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"DEVELOPMENT AND TESTING OF A MOUSE SIMULATED SPACE FLIGHT MODEL"

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INTRODUCTION

We are currently involved in the phase of this research project concerning the development and testing of a mouse model for simulating some aspects of weightlessness that occur during space flight, and the carrying out of immunological flight experiments on animals. The mouse model is an antiorthostatic, hypokinetic, hypodynamic suspension model similar to the one used with rats (1,2).

We have shown that this murine model yielded similar results to those observed using the rat model of antiorthostatic suspension for simulating some aspects of weightlessness (3). We have also shown that mice suspended in this model showed decreased interferon-alpha/beta production as compared to control, non-suspended mice or to orthostatically suspended mice (4). This suggests that the conditions occuring during space flight could possibly affect interferon production (4). We have also continued our basic science studies on the demonstration of the regulatory role of interferon in non-viral diseases. This includes several bacterial and protozoan infections (5-7), indicating the great significance of interferon in resistance to many types of infectious diseases.

Our current studies involve a continuation of the use of the mouse model to simulate some aspects of weightlessness to determine the effects of suspeension on immunological parameters and resistance to infectious diseases. In addition, we have been able to utilize samples from rats flown in mission SL-3 to test for the effects of actual space flight on immunological parameters.

METHODS, RESULTS AND DISCUSSION

We have expanded our studies on the effects of suspension on resistance to infectious diseases. Our earlier studies showed that female Swiss mice that were normally resistant to infection with encephalomyocarditis D (EMC-D) virus became susceptible after being antiorthostatically suspended for one week. These same mice also had suppressed interferon production after antiorthostatic suspension. Orthostatically suspended control female mice retained full interferon production capacity and also retained resistance to infection with EMC-D virus.

Our new studies have been carried out with male Swiss mice. These mice are normally susceptible to infection with EMC-D virus. After either orthostatic or antiorthostatic suspension, the mice became resistant. No differences in the effects of antiorthostatic or orthostatic suspension on interferon production were observed. These results suggest that suspension modelling some effects of weightlessness can affect resistance to viral infections, and that intrerferon production could play a major role in mediating that resistance.

These studies were borne out by additional studies using rats flown in SL-3. Within 8 hr after return to earth, spleens were removed from these rats and challenged with mitogens. The spleen cells of flown rats produced little to no interferon-gamma, while spleen cells from ground control rats produced normal moderate levels of interferon-gamma. These data indicate that the suspension model was predictive of the effects of space flight on interferon production. In addition, the production of interleukin-3, another immunologically important

substance, was not affected in the cells from the flown animals. This may indicate that the effects of space flight on interferon production may be a key factor in any change in immune responses due to space flight.

The following publications have appeared since the last progress report on this agreement. They acknowledge the agreement, and reprints have been included with this report.

A. Wirth, J.J., Kierszenbaum, F., Sonnenfeld, G., and Zlotnik, A. Enhancing effects of interferon-gamma on phagocytic cell association with and killing of Trypanosoma cruzi. Infect. Immun. 49:61, 1985.

B. Mann, D.W., Sonnenfeld, G., and Stein-Streilein, J. Pulmonary compartmentilization of interferon and natural killer cell activity. Proc. Soc. Exp. Biol. Med. 180:224, 1985.

C. Sonnenfeld, G. The natural immunoregulatory role of interferon. In: 8th Forum in Immunology, E. DeMaeyer, Chairman. Annales de L'Institut Pasteur-Immunologie, D:136:77, 1985.

D. Sonnenfeld, G., Wirth, J., Kierszenbaum, F., DeGee, A.L.W., and Mansfield, J.M. In: The Interferon System, Ares-Serono Symposium no. 24, F. Dianzani and G.B., Rossi, eds., Raven Press, New York, 1985, p. 195.

In addition, the following manuscripts are in press:

E. Gould, C.L., Williams, J.A., Mandel, A.D., and Sonnenfeld, G. Effect of flight in mission SL-3 on interferon-gamma production by rats. The Physiologist, In Press, 1985.

F. Sonnenfeld, G. Interactions of the interferon system with cellular metabolism. In: Clinical Applications of Interferons and their Inducers, D.A. Stringfellow, Ed., Marcel Dekker, Inc., New York, In Press, 1986.

G. Sonnenfeld, G., Gould, C.L., Kierszenbaum, F., DeGee, A.L.W., and Mansfield, J.M. Interferon in resistance to bacterial and protozoan infections. In: The Biology of the Interferon System, 1985, H. Schellekens and W.E. Stewart II, eds., Elsevier Scientific Publishers, B.V., Amsterdam, In Press, 1986.

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3. Steffen, J.M., Robb, R., Dombrowski, M.J., Musacchia, X.J., Mandel, A.D., and Sonnenfeld, G. Aviat. Space Environ. Med. 55:612, 1984.
4. Rose, A., Steffen, J.M., Musacchia, X.J., Mandel, A.D., and Sonnenfeld, G. Proc. Soc. Exp. Biol. Med. 177:253, 1984.
5. Kierszenbaum, F., and Sonnenfeld, G. J. Immunol. 132:905, 1984.
6. Rollag, H., Degre, M., and Sonnenfeld, G. Scand. J. Immunol. 20:149, 1984.
7. Wirth, J.J., Kierszenbaum, F., Sonnenfeld, G., and Zlotnik, A. Infect. Immun. 49:61, 1985.