ture modification, which implies that responses normally observed in a normal-gravity environment are no longer appropriate in weightlessness. The results also suggest a concept of otolith signal reinterpretation which is consistent with the sensory conflict theory of space motion sickness. Well-being in space may be related to the ability of the central nervous system to modify response patterns. Individuals with less plastic responses will exhibit more severe symptoms.

The H reflex and dynamic posture tests also provide data on the reestablishment of terrestrial norms of motion behavior. Both tests were extremely sensitive and suggest that more than a single time constant may be involved in man's ability to return to baseline values. While both the sample size and number of measurements were small in this study, the results indicate that an effort to continue this research is warranted. A more complete analysis of the data will appear later (*10*).

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4. The initial design for this experiment called for use of the European space sled to provide a sinusoidal linear acceleration. When the sled was removed from Spacelab 1, D. G. D. Watt, a Canadian investigator associated with the MIT experiments, agreed to the use of his drop system as an alternative method of providing a brief-impulse linear acceleration.
5. Drops in a normal-gravity environment are not equivalent to those in microgravity. In the former the acceleration transition is from 1 *g* to 0 *g*, and in the latter it is from 0 *g* to −1 *g*. Physiologically the primary difference is the bias or position of the otoliths on the saccular maculae. Data from parabolic flight studies by our laboratory suggest that potentiation of the H reflex is sustained in 0 *g*. This supports the concept of a new bias point in a microgravity environment. However, the bias was nulled by adjusting the H reflex in both gravity environments so that it was at 50 percent of its maximum amplitude just before each drop.
6. A full set of responses at each drop-to-shock delay time was obtained before and after flight for all four subjects. Inflight data were collected on two crew members. On day F + 1 (approximately 24 hours into the flight) a complete set of data was obtained with only one of the two inflight subjects. At F + 6 both subjects participated; however, only two drops at each drop-to-shock delay were obtained.
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## Prolonged Weightlessness and Humoral Immunity

Abstract. *Preflight, inflight, and postflight serum samples obtained from crewmen aboard STS-9 were analyzed for immunoglobulin content. Control studies for circadian rhythm were conducted to further validate the analyses. Quantitation of immunoglobulins G, M, A, D, and E indicated relatively minor fluctuations in the concentration of each class of immunoglobulin during the experiment. Thus, microgravity effects on immunoglobulin levels during a 10-day flight were considered insignificant.*

The space environment is characterized in part by the absence of gravity. Because weightlessness is an abnormal condition relative to a 1-*g* environment, microgravity can be considered biologically as a stress factor or perturbation of the normal state. Historically, important basic biological research has capitalized on comparisons between normal and altered states. For example, microbiologists have routinely induced genetic mutations to study basic molecular mechanisms. These artificially created, but controlled, modifications lead to a better understanding of normal states. Similarly, the human immune system is potentially a model for studies in a microgravity environment because of its intrinsic complexity. The human humoral immune response is predicated on poiesis, cell differentiation, complex cellular interactions, regulatory mechanisms, and mitogenic activation with subsequent synthesis and secretion of biologically specific antibody molecules. Such complexity increases potential sensitivity to a variety of external stimuli such as prolonged weightlessness.

The experiment described in this report was designed to analyze and quantitate the humoral immune response under prolonged weightlessness during the 10-day Spacelab 1 (STS-9) flight. The human immunoglobulin (Ig) population, which comprises the humoral response, consists of various classes designated IgG, IgM, IgA, IgD, and IgE. Major classes, such as IgG, also contain subclasses IgG1, IgG2, IgG3, and IgG4. Each class and subclass differs in a variety of properties such as antigenic distinctiveness, average serum concentration, serum half-life, and effector functions. These properties are important in terms of quantitating Ig populations in serum in order to measure the effect of certain conditions such as microgravity.

Four crewmen participated in the Ig studies and were designated MS1, MS2, PS1, and PS2. MS1 and PS1 were members of the red team, while MS2 and PS2 were part of the blue team.

Three separate studies were conducted to validate the Ig measurements and effects of a prolonged microgravity environment. First, in order to control for circadian rhythm effects (*1*), a study was conducted with serum samples from MS1 and PS1 in advance of the STS-9 flight. Serum samples were obtained over a 2-day period, reflecting a shifting of personnel from their routine diurnal

Table 1. Schedule of STS-9 experiment INS105.

| Crewman | Date of bleeding (1983)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | F − 30 | F − 7 | F − 1/1½ | MD7 | L + 0 | L + 1 | L + 8 | L + 12/13 |
| MS1 | 9/24 | 11/21 | 11/26 | 12/6 | 12/8 | 12/9 | 12/16 | 12/21 |
| MS2 | 9/24 | 11/21 | 11/27 | 12/6 | 12/8 | 12/9 | 12/16 | 12/21 |
| PS1 | 9/24 | 11/21 | 11/26 | 12/6 | 12/8 | 12/9 | 12/16 | 12/20 |
| PS2 | 9/24 | 11/21 | 11/27 | 12/6 | 12/8 | 12/9 | 12/16 | 12/20 |

*Day F − 30 is 30 days before flight; MD7 is mission day 7; and L + 8 is 8 days after landing.

schedules to schedules simulating their time in space. Second, serum samples derived from 20 Caucasian males were studied in order to establish a normal range of concentrations (milligrams per milliliter) for each Ig class. Third, preflight, inflight, and postflight serum samples from MS1, MS2, PS1, and PS2 were studied as indicated in Table 1.

In all studies, Ig classes were measured and compared in quantitative assays. The principal assay employed was the radial immunodiffusion test (*2–4*). All serum studies were repeated with a solid-phase radioimmune inhibition assay to measure Ig concentration. In each assay a purified Ig standard (for instance, IgG) was affixed to an immulon well (Dynatech, Inc.) and reacted with radioactively labeled $^{125}I$ soluble antibody against Ig (specific activity, $\sim 10^6$ cpm/mg). Binding was quantitated in terms of radioactivity bound to the plate after adequate washing with buffer (*p*H 8.0). Serum samples from all crewmen at all time points indicated were incubated with the Ig-coated plates before the addition of the radiolabeled specific antibody. Standard inhibition curves were constructed with purified Ig preparations for each class of Ig. All results were closely correlated with the values reported in Table 2.

By use of these assays the serum from 20 Caucasian males (control group) was anlayzed to establish population limits for the various Ig classes with standard reagents and Ig controls employed throughout the studies. Measurements for IgG based on this control group showed a range of 6.16 to 15.54 mg per milliliter of serum with an average standard deviation of 0.10. For IgM the range was 0.57 to 3.43 mg/ml with an average standard deviation of 0.06, and for IgD and IgE the ranges were 0.04 to 0.02 and 0.001 to 0.0001 mg/ml, respectively. Table 2 presents the same analyses of preflight, inflight, and postflight serum samples obtained from MS1, MS2, PS1, and PS2. It should be noted that the concentrations measured for IgG, IgM, and IgA generally fall within the previously established ranges. Only the IgG concentration for MS1 (Table 2) is significantly outside the ranges determined for the human male Caucasian group. In all cases, the IgD concentration for MS1, MS2, PS1, and PS2 was <30 μg/ml and the IgE concentration was below 1 μg/ml. The circadian effect study with serum samples from MS1 and PS1 showed Ig concentration ranges similar to those reported in Table 2 for IgG, IgM, and IgA with no significant changes.

Results of these studies (Table 2) indicated that microgravity, as experienced during the 10-day STS-9 flight, had no significant effect on the humoral immune response as evidenced by the quantitation of each Ig class. The data show only minor variations in the concentration of immunoglobulin and no definite trends when the results are categorized in terms of serum samples taken before flight (days F − 30, F − 7, and F − 1 or 1½), during flight (MD7), in the early postflight period (L + 0 and L + 1), and in the late postflight period (L + 8 and L + 12 or 13). The slight increases during the flight and decreases after the flight may reflect changes in plasma volume resulting in hemoconcentration and hemodilution, respectively.

Table 2. Results of STS-9 experiment INS105.

| Crewman | Ig | Time of bleeding and Ig concentration (mg/ml) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | F − 30 | F − 7 | F − 1/1½ | MD7 | L + 0 | L + 1 | L + 8 | L + 12/13 |
| MS1 | IgG | 18.8 | 19.6 | 18.0 | 18.8 | 19.7 | 21.2 | 18.0 | 15.6 |
| | IgM | 1.8 | 2.3 | 2.5 | 3.5 | 3.5 | 3.2 | 3.0 | 3.2 |
| | IgA | 4.5 | 4.4 | 4.2 | 4.5 | 4.5 | 4.9 | 4.2 | 4.3 |
| | | 25.1 | 26.3 | 24.7 | 26.8 | 27.7 | 29.3 | 25.2 | 23.1 |
| MS2 | IgG | 14.0 | 12.8 | 13.5 | 13.5 | 13.5 | 13.5 | 12.0 | 10.7 |
| | IgM | 2.5 | 1.9 | 1.7 | 2.0 | 1.9 | 1.7 | 1.9 | 1.9 |
| | IgA | 2.9 | 3.5 | 3.3 | 3.7 | 3.7 | 3.7 | 2.9 | 3.0 |
| | | 19.4 | 18.2 | 18.5 | 19.2 | 19.1 | 18.9 | 16.8 | 15.6 |
| PS1 | IgG | 18.0 | 14.0 | 17.7 | 15.0 | 16.0 | 13.5 | 12.8 | 13.5 |
| | IgM | 4.4 | 5.2 | 5.1 | 4.0 | 5.0 | 5.0 | 5.0 | 5.0 |
| | IgA | 4.1 | 4.0 | 4.2 | 4.7 | 4.7 | 4.2 | 3.5 | 3.4 |
| | | 26.5 | 23.2 | 27.0 | 23.7 | 25.7 | 22.7 | 21.3 | 21.9 |
| PS2 | IgG | 8.8 | 10.0 | 7.5 | 7.5 | 7.5 | 7.5 | 6.5 | 7.5 |
| | IgM | 2.5 | 2.6 | 3.0 | 1.8 | 1.8 | 1.9 | 2.0 | 1.8 |
| | IgA | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| | | 12.8 | 14.1 | 12.0 | 10.8 | 10.8 | 10.9 | 10.0 | 10.8 |

The data must be interpreted within the context of the kinetics of the immune response and the 10-day duration of the flight. Invoking a constant rate of Ig synthesis for all Ig classes and subclasses, it appears that the rate of catabolism becomes the distinguishing factor. The average serum half-life values for each human Ig class (in vivo) are IgG1 (23 days), IgG2 (23 days), IgG3 (8 days), IgG4 (23 days), IgM (5 days), IgA (6 days), IgD (3 days), and IgE (2 days). From these values it can be seen that IgG3, IgM, IgA, IgD, and IgE all have half-life values less than the length of the 10-day flight. Preliminary studies of the IgG3 population in the serum samples obtained from MS1, MS2, PS1, and PS2 indicate insignificant changes in concentration as seen with the major Ig classes (Table 2). Similarly, blood group specific hemagglutinin titers remained constant for all crewmen. Relating the results in Table 2 with the catabolic half-life values, it can be concluded that if microgravity had an inhibitory effect on Ig synthesis, and the effect was exhibited shortly after achieving the weightless state (for instance, on MD1), then significant reductions may have been best observed in the IgG3, IgM, IgA, IgD, and IgE populations. The data listed in Table 2 and referred to in the text are not consistent with such an inhibitory effect. These conclusions are similar to those reached in the Skylab flight series (*5*), but the analyses and experimental design presented in this report substantiate the findings.

These results can be correlated with the studies reported by Cogoli *et al.* (*6*), who found no lymphocyte activation on binding of a lectin during the STS-9 flight. Thus, one might conclude that activated immune lymphocytes continue production of Ig's during prolonged weightlessness and are not affected by microgravity. However, microgravity may impair the lymphocyte activation process, altering the response to new antigenic stimuli.

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