Commentary

The Disuse Syndrome

WALTER M. BORTZ II, MD, *Palo Alto, California*

Our cultural sedentariness, recently acquired, lies at the base of much human ill-being. Physical inactivity predictably leads to deterioration of many body functions. A number of these effects coexist so frequently in our society that they merit inclusion in a specific syndrome, the disuse syndrome. The identifying characteristics of the syndrome are cardiovascular vulnerability, obesity, musculoskeletal fragility, depression and premature aging. The syndrome is experimentally reproducible and, significantly, the clinical features are subject to both preventive and restitutive efforts that happily are cheap, safe, accessible and effective.

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Use is a unifying biologic principle. Vital function is highly keyed to the production of energy. Cybernetic mechanics link optimal performance to regular use. For some body systems (musculoskeletal and cardiovascular) this usage implies physical work. For others usage is defined by the specific function served by the organ, such as sense organs, gastrointestinal tract, genitourinary tract and endocrine system. Even for the systems not primarily serving exercise needs, however, exercise plays a modifying role.

Disuse is catabolic. It adversely affects all body tissues and all body functions. The changes due to it in the particular or in the aggregate contribute substantially to the ill health of our bodies. The mechanisms for the deteriorative effects of disuse are varied and specific to the structure or function involved.

The structural changes accompanying disuse involve such diverse phenomena as loss of muscle fiber bulk, calcium resorption or alteration in the number of membrane-binding sites. The functional changes of disuse similarly are varied, such as disruption of rhythmic processes, loss of enzyme activity or distortion of hormonal responsiveness. Whatever the changes, they are probably tightly linked to the chemical pathways of energy generation. The purpose of this paper is to draw attention to some of the adverse end products of disuse. It is further proposed that many of these results are found so systematically and relatedly in clinical situations to merit their inclusion in a single disorder—the "disuse syndrome." It is hoped that by thus focusing attention on these phenomena, increased preventive and restorative efforts will be directed toward them.

The Long View

In characterizing the results of disuse, it is important to place our current state of inactivity in a historical perspective. Anthropologists delight in regressively resetting the birthdate of sapient humans. The latest reckoning puts the date at least two million years ago. Throughout this extended time our biology was being shaped. Accommodation and compromise decreed who lived and who died. Darwin taught us that our heritage was molded through these eons by physical challenge and threat. The fittest of us survived. In the millions of years we lived as hunter-gatherers, our ancestors were likely extremely physically active, running after or away from their dinner or predators respectively. This life-style persisted until the Agricultural Revolution of 10,000 years ago. Food supply became stationary and physical demands slackened. The Industrial Revolution of 200 years ago greatly accelerated the extent of our inactivity. The time span since this major cultural event is only a twinkling of time—0.0017% of our species' lifetime.

There is a basic anthropologic law called the Principle of Least Effort.[1] Simply stated, when an organism has a task to perform it will seek that method of performance that demands the least effort. The economy implicit in this principle is evident.

The contemporary version of our species seems to have embraced the Principle of Least Effort for its very own. Our ardent pursuit of less effort has led to the wheel, pushbutton tuning, the horizontal escalator and—the embodiment of least effort—the motorized golf cart. A major portion of our industrial complex is committed to the refinement of our inactivity. Great economic advantage seems to accompany any breakthrough that enables us to work less hard. We are perfecting the art of spectating—vicarious exercise. The ultimate eventuality of this trend is frightening to contemplate: *"homo robotis."*

Survival no longer depends on physical prowess. For the hunter-gatherer, the least effort was still hard work. The survival pore through which we squeezed was a tight fit. We

From the Health Care Division, Palo Alto Medical Foundation, Palo Alto, California.
Reprint requests to Walter M. Bortz II, MD, Health Care Division, Palo Alto Medical Foundation, 300 Homer Ave, Palo Alto, CA 94301.

were hardened and tempered by millions of years of strenuous work. We are the inheritors of fit genes. Two hundred years have greatly redirected the rigor and vigor of human existence.

With the newness of our inactivity, it is not surprising that so little effort has gone into analyzing its effects on us. The space effort, however, changed that. For the first time it became important for us to understand what the effects of prolonged periods of enforced inactivity had on our bodies. Weightlessness accelerates the effects of disuse as countering gravity per se demands work. We went into space with a sparse understanding of the physical threats that it held. We and the Russians are making earnest efforts to fill the gaps in our knowledge of the effects of disuse on our structure and function. Space medicine is the composite of those efforts.

Structural and Functional Responses to Disuse

Musculoskeletal

Perhaps the most graphic example of the atrophic effects of disuse is the limb that has been immobilized in a cast. After only a few weeks of inactivity the muscles shrivel and stiffen. Biopsy specimens of atrophic muscle show a decrease in fiber diameter.[2] The slow-twitch fibers seem especially sensitive to disuse.[3] Increases in urinary nitrogen content are a reflection of the muscle catabolism that accompanies enforced bed rest,[4] bed rest causing a protein loss of 8 grams per day.[5]

Similarly, calcium wastage is uniformly found with inactivity.[6] Both the mineral content and matrix of bone deteriorate. Bed rest results in a calcium loss of 1.54 grams per week.[6] Between 24% and 40% of the mass of the os calcis is lost during 36 weeks of bed rest.[6] The Skylab astronauts lost appreciable amounts of body calcium in space, enough that space flights longer than nine months may not be feasible.

Cardiovascular

The most vital purpose served by our heart and vessels is the transport of oxygen. The maximum oxygen consumption is the best measure of this capacity. A typically unfit American has a maximum oxygen intake that is 40% less than a fit person of the same age.[7] Cardiac output,[8] stroke volume[8] and left ventricular function[9] decrease with disuse, and total peripheral resistance [10] and systolic blood pressure rise.[11]

Orthostatic hypotension and vestibular hypersensitivity have been repeatedly described by the astronauts and cosmonauts. Tilt-table intolerance follows prolonged inactivity.[12] This is at least partially due to a fall in body water that accompanies disuse. Plasma volume falls 10% to 15% with bed rest.[13]

Blood Components

Red cell mass decreases probably as a result of decreased erythropoiesis with inactivity.[8,11] A thrombotic tendency and fibrinolytic activity correlate strongly with prolonged bed rest.[14,15]

Lungs

The work of the lungs is to breathe. When the function is interrupted by bronchial obstruction or pneumothorax, atelectasis and distorted respiratory function ensue.

Gastrointestinal System

Studies of starvation have shown structural and functional changes of all components of the gastrointestinal tract and its appendages.[16] So, too, have many reports described the state of loops of gut when they are excluded from the enteric pathway[17]; mucosal atrophy and glandular shrinkage occur. Total parenteral nutrition provides an interesting study opportunity.[18] The gut needs to be used to retain its functional capacity. The liver atrophies during starvation and constipation and diverticulosis are outcomes of underused gastrointestinal tracts as well.

Genitourinary System

The kidneys when excluded from filtering requirement[19] and the bladder when excluded from storage[20] atrophy and lose vitality.

Reproductive System

Physical inactivity decreases serum androgen levels[21] and spermatogenesis.[22] Cutler and co-workers report that women with regular sexual activity have more regular menstrual cycle lengths[23] than those with less active sexual lives. Masters and Johnson and Kinsey have written extensively on the linkage of good sexual functioning and regular activity.

Endocrine System

Starvation diabetes follows periods of caloric lack. The glycolytic enzymes decrease in amount and activity when carbohydrates are withheld. Physical exercise, however, increases insulin binding sites on muscles.[24]

The necessity for tropic stimulation of the thyroid, adrenal and sex glands is evident. A lack of stimulation promptly leads to deterioration.

Other Regulatory Functions

The body temperature falls[25] and circadian rhythms[24] desynchronize with inactivity. Vernikos-Danellis and associates reported that enforced bed rest resulted in alterations in the normal fluctuations of metabolic and hormonal indices.[26] Glucose response to insulin,[27] adrenocortical response to adrenocorticotropic hormone[28] and growth hormone responses to hypoglycemia[28] are blunted by inactivity. Disuse leads to the breakdown of feedback-integrating mechanisms. Immunologic alterations have also been described with inactivity.[29]

Sensory Deprivation

One of the prime areas for study in the space program has been the phenomenon of sensory deprivation. When subjects are deprived of visual and auditory cues, significant and progressive disorientation occurs. It is interesting to observe that bed rest also has been noted to result in a decrease in visual, auditory[30] and taste acuity.[31]

Nervous System

Physical inactivity results in decreased activity of the sympathomedullary system[32] and there is decreased catecholamine secretion.[33]

Animals raised in a deprived environment, as contrasted to those raised in an enriched environment, solve mazes slower and have smaller brains and sparser dendritic branching.[34] Electroencephalographic alterations and behavioral changes follow prolonged inactivity.[35] The positron-emitting detector clearly shows the correlation between brain use and vital functioning.

This brief survey indicates that all living cells, tissues and organs participate in the syndrome of disuse when their particular functional activity is impaired. With inactivity so epidemic and universal in our age, it seems appropriate to question whether many of the norms that we apply to functional and structural capacities are in reality faulted and mere descriptors of a lessened potential. This seems to be particularly true of those functions served most highly by exercise demands.

Disease Linkages

Having identified the deteriorative effects that disuse imparts to all body parts, it is logical to inquire how this deterioration may be affecting our overall well-being. My estimate is that the contribution of disuse to human illness is immense. Many sicknesses have components of disuse participating in their pathogenesis, possibly in major degrees.

Mayer has repeatedly drawn attention to the critical role played by inactivity in the development of obesity.[36] There appears to be a highly efficient servomechanism that links energy output with food intake except when inactivity supervenes. Obesity is rare in the wild; it accompanies domestication. Obesity serves survival advantage only when starvation or cold exposure occurs.[37] Otherwise it constitutes a health burden, and its sequelae of degenerative arthritis, hypertension and diabetes compound the problem. Inactivity affects serum lipid values.[38]

Depression responds well to pharmacologic intervention. This prompted the insight into the role of the neurotransmitters in this illness. Peripheral and central nervous system catecholamine content is increased with physical exercise,[33] causing the "runners' high" that is commonly described.[39] It follows that if once we were all more active than we are today, and if physical activity correlates with the mental state, perhaps our entire contemporary sedentary society is depressed.

Disuse certainly participates strongly in changes that are commonly attributed to aging. Indeed, the close correspondence of the alterations ascribed separately to aging and to disuse is striking.[40] Goodrick has reported an 11% to 15% lengthening of the life span of laboratory animals when given an ad libitum opportunity for exercise as contrasted with caged controls.[41]

Stagnation is a derivative of disuse. Whenever a body cavity or duct is rendered stagnant, infection soon follows. The biliary system, the lower genitourinary system, the appendix and so forth reflect this observation.

A number of the above changes are found collectively so frequently and invariably in association with disuse that their aggregation in a clinical syndrome is warranted. The primary characteristics of the disuse syndrome are cardiovascular vulnerability, obesity, musculoskeletal fragility, depression and premature aging. These five features are in many ways interdependent, but all are historical resultants of disuse, as surely as cavitary granulomatous disease is the result of the tubercle bacillus. The features are reproducible in a research setting, and they are correctable by countermeasures. There exist various permutations and formes frustes of the entire syndrome. The syndrome is usually encountered in the middle years of life.

In 1936 Selye first described the concept of the general adaptation syndrome.[42] In his composite thesis he elaborately detailed the body's reaction to excessive input—stress. It is now generally acknowledged that stress and its end products are variably involved in a number of biologic situations. The disuse syndrome can be characterized as the reverse—too little rather than too much. It seems logical that any protracted disruption of the many homeostatic phenomena of our bodies—in one direction or the other—will be harmful.

Discussion

A medical student's first case can be disillusioning. The person's illness does not appear neatly packaged and identified as in the preclinical training. Pathologic conditions do not appear in the way the textbooks say they should. The warp in the clinical presentation of disease is often more impressive than the singular feature of the disease itself. Realization of this fact becomes the challenge and delight of the practice of medicine.

One of the principal distortions of categorical disease is age. Not only do different diseases occur at different ages, but the same disease commonly wears different faces at different ages. A child is not a small adult. An octogenarian is not a wrinkled 20-year-old. Myocardial infarction or a malignant lesion is not the same disease in an 80-year-old person as in a 40-year-old one.

Further, we now know that age corrections are important considerations when assessing some of our basic functional capacities such as arterial oxygen pressure, glucose tolerance, creatinine clearance and others. Identification of the effects of time on disease first led to the establishment of pediatrics as a discipline, and now attention is focusing on the emergence of geriatrics as a major theme of medicine. Disease has an important time dimension.

Illness as we see it has another component that is due neither to disease per se nor to time effects but to disuse, the third dimension.[43] This review is not intended to be encyclopedic with regard to the participation of disuse in our human ailments, but merely to render cohesive what has previously been separately described for each of the circumstances mentioned.

We are blessed with much redundant function. We have two eyes, two ears, two lungs, two kidneys, two testes and two ovaries when only one of them can serve us perfectly adequately. We can run marathons with one lung, or procreate with one ovary or one testicle. The point of this is that we start with 100% of our potential and can surrender 50% with slight or no noted diminution in capacity. It is not until 70% of maximal capacity is lost that a clinical warning sign is lit and medical attention is sought. Unfortunately, a few percentage points of further deterioration mean death. This general observation applies in the lung (oxygen pressure and diffusing capacity), the blood vessels (cross-sectional area), the kidney (creatinine clearance) and the heart (ejection fraction).

Clinical examinations are designed to assess disturbances in the 20% to 30% of maximal range, where disease is manifest. Kerlan has drawn attention to the upper part of the scale, deteriorations from the *norm* that are subclinical.[44(p 22)] This is the range wherein disuse is predominantly manifest. Disuse depletes our reserve capacities and renders us unduly susceptible to disease processes that a fit body may be more easily able to withstand. We are all much more aware of our checking account balance than we are of our health balance.

Inactivity plays a pervasive role in our lack of wellness. Disuse is physically, mentally and spiritually debilitating. But the good news is that it is almost never too late to recognize this. One of the most extraordinary aspects of the human body is its resilience: its ability to recoup is enormous. The latent period of response from an inactive to an active state can be from seconds (sense organs) to weeks and months but tissues of all ages respond to resumed stimulus with vigor and renewal.

As we progressively identify the adverse effect with which the "least effort" of our culture has seduced us and recognize the extensive benefits that can accrue when the disuse syndrome is combatted, we then can aspire to the biogenetic potential with which our millions of years of vigor have vested us.

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