Review



# Cardiovascular Response to Exercise in Vertebrates: A Review

Antonio López-Román , Elena Jiménez-Herranz * , Francisco Javier Calderón-Montero , Juan José Ramos-Álvarez , Raquel Gómez-Lucas

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# Cardiovascular Response to Exercise in Vertebrates: A Review

**Antonio López-Román [1]; Elena Jiménez-Herranz [2,*]; Javier Calderón-Montero [3]; Juan José Ramos-Álvarez [2] and Raquel Gómez-Lucas [1]**

[1] Veterinary Clinical Hospital. Faculty of Health Sciences. Alfonso X el Sabio University. Villanueva de la Cañada (Madrid).
[2] School of Sport Medicine. Complutense University of Madrid.
[3] Faculty of Physical Activity and Sports Sciences. Madrid.
* Correspondence: mariaelj@ucm.es; Tel.: 913947079; Escuela de Medicina del Deporte. Universidad Complutense de Madrid. Plaza Ramón y Cajal nº 1, 28040-Madrid.

**Abstract:** Exercise is the greatest stress for the cardiovascular system, not only for the human being but for the rest of vertebrates. For this reason, the cardiovascular response cannot be considered as only one "anthropocentric" meaning. The adjustment of cardiac output to exercise in the five large groups of vertebrates is highly variable. The response of the heart rate and the stroke volume as the main two basic factors that determine the increase in cardiac output is also highly variable. The difference in the range of heart rate is difficult to determine in many vertebrates, both at rest and maximum effort. The increase in stroke volume also differs among vertebrates. For example, while rainbow trout and leopard increase their stroke volume by increasing final diastolic volume (Frank Starling's law), humans do so at the expense of both increasing final diastolic volume and reducing final stroke volume (contractility). The variation in arterial pressure that occurs during exercise also differs considerably among vertebrates. Large differences in cardiovascular response between different vertebrates could be related to their habitat or living environment. This review aims to analyze the cardiovascular response to exercise, as the most common stress condition in vertebrates.

**Keywords:** vertebrates; arterial pressure; cardiac output; exercise; heart rate; stroke volume

## Introduction

Human interest sport medicine and exercise physiology began in the 19th century. Some decades after, other athletic mammals received some attention, such the racing horses, dogs and camels. In general terms, exercise is the greatest stress for the cardiovascular system, not only for the human being but for the rest of vertebrates. For this reason, the cardiovascular response cannot be considered as only one "anthropocentric" meaning. Athletic performance relies on the aerobic capacity to generate energy for the exercising muscles, and this is facilitated by an increase in resting heart rate, the ability to increase cardiac output (Q) and cardiac stroke volume, among other factors [1]. However, research on the cardiovascular response in vertebrates has serious limitations since its study is conditioned and limited by the methods needed for its assessment, such as stress tests, and the different models of locomotion (aquatic, terrestrial, aerial and their combinations) in the different groups of animals. Therefore, different types of ergometers should be used, such as treadmills, flight tunnels, swimming tunnels and running wheels. Other ways to measure the cardiovascular response to physical exercise are thermal stress due to cold or the straightening reflex [2,3].

Vertebrates that carry out enormous migrations from a few days to weeks [4] need to increase their metabolism eightfold in birds [5] and up to fifteen-fold in salmon [6], having to adjust their cardiovascular system correspondingly to sustain such considerable metabolic activity. Migratory birds maintain a high level of cardiovascular activity similar to the energy cost of a marathon competition in humans, ranging between 62 and 100% of maximal rate of oxygen consumption (VO2max).

The general characteristics of the cardiovascular system in vertebrates has previously been described [7] and can be summarized as follows:

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- Throughout the evolutionary process all vertebrates have possessed a myogenic heart with evident intrinsic activity, although there are exceptions in the fish that have more than one heart. This intrinsic activity of the heart has been demonstrated in the vertebrate precursors, tunicates and cephalochordates.
- Blood flows from the heart to the head and there are also one-way valves, which open and close according to the direction of the blood flowing through them. The venous valves are considered a "passive" system.
- The blood vessels show vasomotor activity, so that the changes in the degree of contraction of the smooth muscles alter the peripheral resistance, the variations in blood pressure and the storage of blood in the periphery.
- Although with certain limitations, the cardiovascular system can be functionally considered as a closed system.

Apart from the general characteristics already mentioned, extraordinary inter and intra-variations occur between the 5 mean groups in which vertebrates are divided (fishes, amphibians, reptiles, birds, and mammals) regarding their cardiovascular response to exercise.

In general, in the closest living relatives of vertebrates, tunicates and cephalochordates, blood is transported in well-defined vessels to numerous separate vascular beds. There are notable differences in the fish division, as for example, some classes of them can breathe atmospheric air for a certain amount of time [8].

The heart of amphibians has two anatomically divided atrium (left and right) that receive blood from the lungs and the systemic venous circulation and that enters to a highly trabeculated and undivided ventricle. The trabeculae, that form deep sacs, collect and retain blood during diastolic filling, providing a mechanism that seems to allow partial separation of the blood during this last phase and even while the blood is being expelled during systole [9]. However, there are notable differences between the two main classes of amphibians: anura (frogs and toads) and caudata (for example the salamander) [10].

The differences among the classes of reptiles have been analyzed previously [11]. The cardiovascular system of non-crocodilian reptiles is a paradigm of intracardiac shunting [7]. The anatomical complexity of the heart and central circulation of reptiles is such that the systemic and pulmonary systems are connected in parallel. The physiological consequences of an intermittent breathing pattern, whether in terrestrial or aquatic activities, have been extensively investigated [12].

The cardiovascular shunts have been adquired during as an adaptation associated with low metabolic activity and intermittent forms of apnea, especially in ectotherms vertebrate. The single ventricle of these vertebrates is partially divided by a ridge and have a spiral valve that expells the blood from the ventricle according to the systemic and pulmonary vascular resistance. Although there are two separate atria, the existence of a single ventricle with this valve device allows the pulmonary and systemic venous blood to be mixed. Therefore, vertebrates with undivided ventricle can perform right-left or left-right shunts. Possible theories regarding the functions of these derivations have been described by Burggren et al., which give them a holistic and integrative sense [13], and may have several implications during exercise. In general, increasing exercise intensity results in cardiovascular bypass [14,15]. The right-left shunt allows the recirculation of venous blood to re-enter into the systemic circulation and as a consequence a decrease in oxygen saturation, while the left-right shunt produces an increase in oxygen saturation and an improvement in tissues oxygenation in reptiles [16,17], aquatic anurans [18,19] and air-breathing fish [20–22]. During exercise, non-crocodilian amphibians and reptiles have a net left-right shunt [2].

The heart of the crocodile is an example of extracardiac shunting, preventing the mixing of blood in the heart, which is common in other reptiles and amphibians, as the cardiovascular shunting is produced outside the heart [23].

Finally, the cardiovascular system of birds and mammals is completely divided in a pulmonary circuit that leaves the right ventricle to irrigate the lungs through the pulmonary artery at low pressure and a systemic circuit that originates from the left ventricle through the aorta at high pressure to perfuse the rest of the body. However, comparisons of the cardiovascular anatomy among genera and families, both of birds and mammals, reveal some differences [24].

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Heart rate is determined by the activity of the heart pacemaker and different factors (temperature, acetylcholine, adrenaline and calcium) which modulate its electrical activity via the nervous or hormonal pathways. Stroke volume (SV) is determined by contractility and the characteristics of the ventricle, mainly with regard to its filling capacity. Similarly, the control of the SV is accomplished by two different pathways (nervous and hormonal).

Although there are many common anatomo-functional characteristics in all vertebrates, the cardiovascular requirement in the 5 groups of vertebrates is highly dependent on the type of circulation and the environment in which it operates.

The "amplitude" of the cardiovascular response is difficult to define because, with the exception of vertebrates used in experimentation, the values of rest and maximum exercise are not very precise.

Previous reviews have focused on factors that limit the exercise performance in vertebrates, without emphasizing in cardiovascular responses [2,3].

The aim of this review is to analyze the cardiovascular response in vertebrates according to hemodynamic parameters and the general hemodynamic equation que indica que la mean arterial pressure es igual al product del cardiac output por total peripheral resistance. The adjustment of the circulatory parameters to exercise experiences great variation among vertebrates due to their body structure and other conditions that determine the adjustment of cardiac output and total peripheral resistance. The variation of the parameters that determine cardiac output (cardiac output = stroke volume x heart rate) is highly variable in the 5 groups of vertebrates. While a number of vertebrates increase cardiac output by increasing stroke volume, others do so by increasing heart rate.

**Adjustment of the heart rate to exercise in verebrates**

Pacemaker rate and heart rate (HR). As mentioned, all vertebrates have a pacemaker. The heart activity is modulated by neural and hormonal factors. The intrinsic rate of the pacemaker shows important differences among the distinct groups of vertebrates [25]. Although all problems related for determining resting HR (temperature, arrhythmic ventilation and definition of the resting state), the differences are related to phylogeny, body mass and temperature and, to a certain extent, the capacity to perform exercise [25].

It has been demonstrated that there is an allometric relation with an exponent of -0.25 between body mass and resting HR, being maximum in birds and small mammals [7]. This relation reflects the great difference in HR between the smallest birds and the largest mammals (table 1). The differences of such magnitude can be due in part to the differences in the conductance of sodium (Na+) that establishes the slope of the potential of slow depolarization in the pacemaker cells [25,26].

Although the data is scarce, there is an allometric relation with a similar exponent in snakes and frogs. Resting HR in fit horses, for example, ranges from 30 to 40 bpm, and from 50 to 60 bpm in athletic humans under the same conditions. Based on limited data, maximum HR (HRmax) during exercise for the majority of the lower vertebrates is 120 beats per minute. Tuna is the only known exception to this generalization, as a maximum HR of more than 200 beats/minute has been found [25].

This higher limit of the HR in the lower vertebrates seems to be independent of body mass, which may reflect a phylogenetic restriction related to the pacemaker rate or the modulating mechanisms [25,26]. Given the recognized scale of HR to body mass, it is probable that the highest HR values are found in early development when the animal is a neonate or still relatively young.

In the studied vertebrates HR and its adjustment to exercise show notable differences, and it could be influenced by several intrinsic factors, as age, as it has already been evidenced in human beings [27]. As illustrated in Table 1, fish, amphibians and reptiles show a limited range of heart rate adaptation [28]. This may be due to the fact that the environment in which they live do not require them to considerably alter their cardiovascular system, that is, increase their cardiac output (Q). Another possible explanation could be that the adjustment of Q is produced by the Frank-Starling mechanism or contractility. Finally, the small increase in HR in response to exercise in these vertebrates may show the increase complexity of the control mechanisms that alter HR throughout evolution.

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During strenuous exercise en el que se alcanza un maximal oxygen consumption (VO2max conditions), Thoroughbred horses are able to reach a HRmax close to 220 bpm, and maximum values ranging from 180-200 bpm have been found in human beings at a similar exercise intensity. These data show the ability to increase the HR from rest to maximal exercise intensity in order of ten and of three to fourfold in the equine and human species, respectively [29,30]. These cardiovascular adjustments in response to exercise are one of the factors that may limit the maximum oxygen consumption in vertebrates (VO2max) [1,2,31].

The index Q (volume of blood expelled by the heart each minute) depends on HR and the stroke volume (SV) so their increase during exercise produces a rise in Q. This response is shown in a greater extent in the equine species than in human beings, and it explains the enormous magnitude of the peak aerobic power in the horse compared to the elite human athlete [32].

Control of the heart rate. The control mechanisms (endocrine and nervous control) seem to show an evolutionary tendency. Catecholamines are common in all vertebrates, but adrenergic cardiac innervation is absent in cyclostomata and elasmobranchii. Thus, from an evolutionary perspective, tachycardia mediated by adrenaline seems to have acquired greater importance in birds and mammals. Cholinergic inhibition of HR is mediated by the muscarinic receptors, affected by a cardiac branch of the vagus nerve, and is found in all vertebrates except some fish [33,34].

Resting HR is influenced by both autonomic and non-autonomic stimuli. Horses and young people are predominantly under parasympathetic control that tends to shift to a sympathetic predominance as aging progresses [35–37]. This modification could be due to a decreased parasympathetic or an increased sympathetic nervous system input, as well as an adjustment in plasma volume and cardiac filling pressure [38], or a combination of all these factors.

**Adjustment of the stroke volume to exercise in vertebrates**

As shown in Figure 1, SV is under the control of the Frank-Starling mechanism and contractility. The participation of each of the mechanisms in different vertebrates depends on several factors as follows:

The Frank-Starling mechanism: The Frank-Starling curves or the curves of ventricular function have been established in several groups of vertebrates (Figure 2) [25]. The right ventricle of mammals is more sensitive to filling pressure than the left ventricle. It is not known if there are differences in the sensitivity of the right and left sides of the heart to filling pressure in amphibians and non-crocodilian reptiles perhaps to help with intracardiac shunting [13].

Pulmonary arterial pressure in reptiles is several times higher than that of mammals when pulmonary blood flow increases [7]. Amphibians, reptiles, birds, and mammals generally increase HR to a greater extent than SV. However, it is well documented that human and equine exercise training increases VO2max, but not HRmax [38,39], so that increases in maximal Q must be due primarily to an increase in SV.

Small increases in SV (10%-30%) are observed in humans during exercise [40]. Thoroughbred horses are exceptional, doubling SV and tripling HR they produce an up to sixfold increase in Q. In these animals, it's been identified an increase of SV from 1000 ml at rest up to 1700 ml at maximal exercise, consequent to an increase in blood volume, venous return and filling pressures according to the Frank-Starling mechanism [41]. In the species in which SV does not appreciably increase with exercise, the heart probably operates at the top of the Frank-Starling curve during the resting eupneic conditions. The Frank-Starling mechanism also ensures a long-term balance between the Q of the right and left ventricles in the heart of mammals. Some amphibians and reptiles show slight decreases in SV during exercise associated with increases in HR. The greatest changes in SV in reptiles and amphibians are decreases associated with apnea. The greatest decrease in SV seen in these animals is associated with apnea required during their physical effort in water [3].

Several fish, including cyclostomata and teleosts, in contrast to other vertebrates, increase SV twofold during exercise [42]. The Frank-Starling mechanism clearly has functional importance in terms of this increase. In fact, fish seem to depend on the modulation of the heart rate (HR) to produce the increases in Q that accompany aerobic exercise [25,43]. These differences in the SV response in

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fish may be a consequence of one of the following factors: 1) a greater sympathetic control of the HR, 2) the atria becoming less sensitive to filling pressure, 3) a greater degree of sympathetic control of the tension in the vein walls and 4) better shortening fraction.

Regarding the above-mentioned factors, it is worth noting that the hearts of fish are almost ten times more sensitive to filling pressure than that of mammals (that is 1-2 mm Hg vs. 10-20 mm Hg for a maximal response), and this in turn may be related to the atria chamber of fish, which is anatomically separated, has thinner walls and is more distensible [7]. Moreover, intracardiac shunting may require a stricter regulation of the dimensions of the ventricle, thus limiting SV but not HR [13].

Contractility. Contractility is an easily defined cardiac function, which is difficult to assess. Contractility is defined as the change undergone by the ventricle or atria when the parameters that can affect myocardial performance (HR, filling volume and pressure and arterial diastolic pressure) are kept constant. The most accurate assessment is through the peak derivative of left ventricular pressure in relation to time, LVdp/dt, and seems to rise progressively with exercise intensity, but remains unchanged with training [7].

It has been shown that the values for mammals and tuna are five times higher than those of teleosts (370-480 mm Hg/s), while the values of the cyclostomata (22 mm Hg/s) and sharks (30 mm Hg/s) are ten times lower. Intermediate values have been recorded for lizards (95-180 mm Hg/s) and anura and the bufo marinus (toad) (60 mm Hg/s and 110 mm Hg/s) [43].

These differences may be due to the following factors:

- Heart rate. Maximum isometric tension decreases with the increase in the frequency of electrical stimulation [33,44]. This inverse relation between contraction rate and maximum isometric tension (Tmax) is called the “negative staircase”.
- Temperature. The action potential duration and Tmax decrease with an increase in temperature, that is Tmax decreases at high temperature as a result of a shorter action potential duration [44].
- Beta-adrenergic stimulation in the cardiac strips of frogs and fish severely increases T max [33,44].
- Extracellular calcium and other inotropic agents. The gradient for Ca2+ through the sarcolemma increases when a rise in extracellular [Ca2+] occurs [45,46], so an increase of extracellular [Ca2+] in the range of 1-9mM triggers an increase in the Tmax of the cardiac muscle. Many other inotropic agents are known, but their relative importance in vivo is not always clearly defined. Negative inotropic effects can be produced with hypoxia, acidosis, acetylcholine and other molecules [47].
- Homeometric regulation, described as the capacity of the cardiac muscle to maintain the blood flow independently of the development of pressure, in contrast to heterometric regulation (Starling’s Law). This factor is well documented in hearts of several classes of fish and may be one of the causes for the SV to be unaffected by alterations in vascular resistance in spite of the change that accompanies cardiac functioning [25].

The result of Starling’s Law and ventricular performance in different vertebrates. Associated to the contractile activity and the relation length/pressure, SV increases as a result of the increase in end diastolic volume (EDV) and decrease in end-systolic volume (ESV), as SV is the difference between them (SV=EDV-ESV). The ventricular ejection fraction in the rainbow trout is normally near 100% [48] and that of the leopard shark 80% [49]. Therefore, the substantial increases in SV that occur in fish are the result of the increases in EDV. In amphibians and reptiles, the duration of the systole is 50% of the cardiac cycle, which potentially leads to a small ESV which can be fundamental for intra-cardiac shunting [13,50]. At high HR, there is a reduction in the filling time that can explain the reduction observed in the perfused rainbow trout heart. Similarly, an increase in HR of 120 beat/min to 180 beats/min in dogs has little effect on Q due to the reduction of the SV [51].

Surprisingly, maximum SV in diverse fish and mammals is not so different (about 0.5-1.5 ml/kg of body mass). This rather small range may reflect an anatomic limitation. Hearts with a larger volume need a disproportionately thicker wall to maintain the same tension (Laplace’s Law) [25]. However, a thicker cardiac wall challenges its O2 diffusion. Therefore, the maximum SV is probably established as a compromise between the generation of wall tension and the adequate supply of

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myocardial O2. The observation that the animals with a large SV have low arterial pressure is congruent with this idea. For example, the SV of amphibians and non-crocodilian reptiles is greater (3-5 ml/kg of body mass) than that of fish and mammals [25]. Furthermore, the hearts of Antarctic fish have an exceptionally high SV (2-10 ml/kg of body mass) and a very poor homeometric capacity [52].

Most vertebrates exhibit a vis-a-tergo (force from behind) cardiac filling, so that central venous blood pressure is the critical determinant of cardiac filling and thus, SV. In the heart of mammals, atria and ventricular filling is produced simultaneously as a result of the favorable pressure gradient between the central veins and the heart chambers. Therefore, filling pressure at the venous level is the main determinant of atria and ventricular filling. Atria contraction by itself contributes about 25% of ventricular filling, with a small portion of the filling due to the elastic recoil of the ventricle.

**Adjustment of mean arterial pressure (map) to exercise in vertebrates**

Resting arterial pressure values in vertebrates. MAP is the product of the Q and total peripheral resistance (TPR). As shown in Figure 1, the parameter under the control of the cardiovascular regulation mechanisms is mean arterial pressure (MAP) because the most important receptors for cardiovascular control are pressure receptors, the baroreceptors. In general, there is an evolutionary tendency towards an increase in pressure as progress is made from primitive circulatory systems to birds and endothermic mammals (Table 2) [7].

Fish. Species of fish adapted to fast swimming and high physiological performance have high levels of arterial pressure, over 100 mm Hg in the tuna and salmon [28].

Amphibians. The heart of amphibians generally does not generate such high pressure as that of the majority of fish. This may be related to the fact that the single ventricle serves both for the pulmonary and the systemic circuits [11].

Reptiles. Turtles have the lowest systemic arterial pressure, and the terrestrial species have slightly higher pressure than the semi-aquatic species. Systemic arterial pressure at rest varies considerably among snakes, in part due to their diversified exposure to gravitational forces. There is an allometric relation in snakes between arterial pressure and body mass (exponent = 0.15), probably because the ventricular mass increases with the increase in body mass. Resting systemic arterial pressure in crocodiles and lizards is similar to that of mammals, and almost double in iguanas [7,53]. Therefore, the functional and anatomical divisions of the ventricle of reptiles are associated with higher systemic arterial pressure [54].

Birds and mammals. The development of high arterial pressures is a feature of birds and mammals. The “average” mammal, with the exception of the giraffe, has a MAP of about 97 mm Hg, while the “average” bird has a MAP of about 133 mm Hg [55,56]. These differences seem to be attributable to a greater Q (related to the mass or metabolic rate) in birds than to differences in peripheral resistance [57]. Compared to mammals, birds have larger hearts, greater SV and lower HR. During exercise, MAP increases more than 50% above resting levels in this groups. As an example, MAP rises from 110–138 mmHg at rest to as high as 200 mmHg during maximal exercise [58].

Physiological mechanisms that explain the control of arterial pressure. Traditionally, books on physiology deal with mechanisms of regulation in the short, medium and long term.

- Short-term regulation. The innervation of the heart is very varied [59]. In teleosts vagal innervation shows a higher tone at rest. The heart of amphibians has sympathetic and parasympathetic innervation both in caudata and anura. The activity of anura increases both HR and arterial pressure, which rises initially because of adrenergic effluents and are maintained by circulating catecholamines. Reptiles present wide variation in the levels of blood pressure attributable to the differences among species, to environmental conditions and to non-steady states derived from different causes. In spite of the high HR in relation to many other vertebrates, the heart of birds is subject to an important cholinergic (vagal) and adrenergic tone. Walking increases blood pressure in several types of birds, particularly at high intensities due to the increase in sympathetic tone and to a lesser extent to vagal inhibition [60].

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All the mentioned data suggest that the baroreflex function in the immediate control of arterial pressure is very important in amphibians (anura), reptiles, birds and mammals, the latter being the group that has provided the most evidence about this issue. Furthermore, in all vertebrates the CNS mediates a wide range of cardiovascular responses, including those that accompany excitement, emotions and cognitive functions. Many of these responses are acute, like the defense reactions that involve tachycardia and increase in blood pressure. The central nervous mechanisms of mammals can suppress the responses of the baroreceptor reflex during exercise and there is some evidence that the brain can alter the reference point around which arterial pressure is controlled or stabilized in the long term. The CNS is very important in integrating both heart and circulation, controlling sustained sympathetic activity which is essential for maintaining peripheral vascular tone and Q. If there is no sympathetic vascular tone, the reflex controls cannot effectively stabilize pressure at any moment. Skeletal muscle arterial and arteriolar vasodilation allows a fall in total peripheral resistance in exercising mammals, which facilitates an increase in Q related to a modest rise in MAP. The control of these events involves a complex array of mechanical, humoral and neural mechanisms [61].

- Regulation of blood volume (medium and long-term regulation). Blood volume in vertebrates varies it hardly exceeds the 10% of body mass. It is supposed that all mechanisms that control blood volume reflect steady state conditions depending on the state of hydration, activity, hibernation and other factors. All the regulatory mechanisms of the vertebrates are summarized below:
- The increase in efferent nervous activity can provoke renal vasoconstriction, which in turn considerably reduces renal blood flow. Renal regulation may be very important in amphibians, some fish and reptiles [62].
- Endocrine factors, like arginine vasopressin, the renin-angiotensin system and the atrial natriuretic peptide. Arginine vasopressin (AVP) promotes the retention of fluid at the level of the kidneys, and its physiological importance for direct effects on blood pressure is secondary. AVP is found in the neurohypophysis of all non-mammal vertebrates. Neurohypophyseal peptides in reptiles and birds are similar to those of mammals [63]. The renin-angiotensin-aldosterone system (RAAS) is present in all vertebrates except cyclostomata and elasmobranchii, and it is one of the most important hormonal systems in the long-term modulation of renal function and hemodynamics in mammals [64,65]. The role of angiotensin II in blood pressure maintenance in fish is demonstrated after a fall in pressure after the administration of inhibitors of the angiotensin converting enzyme. Finally, the atrial natriuretic factor comprises a family of peptides synthesized in the auricular myocytes in response to the tension in the local wall (increase in intra auricular volume) and it is present in all vertebrates [66].
- Factors derived from the endothelium. Numerous peptides produce vasoactive effects and are present in all classes of vertebrates [67].
- Other factors. Different molecules with autocrine or paracrine effects (histamine, bradykinin, adenosine, nitric oxide) are present in the cells and affect the cardiovascular system of vertebrates [68].

As seen, an integrated response to changes in blood volume are controlled by all the afore-mentioned factors. The decrease of volumes of blood and body fluids is the most common natural disturbance in the majority of vertebrates in terrestrial (dehydration by evaporation, convection and irradiation) and marine (dehydration by osmotic imbalances) environments. Mammals are generally less tolerant to loss of blood than other vertebrates. Fish [69], amphibians [70], reptiles [71,72] and birds [73,74] can support a greater degree loss of plasma volume and mobilize compensatory fluid more quickly than mammals.

**Integrated response to exercise in vertebrates**

Metabolic demand in all vertebrates during exercise requires some cardiovascular system adjustments that are not quantitatively proportional, because while VO2max can increase from ten to twentyfold, the changes in Q are smaller. Increased needs from muscle metabolism during exercise impose a strength control by matching between the delivery of O2 and VO2max. This is due to two factors. First, the increase in oxygen extraction allows a greater supply of O2 in musculoskeletal

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muscles without a necessary increase blood flow and secondly, the supply of O2 to tissues does not only depend on the cardiovascular system but also on the respiratory apparatus.

Di Prampero [75] calculated the contribution of each element that contributes to an increase in VO2 to its maximum value. In human beings, the central component (respiratory apparatus and cardiovascular system) is responsible for 75%, minimizing the participation of the peripheral route (mitochondrial oxidation and use of energetic stores). Ventricular size is a limiting factor for the central contribution as it determines SV, Q, and hence aerobic capacity and exercise performance. In mammals, the heart constitutes the same fraction of body mass according to the size of the mammals, from mice to cows. In horses, heart size ranges between 0.9 to 2% of the body mass in elite individuals, which is greater than in other species [1].

Thus, the cardiovascular system of vertebrates during exercise requires an increase in Q and variation of total peripheral resistance (Figure 1). Generalizing, the adjustment of these variables is different in the 5 large groups of vertebrates.

Cardiac output. The mechanism by which Q is increased during exercise varies among vertebrates. Most of them increase Q during exercise between 1.3 and 3.3 times above resting values [76,77]. The known exceptions to this are trained human athletes and Thoroughbred horses. The participation of each of the parameters that determine cardiac output (Q = SV x HR) depends on the class of vertebrate. While maximum HR is very important in the increase of Q during exercise as an allometric function of body mass, SV may be extremely determinant in vertebrates with a certain body weight. Flying pigeons can increase HR sixfold without changing SV [76]. The majority of amphibians, reptiles, birds and mammals depend to a large extent on tachycardia, although the range varies considerably [28] (see Table 1) as SV changes relatively little [78]. For example, in the rainbow trout the considerable increase in end diastolic volume (EDV) during exercise increases from about 0.4 ml/kg to 1.1 ml/kg, that is, almost threefold. In the leopard shark the rise of the EDV during exercise is only 1.5 times, bearing in mind that it weighs 50 times more than the rainbow trout. The human being, in contrast to fish, increases EDV to a lesser degree, but end-systolic volume (ESV) decreases [7]. However, training in mammals increases the role of SV. In mammals, maximum HR in goats and dogs, ponies, calves and horses, is almost identical for animals of the same size, in spite of a difference of 1.4 to 2.5 times in their VO2 max [79]. Tachycardia usually implies both vagal withdrawal and, when possible, adrenergic stimulation.

Total peripheral resistance. Central arterial pressure increases with exercise. However, the species with respiratory and systemic circulations in series (fish and mammals) usually show somewhat higher increases in systemic arterial pressure than species with two parallel circulations (amphibians and non-crocodilian reptiles) [80]. The amplitude of the increase of arterial pressure is reduced because of the decrease in total vascular resistance. The most active mammals seem to be capable of a greater reduction in vascular resistance. The net effect of the increase in Q and arterial pressure is to increase myocardial energy expenditure (Table 2) [7], and this, of course, requires a concomitant increase in myocardial O2 consumption. An additional response is the preferential distribution of blood flow to the working skeletal muscles. The control of these diverse responses is not totally understood, especially in the case of the lower vertebrates. During exercise in mammals, the vasomotor center integrates the afferent information from the active muscles (proprioceptors), the arterial and cardiac mechanoreceptors, the chemoreceptors, the cortex and the hypothalamus to ensure appropriate vegetative efference.

The change in the regional distribution of the blood flow with exercise has been measured in several types of fish. For example, in the rainbow trout and the big-mouthed trout, the blood flow in red muscle is 9% and 0.57% of Q at rest, and increases to 42% and 13.2% during exercise, respectively [81,82]. At the same time as blood flow increases to the skeletal muscles, it is reduced in the abdominal viscera [83]. The decrease in the blood flow in the celiac, mesenteric and intestinal arteries may be especially pronounced being around 30% in Atlantic cod [52] and 70% in Chinook salmon [84]. As systemic resistance decreases, the effect of the vasodilation of the skeletal muscle has to be greater than visceral vasoconstriction. The control of these vascular responses is not well understood. Modulation of the systemic alpha-adrenergic tone is a possibility. And the functions of the locally

produced metabolites [85] adrenergic and non-cholinergic fibers especially in the intestinal circulation have not yet been investigated in depth [86].

However, our understanding of how Q is regionally distributed in amphibians and reptiles during activity is very limited [87–89]. One of the few studies of this type measured the left pulmonary and aortic blood flows during rest and swimming in the green see turtle Chelonia mydas [90]. During exercise, it was assumed that Q would increase, mainly due to an increase in HR of 24 beats/min to 40 beat/min (28ºC). Both the pulmonary and aortic blood flow increased considerably with exercise, but there was scant evidence of a redistribution of Q, apart from that which is usually associated with periods of intermittent pulmonary ventilation and breath holding.

## Conclusions and Future Directions

In conclusion, the cardiovascular adjustments (mainly the cardiac output, total peripheral resistance and pressure gradient) needed during exercise in all vertebrates are quantitatively smaller than the increase in oxygen consumption. The mechanism by which the cardiac output (either the stroke volume or the heart rate) is enhanced during the effort is highly variable among vertebrates. The existing differences found in the pulmonary and systemic circulation systems between vertebrates explain the assorted exercise responses observed in the arterial pressure and total peripheral resistance in vessels.

The study of cardiovascular responses to physical exercise in vertebrates has certain limitations. It would be recommendable in future studies to investigate more specific measurement methods and protocols.

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