Materials and methods. Female Swiss albino mice were obtained from Canadian Breeding Farms, St. Constant, Quebec. At 2 months of age 1 group of mice received an injection of α-tocopherol, while a 2nd group remained as controls. Measurements of lipid peroxidation fluorescent products were carried out when the mice were 3 and 5 months old. The Purina Chow used for the diet was standard mouse chow in pellet form.

In order to inject α-tocopherol, it was solubilized in carrier solution[5]. Experimental animals received 1 i.p. injection of 1.1 IU α-tocopherol in 0.1 ml of carrier. The dl-α-tocopherol used was in oil form, and was obtained from ICN Canada, Montreal, Quebec.

Lipid peroxidation levels were determined by fluorescence analysis. The brain and heart ventricles were excised and processed using the method of Tappel et al.[4]. Fluorescence measurements were made using an Aminco-Bowman spectrophotofluorometer standardized with quinine sulfate (1 mg/ml of 0.1 N H_2SO_4). Measurements were taken with the voltage set at 700 V and wavelength set at excitation 358 nm and emission 438 nm and a slit opening of 5. Measurements were obtained in fluorescent units per 0.2 g tissue sample.

Data were analyzed by means of the standard t-test.

Results and discussion. The results show that the level of lipid peroxidation fluorescent products is lower in the heart and the brain of tocopherol-treated mice as compared to control mice in both age groups examined. Table 1 illustrates the results for heart tissue. By 3 months of age the fluorescence level in the heart of the tocopherol-treated animals is clearly lower (by 23%) than that of the control animals, although there is only a borderline level of statistical significance. By 5 months of age, the level of fluorescence products in the heart is 53% lower than in the control animals, and the difference is highly significant.

Table 2 presents the data for brain. Both at 3 months of age and at 5 months of age, the level of lipid peroxidation fluorescent products is significantly lower in the animals injected with tocopherol than in the control mice.

When we examine the data for both brain and heart in relation to the age of the animals, we note that there is no increase in lipofuscin level between 3 and 5 months of age in the tocopherol-treated animals. In contrast, there is a highly significant increase in the level of fluorescent products between 3 and 5 months of age in the control animals.

The data presented show that the level of lipid peroxidation fluorescent products, or lipofuscin, can be significantly lowered in both brain and heart tissue of young mice by a single i.p. injection of tocopherol. In analyzing these results it is doubtless important to remember that tocopherol can be stored in various body tissues[6] and that parenteral doses are eliminated slowly[7]. Thus the tocopherol that was injected may have gone into a storage pool to be utilized gradually over a period of time. Or, once the level of tocopherol was elevated by the supplementary dose, it may have remained at a new and higher plateau since the animals were receiving an accepted level of tocopherol through the Purina Chow diet. The results can be interpreted in relation to the free radical theory of aging[8]. The presence of tocopherol is believed to reduce the level of free radical reactions at the tissue level, thus retarding the build up of lipofuscin[9], although it is not yet clear whether antioxidants alter the rate of aging in mice.

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Fever and survival in the rat. Metabolic versus temperature response

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Summary. In infected rats, survival was directly proportional to the metabolic cost of fever ($\Delta O_2\%/\Delta$ °C) during its rising phase and inversely proportional to the height of fever. It is suggested that some febrile, metabolic response may be beneficial, while the rise in temperature may be harmful for the host animal.

Although fever is the most common symptom of illness, its role in infectious disease in mammals is not clear. In rats infected with *Salmonella enteritidis*, cooling the spinal cord enhances the febrile, metabolic response to cold without affecting body temperature and increases survival[2]. On the other hand, cooling the preoptic area raises the febrile temperature without essentially increasing metabolic rate and decreases survival[3]. It may then be speculated that in salmonellosis some febrile, metabolic response to cold increases survival, whereas the increase in temperature decreases it. The present work, in which the natural course of this illness was studied, shows that this hypothesis is tenable.

Materials and methods. The results were obtained in 156 specific pathogen free, male Wistar rats, weighing about 350 g and kept at 23 °C with natural illumination and food and water freely available. The animals were anesthetized with pentobarbital and fixed to an antirotatory device that otherwise allowed freedom of movement[3]. At this time, either a preoptic[4] or a spinal[5] thermode was implanted in 70 of the animals but, except for the implantation, these animals were handled like the ones without thermodes.

2-3 weeks after the operation, the animals were i.p. infected with 1 ml of a suspension of live *S. enteritidis*[3]. Body temperature was measured at least once a day (at 12.00 h) with a thermocouple inserted about 60 mm beyond the

anus. Oxygen uptake was additionally determined[2] as required in 69 of the animals, but in each animal always at the same hour to avoid circadian artifacts.

Results. After injection of a sublethal dose of *S. enteritidis* (fig. 1, upper panel), body temperature rose slowly reaching almost 40 °C on the 2nd post-infection day; oxygen uptake, however, increased only during the rising phase of fever ($p < 0.01$, paired t-test). Figure 1 (lower panel) further shows that doses of bacteria high enough to reduce survival drastically did not significantly affect the average height of fever.

In a group of 112 animals, which were infected with a LD_{50} of *S. enteritidis* (fig. 2, upper panel), the highest fever elicited varied between 38.6 and 41.0 °C - average 39.8 ± 0.6 (SD) °C - and the higher the fever the lower was the probability of survival ($p < 0.007$, linear trend in proportions[6]). In 53 of these animals in which metabolic rate was determined, resting oxygen uptake during the rising phase of fever varied between −37% and +87% in relation to the preinfection level but on the average it increased by 17 ± 23 (SD)%. This change in metabolic rate correlated neither with the increase in temperature during the rising phase of fever nor with survival. Survival was, however, proportional to the metabolic cost of fever during its rising phase ($p < 0.01$), that is, to the percentage change in metabolic rate per °C of increase in body temperature (fig. 2, lower panel).

Discussion. Slowly rising fevers seem to be primarily effected by decreasing heat loss[7] because heat production increases only slightly or does not change[2,3] (fig. 1). There is, however, considerable flexibility. In some cases, heat loss increases or decreases in excess[8,9], and heat production, within certain limits, changes in accord to balance heat loss at the febrile temperature[10]. Consequently, irrespective of the height of fever, metabolic rate may be increased, decreased, or unchanged[7-11] (see also 'results').

At the infection levels used in this work, the height of fever was not an index of severity, for lethal and sublethal infections induced the same average fever (fig. 1). On the other hand, when a LD_{50} was injected, the rate of survival was inversely proportional to the height of fever (fig. 2, upper panel). Furthermore, although febrile temperatures retard the growth of *S. enteritidis*, survival decreases if fever is enhanced by cooling the preoptic area[3]. It is well known that very high body temperatures produce lethal thermal injury, but experiments with cells in culture suggest that some cells may suffer irreversible heat damage even at normal body temperatures[12]. Thus, non-lethal, febrile temperatures could cause enough thermal damage to weaken the defences of the host, for example, by producing a substance that depresses the reticuloendothelial system[13]. The febrile rise in temperature could thus aggravate the course of the infection. This may also explain why patients with high fevers seem to have less resistance to infection than those with low ones[14,15].

These experiments also show that survival was proportional to the metabolic cost of the rising phase of fever (fig. 2, lower panel). Since metabolic rate increases only during the rising phase of fever[2] (fig. 1), this increase could be considered a thermoregulatory rather than an immune response. Furthermore, if the metabolic cost of fever is increased by cooling the spinal cord, survival increases[2]. This suggests that some metabolic response to cold is beneficial for the host, perhaps because it stimulates its defences. There are several potential mechanisms. The thermoregulatory system, for example, modulates the endocrine[16], and this controls both the inflammatory[17,18] and the specific immune responses[19,20]. Furthermore, the sympathetic system,

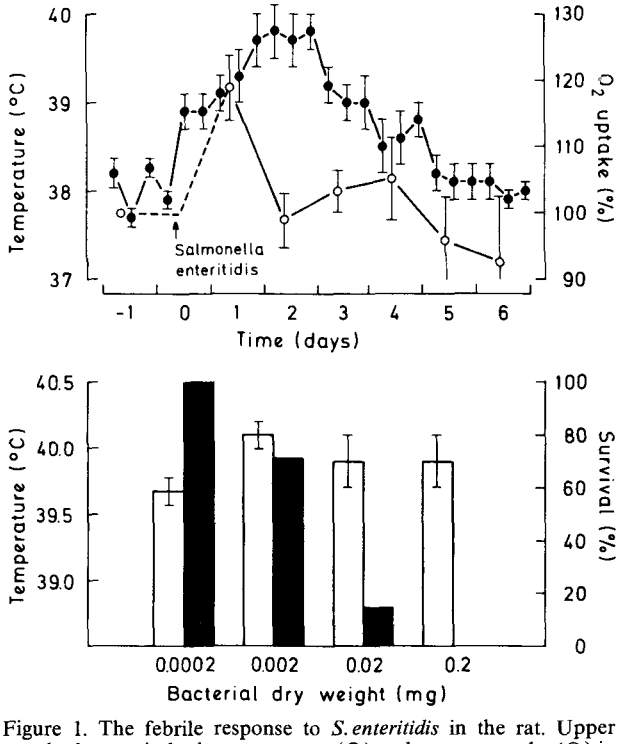

Figure 1. The febrile response to *S. enteritidis* in the rat. Upper panel: changes in body temperature (●) and oxygen uptake (○) in 16 animals infected with a sublethal dose of live bacteria (0.0002 mg bacterial dry weight). Lower panel: febrile temperature (open bars) and survival (solid bars) in rats infected with various doses of live bacteria, 7 animals per group. The vertical lines are standard errors.

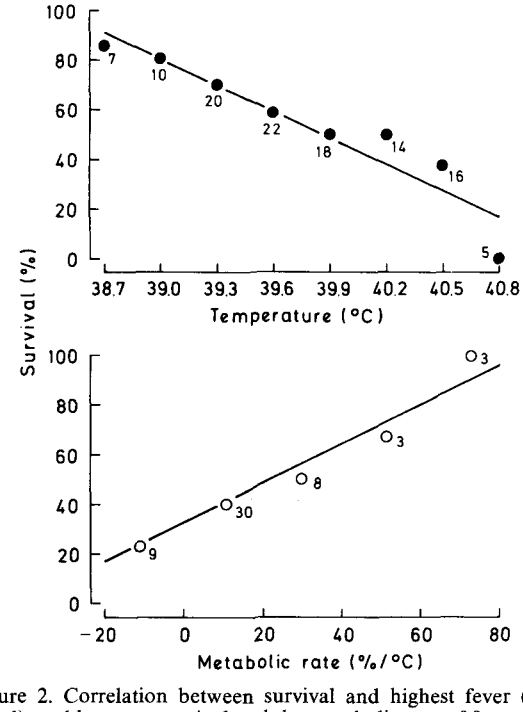

Figure 2. Correlation between survival and highest fever (upper panel), and between survival and the metabolic cost of fever during its rising phase (lower panel) in rats infected with live *S. enteritidis* (0.002 mg bacterial dry weight). The animals were grouped in ranges of 0.3 °C and 20%/°C respectively, and the survival of each subgroup was then calculated. The figures indicate the number of animals in each subgroup.

a thermogenic efferent, may be the mediator[21] of the action of the nervous system on the acute phase reaction[21,22].

To conclude, these experiments suggest that the febrile, metabolic response could be beneficial, and the rise in temperature could be harmful for the host's defences. If this is true, the animals that develop low fever at high metabolic cost would have the highest probability of surviving. The metabolic effect is, however, small. In a population of rats, a metabolic increase of 14% may improve survival by 11% points (fig. 2). Body temperature would, however, increase by 1 °C, thus reducing survival by 35% points. The metabolic effect may thus prevail only at temperatures below 38.5–39.0 °C, because the thermal effect might then be negligible. Consequently, fevers above this level seem to be detrimental for rats infected with *S. enteritidis*. An optimal fever has also been suggested for rabbits[23]; the optimal height may depend on the host species as well as on the invading microorganism[24].

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Electroacupuncture: Effects on digastric muscle activities in the rat jaw-opening reflex

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Summary. Electroacupuncture suppressed the late component of the digastric muscle activity in the rat jaw-opening reflex evoked by buccal skin stimulation, while it scarcely affected the early component. When the jaw-opening reflex was elicited by tooth pulp stimulation, the activity of the digastricus was well suppressed in its whole phase.

It has been reported that the jaw-opening reflex is produced by stimulating various oral and facial areas[2-4]. The reflex is generally considered to be the result of the activation of nociceptors or small diameter nerve fibers[2,5]. Especially when evoked by tooth pulp stimulation, the jaw-opening reflex has been regarded as a possible indicator of noxious reaction, because the tooth pulp is largely innervated by small diameter fibers[6] and also because a sensation of pain is evoked by various stimuli applied to tooth pulp or dentine[7]. However, the jaw-opening reflex can be also evoked by activation of low threshold mechanoreceptors not related to nociception[4].

On the other hand, acupuncture has been shown to suppress selectively pain sensation in patients and in laboratory volunteers[8], and noxious responses in experimental animals[9,10]. It therefore seemed interesting to compare the effects of acupuncture on the jaw-opening reflex elicited by stimulation of tooth pulp or of another oro-facial region.

Materials and methods. The experiments were undertaken with 14 female Wistar albino rats weighing about 400 g. The animals were lightly anesthetized with thiamylal sodium in an initial dose of 80 mg/kg, i.p. For afferent inputs, buccal skin and tooth pulp was electrically stimulated by rectangular constant current pulses of 0.1 msec duration at 1 Hz. Stimulating pulses were delivered to the tooth pulp of the lower incisor using a bipolar stainless steel electrode (0.1 mm in diameter, interpolar distance 2.0 mm, insulated except for the tips) inserted 20 mm from the tip of the incisor. With these conditions, intrapulpal nerve fibers mostly consisting of small diameter ones of Aδs can be selectively stimulated without eliciting a spread of current to the periodontal tissue[11]. The intensity of the stimulus pulses was about 1.5 times the threshold for producing a minimum jaw-opening reflex. The buccal skin was stimulated with the same pulses using a bipolar hook electrode of Co-Cr wire whose interpolar distance was 2.0 mm. The intensity of the pulses in this case was about 3.5 times the threshold for the jaw-opening reflex. With this intensity, both Aβ and Aδ elevations in the compound action potentials recorded from infraorbital nerve were distinguished. The electromyogram of digastric muscle in the jaw-opening reflex was recorded with a bipolar hook electrode of Co-Cr wire, interpolar distance 4.0 mm, inserted into the anterior belly of the ipsilateral digastric muscle, and its magnitude was estimated by the area of the activity. Cathodal electrical acupuncture (electroacupuncture) stimulation pulses (45 Hz, 5 msec) were delivered to the Yin-Hsiang points of both sides which are at the lateral margin of the nasolabial fold. The intensity of the electroacupuncture pulses was 5–6 times the threshold for evoking the compound action