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Metabolic and Regulatory Systems in Space Flight

THE DYNAMICS OF BLOOD BIOCHEMICAL PARAMETERS IN COSMONAUTS DURING LONG-TERM SPACE FLIGHTS

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INTRODUCTION

Long-term stay under conditions of space flight accompanied by forming in man lipid, carbohydrates, protein, and energetic metabolism alterations. The most part of studies of cosmonauts metabolic state had been carried out in post-flight period. In this connection, all conclusions, concerned of metabolism peculiarities during space flight, had probabilistic character.

The purpose of our work was study of metabolism in cosmonauts right during long-term space flights.

METHODS

In capillary blood taken from the finger, by biochemical analyzer "Reflotron IV" (Boehringer Mannheim Co., Germany), which work based on principle of "dry chemistry", activity of GOT, GPT, CK, gamma-GT, total and pancreatic amylase, as well as concentration of hemoglobin, glucose, total bilirubin, uric acid, urea, creatinine, total, HDL- and LDL cholesterol, triglycerides had been determined. HDL/LDL cholesterol ratio also was computed. Crewmembers of 6 basal missions, 17 persons total, had been tested. Biochemical studies carried out 30-60 days before launch, at the 25 - 423 day of flight, at the 1 and 14-th day of recovery.

RESULTS

In cosmonauts during space flight had been found tendency to increase, in compare with basal level, GOT, GPT, total amylase activity, glucose and total cholesterol concentration, and tendency to decrease of CK activity, hemoglobin, HDL-cholesterol concentration, and HDL/LDL cholesterol ratio. Some definite trends in alterations of other determined biochemical parameters had not been found.

CONCLUSION

The same directions of alterations GOT, GPT, total amylase, CK, glucose, total and HDL-cholesterol values, and HDL/LDL-cholesterol ratio allows to suppose existence of connection between noted metabolic alterations with influence of space flight condition upon cosmonaut's body. Alterations of other studied blood biochemical parameters depends on, probably, pure individual causes.

All data, illustrating noted hypotheses will be discussed in the report.

EFFICIENCY OF FUNCTIONAL LOADING TEST FOR INVESTIGATIONS OF METABOLIC RESPONSES TO WEIGHTLESSNESS.

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INTRODUCTION

Biochemical research performed in manned space missions, simulated and in-flight animal experiments to develop and concretize the concept of metabolic balance in microgravity environment indicated that the total metabolic balance in weightlessness is dependent upon the polyhormonal influence of the regulatory systems the function which is reduced to a minimum under these conditions. A specific manifestation of the metabolic balance is the mobilization of the endogenic substrates resulting from the proteins and lipids destruction while inhibition the synthesis of the metabolites, the desintegration of the metabolic cycles with an activation of the deport processes of many substances and the increase of excreting the ballast metabolic products from. The acute periods of adaptation and readaptation to the effect of gravitational factor are aggravated by the development of the stress-reactions having insignificant specificity.

The aim of the present investigation is to examine the advantages of applying the physical load test for men and women metabolism investigation under ground-base simulations of the space flight factors and study of the possibility to using of a stepwise incremental grades load (GPL) on the bicycle ergometer to investigate the metabolic responses of human to a weightless environment during a long-term space mission.

METHODS

The studies with the use of the GPL-test have been done in the experiment with the long-term head-down tilt bed-rest (HDT-BR) with participation of 8 female and 8 male volunteers once before bed rest, respectively on day 60 and day 128 during HDT-BR. The studies with the use of the GPL-test have been performed also with participation of 6 crew members of the prime and back-up spacecrews once pre-flight and post-flight. In the studies there has been used the following GPL-test: a steppers incremental graded leg bicycle ergometry performed in the supine position, with the standard load of 150 W in capacity at the last stage and with total time of pedaling which amounts to 15 min. In conducting the GPL-test, three times - 10 min prior to testing, immediately after completing the bicycle ergometry and within 30 min of rest blood sampling through the catheter inserted into the antecubital vein has been done. In the collected specimens of the blood serum there has been determined the broad spectrum of the biochemical indices characterizing the state of energy metabolism judging from the content of the carbohydrate and lipid substrates and the blood activity of energy - producing enzymes. The studies are performed by using of the biochemical analyzer Technicon RA 1000 with the Boehringer Mannheim commercial test-kits. The data is subjected to multifactorial differential analysis with the fixed effects.

RESULTS

The data of applying the GPL-test in men under ground-based simulation of weightlessness effects are more informative as compared to the performance of biochemical investigations at rest. When studied the effects of long-term HDT-BR on the woman metabolism, the use of GPL-test was also more informative as compared to the at-rest studies. Absolute majority of the observed changes in metabolism is manifested a significant dependence on the level of physical activity of the test-subjects. Physical loads indicated that of 20 blood parameters characterizing the state of carbohydrate and lipid metabolism the 14 indices were reliably changed during experiment. In this case, the maximum amount of changes is revealed with the use of GPT and only 9 indices were registered in the rest state of test subjects. GPL-test has been used for studying the peculiarities of metabolism in cosmonauts of the 18-th crew expedition.

CONCLUSION

The performed studies were the clean demonstration of the high efficiency of applying the GPL-test for studying the peculiarities of metabolism during ground-based simulation of the effects of microgravity both in men and women. The biochemical studies of blood samples taken during GPL-testing are more informative than the investigations performed under at-rest conditions and on this basis have been used for studying the peculiarities of metabolism in a space mission.

Human cellular immunity and space flight .

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Space flight factors may influence many human systems and functions, and in particular, the immune system. In work are presented results of peripheral blood lymphocyte subpopulations studies at cosmonauts, taken part in space flights at the period of 1987-1994, as well as at volunteers, having been in hypokinesia experiments conditions. The flow cytometry method was used to quantify CD3+, CD4+, CD8+, Leu7+ and HLA-DR+ cells. The lymphocyte ability to answer to the mitogen stimulation was studied in cell cultures.

It was shown that already before the flight the reduced contents of CD4+ cells was observed at cosmonauts. After long flights the contents of CD3+, CD8+ and Leu7+ cells was diminished. Lymphocyte functional activity was also decreased after the flight. At the long-duration space flight modeling by means of hypokinesia it was noted a reduction of CD4+ cell count at the beginning of the experiment and an increase of CD3+ cell contents at its end. After the experiment the changes were distinguish from usually observed after the flight. At first days after the end of the experiment it was noted an increase of all T-cell populations, but later a reduction of CD8+ cell amount was happened.

Thereby, the hypokinesia studies do not give a full belief about changes, occur in human immune status in space flight.

At present the methods of immunity evaluation in weightlessness are developed, which will allow to study the cosmonaut immune status right in conditions of space flight. Results of conducted studies are discussed.

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CYTOKINE PRODUCTION AND HEAD-DOWN TILT BED REST

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INTRODUCTION

Head-down tilt bed rest (HDT) is used as an analogue to study physiological effects mimicking those occurring in weightlessness during space flight. An unusual high frequency of infectious diseases during long duration HDT has been described along with a decreased natural killer cell activity.

METHODS

In the present study, 8 volunteers were subjected to a strict HDT of -6° for 42 days. Blood samples were obtained 12 days before, at day 14, 35, and 42 during and 14 and 35 days after HDT. Facscan analysis was used to determine cell subpopulations. Plasma was used to quantify various plasma hormone levels. Whole blood was also triggered with various activators such as LPS, PHA, PMA, anti-CD3, and anti-CD2 antibodies. Supernatants were collected and analysed for interleukin-1, 2, 6, 10, interferon gamma, and tumor necrosis factor alpha.

RESULTS

No significant changes in the percentage and total number of CD2, CD3, CD4 and CD8+ cells was observed. The percentage and absolute number of natural killer cells (CD2+/CD3-/CD56+) decreased in all subjects after 14 days of HDT. No differences in interleukin-2, 6, 10, and tumor necrosis factor-alpha were found. Other cytokine levels have still to be analysed. Hormone levels which might interact with the immune system have shown that 1,25-dihydroxyvitamin D3 and parathormone decreased significantly during HDT whereas cortisol, prolactin, TSH and growth hormone levels remained unchanged.

CONCLUSION

- These results might indicate that the decrease in natural killer cell activity during and after HDT :
- is not due to an increase in stress hormone levels such as cortisol
 - might be due to a decrease in the absolute number in natural killer cells
 - is probably not due to a decrease in cytokine production

PLASMA AND URINE AMINO ACIDS DURING HUMAN SPACE FLIGHT. T.P. Stein, M.J. Leskiw and M.D. Schluter. Department of Surgery, University of Medicine and Dentistry of New Jersey - SOM, Stratford, NJ, 08084.

We measured the plasma and urine amino acid distribution patterns before, during and after space flight on the Shuttle. The urine and plasma samples were collected on two separate flights of the space shuttle. The first flight lasted 9.5 days and the second flight 15 days. Urine was collected continuously for the period beginning 10 d before launch to 6 days after landing. venous blood samples were taken from a forearm vein from the four payload crew of the second mission after an over night fast. The blood samples were taken launch-45 (L-45), 15 (L-15) and 8 (L-8) days before flight, inflight on the flight day 2 (FD-2), 8th (FD-8) and 12th (FD-12) days and after flight on the day of return (R+0), and days 6 (R+6), 15 (R+15) and 45 (R+45) after return. Results: (i) Urinary amino acids: Overall the urinary amino acids showed little change with spaceflight. except for a marked decrease in all of the amino acids on FD1 ($p<0.01$) and a reduction in isoleucine and valine on FD3 and FD4 ($p<0.05$). (ii): Plasma amino acids. Most of the changes found pertained to the essential amino acids, particularly the branched chain amino acids. The plasma aminograms for FD's 8 and 12 were very similar and both aminograms were very different from the FD 2 aminogram. FD2 was not different from the preflight ground control. With increasing duration of time in space, there was an increase in the concentration of the essential amino acids in the plasma. Most of the increase found on FD's 8 and 12 relative to FD2 was due to increases in the branched chain amino acids all of which were significantly increased ($p<0.05$). The concentration of the essential amino acids on landing were decreased. There was no correspondence between the last inflight measurement (FD12) and the sample collected immediately after landing.

DNA FINGERPRINTING: APPLICATIONS TO SPACE MICROBIOLOGY

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INTRODUCTION

DNA fingerprinting techniques have been used to study microbial transfer among crewmembers, microbial dissemination throughout the spacecraft, and to identify sources of contamination. DNA fingerprinting can distinguish different genotypes and provide a molecular identification system for microorganisms. DNA fingerprinting can be achieved by various methods including: restriction fragment length polymorphism (RFLP), Southern blot hybridization, repeated sequence PCR, ribotyping, and others.

METHODS

Microbiological specimens from crewmembers and the spacecraft environment were collected, and *Staphylococcus aureus*, the selected bacterial model, was isolated by standard methods. Crew specimens included nose, throat, skin, urine, and feces; environmental samples included air, surfaces, and water. DNA was extracted from the *S. aureus* isolates and fingerprinted by one or more of the following techniques: RFLP, RFLP with Southern blot hybridization, ribotyping, and repeated sequence PCR. RFLP and PCR products were separated by electrophoresis (pulsed-field, agarose, etc.). Following electrophoresis, the gels were stained (e.g., ethidium bromide) to visualize the banding patterns of the DNA fragments. *S. aureus* displaying the same DNA banding patterns were designated as the identical genotype.

RESULTS

RFLP analysis using Sma I restriction endonuclease demonstrated transfer of *S. aureus* between two crewmembers during a Space Shuttle mission. RFLP analysis following digestion with either EcoRI or HinfI in combination with Southern blot hybridization with repeat fragment 27A probe similarly demonstrated a transfer of *Candida albicans* between crewmembers. However, such transfers appeared to occur infrequently (<1 in 10 Shuttle missions) during the relatively short Space Shuttle missions (<15 days). Repeated sequence PCR analysis of *S. aureus* isolates from crewmembers of the Mir 18 and 19 missions also demonstrated transfer of the bacterium between crewmembers. Ribotyping was used to distinguish different genotypes of waterborne bacteria recovered from Shuttle and Mir water sources.

CONCLUSIONS

DNA fingerprinting proved to be a powerful tool for studying microbial dynamics in spacecraft. Transfer of microbes between crewmembers occurred during shorter duration missions aboard the Space Shuttle as well as during longer duration missions on the Mir Space Station. DNA fingerprinting technologies can be used to validate microbial contamination models. This technology can also serve as an invaluable epidemiological tool to investigate in-flight contamination events and infectious disease outbreaks.