Herald of the Russian Academy of Sciences, Vol. 66, No. 3, 1996, pp. 214–217.
Translated from Vestnik Rossiiskoi Akademii Nauk, Vol. 66, No. 5, 1996, pp. 507–511.

From a Researcher's Notebook

During the last century, humanity has made marked achievements in its eternal struggle against premature death. Although the average lifespan has increased, the number of really longevous people has not increased. However, the period during which people suffer from disorders associated with old age and become dependent on others has increased. Is there a way out of this situation? We believe there is.

Good Health Is Self-Sufficiency

V. N. Anisimov and V. N. Krut'ko*

In the 20th century, science has enriched humanity with a number of discoveries, each of which has worked a qualitative change in civilization. Just like many other formerly unfamiliar terms, the "computer," the "atom," the "sputnik," and the "gene" are associated, on the one hand, with fundamentally new possibilities for accelerated progress and, on the other, with a whole range of extremely difficult social–economic and research problems. Gerontology and lifespan biology have also been developed this century. However, the public at large knows very little about the range and nature of questions that form the subject matter of these young disciplines. Our purpose is to make up for this deficiency.

TRIUMPH AND CRISIS OF THE PUBLIC HEALTH SERVICE

A population's health standard is an important indicator of the quality of life. Many experts maintain that it is the cardinal criterion. At the same time, the main indicator of a nation's health is the healthy, "disease-free" lifespan. For instance, the chief aim of the United State's national health promotion and disease prevention program, which ends in 2000, is a 78-year life expectancy and 65-year healthy lifespan indicator [1]. The World Health Organization's (WHO) European Regional Bureau states that, by the year 2000, the life expectancy indicator in Europe will be at least 75 years [2].

The achievements of medical science and public health services in the 20th century have nearly doubled the lifespan (Fig. 1). This accomplishment is largely due to processes defined as two epidemiological revolutions (ERs) [3].

The first ER, which began in the late 1890s and ended in the 1950s, considerably lowered the mortality caused by contagious diseases. This was made possible by mass vaccination programs and the invention of antibiotics. The second ER occurred in the 1960s–1980s. It enabled economically developed countries to lower mortality from noncontagious chronic diseases, such as cardiovascular disorders and cancer. However, the effect was not as impressive as in the first case. K. Kuper points out that, in the United States in the period from 1968 to 1977, deaths from cardiovascular diseases dropped 23 percent, including 36 percent from insult and 48 percent from hypertension [4].

However, during the same period, the lifespan showed an increase of only 2.7 years. Whereas humanity used to mainly suffer from plague, cholera, and smallpox and later from tuberculosis, diphtheria, influenza, and croupous pneumonia, the character of diseases today has radically changed. In developed countries, 85 out of 100 deaths are due to cardiovascular diseases, cancer, diabetis mellitus, mental disorders, and obesity. As the lifespan becomes longer, the number of years people suffer from poor health and complete or partial dependence on others increases.

The possibilities for prolonging life with the help of the aforementioned means have been practically exhausted. Therefore, the WHO has announced a new

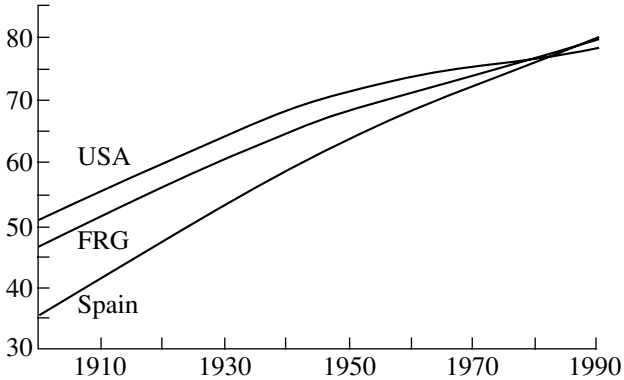

Fig. 1. Dynamics of the number of years of life expected at birth in developed countries in the 20th century: abscissa—calendar years; ordinate—life expectancy.

* Anisimov, V.N., Doctor of Medicine, Professor, Laboratory Head, at the Petrov Scientific Research Institute of Oncology, Ministry of Public Health and Medical Industries of the Russian Federation; Krut'ko, V.N., Doctor of Technology, Professor, Laboratory Head at the Institute of Systems Analysis, Russian Academy of Sciences (RAS).

strategy. Formulated in the Ottawa Charter for Promotion of Health, it is regarded as the third epidemiological revolution [5]. In the drive for health, the emphasis is now on devising and observing self-preserving behavioral patterns oriented toward active longevity. It is the duty of the state to execute a whole range of social–economic measures that would improve the quality of life.

Though this strategy is costly and laborious, it does not promise a sizable increase in the healthy lifespan. Therefore, it would be fair to mention stagnation in the improvement of people's physical condition. The traditional approaches in public health practices, which are based on the "human ecology" paradigm, i.e., on studies of people's relations with their social and natural environment, are hardly effective. Most specialists maintain that medicine and public health services are gripped with a crisis both in separate countries and throughout world. This tendency is illustrated by the fact that the curves reflecting changes in lifespan (Fig. 1) have approached a limit.

What are the causes behind this crisis?

As a natural–social phenomenon, mortality may be represented in the form of a sum of two components: first, environmental factors in a broad sense and, second, evolutionally conditioned biological mechanisms governing the organism's vital activity [6]. The 20th century has witnessed a change in the relationship between these components. In the past, each of them played a big role in determining the mortality rate of a population. However, today, developed countries have managed to practically remove the effect of environmental factors (Fig. 2). Does this affect the lifespan? And if so, how?

Figure 3 clearly shows that the shape of the "living-out" curve (i.e., the curve reflecting the late period of life) approaches that of a right angle. This means that, though the average lifespan has noticeably increased, the maximum length of life remains practically unchanged. However, our calculations show that even in an ideal environment, which is free from harmful agents, the living-out curve will never acquire this shape because the population is genetically heterogenous. It follows that it is impossible to prolong the average lifespan today, unless its maximum indicator increases. This means that the only way to extend an individual's lifespan is to influence the fundamental processes in the organism that determine the length of life of the given species.

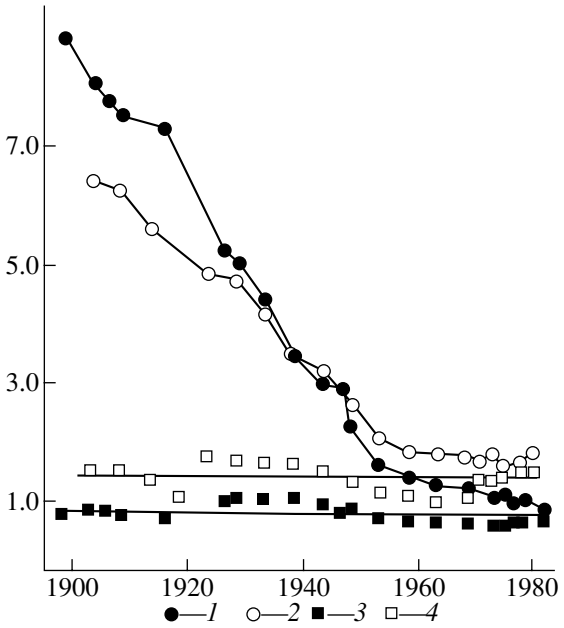

Fig. 2. Dynamics of female mortality in Norway and Denmark at the age of 40 in the 20th century. [6]: (*1*) general female mortality in Norway; (*2*) general female mortality in Denmark; (*3*) age (biological) component of female mortality in Norway; (*4*) age (biological) component of female mortality in Denmark. Abscissa—calendar years; ordinate—mortality rate (per thousand persons).

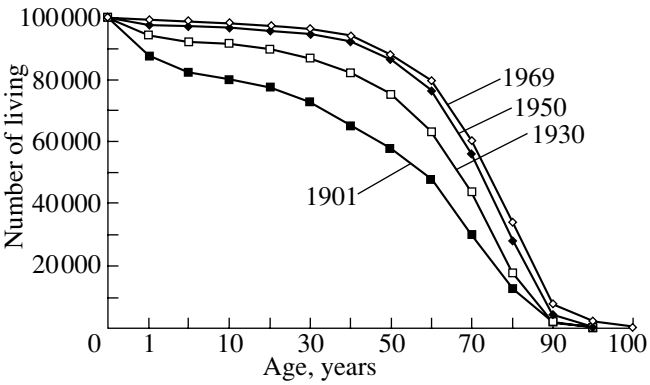

Fig. 3. Dynamics of the living-out curve in the United States from 1901 to 1969.

SOCIAL–ECONOMIC ASPECT OF AN AGING POPULATION

Rapid aging of the population is the direct outcome of increased life expectancy, on the one hand, and a declining birth rate, on the other. In 1975, people 65 and over accounted for 5.3% of the world's population. Specialists say that their share will increase to 6–8% by 2000. In developed countries, people of this age group make up 10–17% of the total population and, by the 2020s, this indicator will double [7]. The bigger towns and cities are gradually developing into "pensioners' homes." This tendency is increasing the "demographic load" on society and its economy (this is manifest in the ratio of the nonworking to the working population). Aging of the population causes changes in the structure of employment, social services, and budgetary resources to assure their timely adjustment to the new conditions. Thus, compared to 1960, federal appropriations in the United States in 1991 for aid to the elderly doubled. Today, these outlays account for one quarter

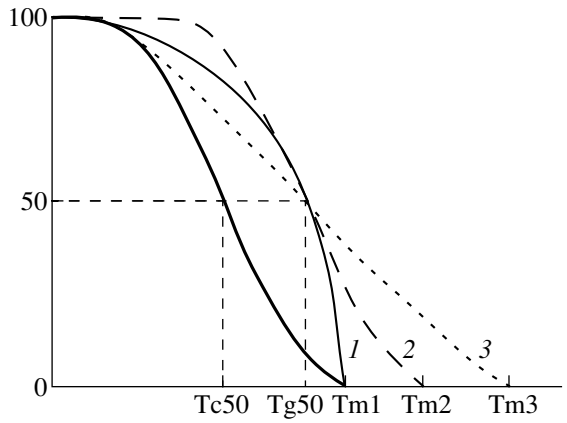

Fig. 4. Types of aging retardation as a result of the use of various geroprotectors [8]: thick line—control specimen; thin lines *1*, *2*, and *3*—employment of geroprotectors: Tc50, Tg50—average lifespan correspondingly of control specimen and of specimens employing geroprotectors; Tm—maximum lifespan. Ordinate—number of surviving animals (%); abscissa—age.

of the federal budget. About 80% of the sum is spent on social security and Medicaid programs for the elderly.

Elderly people fall ill more frequently and remain sick for longer periods of time. Therefore, they consume more medical funds than other groups of the population. As the proportion of elderly people grows, society has to increase its expenditures for the research and development of new medicines and methods of treating diseases caused by old age, such as cancer, cardiovascular disorders, diabetes, and osteoporosis. Thus, 30% of the outlays for the medicare program are spent on a person's final year of life. This gives insight into the so-called "medical armaments race" observed in developed countries. This is characterized by skyrocketing costs of sophisticated medical equipment and medicines and, hence, by mounting outlays for public health in general. At the same time, the medical aid provided to many other sections of the population, children of poor families in particular, is inadequate or totally lacking. US President Bill Clinton regards this unfair practice as a really serious problem that should be resolved without delay.

Such is the economic scope of the problem examined in this work.

In the context of the drastic decline of the birth rate and the economic crisis in Russia, the consequences of aging of the population are even more deplorable, if not disastrous. In pursuit of the State Scientific–Technological Program "Global Environmental and Climatic Changes", the RAS Institute of Systems Analysis conducted a study that showed that, by 2015, the demographic load factor in Russia would be 0.9, i.e., each working individual will have to support one disabled person. At least one out of every two disabled people will be an elderly person who will require more means for life support. The country's already weak economy may collapse altogether. The All-Russia Conference of Gerontologists and Geriatrists held at St. Petersburg in 1994 and the International Seminar on Health Policies for Elderly People in Russia held in Moscow in 1995 discussed urgent measures that should help cope with such a situation.

ON THE THRESHOLD OF THE FOURTH EPIDEMIOLOGICAL REVOLUTION

Thus, traditional solutions to the problem of extending the period of health and fitness (for work) during the lifespan have been exhausted. Research into basic biological mechanisms that determine the lifespan opens new possibilities here. This is traditionally the subject matter of gerontology and, today, also of lifespan biology, a new discipline of a more general character. Achievements in gene and bioengineering may play an important role in this field. This also applies to informatics that is a powerful "catalyst" in mental processes. It helps model and forecast changes caused by various factors in an organism and its life expectancy.

Science has acquired knowledge of a whole range of physical and chemical factors of this kind [8–12]. They are characterized by different mechanisms of action and by varying effectiveness, i.e., the capacity for extending the lifespan (this indicator ranges from 10 to 50% (Fig. 4)). It has been convincingly proven that some of these agents are beneficial for patients. The time is not yet right for using other agents. Before they can be recommended, it is necessary to conduct experiments on animals and clinical studies.

Our analysis shows that the use of such agents (now known as geroprotectors) in the immediate future will make it possible to increase the lifespan by an average of 15 years. This will enable Russia to prevent the demographic load factor from exceeding 0.7 and, in turn, help limit the scope of social–economic restructuring measures that would have otherwise been forced on society by the aging population. An individual approach to every case is even more effective. This is manifest in the application of a whole range of agents to improve the functioning of various levels and systems of the organism. This approach may increase the lifespan by 40–50 years.

However, it is important to know how an individual will live these "additional" years. Another significant point is that employment of geroprotectors "disproportionately" increases the period of active life and youth, though the old-age "phase" remains the same (Fig. 4, curve *2*,). It follows that the purpose is to improve the quality of life in general.

Aging inhibitors (retardants) may produce even more impressive results (Fig. 4, curve *3*). Today, humanity is in a situation where the increase in the average lifespan is not accompanied by positive dynamics of its maximum length (compare Fig. 3 with curve *1* in Fig. 4). In this case, in both animals and peo-

ple, the indicators of old-age disorders, cardiovascular diseases, and cancer, above all, show an increase [11].

Therefore, it would be fair to say that research for considerable extension of an individual's healthy and active life through gerontological research will effectively help solve public health problems. This line requires a fundamental review of public health service policies, methods, and results. This may be regarded as the fourth epidemiological revolution.

The latest achievements in informatics will "catalyze" this revolution. Informatics will present, in quantitative terms, the health-forming process. It will enable the public health service to switch over from a "passive" health protection policy to constructive "health development" practices, to abandon the motto "this is conducive to health," and to adopt the maxim "this promotes health and assures so many 'extra' years of active life." Informatics help optimize the distribution of resources (on the basis of the maximum number of extra years of active life per input unit) and calculate the results of health-promotion measures in terms of lifespan, with respect to both the individual and the population [13]. This approach is being practiced more and more. For example, the World Bank has calculated that, in developing countries, an additional year of life "costs" five dollars per individual if this money is invested in measles vaccination, and $35 if it is invested in antibiotics for the population.

We have tried to draw the attention of the scientific community to this outstanding problem. To solve it, it will be necessary to accomplish a wide range of narrow professional and interdisciplinary tasks, including

research in gerontology and lifespan biology;

development of geroprotector agents, production processes, and methods for the practical employment thereof;

conducting clinical tests (studies) of new agents and methods for prolonging life;

development of models and algorithms for appraising and forecasting changes in the organism's functional reserves, its biological age, and life expectancy under the impact of a whole range of factors increasing or decreasing the lifespan (of individuals or populations); and

analysis of demographic, social, and economic consequences following from one scenario or another designed to increase the lifespan at the population level.

To accomplish the tasks above, the government should launch a National Complex Special Purpose Program for Prolonging the Lifespan.

REFERENCES

1. Mason, J.O., and McGinnis, J.M., Healthy People 2000: An Overview of the National Health Promotion and Disease Prevention Objectives, *Public Health Rep*., 1990, vol. 105, no. 5.
2. *Zadachi po dostizheniyu zdorov'ya dlya vsekh: Politika zdravookhraneniya dlya Evropy* (Health for All Objectives: Public Health Policy for Europe), Copenhagen: WHO, European Regional Bureau, 1993.
3. Krichagin, V.I., Three Epidemiological Revolutions of the 20th Century, *Zdorov'e i prodolzhitel'nost' zhizni*, Moscow: ISEPN RAN, 1993, issue 7.
4. Kuper K. *Aerobika dlya khoroshego nastroeniya* (Aerobics for High Spirits), Moscow: Fizkul'tura i Sport, 1987.
5. World Health Organization Ottawa Charter for Health Protection, *Can. J. Public Health*, 1986, vol. 77, no. 6.
6. Gavrilov, L.A., Gavrilova, N.S., *Biologiya prodolzhitel'nosti zhizni* (Lifespan Biology), Moscow: Nauka, 1991.
7. Anisimov, V.N., Birnbaum, L.S., Butenko, G., *et al*. Principles for Evaluating Chemical Effect on the Aged Population, *Environmental Health Criteria 144*, Geneva: WHO, 1993.
8. Obukhova, L.A., Emanuel, N.M., Types of Experimental Delay in Aging Patterns, *Exp. Gerontol*., 1978, vol. 13.
9. Frol'kis, V.V., Muradyan Kh.K., *Eksperimental'nye puti prodleniya zhizni* (Experimental Ways for the Prolongation of Life), Leningrad: Nauka, 1988.
10. Weindruch, R., and Walford, R.L., *The Retardation of Aging and Disease by Dietary Restriction*, Springfield: Thomas, 1988.
11. Anisimov, V.N., Effects of Factors Prolonging Lifespan on Carcinogenesis, *Ann. N. Y. Acad. Sci*., 1991, vol. 621.
12. Pharmacology of Aging Processes: Methods of Assessment and Potential Interventions, *Ann. N. Y. Acad. Sci*., 1994, vol. 717.
13. Krut'ko, V.N., Mamai, A.V., and Slavin, M.B., Classification, Analysis, and Application of Biological Age Indicators for Life Expectancy Forecasting, *Fiziol. Chel.*, 1995, no. 6.