

GENERALIA

Present state and future developments of experimental gerontology: A memorial to Fritz Verzár (1886-1979)

Editorial remarks.

After Professor Fritz Verzár died peacefully in his sleep in his 93rd year in March 1979, some of his friends and collaborators in his Institute of Experimental Gerontology in Basel came together to discuss in which way a fitting tribute to this man of great initiative and excellent scientist should be made. Rather than to publish the usual academic obituary, they decided that in view of the wide scope of his contributions to research on aging, several scientists active in the field should be asked to examine what has become of Verzár's ideas of the 1950's in the experimental gerontology of the 1980's. The collection of brief essays we present below are the result. They are framed by the remarks of two of his collaborators who discuss Verzár the man, and the future of the field to which he devoted the last 20 years of his scientific life.

Fritz Verzár's contribution to gerontological research was based on 4 important foundations: 1) his concept of systematic experimental investigation to gerontology: he termed his research 'experimental gerontology' in order to distinguish it from 'clinical' and 'social' gerontology, both of which center on man and his special aging problems; 2) his establishment in the early 1950's of an aging colony of rats which was to become the basis for all his further work; 3) his founding of the Institute of Experimental Gerontology in Basel, not only to benefit his own research (he had retired from the Chair of Physiology in Basel in 1956 at the age of 70) but also to provide an international meeting place for the exchange of ideas and experiences of researchers from all over the world; and finally 4) his establishment of an international journal (*Gerontologia*) devoted exclusively to experimental aging research.

For 20 years, from 1956 to 1976, before he finally decided to retire from research at the age of 90, he and his many collaborators in Basel opened up many new areas for experimental research. His concepts

proved to be extremely fruitful with far-reaching consequences:

- He showed that for organism as a whole and at the organ level, aging is marked by a progressively diminishing capacity for adaptation. This fundamental concept has received evergrowing attention in recent years and is now extended to the cellular and subcellular levels.

- He insisted that the investigation of function was superior to merely descriptive work: for example, changes in substrate concentrations or enzyme activities alone do not tell us much about their influence on cellular aging processes unless they are related to the performance of the cell or organ, particularly if these are under conditions of stress.

- He set early markers for modern gerontological research on central nervous system functions by testing aged animals systematically for their cognitive and learning abilities. His and his wife's (Dr. Jean Verzár-McDougall) experiments on labyrinth-running by rats are still of fundamental significance.

- In the classic reductionist approach, he carried his investigations of the aging phenomena from the organ to the cellular, subcellular and molecular levels.

- His extensive studies on age-related structural changes in the collagen molecule formed the basis for numerous investigations on aging of connective tissues all over the world. They also led him to extrapolate his ideas of structural aging of macromolecules to the nucleic acids, and in particular to DNA. He thus paved the way for a molecular biology of aging at a time when the concept of 'molecular' biology had only just started to emerge, from the concern of a limited circle of specialists, to attract the attention of a wider scientific public.

- While he searched for mechanisms and causes of aging at the subcellular and molecular levels he always attempted to tie his experimental findings to the functional impairment - loss of adaptability - of whole cells and organs, studying in particular intermediary and energy metabolism in skeletal muscle.

- He laid a base for a pharmacology of aging by demonstrating that drug action in aged animals differs widely from that in adults.

Today, thanks in great part to Verzár's efforts, experimental gerontology has come of age as a recog-

nized and active field of research in the life sciences. The reports by leading experts presented here are a tribute to this great scientist's interdisciplinary contributions.

H. M.

Introduction: Fritz Verzár's impulse to experimental gerontology

by Daniela Schlettwein-Gsell

Stiftung für Experimentelle Altersforschung, Felix Platter Spital, CH-4055 Basel (Switzerland)

Words of commemoration alone would never have been able to express the extraordinary productivity which characterized Prof. Fritz Verzár's career and the vitality of the man himself. We are therefore grateful, as assistants associated with Prof. Verzár during his final active years, to Prof. Hans Mislin whose initiative has made this far more meaningful tribute to Verzár possible. The following reviews on the present state of experimental gerontology is in many ways a survey of how the ideas and hopes of Verzár have found substantial form.

When Verzár reached retirement age in 1956 it was said that the last all-around physiologist had left University. Already in the 1930's he had written a book on intestinal absorption which was still quoted by American physiologists in the 1960's; in the 1940's he developed hypotheses on endocrine secretion - the volume was still on sale in 1970; and in the 1950's, during his summer holidays in St. Moritz, he tackled problems of atmospheric condensation nuclei which helped to coordinate the work of meteorologists and physicists from all over the world. Furthermore, in all these years he never lost interest in nutritional surveys; after World War II he joined FAO and WHO committees, and in the 1960's he was asked to report to the Swiss Federal Government on the nutritional status of their mountain populations.

In 1956, no one could have imagined that Verzár was on the threshold of work which would turn him into this last all-around experimental gerontologist. Today, as we leaf through the papers in this review, it is astonishing to realize that a single man should have been able to collect thoughts exploring such different directions, and, more importantly, dare to work experimentally with so many different techniques. And yet, in 1956, the only chance for experimental gerontology lay in its being championed by a single personality, pushing research towards every possible direction, not only in order to obtain the necessary financial support, but also to oppose the constant identification with rejuvenation.

Grants - enabling Verzár to buy, with as much optimism as opportunism, the house in Nonnenweg 7

which then would serve as the first Institute for Experimental Gerontology for nearly 20 years - were given to him because he showed that aging had to be included as the 4th dimension of all physiological and morphological research.

His main laboratory was reserved for the work on collagen, where '... his historical experiments on aging of rat tail tendon opened up a new research area on molecular and cellular mechanisms' (Robert, p. 1055). Very soon thereafter he encouraged experiments on aging of nucleic acids and muscle in the laboratories on the 1st floor. Under the roof, with homemade installations, it was discovered that young and old animals react differently to the same pharmaceutical agent... In the neighboring attic, cell numbers were counted histologically in the brains of 'clever' old rats and in those who had lost their memory. Not satisfied with these activities alone, Verzár wrote to centers all over the world and enquired into possibilities of working immunologically with cell and tissue cultures. Unfortunately, good techniques were scarce in those days. I well remember Verzár's disappointment when at this time a well-known immunologist inadvertently killed several dozen of his precious old rats because of poor methodology.

The rat colony itself which populated the cellar of the house and the *Xenopus laevis* groups that swam in the bathroom presented pioneer material for studies on animal lifespan. It is hard to believe today that in 1956, while survival curves were known for men and mice and a few other common laboratory animals, the curves for most species were based on pure speculation. Verzár had at one time planned to work with guinea-pigs. Stables had already been installed when by pure chance he learned that guinea-pigs live as long as 6 and 8 years. None of his grants would have covered even half such a period of time.

Ubiquitous in those days was the claim that Verzár was working on rejuvenation; it was a rather nasty reproach as Verzár was an old man when he started the Institute. Brown-Séguard and Metchnikoff had confronted the same difficulties without success. Perhaps it was their often-quoted example which made