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State of the art

Comments on the history of medical–biological studies of aging, the birth of scientific gerontology



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ARTICLE INFO

Article history:

Received 13 July 2016

Accepted 19 August 2016

Available online 3 November 2016

Keywords:

Metchnikoff

Aging

Gerontology

Longevity

Age-related diseases

Obesity

ABSTRACT

Recent books (*Immunity. How Elie Metchnikoff changed the course of modern medicine* and *Expectations of Life*) reviewed the important contribution of Metchnikoff to the emergence of gerontology as a new branch of biomedical sciences. Here, we insist on Metchnikoff's contribution and pivotal role in the emergence of nutrition as a science and its importance for health and longevity. The discovery of phagocytosis by Metchnikoff and of its evolutionary ancestry are at the origin of the emergence of cellular immunity as an independent science besides humoral immunity. The longevity of Metchnikoff (71 years) at a time when average life expectancy of men did hardly pass 50 years certainly contributed to the acceptance of his teachings. The recent increase of the senior population in most advanced countries is a good opportunity to review the contributions of nutrition to longevity.

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1. Introduction

Most physicians and scientists in these early years of the 21th century do not question the interest of the medico-biological study of aging. Interest in old people, especially centenarians, was popularized in France by an initiative of the IPSEN Foundation to undertake a scientific study of French centenarians [1]. This original enterprise was motivated by the popularization of the oldest French citizen, Mrs Jeanne Calment, who reached over 122 years [2]. There was however in France an internationally famous scientist, Elie Metchnikoff, who worked during most of his scientific career at the Pasteur Institute in Paris and was the object of a recent biography [3]. His original contribution to nutrition to combat aging was to popularize yoghurt, more precisely Bulgarian sour milk as an “anti-aging” nutriment. The recent book on Metchnikoff [3] contains some omissions and misinterpretations of his lectures and writings, which have to be corrected in order to keep an exact record of his important contributions.

2. Some remarks on Metchnikoff's formation and research activity

As reported in his above-cited biography, Metchnikoff did not study medicine, but natural sciences, resembling in this respect

Pasteur's CV who studied chemistry and switched progressively to (immune-) pathology [4]. Pasteur himself received Metchnikoff in his recently built Institute where he (Metchnikoff) accomplished most if not all his remarkable experiments and publications. In retrospect, his most important contribution was phagocytosis, the recognition of its importance for the defence of the organism against microbes, called later cellular immunology which became with humoral immunology an important part of medical sciences. These two branches of immunology, humoral and cellular developed separately as exemplified by the life saving activity of Behring and others who prepared vaccines against several deadly infectious diseases used up to the discovery of antibiotics during the mid-XXth century. But cellular immunity, based on specialized white blood cells, monocytes and macrophages essentially continued to develop as an independent research activity as exemplified by the important contributions of several internationally well-known scientists as Sir McFarlane Burnett, an Australian scientist, author of a voluminous book on cellular immunology [5]. In this respect, we have to insist on an important and original aspect of Metchnikoff's work on the comparative evolutionary aspects of phagocytosis, the basic mechanism of cellular immunology. He demonstrated phagocytosis in unicellular eukaryotes as *Daphnia*, revealing thereby an important fact: the phylogenetic anteriority of cellular “immunity” (phagocytosis) as compared to humoral immunity, which appeared only with the vertebrates. His original formation as a “naturalist” might have played here an important role. It is remarkable in this respect that Metchnikoff recognized the importance of this cellular

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immune-function in the most frequent form of tissue injury, inflammation, object of one of Metchnikoff's monographies [6]. In this series of lectures delivered in 1891 at the Pasteur Institute and published in a volume entitled "Leçons sur la pathologie comparée de l'inflammation" by the well-known Publisher Masson in Paris translated in English [7], Metchnikoff declares in the preface to depart completely from the usual discussion on the "etiology of suppuration" to establish instead a link between pathology and biology of inflammatory processes by starting from the comparative pathology of inflammation, going "down" to invertebrate models. In his last lecture (n° 12), Metchnikoff states "...as shown by the evolution of inflammation, this is the most general means of protection in the animal world and also the most 'active', recognizing thereby the protecting role of the inflammatory process".

3. Studies on aging

The best known and widely popularized activity of Metchnikoff concerned aging and the role of nutrition. His insistence on the role of yoghurt enjoyed an extraordinary worldwide publicity. To some extent, this appears justified a posteriori first by the longevity of Metchnikoff himself (1845–1916, ~ 71 years) at a time when average life expectancy of men hardly passed fifty years. Later, studies on *Lactobacillus* and studies on the importance of the intestinal bacterial flora for human health and resistance to infections confirmed Metchnikoff's work and ideas [8]. Human average life expectancy in the early years of the XXth century passed only slowly over 50 years [9]. Therefore, the longevity of Metchnikoff in those times could well appear as a proof of the efficacy of his yoghurt-doctrine. His work, lectures and books are considered as a strong contribution to the creation of a new branch of medico-biological sciences, gerontology [10], which flourishes nowadays, partly because of the rapid increase of the number of "seniors". This is best reflected by the statistics on centenarians and supercentenarians [11].

4. Longevity, its increase and mechanisms

Longevity increased progressively with time, faster in countries with advanced hygiene and medical progress (Fig. 1). Precise data can be obtained in France from Ined (*Institut national d'études démographiques*). In a recent polemic article published in Figaro, the popular French daily newspaper, Luc Ferry, a well known

Table 1

Increase in average life expectancy in France (average for men and women) from the mid-18th century to present.

| Date | Average life expectancy for men and women (years) | % increase since 1750 |
|------|---|-----------------------|
| 1750 | 23 | – |
| 1850 | 35 | +52 |
| 1900 | 45 | +95 |
| 1950 | 63 | +200 |
| 2016 | 82 | +256 |

Modified from data, communicated by Ined [22].

philosopher, answering pessimistic critiques, proposed the following figures for the increase of longevity in France since the third Republic taken from recent literature, as shown on Table 1 [12]. It can be seen that longevity increased progressively to reach this year an increase of +256% as compared to the 1750-value. This increase is essentially the result of progress in hygiene, public health and even more of rapid advances in medicine, biology, biochemistry [11]. It is interesting to notice the sex-differences. Women have a higher average longevity as compared to men, centenarians are mostly women and supercentenarians (110 years and above) nearly only women. [11]. As the male-female difference is mostly due to genetic mechanisms, females have two X-chromosomes, males one X and one much smaller Y chromosome. Developmental, hormonal and other less well explored mechanisms as immunological as well as the use and contribution of the left – hemisphere of the brain by women more than men may well play a role in this important difference in male-female longevity. The precise genetic mechanisms of this sex-difference deserve to be further explored.

5. Back to nutrition, the obesity epidemics

One of the most important biomedical changes in advanced countries, during the last decades is the rapid increase of obesity. Some of its effects on longevity were well documented as for instance the increased risk of cardiovascular pathologies and also of malignant tumors (Fig. 2). Overeating is not only widespread in affluent societies. Unhealthy diet based on cheap and easily available food concerns the poor also. One example is bacon, mostly from pigs, rich in saturated fatty acids and relatively cheap, its consumption is widespread in middle-European countries. The

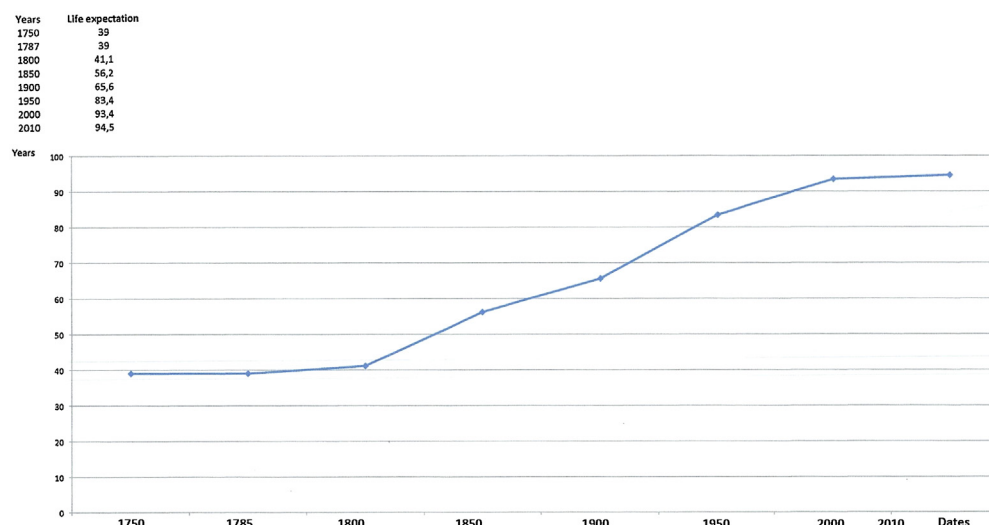


Fig. 1. Increase of life expectancy with medical progress – Jenner's vaccination against small-pox (XVIIIth century), Pasteur's vaccinations (from the XIXth century on), efficient treatment of cardiovascular diseases after the second world war [22].

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