

MRC / BNSC Workshop

‘Space for health, or health for space?’

5 August 2002 at The Royal Society, London

1. Introduction

1.1 Workshop and participants

The workshop was jointly organised by the Medical Research Council (MRC) and the British National Space Centre (BNSC), and was held at the Royal Society in London on 5 August 2002. The workshop brought together 30 leading scientists from both the UK and overseas to discuss the opportunities presented by space-based research programmes in the area of biomedicine, and the benefits that such programmes might provide for terrestrial health needs. The meeting was introduced by Sir George Radda, Chief Executive of the MRC, and was structured to allow discussion of the role of space research in four areas of physiology – bone, muscle, cardiovascular and neuro-physiology.

An expert advisory group was also present throughout the meeting, and met towards the end of the day to draw conclusions and recommendations based upon the presentations and discussions of the workshop.

An agenda for the meeting and a list of the participants is provided as an Annex to this report, while links to the speakers and their presentations can be found by clicking here <http://www.microgravity.ac.uk>

1.2 Aims of the workshop

- To inform MRC's research strategy in relation to biomedicine and space, given that research funded by MRC must ultimately address the health needs of the UK population and UK wealth creation.
- To identify if there are unique opportunities afforded by research in space that might prove beneficial to terrestrial health.
- To inform MRC's and the other Research Council's position on the value of "microgravity" as a platform / tool for research, and on potential UK participation in the ESA Life and Physical Sciences Programme (ELIPS)
- To help assess the competitiveness of the UK in space biomedicine.
- To identify how research activities linked to space programmes might be most effectively linked to the non-space scientific community.
- To identify the opportunities and benefits of engaging more closely with ESA and NASA over the medium/longer term.
- To help prepare for forthcoming MRC bilateral meetings with both NASA and ESA

1.3 Background

The UK has been a member of the ESA European Microgravity Research Programme for a number of years, albeit at a fairly low level, and is represented on this by the

BNSC. The UK has participated in the current ESA microgravity programme, EMIR2-X, since September 2000, but this is due to finish at the end of 2003, and will be superseded by a new ESA programme, termed ELIPS (European Life and Physical Sciences utilising the International Space Station). The UK has not signed up to ELIPS at this time, given the high costs of engagement.

During the discussions relating to the potential UK participation in the ESA ELIPS programme, it was considered timely to review UK biomedical activity in this area. Both NASA and ESA have active life science programmes, and several UK scientists are involved in these. During the summer of 2001 MRC asked both national and international scientists involved in microgravity research to advise on the scientific opportunities afforded by microgravity for research in cell biology and physiology. Plans for the workshop were derived from this consultation, which suggested that the area of human physiology merited further consideration.

2. Workshop presentations

2.1 Bone Physiology

J Reeve

'Current health research goals and strategies'

Osteoporosis is a significant health problem that leads to loss of bone density and to an increased risk of bone fracture. The loss of bone mass is also a major hazard of space flight, and it has been argued that studies of the process in space may inform health-related research on earth. A key issue is to better understand the contribution of mechanical unloading to the bone loss of ageing; bone loss patterns in hip fracture and space flight are very similar. An overview was provided of the current research investigating the mechanisms underlying osteoporosis, focusing on the regulation and turnover of mineralised matrix and the influence of the osteocytes within the matrix. These are the most numerous cells of bone and the evidence that they are responsive to mechanical loading is good. The role of osteocyte apoptosis in promoting normal growth and in initiating repair after matrix damage by attracting bone-reabsorbing osteoclasts was described. Nitric oxide originating from osteocytes, on the other hand, was believed to stimulate bone formation by osteoblasts and to preserve microstructure by inhibiting osteoclast action.

M Horton

'Cellular Biomechanics and New Bone-Active Medicines'

Skeletal disuse due to bed rest or exposure to microgravity in space leads to bone loss, an adaptive process mediated by osteoclast cells. Renewed mechanical stimulation leads to bone renewal through the actions of osteoblasts, and the balance between these adaptive two pathways is controlled through intracellular signal transduction pathways. Cellular biomechanics offers a new approach for better understanding these processes and the behaviour of cells within the skeleton. Atomic force microscopy has been applied as a tool to examine the material properties of bone. This 'nano-indentor' may be used to apply a precise force to 'spherically indent' individual cells in order to examine their mechanical, cytoskeletal and cell signalling responses, thereby allowing an insight into how the cytoskeleton modulates the cell's mechanical response. It is hoped that in the future this can translate into the development of drugs that can be used to prevent bone loss, by enhancing the normal physiological response to mechanical strain at the cellular level

A Goodship

'Bone loss during long term space flight is prevented by the application of a short term impulsive mechanical stimulus'

Bone mass is lost during space flight due to reduced skeletal loading. However, this process cannot be reversed by exercise regimes. Interestingly the loss of bone mineral density (BMD) during space flight is specific to particular sites of the skeleton, reflecting a functional adaptation. For example, the skull appears protected from bone loss.

Studies have been established to investigate whether specific mechanical stimuli can be used to offset this loss by stimulating the production of new bone by osteocytes and osteoblasts. An apparatus has been developed to mimic the heel strike transient, which occurs normally during the motion of walking. This has been tested under conditions of weightlessness, both transiently during parabolic flight, and during the EUROMIR 95 space mission. For the latter, analysis of a single cosmonaut for 6 months following his return to earth revealed that mechanical stimulation selectively reduced BMD loss in the legs, but not in the neck.

H Montgomery

'Weightlessness and exercise in the study of bone remodelling'

The regulation of bone mineral density is influenced by both genetic and environmental determinants, with the genetic component providing up to 70% of the observed variance in BMD between individuals. The interaction between genetic and environmental influences, such as skeletal loading under conditions of exercise, bed-rest or microgravity, is an area of current investigation. The loss of BMD during space flight varies across different regions of the skeleton, as well as between individuals, as shown by a study of two cosmonauts during the EUROMIR 95 mission. To investigate this further, and overcome the difficulties of low sample size in space, a prospective model was established whereby studies were performed on army trainees undergoing exercise training in a controlled environment. BMD changes exhibited 20% variance across individuals, revealing a strong genetic influence. Several genes have been implicated in the control of bone mass, and candidate gene studies within population cohorts have linked *IL-6* and *ACE* gene polymorphisms to this process. These findings are applicable both to young adults and elderly patients with osteoporosis, so it is hoped that common therapeutic targets may be defined in the future. This is being further studied in association with the ESA bed-rest study, which is aimed at studying human physiology in a simulated microgravity environment on earth.

B Elmann-Larsen

'Osteoporosis and genes in space'

The loss of BMD observed in astronauts in space continues for several weeks after return to earth, and different regions of the skeleton recover differentially. For example, the spine does not recover well. Whilst it has only been possible to study low numbers of astronauts, it is apparent that there is vast inter-individual difference in the responses to BMD therapy, despite similar activity patterns during space missions. Nutrition may play a role in bone metabolism, and studies have been designed to investigate the relevance of $\text{Na}^{2+}/\text{Ca}^{2+}$ exchange in this context. The ESA bed-rest study is being used to address these questions. This study involves the immobilisation of volunteers during a 120-day study period, during which time bone densitometry and other physiological parameters are assessed in association with varying exercise and BMD therapy regimes. Results are expected in late 2002.

General discussion

The following points emerged:

- The continued loss of BMD after astronauts return to earth is predictable from cell biology – the regeneration of the bone forming osteoblast population will take several weeks once the stress of microgravity has been removed
- Bed-rest studies do not accurately mimic conditions of microgravity, since the weight of limbs and fluid deposition will be factors of uncertain impact on earth
- The mechanisms underlying bone loss during osteoporosis may be different from those responsible under conditions of microgravity, although mechanical unloading is likely to play a major role in osteoporosis in the very elderly
- In order to accurately assess bone/collagen synthesis better markers are required as well as more appropriate assays
- Defects in the pathways for bone generation may be as important as those regulating bone loss. Some of these pathways link these processes in reciprocal fashion anyway

- Therapeutic intervention will only succeed if the bone formed under such conditions is functionally useful – more knowledge is required concerning what determines the structural orientation of newly formed bone within the skeleton
- Improved statistical methods may be needed since the numbers within each study will always be limited. Candidate gene studies may allow for more targeted studies where a larger effect can be measured. The problem is common to that for the study of rare diseases, and NASA is preparing a report on statistical modelling that addresses this, due to be published at the end of 2002

2.2 Muscle physiology

T Partridge

'Biological basis of maintenance of skeletal muscle'

An overview was provided of the current views of skeletal muscle structure and metabolism. A key player in the maintenance of muscle mass is the satellite cell. Satellite cells are closely associated with the muscle fibre, and normally exist in a quiescent state until activated by damage or excessive work, after which they proliferate rapidly to regenerate myoblasts to achieve growth or repair. Various markers have been identified in recent years that have facilitated the study of satellite cells, and these have been used in conjunction with mouse models to investigate the mechanisms of muscle regeneration. For example, the *mdx* dystrophic mouse model has been used to study the effects of ageing on the regeneration of isolated muscle fibres in culture, and such studies have led to the identification of two distinct populations of satellite cells which may play a role in this process

O Rutherford (presented by M Narici)

'The effects of space flight on skeletal muscle'

Microgravity causes both physiological and biochemical changes to skeletal muscle, including muscle and fibre atrophy, decreased force and power, and increased fatigability and susceptibility to damage. Different muscle groups within the body respond differentially. However, only limited data of variable quality is available from manned space flight, and there are problems in its interpretation due to the low statistical power of such studies, poorly recorded countermeasures and nutrition, and the effects of re-entry and variable flight duration. To circumvent these problems, bed-rest models on earth have been used to simulate weightlessness and provide more amenable experimental conditions. Although such studies have yielded comparable results, it is recognised that such modelling has limitations. For space flight, considerable experimental data has been generated using rodent models. Studies have revealed that type I muscle fibres suffer greater atrophy than type II, and that differential changes occur in the gene expression of type I and IIA myosins. Changes in muscle under conditions of microgravity are thought to occur due to decreased physical activity, under-nutrition, and changes to the endocrine status. Future approaches will need to elucidate the molecular basis for alterations in gene and protein expression, and to better understand neuro-muscular control, with a view to developing effective countermeasures to muscle atrophy. It is hoped that by better understanding the mechanisms involved, therapies might ultimately be developed to counter muscle atrophy on earth due to ageing, disease, immobilisation and spinal injury.

S Harridge

'A mechano-sensitive growth factor in human skeletal muscle'

While the effects of space flight and immobilisation lead to muscle atrophy, mechanical overload produces the opposite effect of muscle hypertrophy. The mechanisms underlying these processes are not fully understood, although emerging evidence suggests that IGF-1 may play a role in mediating the effect of mechanical signals in skeletal muscle. Using transgenic mice models, increases in *igf-1* gene expression have been shown to increase muscle mass. Two distinct IGF-1 isoforms have been characterised, and it is isoform IGF-IEc (or MGF) that is up regulated under conditions of mechanical overload, both in mice and in humans undergoing exercise. The *IGF-IEa*

and *I*Ec genes are differentially regulated, and the isoforms appear to have different functional effects in cell culture experiments. It is hoped that further experiments on IGF-I_{Ec} will help elucidate the mechano-transduction pathways underlying the control of muscle mass.

M Rennie

'The effects of microgravity on muscle and bone mass and protein turnover'

Maintenance of bone and muscle mass depends upon an equilibrium between protein synthesis and breakdown. Muscle atrophy after immobilisation has been measured at 15% per month, and during space flight this process is even more rapid, and cannot be countered by dynamic exercise. Physical activity is required to maintain muscle mass, and affects both muscle-specific gene expression and protein production. Nutritional status is important, and evidence suggests that sensitivity to nutrition may be reduced by both immobilisation and ageing. Insight into the interaction between activity and nutrition has been provided by studies of the effect of amino acids, insulin and contraction on muscle metabolism. These experiments have identified the importance of several cell-signalling cascades, and microarray technology is being utilised to provide a better understanding of the signalling pathways involved. In order to measure bone and muscle turnover, better descriptors are needed. Improvements have been provided by the use of stable isotope techniques; for example, by labelling type I collagen the turnover of bone has been found to be surprisingly rapid, occurring at a faster rate in children than in adults. Further studies are planned to investigate the rates of bone collagen breakdown during space flight. Countering the effects of bone and muscle wastage is important for both manned space missions and the general population, where ageing and frailty are an increasing burden on health care systems. It is hoped that by studying the accelerated effects observable under conditions of microgravity, mechanistic and technological advances may be made that can be used for general benefit on earth.

M Narici

'Adaptations of the musculoskeletal system to ageing and space flight'

Both ageing and disuse lead to loss of muscle strength, which exceeds that expected from simple loss in muscle size. Comparative studies were performed on astronauts exposed to microgravity conditions, participants immobilised in the ESA bed rest study, and elderly patients. A variety of dynamometric, ultrasound and MRI measurements were taken to evaluate adaptations in muscle strength, size and architecture as a result of these various forms of disuse. Alterations in the mechanical properties of tendons and neuro-muscular activity were also monitored. The results indicated that a major reason for the loss of muscle strength could be attributed to atrophy of sarcomeres in parallel as well as in series, which was further compounded by a loss of tendon stiffness and neural changes. Similar patterns were observed in all cases, suggesting that muscle undergoes similar functional and architectural changes in both ageing and disuse.

General discussion

The following points emerged:

- Astronauts always suffer loss of muscle mass during space flight, no matter how much exercise they perform. One explanation might be that the cytoskeleton within muscle cells has a role, and that microgravity conditions are revealing a previously unknown effect of gravity in this process.
- Studies in space are investigating the effects of muscle disuse. Whilst this may provide some mechanistic insight to the clinical problems of ageing, which involve a component of disuse, the loss of muscle mass associated with the ageing process is likely to occur by a distinct mechanism.
- A change in spinal excitability during space flight could play a role in the loss of muscle mass.
- The role of the vascular bed in muscle physiology should be studied further.

2.3 Cardiovascular physiology

D Sheridan

'Cardiovascular research: overview of current research goals and strategies'

Cardiovascular disease now represents the major cause of death in the western world. Although the number of cases continue to rise, death rates have in fact decreased by 40% in the UK in the past 30 years, due to the combined impact of improvements in primary care and medical treatment. Levels of smoking have been reduced by 50%, while there has been increasing use of coronary bypass surgery, and improved control of blood pressure and cholesterol levels. Risk from cardiovascular disease varies across ethnic groups, and is due to the influence of both genetic and environmental factors. Current research efforts are directed at understanding the polygenic nature of cardiovascular disease, and how protective and adverse genes interact. Future priorities will focus on the identification of early markers for disease, such as those indicating endothelial cell injury, smooth muscle cell proliferation and myocardial stress, which should lead to improvements in primary prevention. Another priority is to better understand the pathophysiology of heart failure, which is increasing in prevalence and currently affects 1 in 10 of the elderly. This will involve the use of functional genomics and proteomics to identify new therapeutic targets, as well as advances in the areas of organ and cell replacement therapy.

J Meck

'Overview of space contribution to the field'

Studies on astronauts both during and after space flight have revealed that the cardiovascular system is able to 'adapt' to conditions of microgravity. It is hoped that by studying this adaptation process benefits will be provided by i) reducing the risks involved in manned space flight, and ii) providing new insight into cardiovascular physiology and pathophysiology.

Cardiac output is controlled by pressure gradients which develop along the body axis in relation to the influence of gravity on the body's organs and tissues; these gradients also vary according to whether an individual is upright or supine. Microgravity allows a unique opportunity to assess the various components of this process, and data generated from studies of astronauts has been used to modify the equations underpinning Guyton's models of cardiovascular function. These findings may prove clinically important for the management of a variety of cardiovascular disorders, such as heart failure and hypertension. Current efforts are focused on three aspects of cardiovascular physiology for which reversible changes occur during exposure to conditions of microgravity. An improved understanding of the mechanisms involved is likely to benefit astronauts in space and have clinical significance on earth.

Autonomic dysfunction: Autonomic control of circulation is disrupted in astronauts exposed to conditions of microgravity, although recovery is spontaneous on return to earth. The sympathetic nervous system appears to be the main target of this dysfunction, most likely due to the lack of baroreceptor afferent input.

Cardiac Output: Chronic unloading during space flight leads to changes in cardiac conduction and repolarization, as well as functional modifications such as a reduction in ejection fraction, diastolic dysfunction, and increased ventricular dysrhythmia. All changes recover spontaneously within a few weeks after return to earth.

Gender differences: After space flight, women are found to have a 5-fold greater incidence of orthostatic hypotension, and a 3-fold greater loss of plasma volume. Women have a lower centre of gravity than men, and it is thought that as a consequence microgravity leads to a greater redistribution of fluid in women, and a larger compensatory diuretic response.

The clinical perspective on the data produced from the Meck lab was provided by **Dr R Summers**. Obesity-related heart failure, hypertension, shock, pregnancy and cirrhosis all have gravitational components, although these are not fully understood. For example, the standard treatment of shock by placing patients in the Trendelenburg

position, whereby the feet are raised above the position of the head, might intuitively seem to increase fluid flow to the brain; however oxygenation levels are not found to rise experimentally. Microgravity offers a unique opportunity with which to dissect the effects of diastolic versus systolic loading, and may facilitate an improved understanding of cardiovascular deconditioning and hypertrophy.

R Gerzer

'Integrated team approaches to prepare for individualised medicine of the future'

Studies in space offer opportunities to study integrated physiology and systems biology, and assess physiological function in the absence of gravitational effect. There are also opportunities in telemedicine, since manned space flight will require that effective diagnosis and treatment can be performed at a distance, which will also be relevant as health care advances on earth. The DLR institute in Cologne has been formed to offer a major facility for the investigation of these areas, providing accessible models for space studies. One microgravity simulation is the ESA bed rest study, which is analysing the physiological changes which occur as a result of immobilisation, while iron lung studies are being performed to look at the effects of variations in thoracic pressure. In the area of telemedicine, collaboration with the German military has led to the development of a smart 'health card' for use in the German healthcare system.

M Spyer

'Control of circulation and ventilation by the central nervous system'

Autonomic dysfunction, which may be experienced by astronauts during space flight, affects control of both the cardiovascular and respiratory systems. In particular the environment of microgravity leads to a loss of vestibular input, which impacts upon cardiovascular function. A key question is to understand how vestibular and autonomic functions are integrated, and to gain an insight into the cellular processes that modulate these functions. Electrophysiological and pharmacological approaches have been used to study the baroreceptor reflex in vivo in animal models. Cardiovascular function was analysed following microinjection of GABA or glutamate into the cerebellum of rats, which were found to have either a negative or positive effect respectively. This response was found to operate via uvula stimulation within the Nucleus Tractus Solitarius (NTS). GABAergic neurons reside in the NTS, which is responsible for gating reflex inputs via the baroreceptors, and this has led to the hypothesis that the NTS might act to reset cardiovascular reflex.

P Norsk

'Microgravity: A tool for understanding the effect of gravity on cardiac function'

The distribution of blood and fluids within the human body are subject to the influence of gravity. When humans are upright fluids are drawn towards the legs, which is countered by modulating heart rate and blood vessel contraction in order to maintain adequate perfusion to the brain. A different situation exists during space flight, where conditions of microgravity lead to the expansion of the central blood volume and atrial distension. This distension is greater than that observed in bed-rest patients, indicating that on earth gravity compresses the heart in supine individuals. This might be deleterious in some instances, for example in patients with heart failure, and has led to an evaluation of whether alternate bed positions should be adopted for such patients, such as placement on the side or in the prone position.

Studies have also been performed to assess the effects of prolonged weightlessness on cardiac function. Both cardiac output and stroke volume decline after several days of space flight, which may be caused by both atrophy of cardiac muscle and a decrease in venous return to the heart. Astronauts have also been found to have augmented sympathetic nervous activity and an attenuated renal response to fluid intake, which may be a consequence of reduced cardiac output. The mechanisms underlying these changes are to be investigated further, both for the future benefit of manned space missions, and to provide insight into the treatment of patients with heart failure. Additionally, the use of a non-invasive re-breathing technique developed for these analyses is now being further developed to allow remote biomonitoring in hospitals.

General discussion

The following points emerged:

- The physiological responses observed in space are 'recoverable', and their relevance to pathophysiological processes such as heart failure is unclear.
- Could microgravity be considered as the end point in a continuum between hyper and hypo-gravity? If so, perhaps alternative and more cost-effective approaches could be employed on earth to facilitate studies into gravitational effects? For example, bed-rest, immersion in water and centrifugation have all been used in such studies.
- Countering this argument, there is no evidence that such a continuum exists, and such earth-based models have limitations. For example, the bed-rest model did not predict the effects of gravity on atrial distension and cardiac function, and earth-based studies are unlikely to provide insights into the influence of gravity on venous return.

2.4 Neurophysiology

W Paloski

'The role of neurophysiology in exploring space v. the role of space in exploring neurophysiology'

Gravity is a key reference point for the CNS in controlling balance, spatial orientation and co-ordinated movement. Vestibular function is significantly disrupted during space flight, leading to slower eye-head co-ordination and reduced postural stability. The microgravity environment has been found to trigger a neuro-adaptive response in astronauts to compensate for the loss of gravitational reference, which is then reset upon return to earth. The ear is the major anatomical site controlling this process, and receptors are also known to be present in muscles and joints as well as the skin. However, the relationship between these various sites, as well as the neurological mechanisms involved, are not well understood. Space offers a unique environment within which to study the process of neuro-adaptation, and rodent models are currently being used to analyse the molecular changes that occur in the brain during space flight. Disruption of vestibular function also occurs during the ageing process, with vestibular problems accounting for up to 25% of falls in the elderly and significant health care costs. It is hoped that studies of the mechanisms of neuro-adaptation will ultimately lead to an improved quality of life for the elderly, improved therapies and rehabilitation for patients with spinal cord injuries and vestibular problems, and better training for athletes, pilots and divers.

J McIntyre

'Human neurophysiology: What can be learned from experiments in microgravity?'

The human nervous system has evolved to respond to gravitational cues, which must be integrated with other reference frames within a complex sensorimotor system. The unique conditions of microgravity has been used to study this process further, investigating the role of perception in the vestibular-ocular reflex, head/trunk positioning, and postural control. The gravitational context clearly influences visual processing and vestibular control, but may also provide directional prompts during the development of the nervous system, both within the embryo and post-natally. Animal models are being utilised to study these processes further. Studies of the adaptation of the nervous system to gravitational effects are relevant to both manned space flight, in terms of the development of counter-measures and ergonomic design for tools and apparatus, as well as to improve understanding of neurophysiological processes. Space studies offer the unique possibility to probe the function of the sensorimotor system by allowing an uncoupling of sensory inputs, for example those specifying

visuo-motor function, as well as facilitating a dissection of the neuro-adaptive response. This may in turn have relevance to the clinical problems of dyslexia (loss of spatial memory), cerebellar dysfunction, loss of vestibular function with ageing, and anxiety and schizophrenia (sensory conflict).

N Davey

'The influence of gravity on the control of voluntary movement in man – the effect of dance training'

Studies have been designed to assess the effects of gravity on voluntary or corticospinal control of movement and posture, and thereby assess the influence of vestibular or proprioceptive (joint and muscle) reflexes upon this pathway. These experiments also compared 'naïve' individuals to trained dancers, who possess a greater control of balance and posture, in order to determine whether such training could aid the adaptive response to different gravitational environments. Parabolic flights were used to transiently expose subjects to either 0G, 1G and 2G environments and the effects on postural control determined. Transcranial magnetic stimulation was used to elicit responses in postural muscles within the body, which were measured by electromyography. The results obtained indicated that trained dancers have different corticospinal control of their postural muscles, which enhances their adaptive response to conditions of microgravity. It is hoped that further study of the processes involved may have relevance to rehabilitative techniques for stroke patients or those who have suffered spinal injury.

2.5 Keynote lecture

O Alpar

'Microgravity: a tool for studying microencapsulation technology?'

Microencapsulation and microsphere technologies offer exciting possibilities across many areas of science and technology. In biomedicine, the major possibilities are foreseen in providing 'smart' delivery systems for drug, vaccine and gene therapy, that can address efficacy, toxicity and tissue targeting, as well as application to the tissue engineering and diagnostic fields. A measure of the current interest in this area is provided by the fact that patent applications related to microencapsulation have doubled year on year in the past decade. However to deliver the promise of such approaches, an improved understanding of the microencapsulation process is required in order to improve the quality and reproducibility of microsphere production. Microgravity offers a unique environment in which to study this process, since it may circumvent some inhibitory processes related to fluid physics such as the Marangoni effect. Microsphere preparations made in space outperform those made on earth, and it is hoped that space studies will facilitate microsphere production becoming an exact science. Interdisciplinary research and improved links between space and ground based studies will be needed for the future advancement of this field.

3. Conclusions from the advisory group

The MRC's advisory group met privately towards the end of the workshop and came to the following conclusions:

- Biomedical research in space is clearly needed to support the programmes of manned space flight. The main benefit of such research is to the health of astronauts, rather than to the health of the terrestrial population.
- While the UK has several pockets of excellent research in this area, there is currently a lack of critical mass and co-ordination, while links to the broader biomedical community are weak.
- Microgravity provides an interesting tool with which to probe normal human physiology, although its relevance to pathophysiology needs to be more convincing.

- Investigations into the loss of bone and muscle mass in conditions of microgravity may further our understanding of the basic mechanisms underlying the turnover of such tissue. However it has yet to be established whether this is a useful model in terms of understanding the processes of ageing.
- The studies being performed in space offer some unique possibilities for the area of human physiology. For example, whole organism experiments can be performed on humans to test hypotheses that on earth can only be approached with association studies. However the majority of important questions being posed could be tackled on earth by careful design.
- Cardiovascular research represents an area of opportunity for furthering our understanding of basic physiological processes, although space studies do not provide a good model for heart failure and other cardiovascular disease processes.
- The area of neurovestibular research offers some possibilities, for example in relation to sensory-motor integration studies and cellular/molecular adaptation, although UK efforts in space research in this area are modest. Furthermore there are increasing terrestrial opportunities offered by virtual reality approaches
- Current studies are generally descriptive, and the knowledge base at present is insufficient to ask the critical questions that microgravity might be able to uniquely answer.
- The study population in space research is atypical, since astronauts are a highly selected group of fit and intelligent individuals.
- The small numbers of astronauts that can be analysed gives rise to problems of statistical power in space research, and effort should be put into establishing new biostatistical methodology.
- Space programmes may have a role for the development of bioinstrumentation, such as miniaturised imaging modalities; however the lack of statistical power in space studies will remain to be a problem
- Due to its greater investment in manned space flight, NASA has a more significant biomedical research programme, and a larger physiological database, than ESA.
- Any decision to commit funding towards space research programmes should only be taken once a rigorous cost / benefit analysis has been undertaken
- The UK should establish better links between its biomedical researcher community and those involved in space research (through NASA and ESA). Opportunities exist for improving the design of the experiments performed in space, and UK experts could make valuable contributions in this area.

4. Outcomes

- Bilateral meetings are planned between MRC and both NASA and ESA. These will explore the possibilities for improving the interaction between the UK biomedical community and the research programmes funded by both these agencies.
- The workshop and the output from the ESA and NASA meetings will be discussed by MRC's high level Strategy Development Group (SDG) in early 2003.
- It is likely that this will in turn feed into a broader cross Research Council (RCUK) discussion of the opportunities presented by space research later in 2003.
- MRC will continue to actively participate in the Life and Physical Sciences Network Group (LPSNG), a UK co-ordination group hosted by the BNSC, as well as the related Biomedical and Life Sciences Space Research Group.
- Finally it is hoped that the workshop will help in networking space and non-space researchers so that the possibilities that exist within this area can be exploited to the full.