THE FULFILLMENT OF HEREDITARY LONGEVITY POTENTIAL*

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IN 1928 the First Graduate Fortnight of the New York Academy of Medicine was held under the leadership of Dr. Ludwig Kast. The subject was the problem of aging and old age.¹

During the past half century progress in the training of physicians and other health personnel in the biology of aging and the care of the elderly has been slow and in many areas almost nonexistent. There is presently a marked awakening of interest in these important disciplines, and the next decade should witness greater advances than have been seen since the First Graduate Fortnight in 1928.

My role is to introduce this symposium, dealing with certain aspects of the aging process, to serve as a provocateur, and to present some questions and challenges for which my more learned colleagues may be able to provide answers, or at least place them in a logical frame of reference for future study.

In these days of extensive biomedical research, with all its claims and promises, and philosophical and social discussion regarding the desirability and the possibility of prolonging life we should occasionally sort out the realities from the theories that have entered into our thinking. Is it desirable to prolong life beyond a certain predestined point? Is this possible in our present social and hereditary structure? What point in longevity should we strive for? What are the criteria that make this desirable or even acceptable? Should we be concerned primarily with chronological age or biological age? What can we as individuals and as physicians do to prolong an active, satisfying life? Is existence enough? Is the present pattern of

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mandatory retirement adding to or subtracting from the full expression of our lives as we wish them? Above all, how significant is heredity in controlling our longevity as active, productive citizens? These questions have plagued me for years as I have studied and worked with patients and their families. Obviously, the answers will not be the same for all, and we march to different drums in many ways. We cannot hope to answer all these questions at this time, but we can address them.

Vital statistics regarding longevity and the incidence of disease provide helpful leads for social planners and health officials, and are general guidelines for whatever problems they address. However, such figures may have little or no significance in terms of an individual's life. For example, if the average man in the United States lives to age 68, what help is that to an individual who dies at 40 or lives to 100? That the average life expectancy of man in this country is 68 offers no positive assurance that the man under consideration will reach that age or, looking at it differently, that he will be relieved of his physical and other burdens at that point even though he might be willing to shuffle off this mortal coil. It is too rarely appreciated that these figures are derived from averages of groups and mixtures of people with widely varying expectancy and potential for longevity.

Cardiovascular diseases constitute the major cause of death, and over 52% of the population die from diseases of the heart and blood vessels. In 1975 680,000 died in the United States from coronary heart disease alone. Such much-discussed risk factors as tobacco, hyperlipidemia, hypertension, obesity, stress, chronic fatigue, and such diseases as diabetes occur in different degrees, and customs, smoking, eating, stress, and other factors vary between ethnic groups and families. Involvement of these factors vary from zero to high levels.

The implication of many recent studies is that avoiding or controlling these risk factors can prolong lives. To a certain extent this is true, but to what extent? What is the potential longevity of any specific individual if by good fortune and self discipline none of these risk factors are significantly encountered during his entire life?

Experienced and observant physicians know that the possibilities for long life are not equal in all families. For example, I have studied in some detail a family with a record of longevity exceeding the average for each historical period during 14 generations in this country. In the most recent four generations none of the immediate ancestors died under age 85. One
close relative died at 105 after winning a quilting contest at 104. Another
died at 103 and read the newspaper at 101 without glasses. The hereditary
potential of this family can hardly be considered comparable to that of
another family in which the father, mother, and four sons died under age
55, one at 31, from myocardial infarctions—a condition not usually listed
as congenital or hereditary. These families represent extreme examples,
but similar patterns can be found in any sizable population group.

This suggests that it may be useful to consider the possibility that each
individual is born with a hereditary maximum longevity. The corollary
would be that even were he free from any hereditary disease trait he could
expect a life span beyond that designated time. We cannot predict his
potential genetic life span precisely, but if his family history has shown a
consistent pattern such as the examples mentioned above, there is a fair
chance that he will conform to it unless acquired risk factors or accidents
produce early death.

We may take the position, therefore, that elimination of risk factors will
not prolong life beyond hereditary potential, but that inherited or acquired
risk factors during life actually subtract from this maximum potential.
Actuarial figures indicate that smokers live from six to eight years less
than nonsmokers, that this is related to the degree of smoking from 10
cigarettes to three packs a day, and that at least some of this detrimental
effect on longevity can be recovered by those who stop smoking. Corre-
spondingly, individuals with marked obesity, hyperlipidemia from overin-
dulgence in high cholesterol or saturated fat foods, untreated hypertension,
and type A (stressful, driving) personalities have some reduction in their
expected life span. When two or more of these risk factors are present in
the same individual life span, shortening is frequently very marked. Diabe-
etes mellitus, congenital heart malformations, hereditary hyperlipidemia,
hypertension, and many other disease traits may enter the genetic code at
conception or early fetal life, and such individuals are born with a short-
ened potential longevity. The expected decrease in longevity of some can
be favorably contrainfluenced by modern medicine. Congenital heart
surgery is a striking example of this point.

Fifty-five years ago, before insulin was generally available, the average
child under 10 who developed diabetes mellitus lived about two and a half
years. With the advent of insulin this changed dramatically. When the first
diabetic child in Dr. Joslin's clinic survived 10 years he sent out formal
invitations to doctors working in this field to attend a celebration. I
received one of those invitations. Since then, diabetic children have been able to complete their education, get married, and have children. They have lived full and productive lives, but in their 30s and 40s many develop serious vascular disease resulting in partial or total loss of vision, as well as heart, brain, and peripheral vascular problems. Available treatment—whether by diet, insulin, or oral medication—has not been able to prevent this distressing process, and as a result few childhood diabetics reach old age. This problem is compounded because unless they decide to use birth control some of their descendents will face the same problems. Their children in turn now produce more children. Our diabetic population will continue to increase unless controlled. Present diabetic treatment has prolonged some lives, but we have failed to resolve this major problem, and their hereditary longevity potential is still limited. This syndrome is not to be confused with diabetes developing in middle or late life. Many of these patients live the national average life span, although they may develop severe atherosclerosis, small vessel disease, and retinitis at somewhat different rates from the nondiabetic elderly.

Hypertension can be inherited as well as acquired from a variety of processes. It now appears that in many cases carefully monitored antihypertensive treatment can reduce or significantly delay the mortality and morbidity and hence affect the longevity and quality of life of many hypertensive patients. We are entering a new era in the treatment of hypertension which appears to be significantly decreasing morbidity and mortality, especially from strokes. All of the long-term effects of this therapeutic approach are not yet clear.

Control of hereditary high cholesterol, triglyceride (and other lipid) levels is currently more difficult and the long-term effects less well known. However, diet and several types of medication may favorably affect blood lipid levels in some patients. Whether this affects the life span of those patients is not as yet clear.

There are less common hereditary diseases involving the nervous and other systems that lead to early disability and death. Hemophilia is a noted example. The royal families of Spain, Austria, and Russia were plagued with hemophilia. Other inherited hemorrhagic diseases affect hereditary longevity. Some families show an extraordinary tendency for early death from thrombosis. I reported such a family in 1954 (Figure 1). A woman died at 58, having suffered four attacks of phlebitis, coronary thrombosis, and finally thrombosis of the hepatic circulation (Chiari's syndrome) dur-
ing the preceding six years. Her family history revealed that her father died of a myocardial infarction, her mother of phlebitis with pulmonary embolism, and her mother’s brother of phlebitis with pulmonary embolism. Her two brothers died of pulmonary emboli, one following a myocardial infarction. One nephew died at 35 of pulmonary embolism. Her only sister lived free from thromboembolism, but her son had developed phlebitis at 27. He had survived at the time of the report. The patient’s two children were then free from thromboembolism, but the eldest was only 30 years old. Of the affected members, none lived to 60 years. The cause of this thrombosing disease was never clearly established, but it obviously produced a high risk pattern for a reduction in potential longevity.

Unfortunately, or perhaps fortunately, family history does not predict with certainty the fate of each individual involved. Exceptions are born to both long-lived and short-lived families. What we do to ourselves plus catastrophic events of individual, local, national, and international history may override the expectations based on hereditary endowment."

Potential hereditary predictions are not possible in such areas of the third world as sections of Africa, India, northern Brazil, New Guinea, and the
Philippines, where malnutrition, dysentery, and such unconquered diseases as schistosomiasis or Chargas disease are rampant. Under such conditions true potential hereditary longevity cannot be estimated at this time and may rarely if ever be achieved.

In such areas public health measures can profoundly affect the presently anticipated mortality. I recently visited a remote Mayan tribe in the mountains of Mexico. Here the average life span was formerly 40 years because of infant mortality, dysentery, malaria, typhoid, and a wide variety of other diseases found in primitive societies living in filth. There is no possible way to determine what their potential hereditary longevity is. Within five decades their average life span, however, increased to 60 years as a result of simple public health measures involving outhouses, inoculations, and mosquito control. The water supply is still unsafe to use, although the natives have apparently acquired immunity to the pathogenic organisms it contains. Perhaps in a few more generations the major infectious risks will have been removed from their environment and it will be possible to determine what their potential hereditary longevity really is—provided, of course, that our civilization does not introduce too many new confusing risk factors. Even today, it is stated by the National Social Security Institute (1977) that 25% of deaths in Mexico are from accidents, poisoning, or violence.

Certain societies have had a reputation for unusual longevity while
others are reputed to be characterized by short life spans. The validity of the claims for extraordinary longevity in the communities of Ecuador and the Soviet Union's Georgia are now being challenged and it appears that few live longer than 100 to 105 years, although there may be rare exceptions.

As extreme examples of potential longevity, it is instructive to review the comparative history of the two families previously referred to who have lived in our modern western civilization but under different circumstances.

The family with the unusual longevity by our standards presents a life pattern that is of particular interest. They came to a small village, Nieuw Amsterdam, in 1630. Life was then very primitive, and everybody worked. Family members helped to build a wall to protect their community against the Manhattan Indians, which later gave birth to the name Wall Street, the future of which they could not have possibly conceived. As the population increased they migrated into suburbs, small towns, or country areas. They came from Dutch and English stock with a touch, for a little humor, of Irish. They worked steadily as farmers or artisans from dawn to dusk, far beyond the short work schedules now increasingly popular, and well into their 70s and 80s. Retirement at 60 or 65 was considered neither possible nor desirable. Their wives were active farmers' or artisans' wives without servants. Their lives were regulated by the old adage of "early to bed, early to rise...." In recent generations, where the history is known in detail, only one was a confirmed smoker (three cigars a day). He lived to be 88. One member was considered a liberal consumer of John Barleycorn's products, a habit acquired during an active career in the Civil War and continued with steady devotion until his death, also at 88. Of special interest, none in recent generations, since such diagnoses could be accurately established, have had diabetes mellitus, cancer, hypertension, myocardial infarction, or strokes. Lipid studies have not been available until recently. The present generation has a slight tendency to an increased cholesterol level, probably associated with a very liberal diet. The stress they encountered was that common in families in small communities, and therefore minimal in terms of present life. The exceptions were active participation in the Revolutionary War (six members but no deaths), the Civil War, and the Indian wars. They were not constantly exposed to the shocking events of the rest of the world on an hour-by-hour basis. Good and bad news from distant countries took weeks or months to reach them, and by then it was so remote or stale that the impact was quite different

from our present high-tension media impact. They were active until their last year or so, when deterioration presumably caused by generalized atherosclerosis occurred. Most simply went to sleep and never woke up. With the minimum of hereditary, self-induced, or acquired risk factors, they had a good chance to approach their maximum longevity potential, and most apparently did so.

The short-lived family mentioned knew less about their distant past family history, but they came from central Europe where there had been one or more serious wars involving their actual living areas during each generation. The two generations studied had been subjected to the stress of persecutions (some in concentration camps), and dislocation during World War II. They were tense, nervous individuals, most of whom smoked heavily until they began to realize the risk. The third generation became extremely concerned about their own longevity in the light of their heredity. If all risk factors are minimized in this generation their potential longevity may be more clearly determined.

This suggests that a most important and basic factor in determining the maximum potential longevity is hereditary, and that this should be studied in greater depth in all future statistical analyses dealing with longevity.

Is it the immune function that plays a major role in the hereditary package? What other factors are included? If the immunity potential lessens as we age, is this a mechanism similar to the depletion of a long-lived battery cell or the result of the successive insults of the so-called risk factors, added to the accumulated infections and injuries most of us incur? While the winding down of the activity of the immune, endocrine, and neurological systems may parallel or cause the onset of deteriorative changes in the aging process, the question remains why this happens. One possibility is that small vessel disease, a manifestation of atherosclerosis, limits the blood supply to key target organs and gradually reduces their response to the usual stimuli or demands, or, conversely, does malfunction of any or a combination of these systems initiate atherosclerosis with its widespread and finally devastating effects?

Answers to these questions may help us to understand why some families in the same environment live much longer than others. These may be quite different questions than why some racial or geographic groups are believed to live longer than others.

While I have endeavored to emphasize the importance of hereditary longevity by using examples of extremes, most families do not present
Fig. 2. Family with average to long life. Shortened lives due to ruptured appendix (2) and cancer (1). Reproduced by permission from Wright, I. S.: Can your family history tell you anything about your chances for a long life? Exec. Health 14:5, 1978.

Fig. 3. Eight generations with wide variations in fatal diseases and longevity. This is a common pattern in the United States. Reproduced by permission from Wright, I. S.: Can your family history tell you anything about your chances for a long life? Exec. Health 14:5, 1978.
such clear-cut histories. Most of our American population belongs to families with a greater racial mix, and a study of four to five generations reveals a variety of disease patterns which may include infections, cancer, strokes, hypertension, myocardial infarction, diabetes, accidents, and violent death (Figure 2).

In such families it is frequently difficult to establish a definite hereditary pattern. Future genetic studies may establish which of the genes the patient inherited are predominant (Figure 3).

A purely clinical impression, admittedly not established scientifically at this time, suggests that members of successive generations who look alike and act alike (type A or B in terms of stressful reactions) tend to develop similar disease patterns such as high blood pressure, angina, peptic ulcers, and habituation to smoking or alcohol.

I recently reviewed an interesting family history in this regard (Figure 4). The father, a Protestant clergyman, developed angina at age 35, and this continued in quite severe form for about 20 years, requiring the frequent use of nitroglycerin. However, at about 55 the angina ceased,
probably because of the development of collateral circulation. He had been on a low fat diet and lost considerable weight.

He lived an active life and died at 83. He was a tense, obese man who would probably be classified as a type A personality. He had four sons; three looked and acted like him. All died between 40 and 50 years of age from myocardial infarctions. The fourth son, a physician, was structurally and temperamentally like their mother, who lived to be 93, did not develop angina, never had a myocardial infarction, and is in good health at 78.

Recently, there have been attempts to develop a computerized code, which, by programming the risk factors found in an individual’s history or life pattern, may predict the risk of a myocardial infarction, stroke, or death occurring within one, two, or five years. Unless the hereditary longevity potential is included, a most important item will be missing. These calculations may or may not be significant for a specific individual, but by setting a time estimate for a person to have his heart attack and then inform him, we may change his life plan and style. Some individuals may respond with a serious emotional reaction affecting them and their families. For example, they may become depressed, anxious, retire prematurely, and await a catastrophe which may not occur for years. This attempt at prophecy should be undertaken with great caution and careful selection of the patient. Otherwise, for some patients iatrogenic effects may be serious.

Summary

To return to our basic questions: Are we tagged at or before birth with a potential hereditary longevity? How can we achieve it and can we ever hope to exceed it? It appears that the basic biology of aging is more closely correlated to the potential hereditary longevity of individuals and families than to average longevity for groups or communities which are usually influenced by the insults, be they infectious, malignant, or accidental, acquired in the course of life and which are often a matter of chance.

References
