DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE . BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

c/o Robert B. Livingston, M.D.
Clinical Center, Rm. 3N-242

May 22, 1959

Dr. Jonas Salk
University of Pittsburgh
School of Medicine
Pittsburgh, Pennsylvania

Dear Salk:

Enclosed is a copy of a letter which I received from Jim Watson (Harvard) in response to the memo which I sent you earlier.

Sincerely,

Leo Szilard

Enc.

C
O
P
Y

Harvard University
The Biological Laboratories
16 Divinity Avenue
Cambridge 38, Massachusetts

May 19, 1959

Dear Szilard,

I was most pleased to receive your memo regarding Salk and a possible Cancer Institute. I hope very much that something of this sort can be brought off. I think, however, that its chance of success as a scientific institute will be higher if primary attention is directed toward the reproduction of animal viruses and those fields which bear directly on virology (e.g. biosynthesis of RNA, general nucleotide metabolism), rather than paying equal attention to other fields, such as tissue transplantations which while both biologically interesting and very pertinent to cancer, will probably not substantially help our understanding of the fundamental biochemical picture. Furthermore, other cancer institutes are much involved with these problems. On the other hand, it is obvious that we need a strong base in tissue culture.

I leave on this Friday for Paris and Brussels, returning in 3 - 4 weeks. If I can be of help in any direct way, I can fly down to Washington, etc.

/s/ Jim Watson

THE UNIVERSITY OF CHICAGO
CHICAGO 37 · ILLINOIS
THE ENRICO FERMI INSTITUTE
FOR NUCLEAR STUDIES

June 19, 1959

Dr. Jonas Salk
The Medical School
The University of Pittsburgh
Pittsburgh, Pennsylvania

Dear Salk:

I hear from Roger Revelle that he has been in touch with you over the telephone and that you and he might get together in July for a more or less preliminary conversation upon Revelle's return from Europe. I am attending in Austria the same conference as does Revelle but I have planned to loaf around in Europe until such time as I can do something useful back here. My only commitment in Europe, after the Austrian meeting, is a visit to George Klein's Laboratory in Stockholm. If I can be of any use in connection with your negotiations I trust that you will let me know and I may then hop a plane across the Atlantic. In the meantime, if and when this appears to be useful, I trust you will contact Jim Watson at Harvard - without waiting for my return - and have a good heart to heart talk with him.

I forget whether I mentioned to you that I got somewhat interested in the problem of aging. Attached you will find a one page article which appeared in England. While this article is not entirely correct it nevertheless gives an intelligible summary of my paper.

With very best wishes,

Sincerely,

Leo Szilard

LS/b
cc Jim Watson

AMERICAN NEWSLETTER

A theory of how we age

from JOHN LEAR, our American correspondent

AGEING is plainly a matter of arithmetic. We add one year to another until our time expires. Everyone knows this, and insurance salesmen earn a pleasant living by averaging out the figures and cajoling the rest of us into wagering where we as individuals fit into the scheme. But only a very imaginative man would think of systematizing these mathematics into one equation to comprehend the interval between the cradle and the grave. In all of American science, there are few minds creatively abundant enough to put such a thought into action if the idea did strike. One of these rare intellects graces the disarming corpulence of Dr. Leo Szilard, who has used it to work out mankind's first scientific theory of how we grow old.

It seems to me inevitable that this latest of the Hungarian-born theorist's long line of brilliances will in time be recognized as a major contribution to human thought. It appears, however, with almost innocuous modesty in the pages of the January, 1959, *Proceedings of the National Academy of Sciences*. A dry and frugal footnote tells us that the work was done while Dr. Szilard—ordinarily occupied with the affairs of the University of Chicago's Enrico Fermi Institute of Nuclear Studies—was serving as a consultant to the basic research programme of the National Institute of Mental Health at Bethesda, Maryland. The N I M H is, of course, keenly conscious of the relationship between advancing age and mental illness at a time when the population of this country is ageing markedly.

"This paper represents an attempt to describe a hypothetical biological process that could account for the phenomenon of ageing", the introductory sentence says. "Ageing manifests itself in much the same general manner in all mammals, and we are in a position to learn enough about the ageing of mammals to be able to test the validity of a theory that leads to predictions of a quantitative kind—as does the theory here presented."

Dr. Szilard's thinking takes off from the fact that the basic hereditary unit in our makeup, the gene, can be responsible for the synthesis of a specific protein molecule, and that this molecule in many instances has a specific catalytic function in one of the chemical processes of the body. When the gene mutates, the change renders the gene incompetent to bring about the process for which it ordinarily would be responsible. When the bundle of changes inside us grows sufficiently large, we are incapacitated, we are crippled, and ultimately we die.

How do we begin to die? Just where does the mysterious stroke of death originate? The theory assumes not one all-powerful, felling blow but a series of minor hits. The hits occur at random, with a speed that remains constant from the moment we are born. One hit disables one chromosome, to the extent of knocking out one of the working partners of a pair of genes harnessed to a given biological task. The chromosome continues to function, however, until the second partner also suffers a hit.

Each of us possesses altogether about 15,000 genes. The Szilard theory assumes that only 3,000 of these are important to the healthy life of an adult. To distinguish these effective operatives from all the other genes, the 3,000 are dubbed "vegetative" genes and the mutants of these "vegetatives" are called "faults".

If this were the whole story, the variation in the length of our lives would depend entirely on accidents, murders and wars. But this is not the whole story. The whole story begins generations before we are conceived. It is handed down in the genes of our forebears. By the time the chromosomes containing the 3,000 "vegetative" genes reach us, a certain number of hereditary "faults" have already occurred. In terms of age, it is as though we have already been scraped by the edge of Father Time's scythe before we emerge from the womb. Some of us are born relatively old people.

Whatever individual age one of us has at the beginning of his own phase of the eternal process known as life, that age increases progressively with the number of "vegetative" genes that are disabled by the mysterious hits of time against the species. The progression is not entirely steady, for the really "old" newborn die off rapidly in the first year of existence and then at a slower rate to the age of ten years. After that time, inherited "faults" increase the death rate "only in conjunction with the hits of time, and they increase it appreciably only above 40 (years of age)". From then on, the surviving fraction of vital genes "decreases with age at an accelerating rate".

Here Dr. Szilard begins his ageing equation by writing the symbol "f" to represent the surviving fraction of genes. When "f" reaches a certain critical value, symbolized as "f*", "the individual . . . dies . . . within the year".

"Thus, in its crudest form," Dr. Szilard notes, "the theory postulates that the age at death is uniquely determined by the genetic makeup of the individual."

This, however he adds at once, "cannot be strictly true, for, if it were true, identical twins would die within one year of each other". And the fact is that female identical twins die at differing intervals averaging out to three and a half years. So the reasoning has been refined to account for the variance in manifold ways, including the shielding effects of environmental conditions "prevailing at present in the United States, where essentially no adult dies for lack of food or shelter and no adult has a reduced propensity to procreate because of his inability to provide food or shelter for his offspring".

In underpinning his theory mathematically, Dr. Szilard takes a hypothetical, genetically perfect, white female and designates her age of death as the "lifespan of the (human) species". He finds that she, at 50 years of age, would have the same physiological age as today's average woman of 35 years. Her most probable age of death would be 92 years, twelve years greater than the age at which the average woman dies today.

The Szilard equation encompasses other women by postulating a basic time interval of the ageing process and defining this interval as the difference between the life-expectancy of the genetically perfect woman and a woman whose genetic makeup includes one "fault".

Dr. Szilard stipulates that genes "vegetatively" incapacitated by the hits of age are not thus rendered impotent in their power to duplicate themselves in future generations.

Experiments are now under way in mice to provide supporting evidence for the ageing theory, mice being better than hamsters or dogs for the purpose because the number of their chromosome pairs is closer to the number of man's.