Exercise: A Changing Prescription

The first formal epidemiologic study linking activity to better health took place in the late 1940s, when a researcher in London, Jeremy Morris, and his colleagues compared double-decker bus drivers to conductors. The conductors ran up and down stairs all day collecting tickets while the drivers sat at the wheel. "Morris found that the conductors had lower rates of heart disease," says I-Min Lee, an associate professor at both the Medical School and the School of Public Health. Critics dismissed the study on a variety of grounds, insisting that the other factors it documented—lower blood pressure among the conductors, and lower body weight (indicated by the smaller waists of their trousers)—could explain the differences in rates of heart disease.

But as evidence for the health benefits of activity mounted, the question became, What sort of exercise is needed? The first official recommendations were formulated in the 1970s: adults were advised to engage in at least 20 minutes of continuous vigorous exercise, three times a week. The goal of these initial recommendations—which became the basis for the phrase, "No pain, no gain"—was to improve physical fitness. Then, in 1990, a group of researchers investigating physical activity began to question the necessity of working out intensely for health, as opposed to fitness, benefits. They worried that the recommendations had become a barrier to the average citizen, contributing to low rates of physical activity among Americans. An expert panel convened by the Centers for Disease Control and the American College of Sports Medicine reexamined the literature, and in 1995 issued new guidelines, advising every American adult to accumulate at least 30 minutes of moderate-intensity physical activity a day. The idea that you could walk instead of jog and accumulate activity by adding together exercise bouts of at least 8 to 10 minutes each marked a "radical departure," says Lee. "At that time, there was little direct evidence examining the value of moderate- versus vigorous-intensity activity on disease outcomes like heart disease. There were even fewer data regarding the accumulation of physical activity." Researchers (including Lee) began to conduct studies testing the new approach. Their findings have shown clearly that moderate-intensity activity is beneficial against chronic diseases such as heart disease, stroke, and diabetes.

But what does moderate mean? "We can look at intensity in two ways," Lee says, "on either an absolute or a relative scale." Using absolute measures, a 75-year-old man and a 25-year-old man walking briskly at four miles per hour are said to be engaged in identical, moderate-intensity activity. But in a relative sense, the 75-year-old might rate his effort as fairly hard, while the 25-year-old might say the pace was easy. Current physical activity recommendations generally give examples of physical activity that are "moderate" in intensity for most young to middle-aged persons. But, for older people, who tend to be less fit, perhaps even lighter-intensity physical activity can qualify as "moderate."

In fact, the Harvard Alumni Health Study (a study of Harvard College alumni who matriculated between 1916 and 1950 founded by Professor Ralph Paffenbarger, one of the pioneers of epidemiologic studies on physical activity and health) found that when the alumni were in their forties, vigorous exercise predicted greater longevity and lower risk of cardiovascular disease. "As they aged," Lee says, "relative intensity became a better predictor of heart-disease risk."

Is the intermittent approach to activity valid? Lee and her colleagues found in the Harvard study that as long as the energy expended was the same, it did not matter whether the exercise was carried out all at once in a single bout or broken up into several shorter bouts: the greater the energy expenditure, the lower the risk of heart disease.

phy of muscle and bone. "They're related to indirect effects—for example, [the effects] of exercise on lipid metabolism, as in atherosclerosis. But we are still far from understanding exactly how it works." Better understood is what is happening with muscle and bone during exercise.

Goldberg approaches this subject from a unique perspective: he is an adviser to NASA's space biomedical research program. "One of the big problems for astronauts is tremendous loss of bone and muscle," he reports. When you lose bone mass, what's left becomes brittle and susceptible to fracture. It also releases calcium phosphate and organic components that can make you much more sensitive to renal stones. That is why the loss of bone that takes place with extreme disuse—whether in space, in wasting diseases, as part of aging, or during extreme bedrest—can lead to kidney disease.

Goldberg is co-leader of a team trying to prevent the loss of muscle, which he says, is "absolutely necessary for a long-term space program." The rate of muscle loss—including heart muscle loss—during spaceflight is so great, he says, that "unless this problem is solved, by the time an astronaut got to Mars he wouldn't be strong enough to walk around or even to go out to repair the space vehicle if necessary."

Goldberg's group has discovered that, at the cellular level, the muscular response to disuse is very similar to what is seen in fasting, cancer, AIDS, and renal failure. He says, "We've identified a whole group of genes that are turned on, according to a specific program, whenever a tissue atrophies. Sometimes this program is turned on by disease, and sometimes it is turned on by disuse." His group has dubbed the most critical of these genes atrogin. It tags proteins for destruction—without destroying cells—by a process that is still not fully understood.

Goldberg and his colleagues hope to find a biochemical way to turn off this genetically controlled program of atrophy. Exercise turns it off by causing release of a *(please turn to page 98)*