Deyl et al. point to the probability of such a process[17,18].

The possible post-translational modifications which may occur in the biosynthesis of proteoglycans are less well documented. It appears that the size of the proteoglycan aggregates may change with age and this may be due either to a decrease of hyaluronic acid or possibly to the modification of the proteoglycan core protein itself.

It is hoped that more information will be available in the near future on these important matters.

Conclusion

The brief summary of our present knowledge on the aging of intercellular matrix macromolecules shows the progress which has been made since the original important discovery of Verzár, but it also points out the very considerable gaps which still have to be filled by continued research efforts in this theoretically and practically important area. It is no secret to anyone that most of the disabling and killing diseases of advanced societies concern connective tissues: arteriosclerosis, diabetes, pulmonary obstructive lung diseases, osteoarticular diseases and cancer itself are all age-dependent, so-called aging diseases. The interaction between intercellular matrix and cancer cells plays an important role in the spreading of the tumors. For these other major diseases, the direct involvement of intercellular matrix is well documented. It is therefore hoped that a better grasp of the basic mechanisms involved in these diseases will help us to understand the difference between pathology and aging per se.

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Conclusion: What is the future of experimental gerontology?

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Fritz Verzár's first published articles on aging research were abstracts of three papers presented at the Third International Congress of Gerontology in London, in 1954[1-3]. They concerned adaptation in old age, using as examples compensatory hypertrophy of the kidney and adaptation to low oxygen pressure in the rat. In 1955, his last full year as Professor of Physiology at Basel University, when he was 69, a brief communication in Experientia[4] on 'thermoelastic contraction of skin and nerves' marks the beginning of an astounding period of another 20 years of scientific productivity in an entirely new field, at an age when most of us are or hope to be in retirement. Both of these major topics, loss of adaptation at the physiological and cellular levels, and structural aging of connective tissue, are still central issues of experimental aging research today, as the six reports presented here demonstrate.

Verzár always insisted that only a multi-disciplinary approach would be adequate in attacking the problem of why and how we (and animals, and plants) age. In each of the present reports this point is also evident and insisted upon by the authors. Thus, aging of the immune system (Fabris[5]) cannot be discussed without a detailed understanding of neuroendocrine functions. Neuroendocrinology is also the bridge between the biology of the aging brain and the regulation of cellular genetics (Frolkis[6]). The aging of cells in vitro

in turn cannot be understood or explained without a detailed investigation of their molecular biology and genetics (Macieira-Coelho[7]). The problems of genetics of aging – in particular control of intra- and interspecific variation of lifespan by the genome – lead directly to growth and development, differentiation, mitotic rates, and these lead back to cell culture (Lints[8]). The basis for a rational pharmacology of the diseases of old age is an understanding of cellular metabolism and vascular physiology, of neuropathology, and even of the psychiatry of the age-associated dementias (Meier-Ruge[9]). The most abundant tissue in the vertebrate animal, connective tissue and the intercellular matrix, undergoes major aging changes – and these have their origin in the endocrine system, in genetic factors, and in pathology (Robert[10]).

Each specialized subject of aging research is, clearly, to a large extent dependent on other specialists' results. One comes to realize what an enormously complex problem aging is. Many are those who have tried to find 'the cause' of aging. All have failed. The reports presented here clearly show why. There is no 'cause' of aging. Indeed, on reading the astonshing variety of phenomena that can be discussed under the common heading of 'aging', I come to wonder whether aging is a 'real' biological phenomenon at all – in the sense that embryogenesis, growth and differentiation are. In the gerontological literature we frequently find articles discussing aging and cancer – a most suggestive association. In cancer research, too, development of the past years point to the diversity rather than to the uniformity of what once was considered a phenomenon having a single cause. 'Malignant transformation' and 'aging' both cover so many different phenomena that it appears to be less and less possible to give definitions upon which all those engaged in these fields of research could agree. Wherever we turn to in the six reports presented here, we come upon more questions and fewer answers – as in particular Frolkis[6] vividly demonstrates. We also, for example, find Lints[8] questioning a genetic control of (species-specific) lifespan. He says, in effect, that there is (as yet?) no obvious (genetic) reason why an elephant should live longer than a mayfly. Biochemists will point to specific metabolic rates, to the concept of 'life maximal calorie consumption' and other physiological and functional parameters. But are these explanations, giving cause-and-effect relationships, or rather empirical findings used for inductive reasoning?

What, then, is experimental gerontology about, what are its real aims, what should it investigate? Is it sufficient to simply describe as exhaustively as possible changes in morphological, physiological or biochemical parameters of organisms, organs, or cells of as many animal (and plant) species as possible, in relation to chronological age? This seems hardly satisfactory. Should we continue to search for 'the cause' of aging? More and more, this seems to me to resemble the search for the Philosopher's Stone of the alchemists.

Every day, and more and more, we are confronted with the sociological and medical problems of human aging. Each one of us is sooner or later personally confronted with his or her own aging, and must find a modus vivendi – often a painful giving-up of lifelong habits and a learning of new and not always pleasant facts about one's place in a society so strongly oriented towards the young and active. Surely the challenge of aging research lies here. It is not enough to develop and study animal, experimental models for putative aging mechanisms – much as we need them. In the shorter, foreseeable future our best investement of time, money and effort may be to deal first with the particular, specific problems of man aging in his society. I certainly do not wish to imply that basic, 'pure' research into aging mechanisms in animals or plants is less valuable, but that a concentration of our efforts and of the progressively scarcer resources available today on research on the problems of aging in man – at all levels, biological as well as medical and sociological – appears to me to be the most worthwhile investment. It is in this context also that the Foundation for Experimental Gerontology in Basel, Fritz Verzár's own foundation, small as it may be, can contribute to the resolution of these problems, by continuing to give impulses to those engaged in research, as Verzár gave them so bountifully in his time.

It is frightening to observe the increasing proportions of the impaired elderly in our populations and the increasing numbers of demented patients in our old age homes and geriatrics wards. Here surely lies the challenge to the gerontologist. What is our contribution to solving this world-wide problem? I think that in each of the reports presented here this challenge has been taken up. This is the best memorial we can give Fritz Verzár.

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