Inactivity: Physiological Effects

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Foreword

The Surgeon General of the United States once said, "Smoking is bad for your health," and that message now appears on every cigarette package in the United States.

He could also have said, "Lying in bed is bad for your health." Perhaps this label should be attached to all beds. In fact, we might say that physiologically the most dangerous activity to indulge in is inactivity.

During the Second World War, Sir David Cuthbertson drew attention to the fact that individuals lying in bed, with fractures of one of the major bones of the leg, excreted more calcium and nitrogen than normal, ambulant people. Then he studied some normal, intact people lying in bed for the same period of time and found a similar increase in the excretion of calcium and nitrogen. So this phenomenon did not result from the effects of the fracture as he had thought, but from the effects of lying immobilized in bed.

People who spent a long period in bed because of a fracture, surgery, or some infectious disease always found themselves weak and dizzy when they first attempted to sit up or stand. This was attibuted to weakness brought on by the injury or infection. In fact, normal people lying in bed for the same time have the same symptoms when they try to sit up or stand. So what, in fact, happened was that lying horizontally in bed was causing a deconditioning of the cardiovascular system that created an orthostatic hypotension when they reassumed the erect posture.

Then, when humans began to be exposed to the weightless state in space, it was found that there was increased loss of calcium and nitrogen from their bodies and a cardiovascular deconditioning that became apparent when they returned to a 1 G environment. In many ways, weightlessness resembles bed rest, and thus bed rest experiments became important as a form of ground study of the physiological effects of weightlessness. The study of bed rest also became important as a tool with clinical applications in studying conditions such as osteoporosis and the physiology of the cardiovascular system. One of the methods used to study the physiology of weightlessness in space was to subject humans to sustained bed rest and then spin them in a centrifuge at high G forces. In this way, it was possible to simulate an astronaut's spending some time in space and then being subjected to the higher G forces of reentry.

The two editors of this book have played an integral part in the discoveries just outlined and are uniquely qualified for the job they have taken on. In fact, it would be difficult to find two better qualified individuals for this purpose.

Harold Sandler received his M.D. in 1955 from the University of Cincinnati. After his internship and appointment as a research fellow in medicine, he was introduced to an area he was to make his own for the next 25 years. This was a military service appointment with the U.S. Naval Air Development Center's Aviation Medical Acceleration Laboratory in Johnsville, Pennsylvania. Here Dr. Sandler was brought in contact with the effects of G forces on the cardiovascular system, a system about which he had already published a number of articles. He next held two appointments as assistant professor in medicine and in 1970 joined the National Aeronautics and Space Administration Ames Research Center at Moffett Field, California, as research scientist and the next year was appointed assistant clinical professor of medicine at Stanford University. He has remained at NASA-Ames ever since. From 1972 to 1985, he served as chief of the Biomedical Research Division. Currently, he is chief of the Cardiovascular Research Office at NASA-Ames; associate clinical professor, Wright State University School of Medicine in Dayton, Ohio; associate professor of physiology, Howard University School of Medicine, Washington, D.C.; and clinical professor of medicine at Stanford University School of Medicine.

I have mentioned that Dr. Sandler is responsible for the overall management of NASA's Cardiovascular Research Office, which studies the hazards of aerospace flight with respect to the human body and its ability to adjust physiologically to the stresses of flight. The Office's work includes the study of not only physiological parameters, but also those of a biochemical nature including endocrinology. In this area, Dr. Sandler has had the collaboration of Joan Vernikos, Ph.D. Her experience and expertise not only have been important in their own right, but also have added a new dimension to the Cardiovascular Research Office. The research areas that Dr. Vernikos has made her own include endocrine pharmacology, mechanisms regulating the pituitary-adrenal system, stress and stress response, drug–stress interactions, effects of hormones on the central nervous system, space physiology and pharmacology, neuropeptides and pain, and circadian rhythms.

Dr. Vernikos received a bachelor's degree from the University of Alexandria in Egypt in 1955 and a Ph.D. from the Royal Free Hospital School of Medicine, University of London, in 1960. She was assistant professor of pharmacology at the University of Ohio in the 1960s, and she has been a research scientist at the NASA-Ames Research Center. During 1973–1978, Dr. Vernikos was chief, Human Studies Branch of the Biochemical Research Division at NASA-Ames, and for six months in 1976 she was also acting deputy director, Life Sciences. She is a lecturer in Aeronautics and Astronautics at Stanford University and is also a consultant in the Department of Psychiatry. She has been awarded the

NASA medal for exceptional scientific achievement. She is also a consultant for the European Space Agency, Paris, and the German Space Agency, Cologne, West Germany. Dr. Vernikos has had considerable editorial experience on the editorial boards of a number of scientific journals which, with her scientific expertise, makes her an ideal editor for the current volume.

The work of Dr. Vernikos has been an important complement to Dr. Sandler's studies, and this complementarity also makes them ideal coeditors for the current volume. Their intimate knowledge of their fields has enabled them to gather a distinguished group of contributors, and there is no doubt that this book will be among the most important and most comprehensive works on bed rest as well as a classic on this subject.

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Preface

The flight of Sputnik across the sky on October 4, 1957, catapulted the world into the Space Age and resulted in a vast research program to determine the potential physiological effects that the removal of gravity (weightlessness) would have on humans. This research provided great masses of data not only on what could be expected in space, but also on the results of inactivity and immobilization on earth since these conditions afforded the best method we had to simulate—although not duplicate—the removal of gravity.

This book has been prepared to review the body of information from studies on healthy volunteers conducted in direct support of the space program and to discuss the present state of our knowledge of the physiological deconditioning inherent in inactivity and immobilization in general. It deals, in fact, with that end of the spectrum that is diametrically opposed to the growing literature on the benefits of exercise. It covers the changes that occur in the cardiovascular system, bone and muscle, metabolism and endocrine responses, psychosocial responses, and exercise tolerance. We have stressed clinical effects and clinical management of deterioration while indicating the changes that have been found in healthy, normal bed rested subjects. Where relevant, data on crews that have flown in space may also be included since their physiological responses are qualitatively similar to those observed in bed rested subjects or immobilized patients on earth.

Of primary importance is the development of means of counteracting the many physiological changes brought about by inactivity. As this book will show, few reliable countermeasures are currently available. This is one of the many areas where future research is greatly needed. Others are discussed under the individual subject areas. It is also important that we determine (a) whether the observed changes are due solely to physical inactivity or are compounded by the associated isolation, (b) whether they are reversible, and (c) whether they may result in serious health problems over the long term. Consequently, this book is directed primarily toward research investigators and students interested in this field in the hope of stimulating them to search for answers to the questions that still remain unanswered. The book should also provide useful information for clinicians and nursing staff in the management of their immobilized patients. Finally, it should

offer a basic understanding of the physiology of inactivity for those in allied health disciplines who are concerned with the health problems and care of the sedentary and the aging.

No book like this could be written without help and assistance. We wish to thank the great number of co-investigators and collaborators both within the Space Agency and at various universities and research centers across the United States and abroad who contributed so unselfishly to this cause. We would like also to acknowledge the significant efforts of our Soviet colleagues who have shared invaluable information, and particularly those of A. I. Grigoriev and V. M. Mikhaylov of the Institute of Biomedical Problems, Moscow, who in 1979 worked so diligently to accomplish with us the first joint U.S.–U.S.S.R. bed rest study. Above all, we wish to express to all the healthy volunteers who participated in our studies our enormous appreciation for their cooperation and their willingness to adhere to schedules and strictly controlled experimental conditions. Without them, none of this information would have been available today. We would like to express our particular deep gratitude to two individuals without whose help we could not have prepared this material: first, to Ms. Mary Phares for her assistance in collecting background materials and in drafting and editing the various chapters, and then to Mrs. Doris M. Furman for the typing of the preliminary and final versions of each manuscript.

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Introduction

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Before the nineteenth century, sick people rarely took to their beds until they were too weak to stand or sit. This aversion to bed rest resulted primarily from the fear among working people of losing income critical to family survival and the general superstition that if you went to bed you would never get up again. All of this changed in 1863 when John Hilton concluded that if immobilization could heal a broken limb, it should be helpful in treating other health problems as well (Hilton, 1863). With lack of drugs and modern treatment modalities, the physicians of the time rapidly adopted this concept with so much zeal that they often put to bed many patients who would have been better off up and about, occasionally even forgetting some of them in the process. Starting 50 years ago, certain physicians began to question the prescribed practices then current of 4–6 weeks of bed rest following surgery or treatment of myocardial infarction and pointed out the clinical risks of prolonged bed rest (Asher, 1957; Browse, 1965; Thompson, 1934). Much of this was supported and further confirmed by experiences and findings from World War II, when men who were rapidly returned to ambulation had fewer problems than those bed rested for prolonged periods (Browse, 1965). Yet an understanding of these implications took time, a major reason being that all observations were made on sick people, whose basic illness was the cause of their going to bed. These illnesses could, and did, complicate observed findings.

The first studies to evaluate the effects of bed rest were conducted in the 1920s. The pioneers in the field were Campbell and Webster in 1921 and Cuthbertson in 1929. The first two investigators studied day and night cycles of nitrogen excretion in a 28-year-old male. Cuthbertson had a larger number of

subjects—five males (19–40 years) and two females (19–37 years). This investigator also studied the metabolic effects of immobilization. After these studies, little was done until the late 1940s when the question of whether or not immobilization would have deleterious physiological effects led to two studies (Deitrick *et al.*, 1948; Taylor *et al.*, 1949) that marked the beginning of the modern era of bed rest investigations, which continues to this day.

I. ENTRY INTO THE SPACE AGE

The advent of the space program provided yet another and important contribution. As humans moved to extend their presence in space from hours to days to months, methods for long-term simulation were sought in order to predict adverse reactions and to test and to evaluate various methods for their prevention. It was hypothesized, and later proven accurate, that physiological changes during spaceflight would be similar to those seen after bed rest. The space program provided the justification and resources to study the time course of these changes in large numbers of otherwise completely normal individuals confined to bed for prolonged periods. Rasults showed that all physiological systems of the body change with inactivity and immobilization. Some of these changes appear more rapidly or are longer lasting than others and will be described later in some detail. The severity of many of the changes depends on how long the individual is bed rested or inactive.

After bed rest, or spaceflight, individuals must again adapt to an erect body posture and to earth's gravity. This is often not so readily achieved as is adaptation to the state of inactivity or weightlessness. The return of affected physiological systems to normal can be highly variable and can require days, weeks, or even months. Moreover, certain individuals readapt more readily than others, and why this is so has not yet been determined. Changes in the musculoskeletal system continue to serve as an area for major concern to ground and aerospace medical investigations, because it is uncertain whether the observed changes are ever entirely reversed.

Finally, bed rest has proven to be an important physiological tool. Reactions have now been documented for almost 2000 normal adults and have included individuals up to age 65 years, athletes and nonathletes, and subjects from all walks of life (Greenleaf *et al.*, 1982; Sandler, 1980; Nicogossian *et al.*, 1979). These observations have proven invaluable in attempts to compare the system changes occurring in bed rested subjects with major clinical disease states (Browse, 1965; Steinberg, 1980). Similarly, the findings have also been important to the space program, since it has been difficult to obtain accurate and reproducible data in space. This has usually occurred for three reasons: first, mission operational requirements and crew activities have taken precedence over

medical evaluations; second, since the health and safety of crew members are of primary concern, countermeasures are often employed, some of which alter physiological responses; finally, the relatively small number of astronauts and cosmonauts who have flown in space makes it difficult to extrapolate the data to reach general conclusions about the health and safety of humans during very long exposures to weightlessness. To date, a little more than 300 individuals (9 of whom were women) have flown in space; however, 210 of these persons have been in space for 14 days or less, and only eight, all Soviets, have ever flown 6 months or longer. To overcome these problems, both U.S. and U.S.S.R. investigators continue to rely on ground-based methods, such as bed rest, to obtain statistically significant information on effects and to test the broadest possible segment of the population for change and reaction to proposed countermeasures.

II. GROUND-BASED SIMULATIONS OF WEIGHTLESSNESS

The methods used to simulate null gravity on earth include immersion, bed rest, chair rest, isolation, hyperbaric environments, and immobilization of animals (Sandler, 1980). None of these techniques precisely duplicate weightlessness, because gravity cannot be entirely eliminated on earth. Immersion and bed rest studies, however, have provided possibilities for long-term exposures, with findings closest to those seen with a weightless state. Head-out immersion has the longest history of use (Epstein, 1978; Sandler, 1980). This technique has provided simulations lasting for several hours to as long as 56 days (Shulzhenko *et al.*, 1977). It has been used most extensively to document physiological adaptation to rapid shifts in body fluid distribution. Water immersion longer than 12 hr is difficult, because of problems with temperature control of immersion fluids, personal hygiene, negative-pressure breathing, skin maceration, and associated psychological problems from sensory deprivation. Consequently, bed rest, which does not have these limitations, has been used much more frequently.

More than 160 bed rest studies using healthy individuals have been conducted by U.S., Soviet, and other European investigators to evaluate physiological changes occurring in weightlessness (Greenleaf *et al.*, 1982; Nicogossian *et al.*, 1979; Sandler, 1980). The greatest percentage of studies have investigated cardiovascular changes; those studying exercise tolerance, possible countermeasures, hormonal and metabolic changes, bone mineral losses, and muscle atrophy and neurophysiological changes are the next most common. Subjects have been stress-tested following bed rest with 70° head-up tilt, lower-body negative pressure, centrifugation, and exercise to determine decrements in work performance.

Toward the end of the 1960s, Soviet investigators evolved a new method of bed rest in which subjects were positioned with the head lower than the feet,

rather than horizontal, after subjective comments of cosmonauts after flight suggested that the head-down position more closely reproduced the feelings of head fullness and awareness experienced during flight. The first study (Genin *et al.*, 1969) compared responses from horizontal bed rest and $-4°$ head-down tilt. Since then additional studies have been conducted with head-down positions ranging from $-2°$ to $-15°$ and lasting from 24 hr to 182 days (Kakurin, 1981; Kakurin *et al.*, 1976; Katkov *et al.*, 1982; Sandler, 1980). In general, head-down bed rest induces findings more rapidly and profoundly than its horizontal counterpart.

Both inactivity and removal of postural stimuli, associated with a change in the direction of gravity pull on the body, are suspected to cause the physiological changes seen in spaceflight and immobilization. In both spaceflight and immobilization, these factors are closely interrelated. In space, the body becomes weightless, with loss of load bearing on bone and muscle, particularly the legs, and there is no longer a gravity gradient from the upper to lower body segments on becoming erect. Furthermore, the body cannot move about as readily as it did on earth and essentially becomes inactive. With immobilization, gravity is still present, but head-to-foot loading of the body along its long axis is minimized. Shifting of body fluids footward cannot take place. Loss of these postural cues in bed rest is therefore one of its most important conditioning factors towards subsequent altered physiological reactions. Under such hypodynamic conditions metabolic demands are severely reduced, since the body has had both its type and range of motion restricted, as compared to when it is upright and mobile. Normal basal endocrine and neurophysiological functions require periodic stimulation by such alternating and recurring cues as meals, light and dark cycles, noise, and changes in position. These functions must receive particular and careful attention during either spaceflight or bed rest; otherwise, they can also become factors causing physiological changes.

III. EFFECTS OF INACTIVITY

The human body is constructed for movement, as evidenced by the fact that skeletal muscle constitutes 40% of body mass. During strenuous exercise, blood flow in muscle can be 15–20 times greater than during rest (Steinberg, 1980). The metabolic rate of muscle at peak exercise can be 50–100 times greater than during supine rest (Steinberg, 1980).

The circulation and respiration provide the working muscle with nutrients and oxygen while removing metabolic waste and carbon dioxide. These two systems respond efficiently to any increase in muscular activity. Cardiac output, heart rate, and left ventricular function all increase. Even with moderate exercise, cardiac output may triple, heart rate may double, and left ventricular effort may

more than triple. Oxygen uptake with heavy exercise rises 6 times higher than seen at rest, and minute volume of respiration may increase 10 times over resting values. With maximal exercise, tidal volumes may reach as high as 50% of vital capacity. These changes are greatest in physically fit individuals and are severely reduced in inactive or immobilized persons. With inactivity, physical fitness decreases rapidly, and maximal cardiorespiratory response, a measure of reserve capacity, is severely reduced. Finally, orthostatic intolerance occurs in almost all individuals.

Body metabolic function level is significantly affected by inactivity, although decreases in myocardial and postural muscle work are related to gravity (Browse, 1965; Vernikos-Danellis *et al.*, 1974). General metabolism declines, including caloric and dietary requirements, as part of an adaptive process responding to a new physiologic state.

The efficiency of many other systems also declines with immobilization. Human performance shows decrements over the long term. The intellect is dulled and a state of apathy and depression ensues. Changes are complicated by the associated isolation and confinement, with attendant disassociation from family and friends. Prolonged inactivity also impairs motor ability and task precision. This change occurs because of altered sensory perception and functional maintenance of some muscles and atrophy of others, leading to changes in abilities requiring precise coordination. The immobilized individual loses the ability to coordinate his or her movements rapidly and efficiently.

During prolonged immobilization, the gastrointestional tract is also affected. Immobilized individuals lose their appetite, often for protein-rich nutrients that would contribute to muscle building. Renal problems also occur, because the body is not in a satisfactory position to totally expel urine, and calculi may form in the stagnant pools (bladder or kidney hila) from low-level, long-term increases in urinary calcium content. Prolonged inactivity, in fact, affects every organ in the body, disturbs hormonal and metabolic functions, and contributes to bone mineral loss and osteoporosis. Finally, immobilized individuals cannot respond effectively to stress, and psychosocial interactions may suffer severely.

IV. THE EFFECTS OF GRAVITY

Humans are affected by gravity more than any other animal because of their normal erect posture. Over time the ability to bear weight on the spine and walk upright has required significant adaptive changes. The use of the legs to walk and to return the shifted and reasonably large volumes of blood from the lower extremities has required unique physiological modifications. All such changes are no longer needed or useful in a weightless environment. Let us consider in some detail how gravity affects various physiological systems.

A. Bone and Muscle

Ever since humans attempted to stand upright, gravity has tried to pull them down. The compressive force of gravity on the spinal column and leg joints is such that each astronaut or cosmonaut has reported an increase in body length of at least 2–5 cm during flight. Standing is an active process and results in a small, but significant, expenditure of energy (at least 5.71 kcal/min, 2/hr), which is a 16–19% increase compared to lying down (Browse, 1965). Antigravity muscles come into play and primarily consist of the quadriceps femoris, gluteii, and spinal erectors; the actions of these muscles are balanced by the hamstrings and anterior abdominal muscles. Response and interactions are under central nervous system control, particularly guided by proprioceptive inputs from fibers and receptors in joints and muscles and spinal–cerebellar–vestibular influences. Absence of weight bearing not only removes the direct compressive force on the long bones and spine but also removes the indirect loading on these bones from the pull of these muscles on the various bony structures to which they are attached. Unloading of the skeleton invariably leads to osteoporosis, a weakening of bone strength, and delayed ability to heal fractures, should they occur. Skeletal muscle, as indicated, also makes up 40% of body mass. Disuse and inactivity lead to adaptive changes resulting in change in both size and fiber type for individual groups of muscles, particularly those involved in weight bearing. The underlying reasons for changes in bone and muscle are not known, but the debilitation continues unabated throughout the period of altered gravity if attempts at prevention are not employed. It remains unclear at present whether the changes are irreversible. To date, osteoporotic changes in postmenopausal women and the elderly have generally been refractory to treatment (Steinberg, 1980).

B. The Circulation

Gravity produces significant effects on the circulation and the need for adaptive change. In the upright position, with gravity in full effect, at least 10–15% of the circulating blood volume is shifted footward. Yet such a shift is accomplished with little change in blood pressure or oxygen delivery to the brain. This is the result of the close interaction between the central nervous system (baroreceptors) and the heart (rate and stroke volume). Reactions also include control of venous storage capacity of the lower extremities and supplemental information released by the peripheral tissues as hormones (adrenal and renal steroids) and/or metabolic end products (prostaglandins, adenosine 5′-monophosphate, lactate) that indicate the adequacy of oxygenation. Since we usually spend at least two-thirds of our time erect or sitting, these processes of adaptation and regulation for the headward return of gravity-displaced body fluid have become important steps in our evolutionary process. During weightlessness, however, such mechanisms

are not needed, and in-flight evidence shows that the body once again readily adapts to this new physiological state and does so successfully. Changes during flight and inactivity occur rapidly, and the ability to adjust to an upright body position (lower-body negative pressure [LBNP], stand test, or 70° head-up tilt) are reduced. Using careful hemodynamic and neurohumoral measurements, significant changes can be shown after only 6–8 hr of bed rest, 1–2 hr of water immersion, or 1–2 days of weightlessness. Continued exposure increases both the severity of response and the time needed for recovery. Loss of orthostatic response when used to measure physiological change continues to decrease during the first 3–4 weeks of bed rest or spaceflight and shows much slower, or little, change after the fifth to sixth week, as a state of full physiological adaptation takes place to the new condition of inactivity.

C. Renal and Fluid/Electrolyte Function

Withdrawal of gravity, such as occurs with a supine body position or weightless state, is associated with a significant headward shift of body fluid and sets in motion neurohumoral and central nervous system changes that attempt to handle the apparent excess. Acute hemodynamic changes involve increases in renal pressure and flow. These are followed quickly by neural and hormonal responses designed to increase renal free water clearance (through a decrease in antidiuretic hormone release) and eventually to increase salt and potassium excretion. Renin-angiotensin excretion is also suppressed. Long-term exposure to bed rest of at least several months duration is associated with suppressed adrenal responsiveness and suppressed ability to cope with all forms of physiological stress. Urinary excretion of calcium rises slowly and remains persistently elevated at a low level after the first few weeks of exposure. Such elevated urinary calcium levels have proven troublesome, leading to stone formation in cases with urinary tract abnormalities, particularly in the presence of infection.

D. Sleep and Immobilization

It has been suggested that changes during prolonged bed rest are no more serious than those seen during sleep. However, that is not so. During night sleep in a normal, healthy human, heart rate decreases, blood pressure falls, and peripheral dilation occurs in skin blood vessels, resulting in a secondary loss of body heat. Plasma protein concentration and hematocrit fall, and fibrinolytic activity is decreased so that blood clots form more readily during sleep. Respiration becomes slower and shallower as sleep deepens. In deep sleep, alveolar and total ventilation decreases, and there may be periods of apnea and Cheyne-Stokes respiration. Although the alveolar oxygen concentration remains unchanged, alveolar carbon dioxide concentration increases. The latter change, however, affects the respiratory system very little. Unlike bed rest, sleep decreases urine

production, as well as the excretion of electrolytes, corticosteroids, and hormone breakdown products. The central nervous system shows a decrease in the amplitude of reflex responses resulting from decreased cerebral activity. Although cerebral blood flow may increase to compensate for any fall in blood pressure, cerebral oxygen consumption remains unchanged.

V. SUMMARY

The findings of research personnel and clinicians have demonstrated that no single human physiological system remains unchanged following prolonged periods of inactivity or immobilization. Under these conditions, the various systems deteriorate to a lesser or greater degree and according to different time sequences. Although we have accomplished a vast amount of information on the physiological responses of individuals to these conditions, numerous questions remain to be answered as to why these changes take place, whether they are reversible, and, most importantly, whether they will result in health problems many years later as the individual ages. Research is being conducted at present to find some of the answers. But many comprehensive studies will be needed in the future if we are (a) to understand fully the implications of inactivity and immobilization for research subjects, clinically bed rested or paralyzed patients, and the elderly on earth, as well as for long-term space station dwellers, and (b) to develop countermeasures to offset the observed physiological responses.

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2

Cardiovascular Effects of Inactivity

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I. THE IMPACT OF GRAVITY

Gravity is a consistent factor governing life on earth. As humans, we normally spend two-thirds of our day standing or seated. While erect, a significant amount of intravascular volume and tissue fluids are shifted to the lower body from the pull of gravity, and the body must compensate to maintain blood flow to the head and to distribute blood volume adequately throughout the body. When the compensatory mechanisms are inadequate or retarded, orthostatic intolerance or hypotension occurs, with eventual fainting.

Over time, the human body has evolved a gravity receptor system that uses information gained from muscle proprioceptors, semicircular canals, otoliths, and mechanoreceptors (baroreceptors). These systems, which sense body position and initiate the necessary change, operate continually as we interact with our environment and are most evident when we change from the supine to erect body position. Normally, 70% of the body's blood volume resides in systemic veins, 15% in the heart and lungs, 10% in systemic arteries, and 5% in capillaries. The upright position shifts 700 ml of venous blood from the upper body to the legs, with 400 ml coming from the central circulation (heart and lungs). As shown in Fig. 1, the loss in central blood volume immediately causes a 25% decrease in cardiac output, a 25% increase in heart rate, and a 40% decrease in stroke volume, with little change, or even a slight increase, in blood pressure. Blood pressure is maintained by an increase in flow resistance through arterial and arteriolar constriction, resulting from increased sympathetic nervous system out-

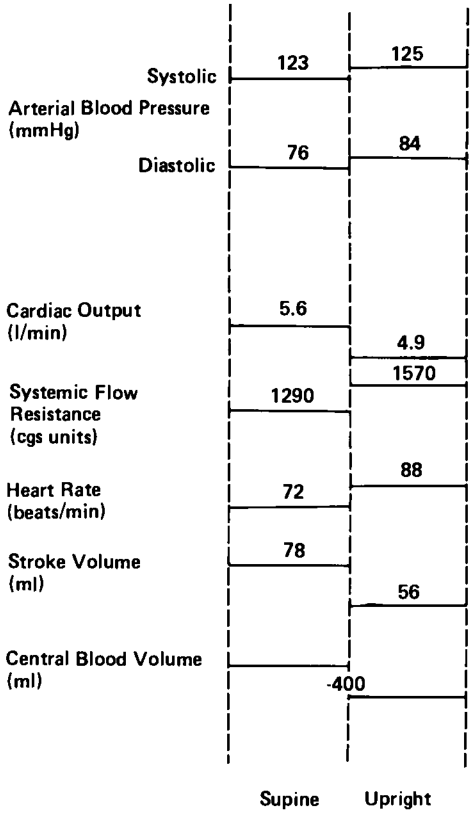

Fig. 1. First level of defense against gravity: hemodynamic changes from supine to upright posture.

put, due to triggering of aortic and carotid sinus baroreceptors. The process is reversed when the body changes from erect to supine.

II. LEVELS OF DEFENSE IN BODY POSITION CHANGES

There are at least three levels of defense to offset cardiovascular changes that occur with changes in body position.

The first is an adjustment in venous capacity and pressure by redistributing contained volume. The magnitude of the venous shift is shown schematically in Fig. 1. When erect, shifted volume is transferred primarily to deep intra- and intermuscular leg veins, with about 200 ml going to the pelvis and gluteus maximus areas. Adjustments for the displaced venous volume occur and rely on

the rapid contraction and relaxation of smooth muscle in the venous wall, respiration (movement of the diaphragm), and particularly, contraction of the lower limb muscles, which by their action squeeze blood back toward the heart.

The second line of defense occurs when the pre- and postcapillary sphincters act to increase or to decrease fluid in the tissues. As shown in Fig. 2, after 10 min of standing this mechanism shifts about 10% the of plasma volume to dependent tissue spaces; such loss stabilizes at about 15% after 20 min. This second line of defense is probably more important in the long run than are fluid shifts within venous vessels, because it increases or decreases the absolute volume of the cardiovascular system, as opposed to redistributing its contents. Factors that can affect this ability for volume change occur at the local tissue level and include nervous, metabolic, or biochemical events.

Finally, there is a third line of defense, which is under neurohumoral control and is used primarily for long-term adjustments. The events associated with these changes are detailed in Fig. 3. Activation of neurohumoral control depends on stimulation of proprioceptors (baroreceptors) which, depending on their design and whether they are located inside or outside the chest, are able to sense (a) the filling of the system, (b) the wall tension in atria or ventricles, or both, and (c) the pulse and mean pressures in the pulmonary and systemic arteries. When activated, the system stimulates sympathetic nerve activity or inhibits the release

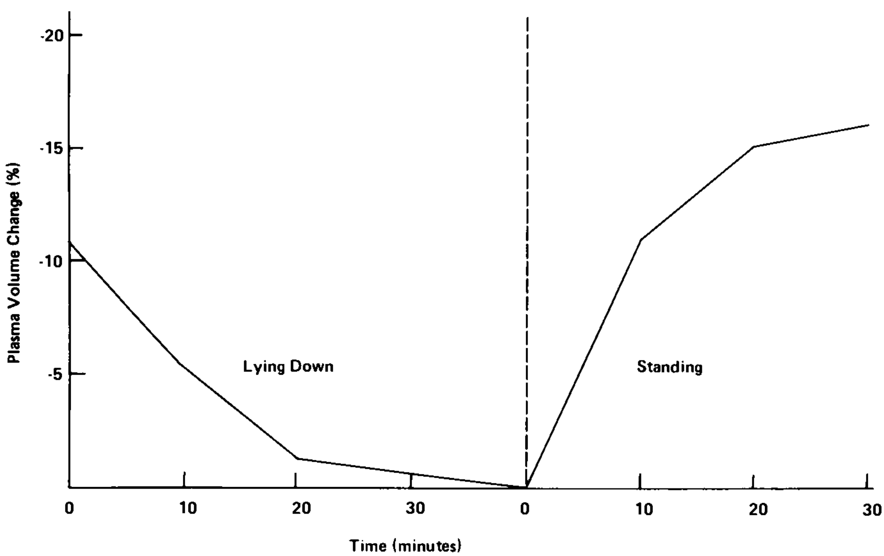

Fig. 2. Second level of defense against gravity: plasma volume changes during lying down and standing. [From Hagan *et al.*, 1978.]

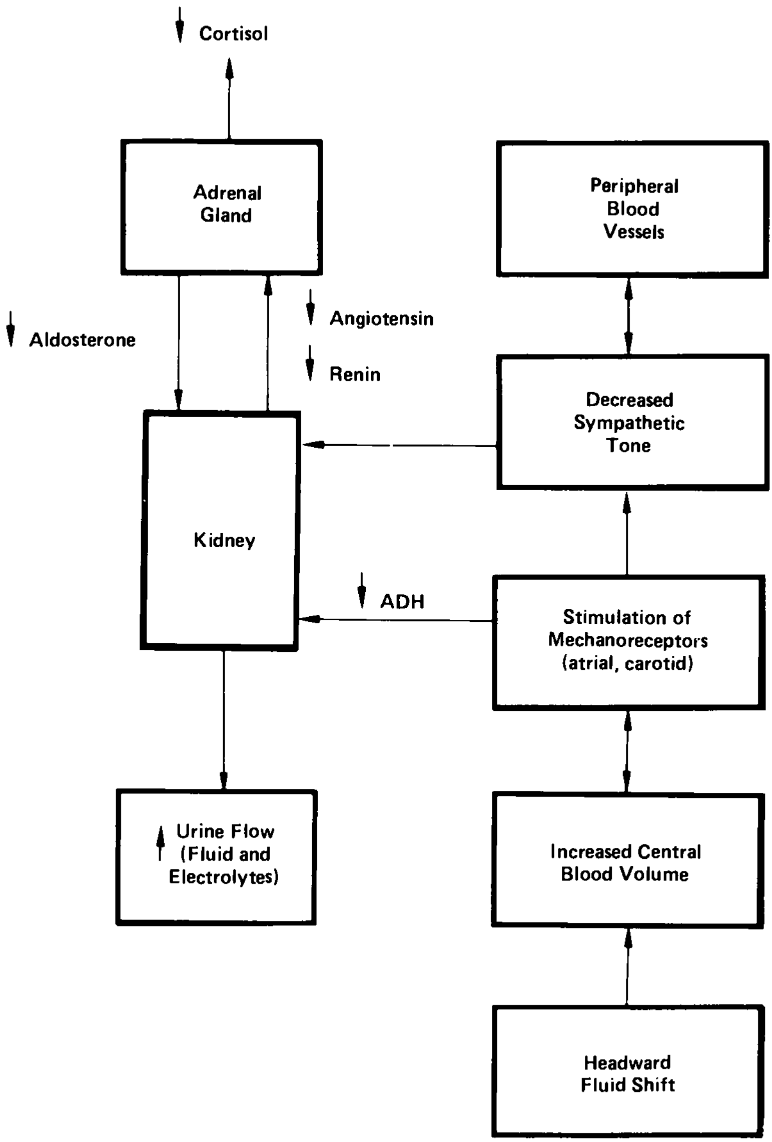

Fig. 3. Third level of defense against gravity: responses in the supine position.