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Does Exercise Stress Alter Susceptibility to Bacterial Infections?

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ABSTRACT

Swimming was used for evaluating alterations in performance capacity and as a means for studying the influence of exercise stress on susceptibility to *Streptococcus pneumoniae* and *Francisella tularensis* infections in two strains of rats, i.e. Fisher-Dunning (FD) and Sprague-Dawley (SD). The performance capacity was reduced by both diseases and was correlated to the dose of the given micro-organism. FD rats, however, were more susceptible to the infection and showed a greater deterioration than SD rats. The effects of exercise stress on disease lethality varied with the time that it was performed. Strenuous exercise immediately before infection drastically reduced susceptibility to either of the bacteria, while a similar bout of exercise performed after infection increased disease-related mortality in both diseases.

INTRODUCTION

In the literature there are only two studies known to us which show that a pre-infection conditioning (training) programme is protective against bacterial as well as viral infections (4,15). There are, however, case reports indicating highly trained athletes to be more susceptible to normally harmless infectious diseases (10). Furthermore, it is well documented that exercise in experimental studies may be harmful in certain infectious diseases, especially in those infections where the infectious process is specifically located within tissues that are activated during physical activity such as in viral myocarditis and poliomyelitis (10, 16). Retrospective clinical data in poliomyelitis also suggest that the timing of exercise during the course of disease may be important in the pathogenesis (13).

For this reason these basic studies were performed in an effort to determine whether there is a critical period around the time of inoculation where exercise stress influences the proneness to develop an infection and subsequently changes the disease-related mortality. We subjected two strains of rats to swimming exercise immediately before and after infection with *Streptococcus pneumoniae* and *Francisella tularensis.* These two bacterial infection models have a well described pathogenesis and do not cause myocarditis (8, 9, 17).

MATERIALS AND METHODS

Animals. Male Fischer-Dunning (FD) rats (F-344/Mai f, MA BioProducts) and Sprague-Dawley (SD) rats (Tac:N [SD] fbr, Taconic Farms, Inc.) weighing 175-200 g, were used and maintained as described in previous studies (8, 9, 17). Rats of each strain were divided into groups for each of the two bacterial infections (see figures 1 and 2).

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals", as promulgated by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council. The facilities are fully accredited by the American Association for Accreditation of Laboratory Animal Care.

Infection. Rats were inoculated subcutaneously (s.c.) in the groin pouch with virulent *S. pneumoniae* Ia5 or intraperitoneally (i.p.) with *F. tularensis* live vaccine strain (LVS), with various doses of either bacteria per 100 g body-weight as shown in the figures. Control rats were sham-inoculated with sterile tryptose-saline. The responses to the diseases were followed and characterized by a rise in rectal temperature and a depression of plasma zinc (data not shown), as described by Neufeld et al (18).

Swimming. All rats were previously experienced with the swimming task through a brief (60min.) swim one week prior to the experiment (9, 17). The effects of various doses of either bacteria on performance capacity were studied 72 h. after inoculation in both rat strains (figure 1). The swim session was performed as previously described

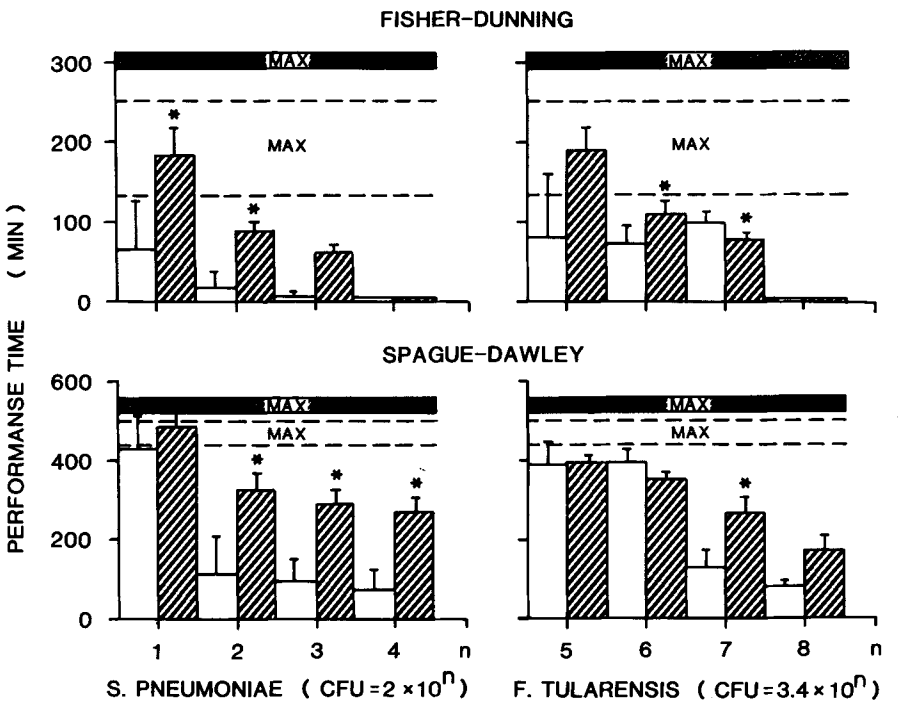

Figure 1. Effects of *S. pneumoniae* and *F. tularensis* on swimming performance capacity of naive (□) and experienced rats (▨) on day 3 of the infections. Each bar represents the mean ± SEM for 20 rats. Horizontal bars represent the maximum swimming time of naive (⁘) and (═) experienced non-infected rats. n=log dilution of each bacteria (CFU) on abscissa. Asterisks denote a statistically significant difference ($p<0.01$) between naive and experienced rats.

(9,17) and according to figure 2. The end-point was chosen as the time when the rat was submerged for approximately 10 sec., ceased all co-ordinated movements and could not return to the surface. Each exercise session was closely monitored by an experienced technician, who retrieved the rats at the moment of exhaustion. Performance capacity was measured in all rats and was defined as swimming time in minutes.

Statistical analysis. The effects of infection on performance capacity was calculated and evaluated for significance by means of ANOVA (unpaired).

RESULTS

A great reduction in performance capacity was observed on day 3 in both *S. pneumoniae*- and *F. tularensis*-infected rats as compared to that in non-infected controls (figure 1). The magnitude of this performance reduction was dose-dependently related to the number of the given micro-organisms. However, Fischer-Dunning (FD) rats were more susceptible than Sprague-Dawley (SD) rats to these infections (figure 2).

Strenuous exercise immediately before inoculation with *S. pneumoniae* or *F. tularensis* drastically reduced disease-related mortality in both FD and SD rats (figure 2). A similar bout of exercise shortly after inoculation, however, seemed to increase the late-phase lethality in both infections (see figure 2). When exercise was performed, before as well as after inoculation, the effect of the latter exercise session was decisive for the outcome, i.e. lethality increased.

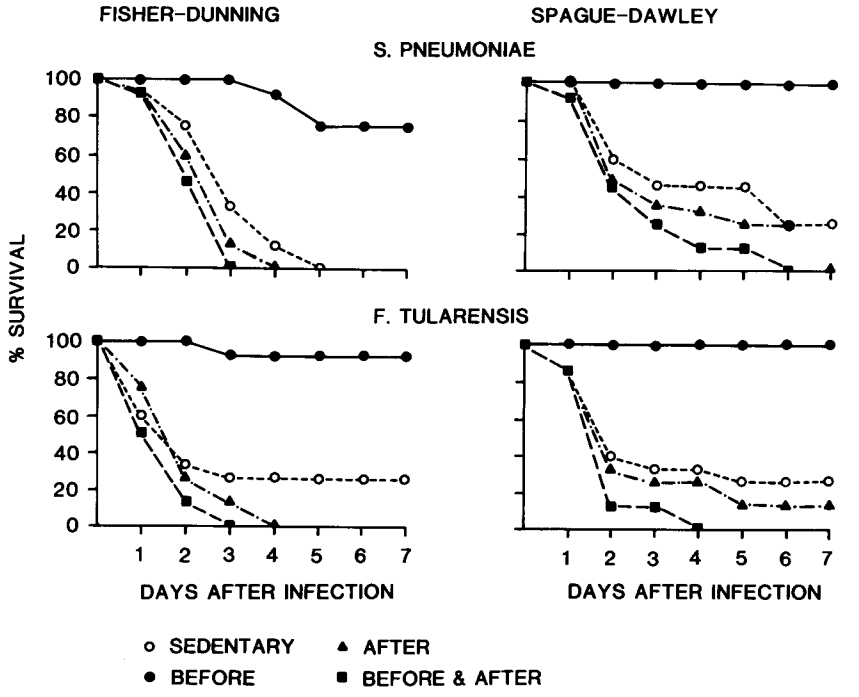

Figure 2. Effects on survival (day 3 post inoculation) of a 3-h swim at various times relative to the time of infection with *S. pneumoniae* (2,1 x 10^1 CFU) and *F.tularensis* (3,2 x 10^6 CFU). "Before" groups were exhausted 3 h prior to the inoculation. "Before and After" groups were exhausted 1.5 h before and 1.5 h after the inoculation (n=15 in each group).

DISCUSSION

This interesting finding of increased resistance to infection after one single bout of exercise performed immediately prior to the inoculation is similar to the early findings by Oppenheimer and Spaeth (20) more than 50 years ago. They showed that exercise before pneumococcus infection in rats increased resistance to the infection by between 67 and 87%. Their results were confirmed with the same bacterial species in two additional animal species, the guinea pig (19) and the rabbit (2).

The mechanisms by which susceptibility and disease lethality in bacterial infections are altered by exercise are still not fully known, but at the time of these early studies results when exercise was performed before the infection were interpreted as being caused by the fatigue that follows after strenuous exercise (2, 5, 19, 20). Regarding the effect of exercise performed after the infection, these workers gave no explanation. Harisch et al. (12) found that a certain amount of swimming exercise imposed during a few days before infection with *Pasteurella multocida* increased survival, whereas, somewhat unexpectedly, either fewer or more numerous exercise sessions at this time were detrimental and reduced survival. A partly similar observation in human athletes is that moderate exercise appears to stimulate the immune system, whereas intense exercise evidently may compromise some immune functions (7).

A single bout of exercise to exhaustion in healthy men may give a transient rise in the number of peripheral blood natural killer (NK-) cells (6). NK cells are an important part of the basic immune defence against several micro-organisms (10, 16). This may explain the observed increased survival in the present study, since there are also reports of increased NK-cell function in peripheral blood of highly trained persons (21)

Forced exercise may also cause lysosomal membrane labilization leading to release of lysosomal constituents and membrane components (24), which can induce lymphoid proliferation (1). Endogenous pyrogen, probably identical to interleukin-1 derived from stimulated macrophages (11), is released during exercise (3), elevating body temperature and possibly increasing unspecific resistance to infection (4). It is not known whether more intense or long-lasting exercise prior to the present infections would have reversed susceptibility.

The cause of the slightly but consistently increased lethality that occurred when exercise was performed after the inoculation is less obvious, but may also be explained by changed immune function. It has been found that exercise in the acute phase of bacterial and viral infections may increase disease intensity (14, 16, 23). The finding of more extensive progression of inflammatory heart disease after exercise is accompanied by lower serum concentrations of specific antibodies and interferon, which might affect host homeostasis and clearance of infective micro-organisms (23). Although not observed in the present study, strenuous exercise during acute tularemia may cause unusual dissemination of the infection possibly due to impaired immune responses (8). In one study respiratory infections were found to be more frequent in ultramarathon runners than in controls for a two-week period following a race (22). Thus, failure to restrict physical activity in the acute phase of both bacterial and viral infections may well contribute to the progression of the disease.

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