Biomedical Investigations in Soviet Long-Duration Space Flights

Introduction

The Soviet Union's manned space program has, in recent years, concentrated its efforts on establishing a permanent human presence in low earth orbit. The Mir space station complex provides the on-orbit infrastructure necessary to fulfill that goal. The 20-metric ton core module launched in 1986 has been more than doubled in weight and habitable volume by the addition of two specialized modules. These modules have also upgraded the technical and scientific capabilities of the complex. Six long-duration prime missions have been launched to Mir, with rotating crews occupying the complex between February 1987 and April 1989, and once again from September 1989 to the present. Durations of individual flights have ranged from four months to one year. Five short-duration visiting flights ranging from eight to 25 days have also been conducted, four of these involving non-Soviet guest cosmonauts.

In the 15 years prior to the launch of Mir, the Soviet Union operated six Salyut space stations, direct predecessors of the current complex. Much of the hardware and many of the procedures used aboard Mir were flown on these earlier stations and were evaluated in ground-based studies using spaceflight-analog environments. Many of the record-breaking long-duration missions were preceded by bed-rest studies of comparable duration, including a 370-day antiorthostatic hypokinesia experiment completed before the start of the one-year flight. Biomedical monitoring techniques, countermeasure procedures, and rehabilitation programs associated with long-duration flights were developed in the course of bed-rest studies.

The Mir complex supports both long-duration prime missions and short-duration visiting flights. The extensive biomedical monitoring, and especially the countermeasure protocols and rehabilitation programs, apply only to flights longer than 30 days and remain relatively constant from flight to flight. The short-duration missions support their own experimental program, often unique for each flight, and usually sponsored by the international partners supplying the guest cosmonaut.

This review is limited to the biomedical investigations conducted before, during and after current long-duration missions on board the Mir complex. The open scientific literature contains varying amounts of information about Soviet investigations, with detailed descriptions in some cases and virtually no details in others. This inconsistency is reflected in the descriptions provided here.

Anthropometric Measurements

Anthropometric measurements pre- and postflight have been performed since the earliest missions (Balakhovskiy & Natochin 1973). Currently, routine inflight anthropometric studies are limited to measurements of body mass and lower leg circumference, with leg volume calculated from the latter values. Anthropometric measurements of long-duration crews are recorded every 2-3 days at the beginning of the flight, and every 2-3 weeks thereafter (Talavrinov et al. 1988).

The Soviet Union's first inflight body mass measurement device was flown on the Salyut-5 station in 1976 (Sarychev et al. 1988) and an essentially identical unit is aboard Mir. The device operates on the principle that a body attached to a spring will, if perturbed, oscillate with a period depending on the spring's properties and the body's mass. After calibrating the unit, the crewmember places his chest and abdomen on the subject support, while his chin rests on a chin support. Footrests and handlebars immobilize feet and hands. A thumb-activated lever unlocks the unit to begin oscillations. The device has a reported accuracy of less than 0.5%.

The first inflight measurements of leg circumference in the Soviet program were recorded during the 140-day Soyuz-29 mission to Salyut-6 in 1978 (Kas'yan et al. 1980). The technique utilizes an elastic stocking-like device, with eight circumferential tape measures located 3 cm apart. Based on the assumption that each segment between tape measures approximates a truncated cone, the volume of the lower leg (a 24-cm length) is calculated as the sum of the volumes of the seven segments.

The Cardiovascular System

Since the first human spaceflight in 1961, much emphasis has been placed on the study of the effects of weightlessness on the cardiovascular system. Operational constraints on early missions limited inflight investigations to cardiac electrical and mechanical activity (Kas'yan et al. 1968) and postflight studies to tests of orthostatic tolerance and exercise capacity (Kakurin 1977). In recent years, more extensive investigations have been conducted on board space stations with the goal of evaluating changes in cardiac electrical and mechanical activity, cardiac size and chamber dimensions, regional blood flow, fluid distribution, exercise capacity, and orthostatic tolerance. Cardiovascular examinations are carried out before, during, and after long-duration flights at rest, during exercise on the bicycle ergometer and the treadmill, during the application of lower body negative pressure (LBNP) and during the application of thigh positive pressure (occlusion cuffs); active orthostatic tests are performed pre- and postflight (see Table 1).

Comprehensive cardiovascular examinations at rest are performed 30 days before launch (L-30), during flight within 48 hours of boarding Mir and approximately every two weeks thereafter, and postflight on the day of landing (R+0), on R+4-5 and again on R+60. Heart rate is monitored by standard 12-lead electrocardiogram (ECG), arterial pressure by auscultation (Korotkov method) and by tachooscillometry, and stroke volume by impedance plethysmography. Cardiac output and total peripheral resistance are calculated from the measured parameters. Regional blood flow is measured by impedance plethysmography, arterial tone by sphygmography (records intensity of peripheral arterial pulses) and jugular vein phase structure by phlebography.

Tachooscillometry, also called differential arterial oscillometry, is a semi-automated technique that records changes in the volume of the brachial artery during graded external pressure changes exerted by a compression cuff. The following arterial pressure (AP) parameters are determined from the arterial volume curve, with reported population normal values: minimal AP (60-80mmHg), mean AP (90-110mmHg), lateral systolic AP (90-100mmHg), end systolic AP (100-130mmHg), and pulse AP (10-20mmHg) (Vinogradova 1986). The relationship between arterial pressures measured by auscultation and tachooscillometry is not known.

Impedance plethysmography, also known as rheography, is a technique that measures variations in local electrical resistance during the cardiac cycle (Akulova 1986). From this, central (stroke volume) and peripheral (regional vascular filling, arterial tone) circulatory parameters can be determined (Tikhomirov et al. 1977). Rheograms of the trunk, limbs, and head (rheoencephalograms) are usually obtained during spaceflight (Yegorov et al. 1988).

Several additional investigations at rest are conducted. Echocardiography is performed using the Soviet built Argument (M-mode only) and Japanese Aloka (M-mode and 2D) devices pre- and postflight, and the Argument and French built Echographie and As de Coeur (M-mode, 2D, and Doppler) units during flight. Ultrasound images of lungs and abdominal organs are also obtained Twenty-four-hour Holter monitoring is performed at L-30, during the first week of flight, at the end of the first month and every three months of flight, and postflight on R+0, R+4, and R+60.

Cardiac mechanical activity is studied by kinetocardiography (KCG), ballistocardiography (BCG), and seismocardiography (SCG) (Yegorov et al. 1988). Kinetocardiography records low-frequency vibrations of the chest wall caused by cardiac contractions and is used to study the phase characteristics of the cardiac cycle of the left ventricle (Krynskiy 1986). Ballistocardiography records the body's displacement in response to cardiac contractions and circulating blood and allows determination of cardiac contractile force (Sergeyeva 1986). Seismocardiography is a modification of ballistocardiography (Bayevskiy and Gazenko 1968).

Surveys of exercise capacity are performed on both a bicycle ergometer and a treadmill. The protocol on the bicycle consists of pedaling at an output level of 125W for five minutes, a one minute rest period, and pedaling at 175W for three minutes, followed by five minute recovery period. The load level, ECG, arterial pressure by Korotkov method and tachooscillometry, and stroke volume by impedance plethysmography are recorded. The surveys are performed at least twice before flight, approximately every two months during flight, and once or twice after flight.

The treadmill protocol consists of a four step graded test consisting of walking for three minutes at 4.5 to 5 km/h, jogging for two minutes each at 6.5 to 7 km/h and 8.5

to 9 km/h, and running for one minute at approximately 11 km/h. The test is followed by a three-minute cool-down walk at 4.5 to 5 km/h. The treadmill speed and the subject's ECG is monitored during the test, which is performed at least once before flight and approximately every two months during flight.

Lower body negative pressure (LBNP) tests use the Chibis device with the following protocol: rarefaction for one minute at -25 mmHg, three minutes each at -35 mmHg and -45 mmHg, followed by a five minute recovery period. Chibis suit pressure, ECG, arterial pressure by tachooscillometry, and cerebral blood flow by impedance plethysmography (rheoencephalography) are recorded. The test is performed twice preflight, approximately every two months during flight and at least once postflight, as soon after landing as possible.

Pneumatic cuffs called Brazlet and measuring 10 to 12 cm wide are worn on the upper third of the thigh for occlusion tests. Positive pressure is applied to the cuffs using the following protocol: ten minutes each at 40, 50 and 40 mmHg, five minutes at 30 mmHg, followed by decompression. The cycle may be repeated up to three times with 30 minute rest periods between tests. Cuff pressure, ECG, and cerebral blood flow by impedance plethysmography are recorded. The test, which sequesters up to 700 ml of fluid in the legs, is performed once or twice preflight, during the first week of flight, and after flight on R+1 and R+4.

Active orthostatic tests are performed preflight on L-30 and postflight on R+0, R+3, and R+7. The crewmember is supine for 10 to 15 minutes and then stands independently for ten minutes with feet shoulder-width apart. After the test, the crewmember assumes a supine position. Heart rate is measured either by palpation or by ECG and arterial pressure by Korotkov method.

Blood and Urine Analyses

Blood and urine samples are routinely collected from long-duration crewmembers before and after flight. Venous blood is obtained from the antecubital vein on L-30 preflight and on R+1, R+7, and R+14 postflight. Twenty-four urine samples are collected on three consecutive days centered on L-30 and L-7 preflight and for the first seven days postflight (JWG 1988). On some flights, inflight 24-hour urine samples are collected, and rarely venous blood is drawn. Capillary blood obtained by fingerstick is a more common inflight protocol, with samples analyzed onboard or stowed for subsequent postflight analysis.

Table 2 summarizes the parameters analyzed in crewmembers' blood and urine to evaluate renal and endocrine function (JWG 1989). Three different loading tests are performed to evaluate renal excretory function of calcium, potassium and water (JWG 1988). The tests are performed on L-30 preflight and on R+2-3 postflight. The calcium test consists of 7.0g of calcium lactate taken with 300 ml of fluid, usually warm unsweetened tea. Urine samples are collected at 2 and 4 hours and analyzed for volume, electrolytes, and creatinine. For the potassium test, crewmembers consume a 10% KCl solution at 0.55 ml/kg body weight. Urine is collected hourly for four hours and analyzed for volume, electrolytes, creatinine, and osmolarity. The fluid loading test consists of drinking 20 ml of water per kg of body weight within 10-15 minutes. Urine is collected for four hours and analyzed for volume, electrolytes, creatinine, and osmolarity.

Studies of energy metabolism are performed on crewmembers' blood samples. Levels of glucose (fasting and in response to a glucose tolerance test), insulin glucogon and enzymes and products of glycolytic and citric acid pathways are determined. Lipid surveys include analysis of free fatty acids. Samples are analyzed for total protein and protein fractions. Levels of various enzymes, such as LDH, CPK, alkaline phosphatase, ALT and AST are also determined (Grigoriev _et al._ 1990, Gazenko _et al._ 1989).

Hematological investigations include complete blood count and erythrocyte metabolic indices such as rate of glycolysis, ATP and glutathione content. Studies of the immune system consist of full leucocyte differential count, including T-cell ratios, and analysis of lymphocyte synthesis of alpha- and gamma-interferon and interleukin-2 (Grigoriev et al. 1990, Gazenko et al. 1989).

Skeletal System Investigations

As flight durations have increased, studies of the skeletal system have gained importance. Mineral density of tibia and calcaneous is determined by single- and dual-photon absorptiometry, using ^{241}Am and ^{153}Gd, respectively, as the gamma sources (Stupakov et al. 1980, Grigoriev et al. 1990, Gazenko et al. 1989). Computer tomography is used to determine mineral density of lumber vertebrae (Grigoriev et al. 1990).

Neurovestibular Studies

Pre- and postflight neurologic investigations consist of testing of the sensory and motor systems, postural control, deep tendon reflexes, and vestibulo-oculomotor interaction (Kozlovskaya et al. 1981). Sensory testing involves vibration threshold sensitivity of the plantar surfaces of the feet, with stimulation at 63, 125, and 250 Hz. Investigations of motor function include isometric Cybex dynamometry to evaluate strength-velocity properties of anterior and posterior leg muscles, during which electromyograms are recorded. EMG activity of leg muscles is also recorded during posture tests, during which graded forces are applied to the crewmembers' chest to disrupt Romberg position. Threshold and amplitude of Achilles tendon reflex are studied.

Vestibulo-oculomotor interactions are studied during the gage-fixation reaction test (Kozlovskaya et al. 1981, Grigoryan et al. 1985), consisting of head turns to randomly-illuminated visual targets in the horizontal plane at 20° intervals up to 60° on either side of center. Eye movements are recorded by electrooculography.

Table 1. Cardiovascular investigations before, during and after Mir long-duration missions.

Parameter/Test	Method/Hardware	Preflight	Inflight	Postflight
Heart rate	ECG	X	X	X
Arterial pressure	Korotkov	X	X	X
	Tachooscillometry	X	X	X
Stroke volume	Impedance plethysmography	X	X	X
Arterial tone	Sphygmography	X	X	X
Jugular phase structure	Phlebography	X	X	X
Echocardiography	Argument	X	X	X
Visceral ultrasound	Argument	X	X	X
Kinetocardiography		X	X	X
Ballistocardiography		X	X	X
Seismocardiography		X	X	X
24-hr Holter monitoring	LENTA	X	X	X
Exercise	Bicycle ergometer	X	X	X
	Treadmill	X	X	
LBNP	Chibis	X	X	X
Occlusion cuffs	Brazlet	X	X	X
Active orthostatic test		X		X

Table 2. Blood and urine chemistry and endocrine parameters studied before and after Mir long-duration missions

Parameter	Source	Method
Calcium	urine	atomic absorptiometry
Calcium, ionized	serum	ion-selective electrode
Calcium, total	serum	colorimetry, atomic absorptiometry
Chloride	serum, urine	colorimetry
Creatinine	serum, urine	colorimetry
Magnesium	serum	atomic absorptiometry
Osmolarity	serum, urine	freezing point
Phosphorus, inorganic	serum, urine	spectrophotometry
Potassium	serum, urine	flame photometry
Sodium	serum, urine	flame photometry
Urea	serum	spectrophotometry
Adrenorcoticotropic hormone (ACTH)	plasma	RIA
Aldosterone	plasma, urine	RIA
Antidiuretic hormone (ADH)	plasma, urine	RIA
Calcitonin	plasma	RIA
Cortisol	serum	RIA
Estradiol	plasma	RIA
Follicle-stimulating hormone (FSH)	plasma	RIA
Glucagon	blood	RIA
Growth hormone	plasma	RIA
Insulin	serum	RIA
Leutenizing hormone (LH)	plasma	RIA
Parathyroid hormone (PTH)	plasma	RIA
Prolactin	plasma	RIA
Prostaglandin E	plasma	RIA
Prostaglandin F2 alpha	plasma	RIA
Renin	plasma	RIA
Testosterone	serum	RIA
Thyroid-stimulating hormone (TSH)	serum	RIA
Thyroxine (T_4)	serum	RIA
Triiodothyronine (T_3)	serum	RIA
25-hydroxy vitamin D_3	serum	RIA

References

Akulova FD. Rheography. In: Vinogradova TS. Instrumented methods of studying the cardiovascular system. Moscow: Meditsina, 1986:340-64 (in Russian).

Balakhovskiy IS, Natochin YuV. Metabolism under the extreme conditions of spaceflight and during its simulation. Prob. Space Biol. 1973:22.

Bayevskiy RM, Gazenko OG. Reactions of the cardiovascular system of man and animals under conditions of weightlessness. In: Parin VV, Kas'yan II, eds. Medicobiological studies in weightlessness. Moscow: Meditsina, 1968:234-44 (in Russian).

Gazenko OG, Grigoriev AI, Bugrov SA, Bogomolov VV, Egorov AD, Kozlovskaya IB. Medical results of the flight of the second prime crew on the orbital station Mir. Presented at the 40th Congress of the International Astronautical Federation, Malaga, Oct 7-12, 1989. Paper IAF/IAA-89-594.

Grigoriev AI, Bugrov SA, Bogomolov VV, Egorov AD, Kozlovskaya IB, Pestov ID, Polyakov VV, Tarasov IK. Preliminary medical results of the Mir year-long mission. Presented at the 8th IAA Man in Space Symposium, Tashkent, Sept 29-Oct 4, 1989. Acta Astronaut. 1990:in press.

Grigoryan RA, Gazenko OG, Kozlovskaya IB, Barmin VA, Kreidich YuV. The vestibulo-cerebellar regulation of oculomotor reactions in microgravitational conditions. In: Keller EL, Zee DS, eds. Adaptive processes in visual and oculomotor systems. New York: Pergamon, 1985:121-7.

Kakurin LI. Purpose of Soyuz manned spacecraft and biomedical research tasks. In: Gazenko OG, Kakurin LI, Kuznetsov AG, eds. Space flights in the Soyuz spacecraft. Biomedical research. (Translation of Kosmicheskiye polety na korablyakh 'Soyuz.' Biomeditsinskiye issledovaniye. Moscow: Nauka, 1976). Washington, DC: NASA TT F-17524, 1977:1-16.

Kas'yan II, Kopanev VI, Yazdovskiy VI. Reactions of cosmonauts under conditions of weightlessness. In: Parin VV, Kas'yan II, eds. Medicobiological studies in weightlessness. Moscow: Meditsina, 1968:52-64 (in Russian).

Kas'yan II, Talavrinov VA, Luk'yanchikov VI, Kobzev YeA. Effect of antiorthostatic hypokinesia and space flight factors on change in leg volume. Kosm. Biol. Aviakosm. Med. 1980;14(4):51-55.

Kozlovskaya IB, Kreidich YuV, Rakhmanov AS. Mechanisms of the effects of weightlessness on the motor system of man. Physiologist 1981; 24(6 Suppl):S59-64.

Kozlovskaya IB, Kreydich YuV, Repin AA, Barmin VA. Coordination of eye and head movements during the gaze fixation reaction. Fiziol. Chelov. 1981;7(1):34-9 (in Russian).

Krynskiy OM. Kinetocardiography. In: Vinogradova TS. Instrumented methods of studying the cardiovascular system. Moscow: Meditsina, 1986:172-80 (in Russian).

Sarychev VA, Sazonov VV, Zlatorunsky AS, Khlopina SF, Egorov AD, Somov VI. Device for mass measurement under zero-gravity conditions. Acta Astronaut. 1980;7:719-30.

Sergeyeva KA. Ballistocardiography. In: Vionogradova TS. Instrumented methods of studying the cardiovascular system. Moscow: Meditsina, 1986;180-94 (in Russian).

Stupakov GP, Kazeykin VS, Kozlovskiy AP, Korolev VV. Evaluation of changes in human axial skeletal bone structures during long-term spaceflights. Kosm. Biol. Aviakosm. Med. 1984;18(2):33-7.

Talavrinov VA, Anashkin OD, Bagramov KhG, Volgin VA, Luk'yanchikov VI, Lyamin VR, Sergeyev AV, Turbasov VD, Chirkov AA. Anthropometric studies of the main crews of the

"Salyut-6" and "Salyut-7" orbital stations. Kosm. Biol. Aviakosm. Med. 1988;22(3):22-6 (in Russian).

Tikhomirov IB, Turchaninova VF, Selivanenko VT, Staferov VA. Tetrapolar rheography used to evaluate the circulatory system. Kosm. Biol. Aviakosm. Med. 1977;11(4):70-4.

Vinogradova TS. Tachooscillography. In: Vinogradova TS. Instrumented methods of studying the cardiovascular system. Moscow: Meditsina, 1986:326-8 (in Russian).

Yegorov AD, Bayevskiy RM, Itsekhovskiy OG, Fyodorov BM, Turchaninova VF, Alferova IV, Lyamin VR, Turbasov VD, Polyakova AP, Domracheva MV, Golubchikova ZA, Funtova II, Tazetdinov IG, Savel'yeva VG. Preliminary results of cardiovascular investigations of the crew of the second expedition on the Mir space station. Kosm. Biol. Aviakosm. Med. 1988;22(6):51-8 (in Russian).