Numerous findings suggest that muscular drives, created by a variety of different stimuli, constitute an important factor in cardiovascular and respiratory regulation during exercise. 

The significance of these drives during different stages and types of exercise, their adequate triggering mechanism, and their afferent fiber groups do not seem to be established adequately. This may be because only a few studies, interrupting the afferents from muscles during strenuous isometric and isotonic contractions, have established the reflex nature of these drives. However, the cardiovascular and ventilatory reactions following sustained isometric efforts seem to be somewhat different from those of dynamic work. Moreover, since isometric contractions substantially enhance intramuscular pressure, it seems conceivable that an increase in intramuscular pressure without contraction produces similar drives. These kinds of afferent signals appear to be transmitted by small group III or IV fibers. It seems necessary to assess the effect of work while excluding possible interference from other stimuli. It appears that this can be satisfactory only if dynamic work is employed. Compared with isometric contractions it can be carried out for a period that is sufficient to produce stronger humoral drives from different extramuscular sites, which then may compete with muscular drives. Such extramuscular receptors can be activated by changes of venous, arterial, or cerebral [H⁺], Pco₂, Po₂, osmolality, and catecholamine concentrations.

Experiments in which the afferent signals from dynamically contracting muscles were eliminated and the cardiovascular and respiratory responses were simultaneously observed are completely lacking. It was therefore the aim of the present study to investigate the role of the supposed muscular reflexes for the adjustment of heart rate (HR), minute ventilation (Ve), mean arterial blood pressure (MAP), and local muscle blood flow (Q) during prolonged dynamic work. Reflex drives were separated from humoral drives by comparison of responses before and after cold blockade of the afferent pathway from the muscles.

Methods

Male mongrel dogs [mean weight, 21.7 ± 0.7 (SE) kg] were used in this study. In the evening and the morning before an experiment, the dogs were premedicated with promazine (4–5 mg/kg of body weight). Anesthesia was induced with hexobarbital sodium (20–50 mg/kg, iv) and supplemented with N₂O (70–75 vol %) in O₂ (25–30 vol %) after the dog had been intubated. Small intermittent
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to restore nerve transmission, the thermode was perfused sciatic nerves to 0–1°C (Fig. 1) with a perfused thermode.

distally or proximally to the electrodes by cooling both tere data (wt/kg of muscle wt).

t output could be computed from these continuously regis-
ted from muscular drives. Third, contraction-induced

ings from different sites outside the muscles could be sepa-

ated from muscular drives. Third, contraction-induced

with warm fluid (37°C). A small thermocouple was care-

fully inserted between the nerves to measure the tempera-

ture changes during cooling and warming. The thermocou-

ple was brought into close contact with the surface of the

erves. The nerves were placed in the trough of the ther-

mode embedded in coagulated blood (Fig. 1). If cooling

was performed slowly (about 1–2 minutes) the tempera-

ture registered by the thermocouple corresponded to the

temperature within the nerves with only small differ-

ences. This was sometimes confirmed by measuring in-

er nerve temperature changes with a minute thermistor.

The temperature was continuously recorded together with

the various cardiovascular and respiratory parameters.

In general the following protocol was observed (Fig. 2).

First, stimulation parameters had to be tested in order to

make use of this knowledge for the subsequent experi-

mental steps. Therefore conduction to the muscles was blocked by cold distal to the stimulating electrodes (distal cold blockade) and muscles were thus paralyzed. Then a stan-

ard procedure was carried out to test the voltages, pulse
durations, and frequencies in a single train which were almost without effect on HR, V̇e, and MAP but which were sufficient to produce strong contractions (2–3 times threshold strength for barely measurable contractions). Stimulation was then continued while nerve conduction to the muscles was reestablished and contractions started. Second, stimulation of the nerve trunks was carried out with the same previously tested parameters while the cold blockade was applied proximally to the electrodes (proximal cold blockade). Thereby muscular contractions could be induced while nerve transmission to and from the centers ceased. Since, however, the blood flow to the muscles was unrestrained, all released metabolites and other constituents could enter the systemic veins and arte-

rial blood. Thus, the contribution of humoral drives aris-

ing from different sites outside the muscles could be sepa-

rated from muscular drives. Third, contraction-induced

The pelvis and the distal ends of the femora were fixed in a specially devised steel frame in such a way that movements of the knee and ankle joints but not the hip joints could be performed. Both sciatic nerves were exposed between the gluteus muscles, and the trunks that innervate the hamstring muscles, the gastrocnemius, and the feet extensors were isolated. The nerves were kept under liquid paraffin and the right and left trunks were stimulated alternately, each with 40 trains/min, through an isolation unit. Each train lasted 350 msec and consisted of rectangular pulses (for parameters see Figure 1 and legends of the other figures). The muscles contracted aux-

tonically against springs. Coordinated flexions of the knee and extensions of the ankle joints were carried out. Cuffs were attached around the lower parts of the feet and connected to fine steel ropes. These were led around a fixed roll and clamped to the springs. During each contraction cycle lengthening of the springs was measured by means of linear displacement transducers connected in parallel, and the forces exerted were measured by means of strain gauges mounted in series with the springs. Work output could be computed from these continuously regis-

ted data (wt/kg of muscle wt).

The stimulation electrodes were put around the isolated nerve trunks and nerve transmission was blocked either distally or proximally to the electrodes by cooling both sciatic nerves to 0–1°C (Fig. 1) with a perfused thermode. To restore nerve transmission, the thermode was perfused

1: STIMULATION ELECTRODE (monopolar) VOLTAGE : 0.2 – 1.0 V
2: THERMODE DURATION : 0.3 – 0.7 m sec
3: CENTRAL NERVOUS SYSTEM FREQUENCY : 30 – 100 Hz

PARAMETERS OF SQUARE WAVE STIMULI IN A SINGLE TRAIN :

FIGURE 1 Arrangement of the stimulating electrodes and thermode on the nerves. A: cold blockade distal to the electrodes. With this arrangement the cardiovascular and respiratory effects of stimulating parameters (bottom) were tested. After the thermode had been warmed the effects of induced contractions were studied. B: cold blockade proximal to the stimulating electrodes. Nerve transmission to and from the centers ceased; however, substances released from the muscles could activate extramuscular receptors. C: details of the thermode. Perfusion with cold or warm fluid could be regulated. The temperature was measured by a small thermocouple between the nerve trunks.
responses were observed while nerve transmission was not blocked in either direction. On completion of each experiment the muscles were relaxed by succinylcholine (2-5 mg/kg, iv) or curare (0.2-0.6 mg/kg, iv) and the dogs were artificially ventilated. The effects on HR, MAP, and Q of the stimulus parameters used, and also of those of increased strength, were again studied. Passive movements of the legs were performed before and after relaxation, to produce sudden stretch of the muscles. These passive movements were carried out with the same rhythm and caused similar displacements and exerted similar forces on the springs as did active contractions. Since the first part (testing stimulation parameters) and the last part of the experiment (relaxation with succinylcholine or curare) were not interchangeable with any of the other parts, randomization of this schedule did not seem to be warranted.

Between the periods of exercise the different circulatory and ventilatory variables attained their control values within 5-25 minutes (see Fig. 2-6). If control values had been reached this was regarded as one criterion of recovery. At this time arterial pH, Pco2, standard [HCO3-], and PO2 were determined as the second criterion of recovery. Additionally, end-expiratory Pco2 was continuously measured. New periods of exercise usually were not started if these various parameters were beyond the control values given in the various figures (Fig. 2-6). If, however, a dog did not recover and its Ve and arterial pH, PO2, and standard [HCO3-] decreased whereas Pco2 and HR increased beyond these limits, it was assumed that the dog’s condition was not satisfactory. In this case the experiment was not discontinued but the data for such a dog were not included in the statistical evaluations. Similarly the data were discarded if the electrical stimuli needed to elicit contractions had to be augmented above the previously tested limits (Fig. 1). Thus out of 42 dogs the data from only 26 dogs could be used. The number of dogs used in each part of the experiments is given in the legends of the figures.

HR, tidal volume (VT), ventilatory frequency (Ve), VO2, Q, MAP, and mean inspiratory and expiratory O2 and CO2, as well as end-expiratory CO2 concentrations, were continuously recorded. HR was measured from the electrocardiogram (ECG) by a cardiotachometer which delivered a linear analog and also a beat-by-beat output. Vr, Ve, and Ve (liters/min, BTPS) were registered by means of a pneumotachograph. O2 and CO2 concentrations were analyzed by quick paramagnetic O2 and infrared CO2 analyzers. VO2 and VCO2 (ml/min, STPD) were calculated from these measurements. MAP was obtained from a catheterized radial artery by a pressure transducer. Mean Q (ml/min · 100 g) in the femoral arteries was determined by square wave electromagnetic flowmeters. Since we wished to obtain changes in the arterial inflow and not absolutely correct perfusion rates, only such collateral vessels were ligated as could be isolated easily without any greater surgical manipulation. The flow probes were placed around the arteries, embedded in an electrolyte paste, and attached to the connective tissues to maintain proper position. After the experiments had been finished the probes were calibrated by measuring various defined and constant flows through the same segments of the arteries. The involved muscles were removed from bones and skin and weighed to normalize the flow to 100 g of muscle weight. Catheters were introduced into the femoral veins so that arterial and venous blood samples could be withdrawn simultaneously and anaerobically. They were immediately tested for PO2 (Clark electrode), O2 saturation (SO2, photometrically), Pco2, pH, standard and actual [HCO3-] (Radiometer Astrup microequipment 1) at 37°C. Plasma osmolality (mOsmol/kg of H2O) was determined by freezing point depression, and [K+] by atomic absorption photometry. Regression and correlation analysis and t-tests for mean and paired differences were employed for statistical evaluation of the data.24

**Results**

**EFFECTS OF STIMULATION, IMMOBILIZATION, PASSIVE MOVEMENTS, AND CONTRACTIONS**

The electrical stimuli used to evoke contractions activated mainly group I and probably groups II nerve fibers,5 8 which terminate in various muscular mechanoreceptors.56 Their effects due to electrical activation were compared with those of passive movements, contractions, and electrical stimulation of group III and IV fibers.

Figure 3 demonstrates the effect on HR, Ve, and MAP.
of the stimuli (see Fig. 1) which were used to elicit contractions. When the nerve trunks were excited by these stimuli during distal cold blockade only small increases in HR, VE, and MAP occurred (HR, P < 0.0125; VE, P < 0.025; MAP, P not significant). If, however, the thermometer was warmed and stimulation continued, the muscles contracted and only thereby were strong increases in HR, VE, and MAP triggered (P < 0.0005 for all variables). After cessation of work control values were reached again in 6-8 minutes. When, during contraction of both legs, the nerves of only one side again were blocked distally, while stimulation of both nerves continued as did constant work of the contralateral leg, increments in HR and VE were almost halved. Thus, the inputs from various muscle groups were nearly additive (Table 1).

Table 2 shows the influence of electrical stimulation of the sciatic nerves on HR, MAP, and Q when the dogs were immobilized by curare or succinylcholine and artificially ventilated. The results were identical for both succinylcholine- and curare-treated dogs and were therefore pooled. Stimulation parameters in the lower range (0.79 and 1 V, exciting group I and II fibers) were ineffective. Stronger stimuli that activated group III and IV fibers8,9 evoked significant increases in HR and MAP (P < 0.01 for HR and MAP at 5 V, 1-msec duration, and 25 Hz; P < 0.0005 for HR and MAP at 10-20 V). The small increases of Q were not significant.

Rhythmic movements of the legs per se could account for only a small fraction (5-10%) of the total increases observed during contraction. Thus, passive movements of the leg muscles which were not immobilized by curare or succinylcholine caused only slight increases in HR, MAP, and Q while the nerves were not blocked. Moreover, these small drives disappeared after administration of the relaxing drugs (Table 3, data with curare and succinylcholine were again identical and were pooled). End-tidal PCO2 remained essentially constant during the course of passive movements, thus indicating that muscular drives were not masked by simultaneously decreased drives from the arterial chemoreceptors. In addition, passive movements of...
However, arterial PO₂ decreased (P < 0.05). Thus it seems likely that VA was not sufficiently augmented during withdrawal.

The effects of contractions during proximal cold blockade

By these procedures the interaction of muscular with extramuscular humoral drives during prolonged dynamic work could be investigated. One group of dogs exercised at a lower rate (Figs. 4 and 5) while a second group worked at a higher load (Fig. 6). These changes were, however, insignificant although in a direction typical of exercise.

The legs before immobilization were accompanied by changes in the composition of femoral venous blood (Table 4). These changes were, however, insignificant although in a direction typical of exercise.

**EFFECTS OF CONTRACTIONS DURING PROXIMAL COLD BLOCKADE**

By these procedures the interaction of muscular with extramuscular humoral drives during prolonged dynamic work could be investigated. One group of dogs exercised at a lower rate (Figs. 4 and 5) while a second group worked at a higher load (Fig. 6).

Figure 4 demonstrates responses of HR, VE, arterial H⁺, Pco₂, and Pao₂. At first, work was electrically induced while the cold blockade abolished conduction to the centers (compare Fig. 1B). This procedure only accounted for moderate increments in HR (P < 0.05) and VE (P < 0.025). However, arterial Po₂ decreased (P < 0.05). Pco₂ and [H⁺] increased (Pco₂, P < 0.05; [H⁺], P < 0.0125).

Warming the thermode reestablished the muscular drives and VE and HR increased further (P < 0.0005 for both). Now VE was sufficiently enhanced to compensate for the arterial disturbances of [H⁺], Pco₂, and Pao₂ and all three parameters were no longer significantly different from the control values. Figure 5 shows the corresponding alterations of MAP, Q, Vo₂, and Vco₂. Work during proximal interruption of nerve transmission caused a decrease in MAP (P < 0.0005), but an increase in Q, Vo₂, and Vco₂ (P < 0.0005 for all three). If the transmission was restored, and work performed at a constant rate, further substantial increases in Q, Vo₂, and Vco₂ occurred and MAP also rose (P < 0.005 for all four variables).

From the data in Figures 4 and 5 the alveolar ventilation (VA, at 37°C) could be calculated according to the equation: VA = Vco₂ · 863/Paco₂. During the control period the calculation yielded VA = 2.24 liters/min and during work with blocked conduction it amounted to 2.61 liters/min (calculated from the means). This corresponds to an increase of 16.5%, whereas Vo₂ increased by 60–70%.

Considering the changes during work without proximal blockade, Vo₂ increased by 90–100%, despite the fact that the workload decreased somewhat. However, VA rose to 4.65 liters/min or by about 207%. Thus it seems likely that VA was not sufficiently augmented during withdrawal and [H⁺] increased (Pco₂, P < 0.05; [H⁺], P < 0.0125).
of muscular drives to match the increased metabolic demands and to compensate for the arterial \( \text{Po}_2 \), \( \text{pH} \), and \( \text{PCO}_2 \). The changes in \( \text{VO}_2 \) during blocked and unblocked nerve transmission seem to be related to the changes in \( Q \), as will be discussed below.

Experiments repeating the proximal cold blockade, after prolonged work with intact nerve transmission, yielded similar results (Fig. 5).

**TIME COURSES AND METABOLIC CHANGES**

Figures 6 and 7 and Table 5 summarize the responses of HR, \( V_E \), MAP, and \( Q \), and of some blood constituents

---

**Figure 6** Time courses of HR, \( V_E \), MAP, and \( Q \) during contractions of hindlimb muscles. Lower curves (open circles, \( n = 12 \)): data obtained during the onset and steady state of work with proximal cold blockade (about 1°C) in both sciatic nerves. Upper curves (closed circles, \( n = 13 \)): time courses if muscular drives from contracting muscles were not eliminated. The corresponding half-times of the increases during the first 60 seconds are indicated. The values of the lower curves at about 14 minutes were obtained if, after a period of work with unblocked reflexes, the proximal cold blockade was repeated (for details see Fig. 2 and text). Work rate under both conditions: \( 5.6 \pm 0.6 \) W/kg of muscle weight. Parameters of square wave pulses: \( 0.62 \pm 0.03 \) V, \( 0.4 \pm 0.00 \) msec, \( 65 \pm 0.00 \) Hz. Mean values \( \pm \text{SE} \).
Thereafter it fell again and was no longer significantly different from the control value. The increase in HR could be elicited by a change in discharge from the arterial pressoreceptors since this required an oppositely altered MAP. Q rose during the first 60–120 seconds with a rate and half-time similar to those of HR, but without an overshoot ($P < 0.0005$, 5 seconds after start and for all subsequent values). $Q$ increased exponentially and to obtain the time constant, $\tau$, $t/2$ could be divided by 0.675 to yield 12.0 seconds (Fig. 6). In the recovery period the four variables decreased rapidly within the 1st minute and thereafter only slowly. The rapid fall must have been caused by withdrawal of the reflexogenic drives.

In Table 5 arterial and femoral venous $P_{CO_2}$, $[H^+]$, $P_{O_2}$, $So_2$, plasma osmolality, and actual $[HCO_3^-]$ are shown during work without blocked muscular drives. These variables in the venous outflow are well known to reflect the work intensity of contracting muscles. The changes in femoral venous blood were highly significant (Table 5) but the values were normalized after passage through the lungs. Thus the reflex increase in $V_{E}$ was sufficient to compensate for these alterations in composition of venous blood. The compensation of plasma osmolality can be explained by equivalent changes of actual $[HCO_3^-]$ due to CO$_2$ output. In contrast to this, values of arterial pH, $P_{CO_2}$, and $P_{O_2}$ were not restored to normal if the muscular drives were blocked (Fig. 4). Table 5 also shows that the reflexogenic increase in $V_{E}$ was predominantly caused by an accelerated $V_{E}$ and to a lesser extent by an augmented $Q$. In Figure 7 the individual values of HR and $V_{E}$ were displayed as a function of $V_{O_2}$ during dynamic work without nerve blockade. The data were determined for periods after the onset of exercise at the times denoted in the various figures (2, 7, 14 minutes and rest).

**Blocked Muscular Drives (Fig. 6)**

When the time course of the variables was observed during contractions while nerve conduction to the centers was blocked proximal to the stimulating electrodes, neither HR nor $V_{E}$ rose significantly during the first 20 seconds (Fig. 6, left). Thus, muscular reflex drives were completely withdrawn by the cold blockade. Only after 2 minutes did HR and $V_{E}$ rise significantly ($V_{E}$, $P < 0.005$; HR, $P < 0.05$); however, they remained significantly below the values of the upper curves which referred to "no blockade" (significance for HR after 10, 30, and 120 seconds: $P < 0.05$, $P < 0.005$, $P < 0.0005$, respectively; for $V_{E}$ after identical times: $P < 0.0005$, $P < 0.0005$, $P < 0.0005$). MAP (Fig. 6, upper right) decreased rapidly during contractions with blocked muscular reflex drives (after 10 seconds, $P < 0.0005$). At equivalent times during the first 2 minutes MAP was significantly different from the values recorded during unblocked drives (after 10 seconds, $P < 0.025$; after 30 seconds, $P < 0.0025$). $Q$ (Fig. 6, lower right) rose with the same rate and $t/2$ during work with blocked as with unblocked reflex drives. Although the control data varied by about 4 ml/min per 100 g ($P < 0.0125$) it is obvious that the differences between $Q$ with blocked and unblocked reflexes became magnified and amounted to 12 ml/min after 2 minutes of work ($P < 0.001$).

The data for HR, $V_{E}$, MAP, and $Q$ which referred to
### Table 5 Work-Induced Changes in Some Femoral Venous Blood Constituents

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>After 6.8 min work</th>
<th>After 13.1 min work</th>
</tr>
</thead>
<tbody>
<tr>
<td>Art. $P_{CO_2}$ (mm Hg)</td>
<td>36.3 ± 1.8</td>
<td>35.7 ± 2.0</td>
<td>36.2 ± 1.7 NS</td>
</tr>
<tr>
<td>Art. $P_{CO_2}$ (mm Hg)</td>
<td>40.9 ± 2.1</td>
<td>53.5 ± 2.7</td>
<td>55.7 ± 3.4 *</td>
</tr>
<tr>
<td>Art. $[H^+]$ ($10^{-8}$ Eq/liter)</td>
<td>4.13 ± 0.12</td>
<td>4.23 ± 0.16</td>
<td>4.40 ± 0.10 NS</td>
</tr>
<tr>
<td>Art. $P_{O_2}$ (mm Hg)</td>
<td>94.1 ± 4.6</td>
<td>89.8 ± 5.3</td>
<td>86.3 ± 4.1 NS</td>
</tr>
<tr>
<td>Art. $P_{O_2}$ (mm Hg)</td>
<td>48.6 ± 2.1</td>
<td>29.9 ± 1.4</td>
<td>27.3 ± 1.6 *</td>
</tr>
<tr>
<td>Art. $S_O_2$ (%)</td>
<td>93.7 ± 0.9</td>
<td>90.0 ± 2.0</td>
<td>90.4 ± 1.5 NS</td>
</tr>
<tr>
<td>Art. $S_O_2$ (%)</td>
<td>68.9 ± 3.1</td>
<td>34.2 ± 2.9</td>
<td>30.0 ± 3.3 *</td>
</tr>
<tr>
<td>Art. osmolality (mOsmol/kg H$_2$O)</td>
<td>300.7 ± 1.8</td>
<td>300.9 ± 2.5</td>
<td>300.8 ± 1.6 NS</td>
</tr>
<tr>
<td>Ven. osmolality (mOsmol/kg H$_2$O)</td>
<td>303.0 ± 1.9</td>
<td>307.0 ± 2.0</td>
<td>308.1 ± 1.8 *</td>
</tr>
<tr>
<td>Art. actual $[HCO_3^-]$ (mEq/liter)</td>
<td>22.3 ± 0.70</td>
<td>21.7 ± 0.82</td>
<td>20.5 ± 0.67 NS</td>
</tr>
<tr>
<td>Ven. actual $[HCO_3^-]$ (mEq/liter)</td>
<td>24.6 ± 0.86</td>
<td>29.2 ± 1.13</td>
<td>27.9 ± 0.86 *</td>
</tr>
<tr>
<td>$V_F$ (min$^{-1}$)</td>
<td>15 ± 2.3</td>
<td>28 ± 3.1</td>
<td>34 ± 4.1 *</td>
</tr>
<tr>
<td>$V_T$ (ml BTPS)</td>
<td>307 ± 22</td>
<td>402 ± 28</td>
<td>409 ± 30 *</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SE; $n = 13$. The femoral venous blood constituents listed are well known to be altered by contraction.$^{19,21}$ The changes in venous blood were normalized in the arterial blood due to the reflexly augmented minute ventilation ($V_F$) if nerve transmission was not blocked. $V_F$ = ventilatory frequency; $V_T$ = tidal volume; NS = not significant. Significance between arterial (Art.) and venous (Ven.) data is specified between two lines over the columns. Significance for changes compared to control is given at the end of the corresponding lines.

* $P < 0.0005$.
† $P < 0.025$.
‡ $P < 0.0125$.

### Discussion

#### INVOLVED FIBER GROUPS AND REFLEX MECHANISM

The present findings give convincing evidence in favor of the hypothesis that specialized reflexes originate in the dynamically working muscles which simultaneously exert their drives on the heart, the lung, and the systemic circulation. However, the present experiments differ in some respect from previous investigations. The experimental protocol allowed further insight to be gained into the fiber groups involved and the interaction of muscular and extra-muscular drives. Another important difference from previous papers$^{13-18}$ is that we used an adequate stimulus, i.e., dynamic work, to evoke responses whereas former investigators used more or less inadequate or undefined mechanical, chemical, or electrical stimuli. Compared to isometric contraction dynamic work may be defined as muscular activity consisting of rhythmic contractions which cause predominantly a shortening of muscle fibers. The development of tension, pressure, and hypoxia within the muscles is minimized. This was reflected by a...
normal increase in Q and VO2 (Fig. 5-7) which in turn led to only a moderate decrease in femoral venous PO2 (Table 5) which was typical of dynamic work.18,30 Cardiovascular and respiratory responses evoked by isometric contractions differ in some respect from those obtained during dynamic work.21 In this regard it is of interest that isometric contractions with multiple muscle groups exerted no additive effects.21 However, that seems to be the case during dynamic work with multiple muscle groups, as shown in Table 1.

Group I and II nerve fibers and their corresponding receptors cannot play a dominant role in triggering the reflexes as it has often been supposed.7,26 These fibers chiefly innervate spindle, tendon, joint, and pressure receptors in the muscles.25 On the one hand, we excited these fibers with appropriate electrical stimuli (Fig. 3); on the other hand, by passive movements (Table 3). Both techniques evidently produced rather similar drives, but they cannot by any means explain the increase evoked by contractions (Fig. 3-6). In addition, these small drives via group I or II fibers disappeared after paralysis with immobilizing drugs (compare Tables 2 and 3 with Fig. 3). Therefore it might be possible that in nonparalyzed animals muscle tension was reflexly augmented by a compound input to the spinal cord following electrical or mechanical stimulation. Thus it can be argued just as well that these drives were caused secondarily to increased muscle tension which caused an augmented metabolic rate as demonstrated in Table 4. Beside these metabolic changes a reduction in peripheral resistance during passive movements follows (Table 3). This reaction is also metabolic in origin.37 Moreover, it is known that passive movements of the legs increase VO2.8 Thus there are several reasons to assume that proprioceptive mechanoreceptors whose impulses are conducted via group I and II fibers can be ruled out as receptors which are essentially involved in triggering the reflexes (see also Hodgson and Matthews29).

This notion receives strong support from the fact that the major portion of the reflexogenic drives still persisted at a nerve temperature between 4-8°C. Within this temperature range most of the myelinated fibers are blocked.23 Since the drives were only completely abolished after a latency of about 2°C it seems justified to suppose that identical fiber groups and mechanisms of excitation were involved. No convincing evidence has been found up to now to indicate changes in local PO2 or SO2, due to a lack of O2 supply, could be involved in the reflex initiation. For, HR, VE, and Q are adjusted much more quickly than changes in oxygen-consuming processes.20,33 In addition, ischemia activated group IV fibers only after a latency of about 2 minutes or not at all.31 The increase of [K+] was the only metabolic change in contracting muscles that corresponded to changes in blood flow and cardiorespiratory adjustment.20,34 Furthermore, enhancement of local [K+] by infusions induced, in addition to vasodilation, not only a reflex increase in HR, VE, and arterial blood pressure, but also an increase in sensory outflow via group III and IV nerve fibers.18,30,32

**IMPORTANCE OF EXTRAMUSCULAR DRIVES**

The present data demonstrate that neither arterial nor venous or cerebral chemoreceptors5-14 can be responsible for the principal cardiovascular or respiratory responses during exercise. Since the arterial osmolality remained unaltered (Table 5) it did not constitute a stimulus for cerebral osmoreceptors14 in our experiments. However, it appeared from Figure 6 that extramuscular humoral drives became more effective with increasing duration of work.

With regard to VE it may be supposed that humoral drives arose from the arterial chemoreceptors. However, during work with intact reflexes no significant arterial disturbances occurred (Fig. 4 and Table 5). Thus, under this condition the influence of the arterial chemoreceptors must be smaller than 21%. This minor importance of the chemoreceptors on respiratory control during exercise agrees with recent findings in chemodenervated animals.35 The increase in HR at the onset of work with blocked reflexes might be elicited by stimulation of the arterial pressoreceptors because the blood pressure correspondingly decreased (Fig. 6). However, at the end of work MAP was not significantly altered. Therefore it may be speculated that at this time a direct effect of bloodborne agents such as catecholamines might have been of importance. This speculation can be supported by the fact that in dogs exercising with denervated cardiac efferrnts HR increased similarly by about 20-30%.36

To explain the diminished MAP and Q during nerve blockade a reduction in the sympathetic tone of resistance arterioles throughout the body seems to be the most apparent cause. A smaller fraction of the cardiac output was
therefore directed through the working muscles. Whether the cardiac output was also diminished by the loss of muscular drives can only be the subject of speculation. However, it seems that the reduction of \(Q\) elicited the fall of \(V_o_2\) and \(V_c_o_2\) shown in Figure 5. \(V_o_2\) and \(V_c_o_2\) have been reported for resting as well as active muscles when blood flow was depressed.37, 38

With respect to the implications of the reflexes in the cardiorespiratory adjustments in conscious dogs, comparison is complicated by the different experimental conditions. However, it appears that the rate of increase in HR and \(V_e\) and the typical overshoot at the onset of exercise are rather similar in conscious and narcotized animals.35, 36, 39 As a function of \(V_o_2\), HR and \(V_e\) rose in the same way as in conscious dogs9 (Fig. 7).

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U Tibes

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