamic resistance from the renal artery to the glomerular capillary is large, the Bowman capsule pressure is high, the total surface for filtration is small, the capillary permeability is low, or a combination of these factors. Another potential explanation would be high osmotic activity of plasma, but as already mentioned giraffe plasma osmolarity is about 25 mm Hg, as in other mammals (14, 23). If the filtration area or capillary permeability were small, the filtration fraction could be expected to be low. We therefore calculated the filtration fraction from GFR and effective renal plasma flow [renal plasma flow was determined from the clearance of para-aminohippuric acid (PAH)]. The filtration fraction of giraffes is not different from other mammals, making it unlikely that the low GFR is explained by small filtration areas or capillary permeabilities (35). To obtain some information on the renal hydrodynamic resistance, ultrasound recordings of renal blood flow were made. From these measurements the resistive index, calculated as (peak systolic flow–end diastolic flow)/(peak systolic flow), was shown to be low in giraffes. The interpretation of this is ambiguous (36–38), and it is possible that the low resistive index reflects the hemodynamic situation of giraffes with high mean blood pressure but somewhat normal pulse pressure relative to other mammals rather than a low hydrodynamic resistance in the kidney. From the renal arterial and venous pressures, the effective renal plasma flow, and the hematocrit it is also possible to calculate the vascular conductance in the kidney. The conductance may be 40–50% lower in the giraffe compared to the human kidney. If this low conductance reflects changes in the afferent arterioles (but this is unknown), it would lead to an increased pressure drop in the giraffe and thereby bring the capillary pressure closer to the values of other mammals. There is also evidence that the Bowman capsule pressure may be higher in giraffes compared to Bowman capsule pressures in other mammals. At least the interstitial pressure in the medulla measured in anaesthetized giraffes was 45–50 mm Hg, and it seems likely that Bowman capsule pressure may be around the same value, which is much more than the 0–5 mm Hg seen in other mammals. Thus, although it is not known why giraffes have a low GFR, the most likely explanation is that the filtration pressure in the glomeruli is small despite the high pressure in the renal artery.

The high interstitial pressure would indicate that the pelvic pressure and renal vein pressure should also be high to prevent them from collapsing, which is indeed the case. Renal pelvic pressure is about 40 mm Hg (and ureter pressure 5 cm proximal to the bladder is 24 mm Hg), and the renal vein pressure is 32 mm Hg. The pressure decreases 12 mm Hg from the renal vein into the caval vein, which has a pressure of 20 mm Hg. At the ostia of the tributaries of the renal vein, and where the renal vein enters into the caval vein, membranous (nonmuscular) valves are present. The semilunar valve at the junction of the renal vein and caval vein may direct the high-pressured venous blood from the kidney toward the heart. The role of the tributary valves is unknown.

The high venous pressure of the renal vein may also relate to a structural feature of 2 cm of the caval vein around the inlet of the renal vein. At this stretch of the caval vein, the wall is 3–4 times thicker than near the atria and near the confluence of the iliac veins. Furthermore, the density of smooth muscle is about two times higher at this site than in other parts of the caval vein. It is tempting to speculate that this reflects the arrival of the high-pressured venous blood from the kidney.

Finally, the giraffe kidney capsule is about twice as thick as that of the cow and has a higher density of collagen per capsule area. This confers the giraffe capsule higher strength compared to that of the cow; however, when normalized for collagen content the strengths of the giraffe and cow capsules are similar. Based on the biomechanical measurements it is possible to calculate the burst pressure, which is 600–650 mm Hg for giraffes compared to only 125 mm Hg for cows (35). It is not known why such a high burst pressure of the renal capsule is necessary.

HOW ARE CEREBRAL ARTERIAL PRESSURE AND FLOW CONTROLLED?

Arguably, the most pressing question relates to how the cerebral circulation is controlled and protected when giraffes lower their head to drink and, similarly, how cerebral perfusion is maintained when giraffes lift their heads again—a smooth movement that is completed within 1–2 s.

Even the basic concept of how the cerebral circulation is established at rest has created debate. One school suggests that a siphon mechanism, where the blood flows down the jugular vein, helps draw the blood up through the carotid artery and thereby reduces work by the heart (39–44). Another group maintains that the flow of blood down the partly collapsed jugular vein provides no support for the heart, and the heart works against gravity when lifting blood through the carotid artery (14, 45–49). The discussion has been based on the assumption that the jugular vein of giraffes is partly collapsed in the standing position, and many of the discussions have been based on the behavior of mechanical models rather than actual measurements (7, 45, 47). The collapsed jugular vein was later confirmed with ultrasound in anaesthetized hoisted giraffes (24), where only a small lumen of the jugular vein is seen when the head is in near vertical position (**Figure 4*a***). In contrast, the jugular vein lumen is large when the head and neck are in the horizontal position, which reflects accumulation of blood in the jugular vein (**Figure 4*a***). From an energetic point of view, there is no doubt that the heart needs to produce about 200 mm Hg—the systemic blood pressure of giraffes (5–10, 14, 17, 24)—to provide an arterial pressure of about 100 mm Hg at the entrance to the brain (5–10, 14, 17, 24). In the section on the heart, we have already explained why this does not provide an extraordinary strain on the heart. Interestingly, the pulmonary pressures are reported to vary between 30/10 mm Hg and 50/22 mm Hg (7, 8, 26). In contrast to systemic blood pressure, pulmonary blood pressure is therefore—as expected—close to that of other mammals. The high-energy content of the blood provided by the left ventricle is lost as viscous resistance. Part of this resistance resides in the small arteries and capillaries of the neck and head. However, the collapsed jugular vein (24) also provides substantial viscous resistance, which matches the conversion of potential energy of the blood flowing down the jugular vein to hydrostatic pressure energy. Thus, venous pressure along the jugular vein falls slightly (14) or stays constant (24) rather than increasing, as would be expected from the conversion of potential energy to hydrostatic pressure energy close to the heart.

In relation to this discussion, one question is whether giraffes have high hydrodynamic peripheral resistance and, surprisingly, it has been suggested that they may have low peripheral resistance (49). A measure of total peripheral resistance requires measurements of cardiac output and blood pressure. There is no doubt that the blood pressure of giraffes is substantially higher than that of

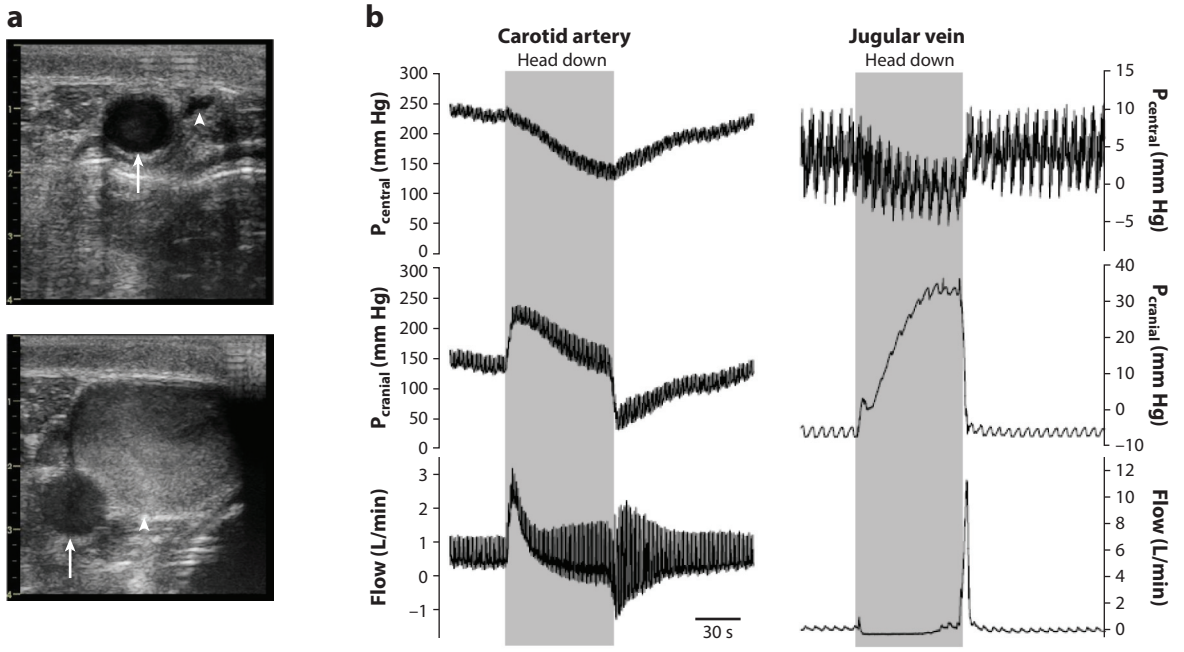

Figure 4

(*a*) Ultrasound recording of the carotid artery (*arrows*) and the jugular vein (*arrow heads*) in an anaesthetized giraffe. Top image with head in vertical position; bottom image with head in horizontal position. (*b*) Original measurements of flows and pressures in the carotid artery and the jugular vein of a hoisted and anaesthetized giraffe where the head is lowered to immediately below heart level and raised again after 1 min. Figure adapted with permission from Reference 24.

similar-sized animals, and as discussed in the section on the heart, the cardiac output is less than in similar-sized animals. Therefore, the total peripheral resistance calculated as (blood pressure)/(cardiac output) is substantially increased in giraffes compared to similar-sized animals, and this "causes" the high blood pressure.

The question of how the circulation of the head is protected when giraffes drink has not been addressed in detail experimentally. One behavioral protective measure is, however, easily observed in a drinking giraffe. Since the neck is shorter than the legs, giraffes either spread the forelegs or bend them when they drink (**Figure 1**). This brings the heart closer to the ground (and reduces the vertical distance between the heart and head), and the hydrostatic pressure in the neck and head vasculature is therefore less than it would have been, had the heart remained in the same horizontal position as in the upright giraffe. In 1966, Van Citters et al. (10) measured carotid pressure (ca. two-thirds of the way up the neck, 40 cm from the jaw) in two free-ranging giraffes using telemetric equipment. In a subsequent and equally impressive paper, Van Citters et al. (8) reported a pressure increase from ~130 mm Hg to ~300 mm Hg in one giraffe during drinking (**Figure 1**). They also stated that the jugular pressure and cerebral spinal fluid pressure "tended to vary in the same direction as distal carotid artery pressure during postural changes" (8, p. 301). Interestingly, head lowering was accompanied by a reduction in arterial pressure at heart level and heart rate. Apart from this, we know nothing about pressure changes at both the arterial and venous sides during spontaneous drinking in awake giraffes. However, in a notable study, McCalden et al. (50) investigated the pressure-induced autoregulation of flow in the carotid arteries of giraffes. In these experiments, changes in blood pressure were induced by angiotensin II injections

in sedated giraffes placed in a sternal position, and pressure and flow were measured in the carotid artery. Remarkably, the flow was not significantly changed when arterial pressures ranged from 70 to 210 mm Hg. This autoregulatory range is substantially larger than that in other mammals and strongly suggests that the increase in arterial pressure when the giraffe lowers its head to drink is associated with vasoconstriction in the head (and possibly neck). With this background, it is surprising that researchers have suggested that cranial resistance increases when giraffes raise their heads (49) and the pressure decreases. This seems counterintuitive, but it was suggested that extracranial vasoconstriction could shunt the blood away from the extracranial circulation to support the brain. The statement (49) is based on a review of measurements (17) from three earlier studies (9, 16, 50). However, data from one of these studies (50) suggest that the resistance increases when the head is lowered, while data from two other studies (9, 16) suggest that resistance increases when the head is lowered. For all three studies, the experimental details provided are limited, and it is difficult to evaluate the experimental background for the statements and therefore why they yielded different results. The role of a baroreceptor function is also limited, although evidence for a carotid body has been provided (51). There is also evidence that the carotid artery and the internal maxillary artery, which provides blood to the brain, have substantial sympathetic innervation (52) that appears to extend into the smaller arteries in the head (53). It is therefore likely that a baroreceptor-mediated effect may also contribute to protection of the circulation in the head.

More recently, we measured jugular, central, and cranial carotid pressures and flow in hoisted, anaesthetized giraffes while the neck and head were lowered from a near vertical position to a horizontal position for 1 min and then lifted again (24) (**Figure 4*b***). Lowering of the head to the horizontal position was associated with a slow reduction of the central carotid pressure, amounting to ca. 60 mm Hg over the 1 min. This is consistent with earlier findings by Goetz et al. (7) and Van Citters et al. (8) in free-ranging giraffes. The cranial arterial pressure increased more than 50 mm Hg within a few seconds and then slowly fell, over the course of a minute, toward a pressure resembling that of the head in the upright position (**Figure 4*b***). The cranial venous pressure increased slowly by around 40 mm Hg when the head was lowered. In addition, when the head was lowered, the arterial flow transiently increased over the initial 30 s, whereupon it returned to the value in the upright position. The flow in the jugular vein virtually ceased when the head was lowered, leading to a progressive filling and distension of the vein. The accumulation of blood caused a dramatic, transient surge of blood flowing toward the heart as soon as the head was returned to the upright position. This confirmed the pooling of venous blood in the jugular vein that was suggested many years earlier by Goetz et al. (7) and could be visualized by ultrasound; the jugular vein, which was large and full of blood when the head was lowered, collapsed quickly toward a small lumen as soon as the head was lifted (24). These findings show that it may be problematic to use the Poiseuille equation to calculate resistance during head movements because of the nonsteady-state situation of blood flow and arterial pressure. However, 1 min after lowering of the head, at steady state, the perfusion pressure of the head and the flow to the head were similar to the perfusion pressure and flow with the head in the upright position. Consequently, there was no indication of a change in hydrodynamic resistance. Because the arterial pressure was similar in both situations, there is no stimulus to the baroreceptors, which appear to be located in the distal part of the carotid (51), and no stimulus for a myogenic response. Therefore, the unchanged hydrodynamic resistance may be expected. However, it is highly likely that the hemodynamic events differ substantially in an awake giraffe that voluntarily lowers its head to the ground to drink. Thus, there is clearly a need for obtaining measurements of jugular and carotid pressures and flow under these conditions. The reason for the reduction of blood pressure when the head is lowered is most likely due to the storage of blood in the veins of the neck, which would lead to a

reduction of diastolic filling and a reduction of stroke volume (24). In this manner, the relocation of central blood volume in the drinking giraffe resembles the hemodynamic changes that occur when humans move from a supine to standing position.

Van Citters reported (8) that arterial pressure at the head falls "precipitously" when the head is raised after drinking. This suggests that the perfusion pressure for the head falls. However, evidence from anaesthetized giraffes suggests that the venous pressure at head levels also falls (24), which supports a maintained perfusion pressure. Based on a comprehensive series of experiments with a mechanical model of the circulation of the giraffe head, Mitchell et al. (54) concluded that a noncollapsible venous drainage, perhaps via the vertebral venous plexus, where a negative pressure could be generated, and a diversion of blood from the extracranial part of the head to the brain could be important protective mechanisms against reduced blood flow to the brain when the head is raised.

Rete Mirabile

Almost all species of the mammalian order Artiodactyla (the even-toed ungulates), to which the giraffe belongs, have a specialized vascular structure called the rete mirabile (55). The rete is an extensive, subdural branching of the internal maxillary artery, i.e., a meshwork of arteries, embedded in a venous sinus. The venous sinus receives blood from the anterior cerebrum and meninges and cooler blood from the facial veins. The rete provides the major arterial blood supply to the brain and meninges and functionally replaces the internal carotid artery. There is little doubt that the rete contributes to brain cooling in other artiodactyls (see 56, 57); however, the role of the rete in temperature regulation needs to be confirmed in giraffes (58). The rete may be hemodynamically important by protecting flow and pressure in the brain during sudden increases of pressure (8, 59). However, no convincing description of how this should be achieved has been provided, and arguments against a role of rete in control of cerebral circulation have also been voiced (6). Recently, the rete's importance in changes in arterial pressure, hemodynamic resistance, and shear stress during changes in input pressure to the rete was tested in computational models (60). This comprehensive discussion of the potential hemodynamic consequences concluded that the rete is unlikely to play a role in regulating cerebral arterial pressure and flow. It may therefore be suggested that the rete is unlikely to play a protective role in relation to cerebral hemodynamics when giraffes lower their heads to drink. This conclusion was further supported by the paucity of sympathetic innervation of the arteries in the rete (52).

SUMMARY POINTS

1. Giraffes have a mean pressure of about 200 mm Hg and an arterial pressure at the head of about 100 mm Hg.
2. A sphincter-like structure in the conduit arteries at the knees and elbows, in combination with thick-walled small arteries in the legs, protects the lower limbs against high arterial pressure.
3. The heart relative to the body weight of giraffes is similar to other mammals despite the high blood pressure, but the cardiac output is low and therefore the energy expenditure of the heart (relative to body weight) is similar to other mammals.
4. The kidney has a strong fascia and high interstitial pressure, which reduces filtration pressure, and the renal vein and the caval vein at the entrance of the renal vein are structurally adapted to high (about 40 mm Hg) venous pressure.

5. There is no good understanding of how the hemodynamics of the head is controlled when the head is lowered to drink and lifted again after cessation of drinking. Storage of blood in the veins of the neck and head, baroreceptor-mediated control of vascular tone, noncollapsible vertebral veins, and venous valves in the jugular veins are elements that likely play a role.

FUTURE ISSUES

1. Research should provide an understanding of when the sphincters of the conduit arteries at the knee and elbow are activated in free-ranging giraffes.
2. We aim to understand whether the low cardiac output of the giraffe is associated with enhanced extraction of oxygen or whether the metabolism of giraffes is unexpectedly low.
3. It is critical to discern whether the afferent arterioles of the giraffe kidney exert an unusually high hydrodynamic resistance.
4. We need to describe hemodynamics, i.e., the central and distal pressure and flow in the jugular vein and the carotid artery, when giraffes lower their heads to drink and lift them again after cessation of drinking.

DISCLOSURE STATEMENT

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