- 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 recognized 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

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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 historial 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 nucleid 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 inadvertantly 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-Séquard and Metchnikoff had confronted the same difficulties without success. Perhaps it was their often-quoted example which made

the topic of clinical or sociological gerontology a taboo in Verzár's group for many years.
Verzár was convinced that only experimental gerontology would be able to provide realistic solution to the problems of geriatrics or sociogerontology. He considered it possible that age changes in the individual occurred randomly, rendering preventing measures apparently meaningless. But he sincerely hoped that experimental gerontology would help man to age in good health.
His own personality attested how important healthy elderly human beings are for our society (we need only remember the many young people, academic and non-academic, who used to crowd his institute or drop in just for a cheerful chat), and for science. He made us realize that the sense for interrelationships and the capacity to evaluate facts can improve at an age when memory and reaction time have long started to decline.
Verzár would have loved to read this review - happy to sense the evolution of his now accepted ideas, and full of interest for new facts and figures.

Immunology and aging

by N. Fabris

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Among the experimental and theoretical approaches to the study of aging, the immune system has received particular attention during the past ten years in the context of both stochastic theories of aging (random primary events) and of programmed events such as the deterioration of some relevant immune functions 1-4.
If it is generally accepted that with advancing age a progressive deterioration does affect the immune system; the exact target of this deterioration and the mechanisms involved are, however, still a matter of hypothesis. The dearth of knowledge in this area is certainly linked to the complex working pattern of the immune system, which is largely based on cooperation among different cell types, and, within the lymphoid system itself, among different subsets of lymphocytes[5]. The existence, moreover, of a complex network either of self-regulatory mechanisms, possibly mediated by different humoral factors such as lymphokines and interleukins[6], or of homeostatic actions, generated outside the immune system, e.g. in the nervous and in the endocrine system[7,8], has further hindered the attempt to reach a comprehensive picture of the aging of the immune system. Nevertheless a good number of experimental approaches have offered us fundamental information upon which further work may be grounded.

Environmental changes

Considerable experimental evidence has provided support in the past years to the hypothesis that immunological decline with advancing age might be due to changes in the 'internal milieu'[7,9,10]. By employing cell transfer methods, it has been shown that the responsible factors are systemic and likely to be dependent on three orders of age-related environmental changes:

a) *neuro-hormonal balance:* Since the pioneering observations of F. Verzár[11], much information has been accumulated on the fact that with advancing age a number of alterations modify the functional balance of the neuroendocrine system: at the level of hormone and/or neurotransmitter producing organs, substantial modifications in the synthesis or of the release of such humoral factors has been documented[12]. It has also largely been proven[8,10], that the neuroendocrine balance affects the immune efficiency. More direct evidence has recently been provided by the observation that by reconstituting the abnormally low T_4 level in old mice by exogenous administration of L-thyroxine, a significant recovery of different immunological functions can be achieved[13].

b) *'death' hormone appearance:* It has been shown that, at least in rats, hypophysectomy performed in young adults followed by a substitutive hormonal therapy, may prevent the immunological decline[14]. Such a phenomenon has been explained on the assumption that with advancing age the pituitary may begin to synthetize a hormone, at present not yet identified, which, by interfering with the peripheral utilization of thyroid hormones, can cause the age-dependent modifications of the immune capacity.

c) *metabolic conditions:* A consistent increase in the viscosity of the membrane of the lymphocytes has been shown to occur with advancing age[15]. This alteration seems to be strictly linked to the ratio between phospholipids and cholesterol, which is known to increase in such different processes and conditions as normal aging, obesity, adult-onset diabetes, atherosclerosis and in various type of cancer[16]. Further proof of the relevance of these metabolic factors for the age-dependent decline of the immune system comes from the observation that