1 Supported by the Deutsche Forschungsgemeinschaft. The excellent technical assistance of Miss Claudia Zeugner is acknowledged.

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Effect of metabolic versus respiratory acid-base changes on isolated coronary artery and saphenous vein

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Summary. Experiments were performed on helically cut strips from coronary artery and saphenous vein to determine the relative influence of metabolic versus respiratory acid-base changes. Tensions were measured over a range of various HCO_3^- concentrations and pCO_2's. The results suggest that tension is influenced by extracellular pH and is independent of pCO_2.

Previous studies on the relative potency of metabolic versus respiratory acid-base changes on isolated blood vessels have conflicted. Isolated arteries were more sensitive to respiratory pH changes[2], and veins were more sensitive to metabolic pH changes[3]. In view of these conflicting reports, we compared the relative effectiveness of respiratory and metabolic acid-base changes on contractile tension of arteries and veins suspended in the same muscle bath.

Materials and methods. Helically cut strips from segments of canine left anterior descending or circumflex coronary artery and saphenous vein were attached to Grass FTO_3 force transducers and suspended in the same 40-ml organ chamber containing physiologic salt solution (PSS) bubbled with a 95% O_2 - 5% CO_2 gas mixture and of the following composition in mM: NaCl, 119; KCl, 4.7; KH_2PO_1, 1.18; $MgSO_4 \cdot 7\ H_2O$, 1.7; $NaHCO_3$, 21; $CaCl_2$, 1.16; dextrose, 5.5; sucrose, 50; $CaNa_2$ ethylenediaminetetra-acetate, 0.026. Initial tension was set at 100 mg in saphenous vein, and 500 mg in coronary artery. 35 mM K^+ (with NaCl reduced to maintain constant osmolarity) was placed in the chamber. The elevated K^+ caused tension to increase to 1903 ± 107 mg in coronary artery and to 460 ± 51 mg in saphenous vein. Bath pH was altered in 2 ways. In 1 case pH was varied by changing the bath pCO_2 at a constant HCO_3 (21 mM), and the relationship between tension and pH was determined for both types of vessels over pCO_2's ranging from 20 ± 2 mm Hg to 56 ± 3 mm Hg. In the 2nd case pH was altered by exchanging the control 35 mM K^+ PSS for either acidic PSS (35 mM K^+, 14.0 M $NaHCO_3$, adjusted NaCl) or basic PSS (35 mM K^+, 33.0 mM $NaHCO_3$, adjusted NaCl). Again, after equilibration the tension vs pH relationship was determined for several values of pCO_2. In each experiment pH, pCO_2 and pO_2 were measured 10–15 min after changing gas composition by anaerobically drawing PSS from the chamber into a glass syringe and immediately analyzing it with a Corning Blood Gas Analyzer. The experimental maneuvers were performed in various orders to prevent time-dependent errors.

Results. Tension is expressed as the percent change in tension from control. Control tension is defined as tension during 35 mM K^+ and 5% CO_2, and was obtained before and after each experiment. In figures 1 and 2 the triangles show the relationship between change in bath pH and change in bath pCO_2 when $\%CO_2$ was varied in control PSS. Open circles indicate values obtained by varying pCO_2 in the presence of low bicarbonate PSS, and closed circles indicate those values obtained by varying pCO_2 in high bicarbonate PSS. Indicated next to each point is the change in organ chamber pCO_2 from control. The main finding is

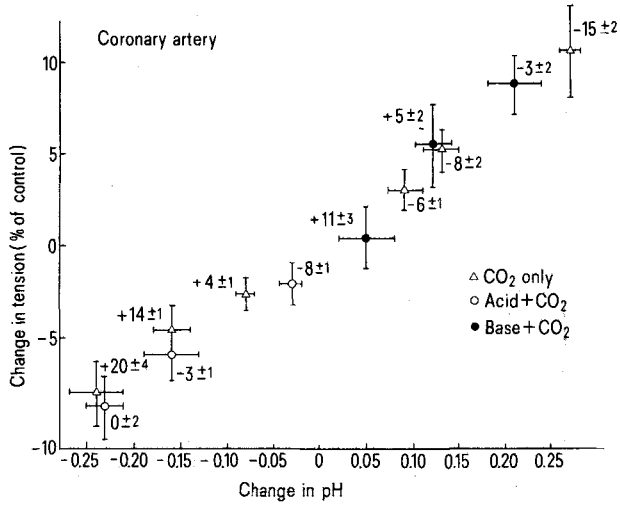

Figure 1. Effect of changes in bath pH on contractile force of coronary artery strips from 4 dogs. Data were grouped according to change in pH, means ± SEM for change in pH, change in tension and change in pCO_2 (values beside points) were calculated. Triangles show data obtained when bath pH was adjusted by changing pCO_2 alone; open circles represent effect of lowered bicarbonate concentration plus changing pCO_2; closed circles represent effect of raised bicarbonate concentration plus changing pCO_2. Note that change in tension is independent of the change in pCO_2. The change in pH of the bathing solution determines the change in tension independent of the change in pCO_2.

readily apparent: changes in tension depend only upon PSS pH and are independent of changes in pCO_2. For example, in coronary artery the pH in control PSS was increased approximately 0.13 units above control by lowering bath pCO_2 8 ± 2 mm Hg below control pCO_2 (triangle). The PSS pH for these same vessels was also raised a similar amount ($\sim$ 0.12 units) by replacing with basic PSS and then raising pCO_2 by 5 ± 2 mm Hg. The change in PSS pH and the increase in tension produced by these different procedures was identical (+5.5%) despite the fact that the change in pCO_2 was qualitatively different. This finding was true for both types of vessels throughout the entire range of pH's tested. In general, the saphenous vein was more sensitive to changes in pH than was the coronary artery.

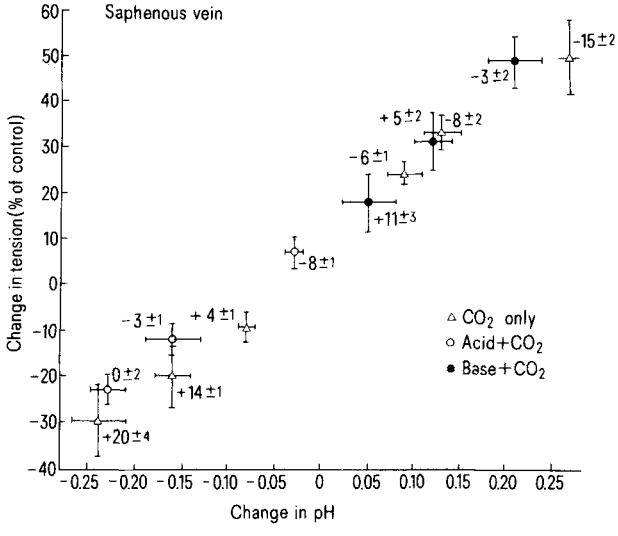

Figure 2. Effect of change in bath pH in contractile force of 4 saphenous vein strips from 4 dogs. See figure 1 for explanation.

Discussion. It is generally accepted that a) cell membranes are relatively impermeable to H^+ but readily permeable to CO_2 and b) CO_2 interacts with intra- or extracellular water to affect pH. One would predict from this that altering extracellular pH while holding pCO_2 constant should have a relatively small effect on intracellular pH, while changing pH an equal amount by varying only the pCO_2 should produce a much greater change in intracellular pH. Evidence from studies in several types of tissue supports this idea[5]. It has been proposed that pH affects vascular tone via changes in intracellular pH[6]. However, we found that similar changes in coronary artery and saphenous vein strip tension were produced by alterations in PSS pH regardless of the pCO_2. This suggests that changes in blood vessel diameter are influenced more by extracellular than intracellular pH. In vivo work by Kontos[7] on the dog pial artery supports this idea. In addition, Vanhoutte and Clement[3] showed in isolated dog saphenous vein that extracellular pH changes alone are more potent at affecting contractility than are changes of equal magnitude produced with CO_2. We have confirmed and extended these observations, showing that 1. the sensitivity of isolated arteries and veins to bath pH is not influenced by pCO_2; 2. the exterior of the plasma membrane may be the site of action of H^+ on vascular smooth muscle tension.

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Zeitgeber-schedule dependent resynchronization of circadian rhythms in nocturnal mammals (Primates and Chiroptera)[1]

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Summary. Changing the L: D time ratio of an entraining light-dark regime leads to characteristic alterations of the resynchronization behaviour of the circadian activity rhythms in night monkeys *(Aotus trivirgatus)* and African fruit bats *(Rousettus aegyptiacus)* after 8 h advance and delay shifts of the LD-Zeitgeber. Reduced speed of re-entrainment and occurrence of antidromic resynchronization point to a lower Zeitgeber strength of 24-h LD-cycles with a prolonged D-phase.

Entrained circadian activity rhythms usually do not follow a sudden phase shift of the Zeitgeber cycle immediately. Various numbers of shortened or lengthened transient cycles are needed for resynchronization. The various times needed for re-entrainment depend on different factors. Up to now the following have been proven: a) Dependence on the amount of the phase shift of the Zeitgeber[2]. b) Dependence on the direction of the Zeitgeber shift called 'asymmetry effect'[2], better yet 'directional effect'. Some species resynchronize more rapidly after a phase delay than after a phase advance of the Zeitgeber cycle whereas in other species the responce is exactly reversed[2,3]. c) Dependence on the oscillation range, that is the difference between the maximum and minimum of the signal intensity of the Zeitgeber cycle (temperature cycles: 4; light-dark cycles: 5). The greater the oscillation range of the entraining Zeitgeber cycle the higher the speed of re-entrainment. d) Dependence on the degree of plasticity of the circadian system of the individual species. Species with a very plastic endogenous timing system resynchronize more rapidly than species with a very rigid circadian system[6].

In order to check whether the Zeitgeber pattern, specifically the length of the photo and scoto periods, also influences the resynchronization behaviour, we carried out experiments with 4 night monkeys *(Aotus trivirgatus)*, and 12 African fruit bats *(Rousettus aegyptiacus)*. In the case of