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.

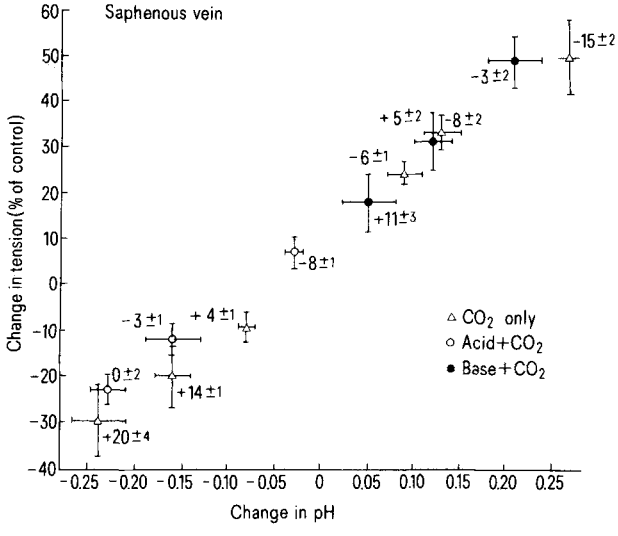

Figure 2. Effect of change in bath pH in contractile force of 4 saphenous vein strips from 4 dogs. See figure 1 for explanation.

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.

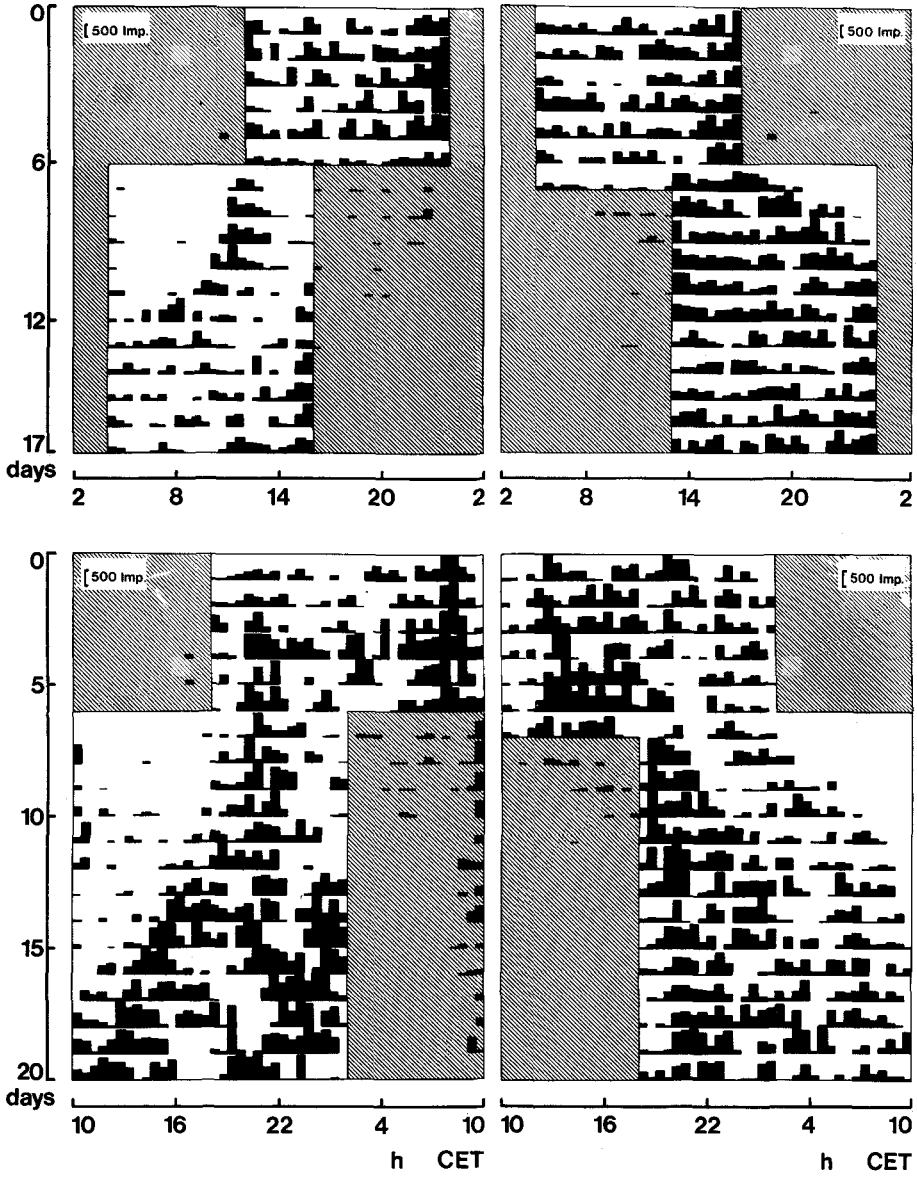
Entrained circadian activity rhythms usually do not follow a sudden phase shift of the Zeitgeber cycle immediately. Various numbers of shortened or lengthened transient cycles are needed for resynchronization. The various times needed for re-entrainment depend on different factors. Up to now the following 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

Aotus an LD 12:12 and an LD 8:16 h (10^2:10^0 lx) were abruptly delayed or advanced 8 h, and in the case of *Rousettus* the same resynchronization experiments were carried out with an LD 12:12, an LD 8:16, and an LD 16:8 (10^{-1}:10^{-5} lx). Before each Zeitgeber shift the test animals remained entrained to the respective LD-schedule for at least 20 days. By this means the probability of interfering after-effects of the preceeding resynchronization experiment with the following one was reduced to a minimum. The animals were fed ad libitum 1–2 h before the onset of the dark phase. For recording the locomotory activity of the monkeys and bats we used an electroacoustical method in which substrate-conducted sound caused by the movements of the animals was picked up by a special microphone, amplified, and used to trigger a series of square wave pulses. These were added by a data processor and printed out at 30-min intervals.

The resynchronization of the activity rhythm observed in both species was faster following the respective delay shift than the advance shift. This directional effect can be accounted for by the fact that the spontaneous period exceeds 24 h in both species. Whereas the night monkeys with LD 12:12 only needed 4 (delay shift) and 7 (advance shift) transient cycles respectively on the average in order to resynchronize, with LD 8:16 they needed 6.5 and 11.5 days respectively (fig.). Even the fruit bats with LD 8:16 resynchronized significantly slower than with LD 12:12 (t-test: $p < 0.001$). On the average, the bats with LD 8:16 needed after the delay shift 13.8 ± 3.1, and after the advance shift 17.9 ± 3.4 transient cycles, and only 9.1 ± 1 and 12.7 ± 2 respectively with LD 12:12. The time *Rousettus* needed for resynchronization with LD 16:8 was 7.5 ± 2 and 11.7 ± 3.5 days respectively which was somewhat shorter than with LD 12:12. The differences were, however, not significant. Whereas the fruit bats with LD 12:12 always resynchronized orthodromically, in other words a change of the period in the direction of the Zeitgeber shift, half of them with LD 8:16 resynchronized antidromically after the advance shift by lengthening instead of shortening the period. Also when exposed to an LD 16:8 several resynchronized antidromically after the advance shift.

These results show that the Zeitgeber pattern influences the



Resynchronization behaviour of the circadian activity rhythms of 2 night monkeys, *Aotus trivigatus*, after 8 h advance (left) and delay shifts (right) of an entraining LD 12:12 (top) and an LD 8:16 h regime (bottom). L = 10^2 lx, D = 10^0 lx. The histograms based on the recorded 30-min values represent the activity pattern on successive days (from top to bottom) before and after the respective phase shift of the Zeitgeber cycle. The activity bouts the monkeys show in the last 2 h of the light time of the phase advanced LD 8:16 (bottom left) are caused by feeding behaviour immediately after supplying the animals with food.

course of resynchronization of the circadian activity rhythm after a phase shift of the Zeitgeber cycle. These effects can hardly be referred to as after-effects of short and long photoperiods on the circadian period as described by Pittendrigh and Daan[8] because in both species the period length of the free-running circadian activity rhythm varies only within a very narrow range[3]. Both the reduced speed of resynchronization and the occurrence of antidromic resynchronization point to the fact that 24-h LD cycles with a prolonged D-phase possess a lower Zeitgeber strength for the circadian system of nocturnal species than LD's with L- and D-phases equal in duration. We assume that this generally holds true and that light-active species would react in a way analogous to the nocturnal species tested, if the duration of the L-phase of an 24-h LD cycle exceeds 12 h. In this respect also human beings - in whom LD cycles are not fully ineffectual, despite the fact that social factors are the principle Zeitgeber[9] - should be tested to see whether the time needed for resynchronization after transmeridian flights at higher latitudes is larger in summer than during the equinoxes, and whether a pronounced temporary internal desynchronization of circadian functions[10] can occur as a result of the lower Zeitgeber strength of the natural illumination cycle with a greater day length.

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Fever and survival in the rat. The effect of enhancing the cold defence response

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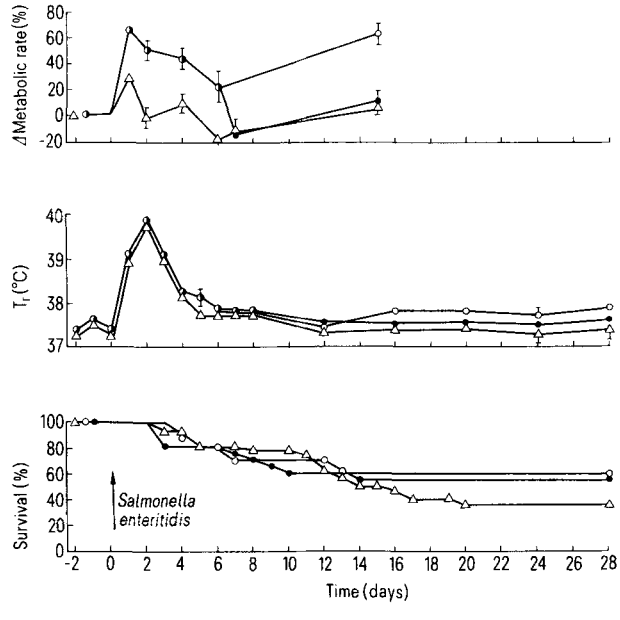
Summary. Continuous cooling of the spinal cord for 6 and 28 days had a probably beneficial effect on the outcome of salmonellosis in the rat, suggesting that the apparently harmful effect of high fevers is not due to the cold defence response but may rather be caused by the high body temperature.

The febrile response of a mammal may be a defence against invading microorganisms[2]. However, the enhancement of the normal febrile response of rats by cooling their preoptic areas increases mortality from salmonellosis[3]. High fevers, furthermore, are associated with increased mortality in both humans[4] and rabbits[5]. This effect could be caused by the febrile activation of any of the cold defence responses - the increase in metabolic rate is thought to be particularly detrimental[6,7] - or by the high body temperature. To investigate the former possibility, I cooled the cervical spinal cord of rats infected with *Salmonella enteritidis*. Spinal cord cooling enhances the cold defence responses but has no effect on body temperature in the rat because the rise in heat production so induced equals the amount of heat lost to the thermode[8,9]. This methode of enhancing the cold defence responses seemed preferable to cold exposure, for cold exposure cools the peripheral tissues and, in infected rats, it usually induces hypothermia[10].

Materials and methods. Spinal cord thermodes were chronically implanted in 130 specific pathogen free, male Wistar rats under pentobarbital anesthesia. The animals, weighing about 350 g at the time of operation, were then fixed to an antirotatory device[3] that allowed freedom of movement otherwise, and caged individually in a room at 23 °C with natural illumination. Food and water were continuously available. 3 weeks after the implantation, 60 animals that showed no apparent signs of spinal compression were i.p. infected with 1 ml of a suspension of live *S. enteritidis*[3] containing 0.002 mg bacterial dry weight/ml. In 30 randomly chosen control animals, the disease was allowed to follow its natural course, while in the other animals the spinal cord was continuously cooled with water at 23 °C starting shortly after the induction of the infection. In 20 of



Average changes in metabolic rate and body temperature, and survival in rats infected with live *S. enteritidis*. In the control (△) and in the experimental animals, the pathogen was injected on day zero and the spinal cord of the experimental animals was then continuously cooled for 6 (●) or 28 (○) days. Note that in the first 6 post-infection days, the temperature and metabolic data for both groups of experimental animals were pooled because they were treated the same, and that after the 1 infection day the metabolic rate was determined in only 8 control and 8 experimental animals. The standard errors (vertical lines) are shown only when larger than the symbols.