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ONE HUNDRED YEARS AND MORE — THE CHANCE FOR LONGEVITY

The United Nations Organization has announced 1999 as the Year of the Senior. Last decades have brought about dramatic changes in the age structure of societies, particularly in developed countries. Humanity is ageing. It is quite predictable, that in 2025 people above 60 years old will represent 15% of the world population. One third of the populations in Italy, Sweden, Germany and Japan will correspond to seniors. This new demographic situation evokes several problems from a social, medical and political point of view. That is why the mechanisms of ageing and longevity require consideration. In particular, the most interesting seems to be the effect of life style and gene interactions in revealing phenotypes that favour a prolonged lifespan. The increase of mean human lifespan brings both advantages and disadvantages, as well. Who would not like to live longer, wealthy and healthy — under this condition the majority of us would accept ageing. However, senescence is commonly noticed as the decline in physical and mental activity including a change for the worse in mobility, sight, hearing and memorising. There is also an increased probability of falling ill of age-associated disorders such as diabetes, cardiovascular disease, cancer, immune disorders and senile dementia. All of these are not very tempting. On the other hand, during the last decades, the progress in medicine and science, as well as changes in our life style have significantly limited the risk of age-associated disorders, thus giving the possibility to prolong the period of satisfactory physical and mental condition. In the near future, we are to face the phenomenon of a constantly growing subpopulation of relatively healthy seniors in human society. With no doubt, this situation will change the way of thinking about the elderly. The elderly will be no more the synonym of physical and mental disorder.

This issue of KOSMOS shows a broad spectrum of problems associated with the ageing and longevity, humans and other species that represent perfect models for scientific research since they show high homology with some aspects of human ageing. Here, one can find articles by gerontologists that know the issue from a medicine cabinet and the articles by scientists who investigate the molecular basis of ageing in their laboratories. The present KOSMOS is an attempt to familiarize one with the current topics in the field showing trends in ageing research all over the world.

An American scientist, Edward Schneider said "If you think that cancer is complicated, look at ageing". Three centuries passed since the first hypothesis of ageing was proposed and now there are hundreds of them. However, none is universal and they only show part of the truth. It is quite often that investigations into the mechanisms of ageing concern studying longevity. The lifespan of people suffering from premature ageing syndromes is shortened. On the other hand, the study of *Saccharomyces cerevisiae*, *Drosophila melanogaster* and mice with caloric restriction show that the phenotype of longevity reflected by an increased of mean lifespan, or even the extension of maximal lifespan, bore delayed ageing. Majority of reviews presented in this issue show data and hypothesis concerning the effect of environment and genetics on ageing process and lifespan. A.MYŚLIWSKI in his article entitled "Process of ageing — course and consequences" calls our attention to the physiological aspect of ageing as a process that renders the disorders to happen, but is not a disorder itself. The study of relatively healthy elderly has supplied some nice data that confirms the hypothesis mentioned above. J. MYŚLIWSKA in her review "Age-related changes of the immune response" claims, that age-

associated alterations of immune responses do not reflect a change for the worse but would rather compensate for the collapse of some other cell activities. A proper immune response is likely to play a pivotal role in healthy ageing. But among age-associated diseases one could not only find immune disorders, but also brain illnesses such as Parkinson (A. FRIEDMAN) or senile dementia i.e. Alzheimer (M. BARCIKOWSKA and M. DESPERAT, T. GABRYELEWICZ). However, physiological ageing of the brain does not cause such dramatic symptoms. Typical for neurodegeneration dying of neurones by apoptosis (B. KAMIŃSKA) or significant collapse in perception and learning (G. NIEWIADOMSKA) do not occur in physiological ageing. Apparently, immune and neuronal disorders are age-associated and could accompany the ageing process but are not ageing symptoms themselves.

J. WITKOWSKI in his article "Genetics of ageing and longevity: can we stop ageing and do we want to?" presents a current knowledge of longevity genes in several models and genes that are suspected to favour human longevity. Both, J. WITKOWSKI and A. MYŚLIWSKI give their attention to the problem of replicative senescence, pointing out a still controversial correlation between ageing *in vitro* and *in vivo*. Replicative senescence defined as the limited capacity of normal somatic cells to divide beyond a finite number of population doublings seems to be well characterized. In the article entitled "Regulation of the cell cycle, ageing and cell death" E. RADZISZEWSKA shows that factors regulating cell cycle are responsible for proliferation arrest and the key switchpoint corresponds to phosphorylation of Rb protein. The inhibition of Rb phosphorylation by cyclin-dependent inhibitors in response to the increased activity of p53 protein is observed in old, non-dividing cells. According to the telomere hypothesis of ageing, it is assumed that shortening of chromosomal termini is involved in signal transduction resulting in alterations of the regulatory proteins. E. JARUGA presents this difficult but fascinating problem in her article entitled "Telomeres in regulation of proliferation and cell ageing".

Until recently, the cause of ageing has given rise to much controversy on the role of genes in the ageing process presumed by evolution theories and the participation of stochastic factors that depend on time and evoke cell component damage quite in a random manner (stochastic theories). It seems that the free radical theory of ageing, first presented by Harman in 1956, supplied numerous data confirming the engagement of genes and their casual damage in the the ageing process. More information about the involvement of reactive oxygen species in cell ageing is found in two articles: "Oxygen and ageing" by G. BARTOSZ and "Nuclear and mitochondrial DNA damage in ageing" by M. JURGOWIAK and R. OLIŃSKI.

What is the prescription for long life and healthy senescence? Which genes are good and which environmental factors are bad? How could we possibly help ourselves to experience long life and successful ageing? Still, we do not know the miraculous youth elixir. Still we are short of scientific data confirming the rejuvenating effect of such hormones as dehydroepiandosteron and melatonin or even a commonly used antioxidant like vitamin E (G. BARTOSZ). However, substitute hormonal therapy for women in the postmenopausal period gives positive results, unless it renders breast tumour that unfortunately is likely to occur in the presence of estrogens (A. MYŚLIWSKI). Yet, long lifespan is the price for the lucky owners as some allele of a major histocompatibilty complex and for apolipoprotein A (J. WITKOWSKI). Epidemiological study within Poland showed a beneficial, reducing effect of education on the rate of ageing, analysed by mortality factor and parameters characterizing the biological condition of the organism (E. ROGUCKA). Mental activity of the elderly is one of the factors that delay the symptoms of senile dementia (T. GABRYELEWICZ). Some answers for the question, what should be done to live longer and relatively healthy, one can find by investigating people that are above one hundred years old, namely centenarians. The article of E. SIKORA "Centenarians" is an invitation to participate in the Polish Centenarians project concerning a broad spectrum of scientific research including sociological, anthropological, medical and biological approach to centenarians ageing and longevity.

Reviews on ageing are published quite often, since they call our attention. The present issue of KOSMOS gathers already articles describing different points of view, thus giving an enriched look into the problem that will concern all of us. In spite of the fact that many scientists in Poland consider the ageing process as an extraordinary and interesting problem, only few of them are engaged in research on it. We hope, that young people dreaming about a career as a physician or scientist will be encouraged to set about solving the problems of ageing and longevity that probably now seem for them quite exotic and unreal.

I greatly acknowledge the KOSMOS Editors for favouring the initiative to publish this issue. I would also like to thank the authors of this

monograph for the effort that made this initiative possible. I hope that the Readers will find this monograph very useful as it presents good, comprehensive reviews enriched in the personal opinion of the authors. I would like to apologize to all those working in the field and were not invited to participate in this monograph, but my intention was to avoid topics that had already been published in KOSMOS. I do hope that this monograph will be kindly accepted by all KOSMOS Readers.

Ewa Sikora