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LEFT VENTRICULAR OXYGEN EXTRACTION DURING SUBMAXIMAL AND MAXIMAL EXERTION IN PONIES

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SUMMARY

1. Left ventricular (LV) myocardial O_2 extraction was studied in five healthy ponies which had catheters implanted in the great cardiac vein and main pulmonary artery 15–30 days before the study. The abdominal aorta was percutaneously catheterized to sample arterial blood.

2. In addition, phasic LV and aortic pressures, LV dP/dt_{max} and rate–pressure product were also studied; dP/dt_{max} is the maximal rate of rise of the left ventricular pressure during the isovolumic phase, and is considered an index of myocardial contractility. Measurements were made at rest (control) and during adenosine infusion (3 μmol kg^{-1} min^{-1}) at rest, moderate exercise (heart rate 169 ± 10 beats min^{-1}), heavy exercise (heart rate 198 ± 7 beats min^{-1}), maximal exercise (heart rate 232 ± 7 beats min^{-1}), and adenosine infusion (3 μmol kg^{-1} min^{-1}) during maximal exercise (heart rate 230 ± 6 beats min^{-1}).

3. In resting ponies, LV arterial to coronary venous O_2 content difference (ΔLV_{a-v} O_2) was $8{\cdot}9 \pm 0{\cdot}5$ ml dl^{-1} and O_2 extraction was $59{\cdot}9 \pm 2{\cdot}2$%. Adenosine infusion at rest decreased ΔLV_{a-v} O_2 and O_2 extraction precipitously ($2{\cdot}6$ ml dl^{-1} and $14{\cdot}3 \pm 1{\cdot}7$%, respectively), thereby indicating superfluous LV myocardial perfusion.

4. Moderate, heavy and maximal exercise increased ΔLV_{a-v} O_2 to 185, 194 and 218% of its control value and O_2 extraction rose to 71 ± 2, $75 \pm 1{\cdot}5$ and $78 \pm 0{\cdot}9$%, respectively. The widening of the ΔLV_{a-v} O_2 gradient was due to the increased arterial O_2 content during exercise.

5. Combining these observations with equine myocardial perfusion, the LV O_2 consumption was calculated to be 7·8, 47·9 and 103·6 ml min^{-1} 100 g^{-1} at rest, moderate and maximal exercise. In order to achieve the 13·4-fold increase in LV O_2 consumption, the LV perfusion rose only 6-fold; the rest being met by widening the ΔLV_{a-v} O_2.

6. Adenosine infusion during maximal exercise decreased ΔLV_{a-v} O_2 and O_2 extraction ($10{\cdot}7 \pm 1$ ml dl^{-1} and 45%, respectively; $P < 0{\cdot}0001$). This indicated that coronary vasodilator capacity was not being completely expended in maximally exercising ponies. It is concluded that coronary circulation is unlikely to be a limiting factor to further exertion in ponies.

INTRODUCTION

Organ/tissue perfusion studies in exercising ponies have demonstrated that of all working muscles, the left ventricular (LV) myocardium received the highest level of blood flow. For example, during maximal exercise the LV myocardial blood flow was 534 ± 31 ml min^{-1} 100 g^{-1} (Parks & Manohar, 1983), while in the principal muscle of propulsion, the gluteus medius, it was 226 ± 22 ml min^{-1} 100 g^{-1} and in the diaphragm 265 ± 36 ml min^{-1} 100 g^{-1} (Manohar, 1986). Since exercising equine subjects also exhibit large (about 50%) increments in haemoglobin concentration (and therefore, arterial O_2 content), it follows that LV coronary O_2 supply rises dramatically with maximal exercise in ponies (Parks & Manohar, 1983; Manohar, 1986). However, little is known about LV myocardial O_2 extraction. Thus, the primary objective of the present study was to examine LV myocardial O_2 extraction in ponies during graded exercise.

Despite the fact that pony LV myocardium had the highest level of perfusion of all working tissues, it was noteworthy that coronary vasodilator capacity was not being completely expended in maximally exercised healthy ponies (Parks & Manohar, 1983). In fact, in comparison with dogs (Barnard, Duncan, Livesay & Buckberg, 1977) and swine (White, Sanders & Bloor, 1981), the relative extent of unutilized transmural LV coronary vasodilator reserve was much greater in maximally exercised ponies. Thus, another objective of the present study was to assess the impact of unmasking the coronary vasodilator reserve on LV myocardial O_2 extraction in maximally exercising ponies.

METHODS

Experiments were carried out on five healthy-grade ponies, 2–4 years old and weighing 173 ± 10 kg (mean $\pm$ S.E.M.). They were housed in an air-conditioned building (about 20 °C) and were fed a ration of alfalfa hay and oats. Water was provided *ad libitum*. All animals had been dewormed and inoculated with tetanus toxoid several days before surgery. The ponies were accustomed to being handled by people and were trained to run on a treadmill.

Surgical preparation of animals

About 15–30 days before the study, a left lateral thoracotomy was performed by resecting the fourth rib. Anaesthesia was induced with intravenous sodium thiamylal + glyceryl guaiacolate, and maintained with halothane administered in O_2 using a circle absorber system and a ventilator. Via a 1·5 cm diameter aperture made in the pericardium below the origin of the left circumflex coronary artery, a 20-gauge silastic catheter was implanted in the great cardiac vein draining the left ventricle. A 16-gauge Tygon catheter was also implanted in the main pulmonary artery. The catheters were exteriorized in the 7th intercostal space and the thoracotomy was closed in the conventional manner. The ponies recovered uneventfully and were afebrile at the time of the study.

About 24–48 h before the study, the abdominal aorta was percutaneously catheterized following local infiltration of 2% lidocaine HCl in the 16th intercostal space (Manohar, Kumar, Bhargava, Nigam & Tyagi, 1973).

On the day of the study, following local infiltration of 2% lidocaine HCl in the mid-cervical region, the left carotid artery was carefully exposed. An 8F cardiac catheter equipped with dual-tip micromanometers (Millar Instruments Inc., Houston, Texas) was advanced such that the distal sensor was located in the left ventricle while the proximal sensor remained in the ascending aorta. The catheter-tip-micromanometers were calibrated against a mercury manometer in a waterbath maintained at the pony's rectal temperature and the signals were matched with fluid-filled transducer signals obtained from the same locations as described previously (Manohar, Bisgard, Bullard, Will, Anderson & Rankin, 1979).

Experimental protocol

The ponies were studied during the following steady-state conditions. Existence of a steady state was judged based on the stability of heart rate, arterial pressure, and blood-gas tensions. At each step of the protocol, heart rate, phasic and mean pressures in the aorta, LV pressure and its dP/dt, as well as arterial and LV coronary venous blood-gas tensions, pH, haemoglobin O_2 saturation, and haemoglobin concentration (Models BMS3MK2/PHM73 Blood-gas/pH analyzer and OSM2 Hemoximeter, Radiometer, Copenhagen, Denmark) were determined. Simultaneous arterial and LV coronary venous blood samples were withdrawn anaerobically in heparinized blood-gas syringes (Sarstedt, F.R.G.). Bicarbonate concentration was calculated using Henderson–Hasselbalch equation with $pK = 6{\cdot}1$. Blood O_2 content was calculated as haemoglobin concentration in g $dl^{-1} \times 1{\cdot}34 \times O_2$ saturation plus (O_2 tension $\times 0{\cdot}003$). The LV myocardial O_2 extraction (%) was determined as arterial to LV coronary venous O_2 content difference divided by arterial O_2 content. Rate–pressure product, calculated as heart rate $\times$ aortic systolic pressure $\times 10^{-2}$, was considered an index of myocardial O_2 demand, and the LV dP/dt_{max} was regarded as an index of LV myocardial contractility.

Rest (control/baseline). Measurements were made on ponies standing comfortably as described previously (Parks & Manohar, 1983; Manohar, 1986).

Adenosine infusion at rest. Adenosine was infused into the main pulmonary artery via the previously implanted catheter at 3 μmol kg^{-1} min^{-1}. During the third and fourth minutes of infusion, haemodynamic and blood-gas measurements were made when a steady state existed (Parks & Manohar, 1983).

Moderate exercise. Ponies were exercised for 4 min on a treadmill at a speed setting of 16 km h^{-1} Simultaneous arterial and LV coronary venous blood samples were obtained at 30 s intervals during the 4 min of exercise. Thereafter, the animals were allowed to rest for at least 90 min to permit return of cardiorespiratory parameters towards control values.

Heavy exercise. Exercise was performed at a treadmill speed setting of 24 km h^{-1} for 4 min, during which period simultaneous arterial and LV coronary venous blood samples were obtained at 30 s intervals. A rest period of at least 90 min followed so as to permit recovery of various parameters towards control values.

Maximal exercise. Ponies were exercised at a treadmill speed setting of 32 km h^{-1} for 4 min. None of the animals could sustain this work intensity for longer than 4 min. Blood samples were collected anaerobically at 30 s intervals during maximal exercise. A rest period of about 120 min followed.

Adenosine infusion during maximal exercise. Ponies were exercised at 32 km h^{-1} for 4 min. Adenosine infusion (3 μmol kg^{-1} min^{-1}) into the main pulmonary artery was initiated at the start of the exercise. Arterial and LV coronary venous blood samples were obtained at 30 s intervals starting at 90 s of exercise.

The sequence of moderate exercise, heavy exercise, and maximal exercise was randomized for each pony, and the resting blood samples and haemodynamic measurements were obtained before every exercise step.

Statistical analysis of the data

The data were subjected to a two-way analysis of variance followed by Newman Keuls multiple range test when significant F values were encountered (Steel & Torrie, 1960). A probability level of $P < 0{\cdot}05$ was considered statistically significant. Data are presented as mean $\pm$ S.E.M.

RESULTS

Rest

Haemodynamic data and arterial, as well as LV coronary venous blood-gas variables are listed in Tables 1 and 2. Control resting values obtained before each of the exercise steps were similar. The arterial to LV coronary venous O_2 content gradient was $8{\cdot}9 \pm 0{\cdot}5$ ml dl^{-1} at rest and the LV O_2 extraction amounted to $59{\cdot}9 \pm 2{\cdot}17$ %.

TABLE 1. Haemodynamic variables from five healthy ponies at rest and during exertion before and during adenosine infusion (3 μmol kg^{-1} min^{-1})

	Control (rest)	Adenosine infusion at rest	Moderate exercise	Heavy exercise	Maximal exercise	Addenosine + maximal exercise
Heart rate (beats min^{-1})	54±2	89±4*	168±10*†	198±7*†‡	232±7*†‡§	230±6*†‡§
Aortic systolic pressure (mmHg)	150±4	130±8*	192±13*†	208±14*†	244±18*†‡§	225±20*†‡
Mean aortic pressure (mmHg)	125±4	98±6*	141±10†	155±8*†	186±11*†‡§	168±14*†‡
Aortic diastolic pressure (mmHg)	109±5	82±5*	116±8†	129±6*†	158±8*†‡§	141±12*†‡
LV dP/dt_{max} (mmHg s^{-1})	2200±141	2450±457	7050±750*†	8425±525*†‡	9850±656*†‡§	10150±392*†‡§
Rate–pressure product (mmHg × beats min^{-1} × 10^{-2})	84±5	116±13	327±47*†	416±50*†‡	565±39*†‡§	514±43*†‡§

All values are mean ± S.E.M.

* Significantly different from control. † Significantly different from adenosine infusion at rest. ‡ Significantly different from moderate exercise. § Significantly different from heavy exercise.

TABLE 2. Arterial and LV coronary venous blood-gas variables from five healthy ponies at rest and during graded exercise

	Arterial blood				LV coronary venous blood		
	pH	O_2 tension (mmHg)	CO_2 tension (mmHg)	O_2 content (ml dl^{-1})	O_2 tension (mmHg)	O_2 saturation (%)	O_2 content (ml dl^{-1})
Rest	7·402±0·012	97±1	38·3±0·9	14·4±0·9	22·4±0·4	39·9±0·8	5·5±0·4
Adenosine infusion at rest (3 min)	7·533±0·010*	107·5±3·5*	25·7±1·3*	18·6±1·2*	40·3±1·7*	85·8±1·5*	16·1±1·3*
Moderate exercise							
120 s	7·391±0·029†	85±2*†	32·3±2·6*†	23·5±1·2*†	17·6±1·5*†	29·0±2·0*†	7·0±0·8†
240 s	7·409±0·023†	88±1*†	30·9±2·2*†	23·1±1·1*†	16·0±1·3*†	28·1±1·6*†	6·6±0·7†
Heavy exercise							
120 s	7·328±0·021*†‡	85±2*†	27·5±1·7*‡	23·2±1·1*†	15·6±0·9*†	24·9±1·4*†‡	5·9±0·6†
240 s	7·303±0·021*†‡	85±1*†	25·0±1·4*‡	24·0±1·2*†	14·5±1·3*†	24·8±1·2*†‡	6·3±0·7†

All values are mean ± S.E.M.

* Significantly different from rest/control. † Significantly different from adenosine infusion at rest. ‡ Significantly different from moderate exercise values.

Adenosine infusion at rest

The heart rate of ponies increased and the arterial blood pressure decreased (Table 1). The ponies also exhibited marked alveolar hyperventilation as demonstrated by a significant fall in arterial CO_2 tension and the arterial pH rose markedly (Table 2).

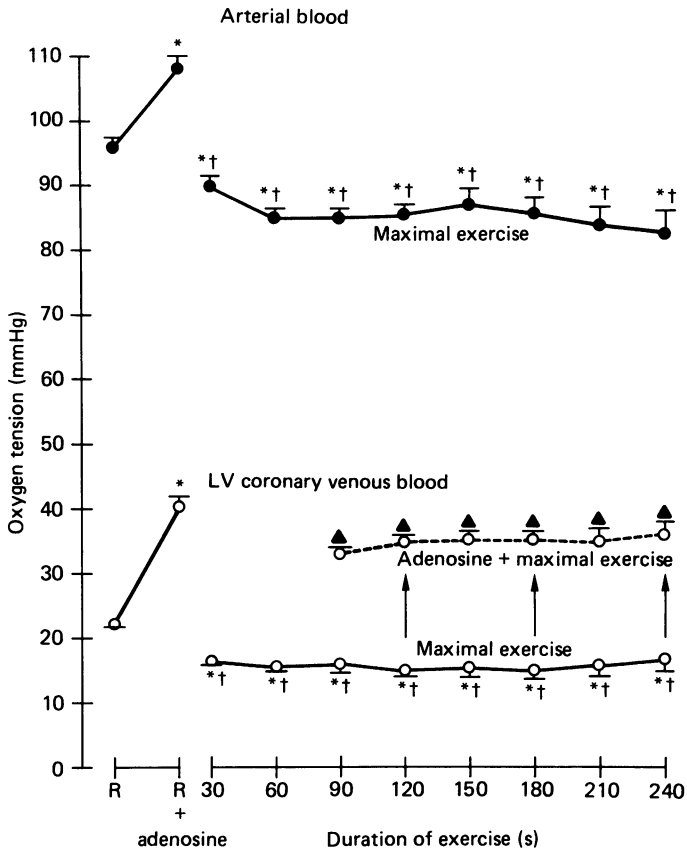

Fig. 1. Arterial and left ventricular (LV) coronary venous blood O_2 tension at rest (R; control) and during 240 s of maximal exercise. Note that adenosine infusion at rest (R + adenosine) as well as during exercise caused coronary venous O_2 tension to increase markedly. * Significant differences from control values at rest; † significant difference from rest + adenosine values; ▲ significant differences from maximal exercise values.

The arterial O_2 tension also increased (Fig. 1). The infusion of adenosine at rest also markedly increased LV coronary venous O_2 tension (Fig. 1) and O_2 saturation (Fig. 2). The arterial to LV coronary venous O_2 content difference decreased from its control value to $2{\cdot}6 \pm 0{\cdot}2$ ml dl^{-1} and the LV O_2 extraction was only $14{\cdot}3 \pm 1{\cdot}7$ % (Fig. 3).

Moderate exercise

As expected, heart rate, aortic pressure, rate–pressure product, and the LV dP/dt_{max} increased from control values (Table 1). The arterial CO_2 tension decreased

markedly while O_2 content increased (Table 2) due to an increase in haemoglobin concentration. Arterial pH and the O_2 saturation were, however, not significantly affected.

Moderate exercise resulted in a significant reduction in LV coronary venous O_2 tension as well as O_2 saturation within 30 s, but the O_2 content did not change significantly (Table 2). However, due to the rise in arterial O_2 content, the arterial

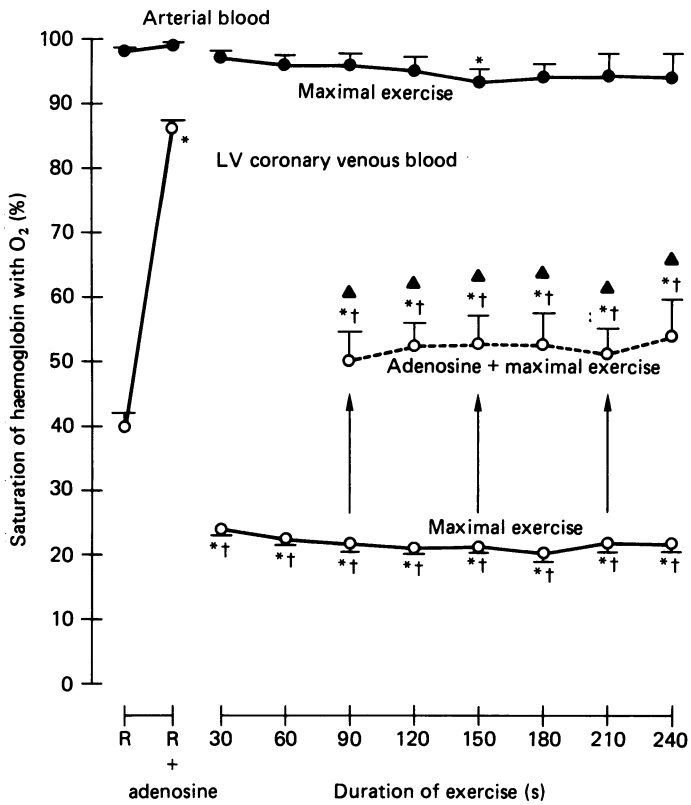

Fig. 2. Arterial and left ventricular (LV) coronary venous haemoglobin O_2 saturation at rest (R) and during 240 seconds of maximal exercise. With adenosine infusion at rest (R + adenosine) as well as during exercise coronary venous haemoglobin O_2 saturation increased significantly. *Significant differences from resting values; †significant difference from rest + adenosine values; ▲ significant differences from maximal exercise values.

to coronary venous O_2 difference increased to $16{\cdot}5 \pm 0{\cdot}7$ ml dl^{-1} (185% of its control value) and the LV O_2 extraction rose to $71 \pm 2\%$ at 120 s of exercise (Fig. 3).

Heavy exercise

Further increments in heart rate, aortic pressure, LV dP/dt_{max} and rate–pressure product were observed during heavy exertion (Table 1). Compared with moderate exercise, arterial O_2 tension, O_2 saturation, and O_2 content were not found to be different (Table 2). However, arterial CO_2 tension and pH from the second to fourth minute of heavy exertion were significantly less (Table 2).

Heavy exercise caused only insignificant further changes in LV coronary venous O_2 tension, and O_2 content compared with moderate exercise (Table 2). Thus, arterial to LV coronary venous O_2 content difference and LV O_2 extraction during heavy exercise ($17{\cdot}3 \pm 0{\cdot}6$ ml dl^{-1} and $75 \pm 1{\cdot}5\%$, respectively, at 120 s) were also not different from moderate exercise values.

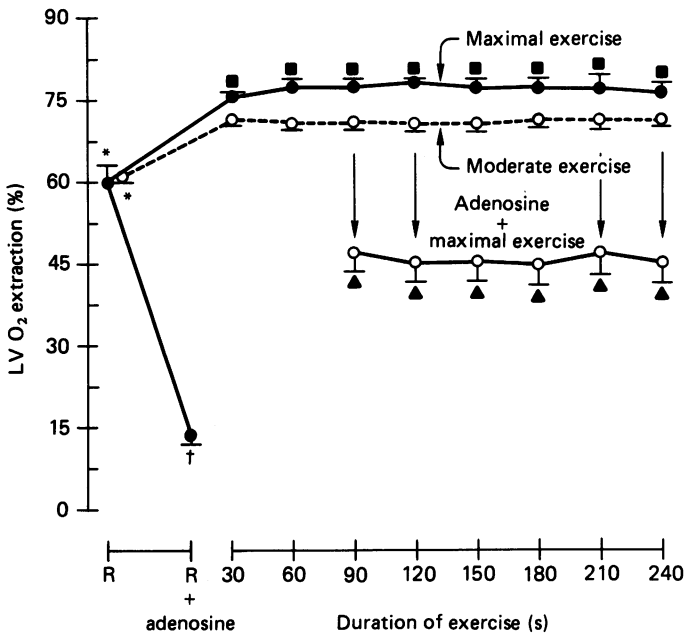

Fig. 3. Left ventricular (LV) myocardial O_2 extraction at rest (R; control), adenosine infusion during rest (R + adenosine), and 240 s of maximal exercise. Values for moderate exercise are also included for comparison's sake. Notice that adenosine infusion during maximal exercise significantly decreased LV myocardial O_2 extraction. * Significantly different from all exercise values; † significantly different from rest as well as all exercise values; ■ significantly different from moderate exercise values; ▲ significantly different from maximal exercise values.

Maximal exercise

Heart rate, aortic pressure, LV dP/dt_{max} and rate–pressure product registered further increments from heavy exercise values (Table 1). Marked alveolar hyperventilation (arterial CO_2 tension of 32 ± 2 and $31 \pm 1{\cdot}4$ mmHg at 120 and 240 s of exercise), and severe metabolic acidosis (arterial pH of $7{\cdot}117 \pm 0{\cdot}019$ and $7{\cdot}084 \pm 0{\cdot}024$ at 120 and 240 s of exercise) occurred. Arterial O_2 tension also decreased from its control value (Fig. 1).

The LV coronary venous O_2 tension ($15{\cdot}1 \pm 0{\cdot}9$ and $16{\cdot}3 \pm 1{\cdot}7$ mmHg at 120 and 240 s of exercise; Fig. 1) was similar to that during heavy and moderate exercise values (Table 2). However, LV coronary venous O_2 saturation during maximal exercise ($21 \pm 0{\cdot}8$ and $21{\cdot}9 \pm 1{\cdot}0\%$ at 120 and 240 s; Fig. 2) was significantly less ($P < 0{\cdot}05$) than corresponding values for moderate and heavy exercise (Table 2). The arterial to coronary venous O_2 content gradient was $19{\cdot}4 \pm 0{\cdot}4$ ml dl^{-1} (218% of the resting value) and the LV O_2 extraction was $78 \pm 0{\cdot}9\%$ at 120 s of maximal exercise

(Fig. 3). At 240 s, their corresponding values were $18{\cdot}1 \pm 0{\cdot}5$ ml dl^{-1} and $76 \pm 1{\cdot}5\%$ (Fig. 3).

Adenosine + maximal exercise

Compared with maximal exercise values, adenosine infusion did not cause significant variations in heart rate, aortic pressure, LV dP/dt_{max}, and rate–pressure product, arterial pH, O_2 tension, and O_2 content. However, during adenosine + maximal exercise, the LV coronary venous O_2 tension, percentage O_2 saturation, and O_2 content were more than double their values during maximal exercise without adenosine (Figs 1 and 2). During adenosine + maximal exercise, the LV arterio-venous O_2 content difference ($10{\cdot}7 \pm 1{\cdot}0$ and $10{\cdot}7 \pm 2{\cdot}5$ ml dl^{-1} at 120 and 240 s) was significantly less ($P < 0{\cdot}0001$) than that during maximal exercise carried out without adenosine. As a consequence, LV O_2 extraction decreased dramatically during adenosine + maximal exercise (Fig. 3).

DISCUSSION

The present study clearly demonstrated that equine LV myocardial O_2 extraction increased significantly with exercise. Also demonstrated was the fact that adenosine infusion during maximal exercise caused a significant reduction in LV O_2 extraction.

In exercising ponies, heart rate, aortic systolic pressure, and LV dP/dt_{max} increased progressively with increasing work intensity (Table 1). These variables are believed to be significant determinants of myocardial O_2 utilization (Braunwald, 1971; Rowe, 1974). It has been previously demonstrated that graded exercise caused appropriate increments in LV myocardial blood flow which resulted from progressive increments in coronary vascular conductance (Parks & Manohar, 1983). The data presented in Table 2, and Figs 1–3, suggest that exercising ponies also increase their myocardial O_2 extraction along with their coronary perfusion and arterial O_2 content in order to meet the augmented LV myocardial O_2 requirements. Hoffman (1987) noted that canine myocardial O_2 extraction is about 65% at rest, and it increased to about 80% with severe exercise (Khouri, Gregg & Rayford 1965). The data from ponies (Fig. 3) are similar to these values.

Adenosine infusion in resting ponies resulted in large superfluous myocardial blood flow as demonstrated by the rise in coronary venous O_2 tension and saturation (Figs 1 and 2) and a precipitous drop in LV myocardial O_2 extraction (Fig. 3). These observations are consistent with direct measurements in awake ponies, where adenosine infusion caused transmural myocardial blood flow to rise far in excess of that needed to meet the metabolic requirements (Parks & Manohar, 1983). Similar observations have also been made in other species (Hoffman, 1987).

A more interesting observation from the present experiments, however, was the ability of adenosine infusion during maximal exercise to increase significantly coronary venous O_2 tension and saturation (Figs 1 and 2), and thereby decrease myocardial O_2 extraction (Fig. 3) despite the fact that heart rate, LV systolic pressure, dP/dt_{max} and rate–pressure product were similar to that during maximal exercise performed without adenosine (Table 1). This indicates that adenosine infusion was able to cause a further increment in LV myocardial perfusion of

maximally exercising ponies in excess of tissue metabolic needs. The fact that coronary venous O_2 saturation of maximally exercising ponies rose from nearly 21 to about 50% with adenosine infusion (Fig. 2) as LV O_2 extraction decreased precipitously (by more than 30%; Fig. 3) clearly establishes the presence of a considerable unutilized coronary vasodilator capacity in the maximally exercised pony. This conclusion is also supported by transmural myocardial perfusion data reported previously (Parks & Manohar, 1983).

Combining the LV coronary arteriovenous O_2 content differences observed in the present study with LV myocardial blood flow data (Parks & Manohar, 1983; 89 ± 7, 290 ± 19, and 534 ± 31 ml min^{-1} 100 g^{-1} at rest, moderate exercise and maximal exercise, respectively), the following values of LV myocardial O_2 consumption ($\dot{V}_{O_2,M}$) were obtained: rest = 7·75 ml min^{-1} 100 g^{-1}; moderate exercise = 47·9 ml min^{-1} 100 g^{-1}; maximal exercise = 103·6 ml min^{-1} 100 g^{-1}. These data reveal that although maximal exercise increased LV flow 6-fold from its resting value, the $\dot{V}_{O_2,M}$ rose 13·4-fold. Clearly then, increased O_2 extraction also plays a major role in adequately meeting the augmented LV metabolic O_2 demand during exercise. The fact that ponies have a large splenic reservoir of erythrocytes which allows a rapid increase in arterial O_2 capacity (Table 2) is an important factor in their ability to expand the LV coronary arteriovenous O_2 difference during exercise. This is underscored by the observation that coronary venous O_2 content of exercising ponies did not change significantly from the control resting values (Table 2). This is not the case in dogs (Khouri *et al.* 1965).

In conclusion, the results of the present study revealed that during vigorous exercise, equine LV myocardial O_2 demands are met by both an increase in perfusion and the arteriovenous O_2 content gradient; during maximal exercise the latter was 218% of its control value (rest). Adenosine infusion during maximal exercise caused superfluous LV myocardial perfusion such that coronary venous O_2 saturation rose markedly and LV O_2 extraction decreased. This indicated a considerable unutilized coronary vasodilator capacity in the LV myocardium of the maximally exercising pony. Therefore, it is believed that coronary circulation is not a limiting factor to further exertion in healthy ponies.

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