reactor wastes at sea may release quantities of thorium and lead, among other radioactive isotopes, the effectiveness of these presumably biological mechanisms is of no little interest.

In proposing the Geosecs program, marine geochemists held out the idea of establishing a baseline against which man-made changes in the global environment could be measured. Unexpectedly, shipboard measurements of atmospheric nitrous oxide (N_2O) concentrations made during Geosecs cruises and some earlier measurements of the gas 10 years ago in the Pacific have shown the value of a baseline and of a sample bank for later analysis. Nitrous oxide is produced in soil and in the surface layers of the oceans and destroyed in the stratosphere, where it is also the main moderator of ozone. Several scientists concerned with threats to the ozone layer have suspected that widespread use of fertilizers was accelerating N_2O production in the soil. Harmon Craig and Ray Weiss of Scripps compared the recent samples with those collected earlier by the late William Dowd of Scripps and found that average concentrations for equivalent sites in the Pacific had increased by about 4 parts per billion in a decade—a rate that they project would cause a 7.4 percent increase in atmospheric N_2O and a corresponding 1 percent decrease in ozone by the year 2000 and a far more serious effect thereafter. Craig proposes, however, that at least half of the increase in N_2O is probably due to combustion of coal and oil in electric power plants, not fertilizer use. Whatever the source, the result appears to be the first definite indication of a long-term increase in atmospheric N_2O.

Another Geosecs result has proved of interest to solid earth geochemists. Craig and his co-workers found concentrations of the helium isotope ^3He in the Pacific Ocean in excess of the amount expected from its atmospheric abundance relative to ^4He, the more abundant isotope. The excess ^3He was most concentrated in the eastern equatorial Pacific above the East Pacific Rise, where new oceanic crust is being formed by sea-floor spreading. J. E. Lupton and Craig subsequently found that basalts from the Rise are also enriched in ^3He, an indication that the oceanic ^3He is primordial—part of the earth's initial endowment and not of recent atmospheric origin. They conclude that the earth has not completed its internal evolution and is still outgassing, injecting helium from the mantle into the deep Pacific from the crests of the mid-ocean ridges.

What has been obtained from the Geosecs project so far is only preliminary; study of the massive amount of data has just begun. Broecker believes that the data will dominate efforts to understand ocean circulation and mixing processes for the next decade. In any case, it is likely that the increasing sophistication of geochemical research in the oceans will be productive in ways not yet knowable and perhaps vital to managing an increasingly crowded planet.

—ALLEN L. HAMMOND

The Aging Heart: Changes in Function and Response to Drugs

Most studies of heart disease have been concerned with heart disease in those under 65—the so-called "premature" heart disease. This emphasis is understandable both because premature heart disease strikes people who are more likely to be economically productive and because it usually is more shocking to see a younger than an older person die or become disabled. But the fact remains that most heart disease occurs among people aged 65 or older. Heart disease is so common among old people that it accounts for more than 40 percent of the deaths in this age group.

Heart disease in old people may have different causes and require different treatment than premature heart disease. The changes in the heart that come with age are likely to affect its susceptibility to damage and its response to drugs. In order to determine the degree to which conclusions from data on premature heart disease can be generalized to older people, investigators are studying the epidemiology of heart disease in the elderly and the biochemical changes that occur in the aging heart.

It would be desirable to study the effects of aging on the cardiovascular system by recording physiological changes that occur in members of a group of people as they relate to their chances of dying from heart disease over the course of their adult lives. This is not often done because it is expensive and because people tend to drop out of long-term studies. Thus, only a few studies of this type are being conducted.

One of the most successful long-term studies began in 1949, when the U.S. Public Health Service began recruiting about 6000 people between the ages of 30 and 59 from the town of Framingham, Massachusetts. This continuing investigation is providing some insights into the effects of risk factors for heart disease on people of all ages, including those over the age of 65.

This is the ninth in a series of Research News articles examining recent developments in research on heart disease.

According to William Kannel, who directs the Framingham study, some major risk factors in younger people do not seem to affect the elderly. Serum cholesterol concentrations and cigarette smoking, for example, are not good predictors of heart attacks or strokes in the elderly. (Smoking is associated with the development of lung cancer and emphysema in the elderly, however.) And diabetes seems to have less effect on old men than young, although it does predispose old women to develop heart disease. Kannel says that the best predictors of heart disease in old people are hypertension, electrocardiogram findings, high-density lipoproteins (which are associated with lowered risks) and, in women, diabetes. He emphasizes that, contrary to a widespread belief, hypertension is as much a threat to the old as to the young. The lower an old person's blood pressure, the lower his or her risk of developing heart disease. (Old women with low blood pressure, Kannel says, are "practically immortal.")

Since risk factors for heart disease in the young may not be risk factors for the elderly, not all research on the causes of premature heart disease may be applicable to heart disease in old people. In order to understand the genesis of heart disease in the elderly, it is helpful to know both the biochemical and the physiological changes that occur with age. An emphasis on studies of both physiology and biochemistry is the thrust of research at the National Institute of Aging (NIA) in Baltimore, where investigators are now beginning to piece together a picture of changes in the aging heart.

One of the most striking physiological changes that occurs with age is a decline in the heart's ability to respond to stress. This decline, first reported as early as 1929, has been confirmed by numerous investigators. During the stress of exercise, heart rate and blood flow increase, but the magnitude of these increases is smaller in older than in younger people.

James Conway of Imperial Chemicals in Cheshire, England, and his associates find that these age differences in re-

sponse to stress are obliterated when younger people are given propranolol. Propranolol blocks the response of the heart to catecholamines—agents that are secreted in response to stress. Catecholamines bind to specific receptors on heart cells and cause the heart to beat faster and increase the strength of its contractions. Propranolol prevents the binding of catecholamines.

Conway's result indicates either that old people secrete fewer catecholamines in response to stress or that their hearts respond less well to them. Edward Lakatta of the NIA reports evidence that supports the latter explanation. He and his associates found that the response of people, rats, and dogs to catecholamines diminished with age.

In order to study the basis of this decreased response to catecholamines, Lakatta and his associates, together with Myron Weisfeldt of Johns Hopkins University Medical School, isolated heart muscle from old and young rats and compared the responses of these muscles to catecholamines and calcium. Catecholamines increase the amount of calcium supplied to the contractile proteins of heart muscle cells and thereby cause the muscle to contract. It had been previously shown that heart muscle from young rats is stimulated equally well by both catecholamines and calcium. The muscle from old rats responded as well to calcium as muscle from young hearts but less well to catecholamines. Thus the effect of aging seems to be in the ability of catecholamines to affect the release of calcium rather than in the response to calcium per se.

Investigators at the NIA find that there is an age-associated decline in the number of catecholamine receptors on heart muscle cells. Isolated heart muscle from both old dogs and old rats has fewer receptors than muscle from young animals. Such a decrease could be a cause of the observed lack of responsiveness. Roth and others believe that diminishing numbers of hormone receptors are a universal characteristic of aging. Such decreases have been shown to occur in cells other than heart cells and to affect receptors for several kinds of hormones.

It is also possible that cardiac receptors for digitalis are lost with age. Digitalis binds to cardiac receptors and increases the strength of contractions. Roth finds that heart muscle from old rats responds poorly to digitalis. If human hearts respond similarly, digitalis may be less effective in old than in young people. Digitalis is commonly used to treat congestive heart failure, but patients who take it may suffer from serious side effects. According to Paula Goldberg and Jay Roberts of the Medical College of Pennsylvania in Philadelphia, old people have often been reported to react severely to concentrations of digitalis that do not generally injure younger people. These reactions include cardiac arrhythmias and neurological disturbances.

A second reason for the heart's decreased response to stress with age may be that the heart muscle changes its mechanical and biochemical characteristics. Many investigators have found that contractions are prolonged in hearts of old people and old laboratory animals. A contraction consists of a period during which the heart muscle builds up tension and one in which the tension is released. Harold Spurgeon and his associates at the NIA report that isolated heart muscle from old rats and old dogs relaxes more slowly than muscle from younger animals.

Studies by other investigators have shown that several reasons for the prolonged relaxation period of old heart muscle are possible. In order for heart muscle to relax, calcium must be removed from the contractile proteins and taken up by the sarcoplasmic reticulum, which is a separate compartment in the muscle cell. An increase in relaxation time may be caused by a decrease in the rate of calcium removal by the sarcoplasmic reticulum. Jeffrey Froehlich and his associates at the NIA recently isolated sarcoplasmic reticulum from rat heart muscle. Their preliminary results indicate that the isolated material absorbs calcium less readily as the animal ages.

Froehlich has not ruled out the possibility that other mechanisms of calcium uptake may compensate for these age-associated changes in the sarcoplasmic reticulum. But he does think his results are a first step to discovering why old heart muscle relaxes slowly.

Froehlich and Robert Tomenek of the University of Iowa point out that changes in the sarcoplasmic reticulum could be secondary, rather than primary, effects of aging. Heart muscle tends to hypertrophy with age, and there is some evidence that hypertrophy may be associated with a decrease in the activity of the sarcoplasmic reticulum. This does not necessarily mean that hypertrophy causes this decrease in activity.

Most results on the effects of hypertrophy are based on studies of rat muscle. But these changes also seem to occur in people. Gary Gerstenblith and his associates at the NIA report that human hearts become thicker with age. For example, the left ventricular wall is about 25 percent thicker at age 80 than at age 30.

Although the recent studies of the biochemistry and physiology of the aging heart do not provide direct evidence of why old hearts become damaged, they do indicate that specific changes occur with age. Knowledge of these and other changes may have important implications for drug therapy.

Roberts and Goldberg have been studying the aging heart with an eye to assessing the use of drugs that counter arrhythmias in the elderly. They found that the electrical activity of cardiac pacemaker cells decreases as rats grow old. This decrease in activity occurs in the pacemaker cells in the right atrium, which normally set the rhythm of the heartbeats, and in pacemaker cells in the ventricles, whose activity becomes apparent only when the heart is damaged in such a way that conduction between the atria and ventricles is blocked. When such a blockage occurs, the ventricular pacemaker cells cause the ventricles to beat at their own rate independently of the atria. Roberts and Goldberg speculate that the possible slowing of the electrical activity of human cardiac pacemakers with age may explain why old people are more susceptible to cardiac arrhythmias.

Roberts and Goldberg find that age-associated changes in the pacemaker cells of rats seemed to modify their response to three antiarrhythmic drugs. One of these drugs, quinidine, is often given to people with arrhythmias arising in the atria. These investigators found that the effects of quinidine on the electrical activity of both atrial and ventricular pacemakers of rats decreased with age. Lidocaine, which is given to people with ventricular arrhythmias, also had a decreased effect on the ventricular pacemakers from old rats. But it had a greater effect on the atrial pacemakers as the rats aged. And propranolol, which is thought to act in a way similar to that of quinidine, had the same effect on old as young pacemaker cells from the atrium and from the ventricle of rats.

Goldberg and Roberts point out that old people may have different reactions to drugs than the young for reasons other than changes in their heart cells. The effects of drugs are related to their absorption by the gastrointestinal system, their distribution in the body, and their metabolism. All change with age.

A complete picture of how and why heart disease occurs and how old people with heart disease should be treated cannot emerge until the aging heart is understood in light of age-associated changes in the rest of the body. But the recent studies of the aging heart are providing direction to the study of heart disease in the elderly.—GINA BARI KOLATA