

Handbook of the Biology of Aging (Seventh Edition)

# 衰老生物学手册

(原著第七版)

Edward J. Masoro and Steven N. Austad



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Edited by Edward J. Masoro and Steven N. Austad

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定价:148.00 元 (如有印装质量问题,我社负责调换) 随着医学的发展和社会的进步,人类的寿命越来越长,目前导致老年人死亡的主要因素如心血管疾病等都有了较为有效的治疗手段,因此老年人的死亡率大幅度降低,总的结果是老年人所占人口比例越来越高。根据国际公认标准,一个国家或地区 65 岁及以上人口占总人口的 7%以上,60 岁及以上人口占总人口的 10%以上,就属于老年型国家或地区。按照我国 2000 年 11 月底第五次全国人口普查,65 岁以上老年人口已达8811 万人,占总人口 6.96%,60 岁以上人口达 1.3 亿人,占总人口 10.2%,此时我国就已经进入老年社会。2010 年第六次全国人口普查数据显示,我国 60 岁及以上老年人口已达 1.7765 亿,占总人口的比重达 13.26%,65 岁及以上老年人口已达 1.1883 亿。而且我国老年人口还在以每年八九百万的绝对数量递增。照此计算,2015 年,我国 60 岁以上老年人口将达到 2.16 亿,约占总人口的 16.7%;80 岁以上的高龄老人将达到2400 万,约占老年人口的 11.1%。这些数字表明中国已开始快速进入了老年型社会。发达国家老龄化进程长达几十年至 100 多年,如法国用了 115 年,瑞士用了 85 年,英国用了 80 年,美国用了 60 年,而我国从 1981~1999 年只用了 18 年就进入了老龄化社会,而且老龄化的速度还在加快。

虽然说老龄化已成为21世纪不可逆转的世界性趋势,但随着年龄的增长,老年人的生活质量并没有得到相应的改善,一些疾病仍然困扰着老年人。以老年痴呆症为例,有数据显示,65岁以上人群的发病率为4.8%,85岁以上人群的发病率即增加到8%。目前我国患老年痴呆症的失智人口已高达600多万人,而每年还有大约30万老年人加入其中。因此改善老年人的健康状况,提高老年人生活质量就成了当前社会广泛关注的重要问题。当前我国从事衰老研究的人员队伍在不断壮大,但相应的指导书籍出版却相应滞后,特别是能反映衰老研究领域最新进展的书籍明显缺乏。因此,《衰老生物学手册》通过版本的不断更新,在很大程度上弥补了这一缺憾。

本书《衰老生物学手册》(Handbook of the Biology of Aging, 7<sup>th</sup> Edition)是《衰老手册》(The Handbooks of Aging)丛书中的一本,其他两本是《衰老心理学手册》(Handbook of the Psychology of Aging, 7<sup>th</sup> Edition)和《衰老和社会科学手册》(Handbook of Aging and the Social Sciences, 7<sup>th</sup> Edition)。本系列丛书从生物学、心理学和社会学角度对从事相关领域研究的学者、医生和学生进行指导,也适用于其他研究人员。从生物学上讲,衰老是生物随着时间的推移,自发的必然过程,它是结构和机能衰退、适应性和抵抗力减退的一个综合表现。因此《衰老生物学手册》这本书对于较为系统地了解衰老过程中的生物学特点和分子机制就显得十分重要。《衰老生物学手册》内容包括了基础与临床两大部分。其中基础部分详细介绍了衰老过程中一些组织器官发生的生物学改变,这些组织包括肌肉、脂肪等,以及干细胞和白细胞的改变及其机制。这部分内容不仅涉及最新研究进展,如细胞凋亡相关进展、自由基在衰老中的作用、衰老过程中的信号转导机制,以及一些环境因素和炎症等对衰老的影响等,还详细阐述了一些传统的衰老理论,如饮食摄人限制对延缓衰老的影响,并介绍相应的分子机制。《衰老生物学手册》的第二部分从临床角度出发,主要介绍了衰老过程中神经系统、心血管系

统、内分泌系统和呼吸系统的病理学改变。这些内容有从人类研究观察的结果,也有从 其他生物获得的数据。书中在第十八章和第二十三章还特别介绍了寿命为什么在性别之 间存在差别。

这本书是本系列丛书的第七版,其特点有两个,第一是既传承以前几版的主要内 容,但又不断加入新的论题、新的进展,并增加新的作者。这样可以使读者从新版中不 断获取最新信息,也可以了解衰老研究中涌现出的新的突出人物及其研究领域工作。要 彻底阐明衰老的机制. 就必然需要以分子生物学技术为手段进行研究, 特别是需要研究 导致衰老过程的信号转导机制。本书在第四章介绍了细胞凋亡的基本信号机制,在第九 章详细地介绍了衰老相关的 TOR 信号途径,在第十一章详细地介绍了长寿蛋白(Sirtuins, NAD 依赖的去乙酰化酶类) 在衰老中的分子机制, 在第十七章又简述了胰岛素 信号途径等。在这里值得说明的是,体内与衰老过程相关的信号网络是如此复杂,远不 是几个个别途径就能解释清楚的。我国科学家在衰老机制研究领域、特别是分子机制方 面也取得了许多令人瞩目的成绩,有兴趣的读者可关注北京大学衰老研究所童坦君院士 团队在该领域的工作。第二个特点是基础与临床的相互融合。在读了本书后就会发现, 虽然书中内容人为安排为基础与临床两大部分,实际上各个具体章节中都有基础与临床 的高度结合,其内容融贯全书。如在基础内容第一章中就讲述了饮食限制对寿命延长的 遗传网络。在临床内容中第十章、第十四章和第二十一章等中也介绍热卡限制与寿命的 关系,内容既有重复又有各自特点。在基础篇的第十一章详细介绍长寿蛋白的基础知识 与临床意义。在第十二章也介绍炎症与衰老、动脉硬化和阿兹海默症等相关内容。

本书不同于我们一般理解的实用手册,与其说本书是一本手册,不如说是一些综述的汇集。虽然说由于参加编写人员研究领域的限制,本书不可能十分全面地详述整个衰老机制的进展,但我们仍然可以从本书中获取大量衰老基础与临床的基本信息和相关进展。所以本书对于从事衰老相关领域研究的科研人员仍然具有指导作用,是一本值得参考的好书。

李 刚 北京大学医学部生物化学与分子生物学系 2011.9 20 世纪的科技进步在世界范围内重塑了工业化国家的生活。生活条件的改善使婴儿和儿童的死亡率大大降低,导致成年人死亡的主要疾病如心脏病、肿瘤在预防和治疗的医学成就也进一步延长了老年人的寿命。其结果是使得在一百年的过程中,发达国家的平均寿命几乎延长一倍。人类有史以来第一次把老年当做是生命历程中的一个基本阶段。不仅仅是个人平均寿命延长,而且寿命延长的同时生育率急剧下降,其结果是人口也开始老化。发达国家的人口结构正迅速达到六十岁以上人口多于十五岁以下人口这样一种状态,因此老年人口的状况直接制约着整个社会的运作。

虽然寿命延长近乎加倍是一个重大的成就,但就我们在减轻晚年生活的无助状况方面却没有相应的进展。对于很老的人群,也没有像对青年人的需求一样,去为他们创造一个他们的世界,这样的社会进步也显得十分不足。为了开发生命延长的巨大潜力,科学家必须更加充分地去了解人的衰老过程,以及那些有助于延长寿命的社会、心理及生物学因素。随着在长寿和年龄相关疾病易感性的遗传因素研究领域所取得的重要进展,认知那些可以调节、甚至取代遗传倾向疾病的环境因素显得至关重要。这一系列丛书全面地介绍了促使人类衰老的各种相互作用的因素。

《衰老手册》系列丛书分为独立的三卷,即《衰老生物学手册》、《衰老心理学手册》和《衰老和社会科学手册》。该丛书现在已经是第七版,丛书详细地介绍了了解个体和社会相关衰老问题的基本原理。由于在这些领域的发现是快速和广泛的,这一丛书对于学生和科学家都起着特有的重要作用。通过整合和更新,丛书对最新进展进行了当前最高水平综述。通过不断提出一些有特点的新论题和加入一些新的作者,丛书推动了创新,也培育了一些新的论点。随着近几十年信息爆炸和衰老研究进展,在衰老和长寿方面的大学课程和研究项目数量也随之增加。《衰老手册》系列丛书提供了一些知识基础以指导这些持续变化的领域。

确实如此,《衰老手册》作为教师以及学生的资源,提供了教学法的信息和进一步研究的灵感。该系列丛书内容覆盖广泛和深入,可作为最新信息的来源和不同领域工作的综览。《衰老手册》章节上最大的优点之一是把作者提供的内容综合在了一起,这些作者都工作在本研究领域的前沿,因此对一些问题的界定和每一领域的挑战都提供了专业的评价。衰老研究具有交叉学科性质,从基础生物学到社会学,各章节在概念上相互重叠就是最好例证。

我们对于各卷编撰人员忘我的献身精神和贡献表示崇高的敬意。正是由于他们的不懈努力,才赋予了本丛书优秀的品质。我们感谢《衰老生物学手册》编撰人员 Edward J. Masoro 和 Steven N. Austad 博士,《衰老心理学手册》编撰人员 K. Warner Schaie 和 Sherry L. Willis 博士和《衰老和社会科学手册》编撰人员 Robert H. Binstock 和 Linda

K. Geoge 博士。我们也万分感谢我们在 Elsevier 的出版商 Nikki Levy, 他对本书的高度兴趣和献身精神使《衰老手册》顺利地出版了许多版。最后我们也深深地感谢 James Birren, 他创建和指导了本系列丛书的前六版。

托马斯 A. 朗多,卡斯坦森 L. 劳拉斯坦福大学长寿中心

(李 刚 译)

我们对衰老生物学基础,以及怎样控制生物学以改善健康状况和长寿的理解正在不断地快速提升。这本书就像本系列丛书的前些版本,综述和整合了本领域的最新研究结果和发现。不仅如此,在这一版我们还包括了较多临床上有关衰老医学生理学进展的内容。本书主要适用于基础研究人员,他们希望与自己亚学科外的新研究保持并进、并想了解一些最新的临床发现。本书也适用于那些从事医学的、行为学的和社会老年病学家们,看看基础科学家和临床医生们在做什么。为确保本书有广泛的读者,我们也尽可能让所有章节容易被普通读者所接受。

如上所述,本书的组织结构宽松,其中一部分内容介绍基础衰老过程,另一部分集中在医学老年生理学上,但这两方面内容难免相互融合。例如,在基础生物学章节中,肌肉、脂肪组织和干细胞的内容都与临床研究有关。一些最令人兴奋的新发现也会与一个衰老生物学中最古老的观察一起介绍,例如饮食限制,简单地减少食物摄入量就能够延缓许多种属生物的衰老和延长生命。这样一个简单的干预就可有显著的效果,其分子机制却让研究者困惑了几十年,但是现在开始有所改变,在第一章和后续的几章中将尤为明显。另外,在饮食限制论题中,对灵长类动物包括人类的长期饮食限制实验现在也开始涉及到水果。

有时,对一些衰老特定的可能机制如自由基损伤,其到底如何影响寿命,只有先在特定研究方法和动物种类范围内进行实验,再对实验结果进行打分并进行评估,然后才能知道其真实情况。但在读了专门论述人类衰老氧化应激理论相关章节,以及保守的调节长寿生化途径如 TOR、胰岛素信号和长寿蛋白途径相关章节后就会比较清楚。

医学生理学部分包含了几章关于人脑衰老的章节。在衰老大脑相关疾病论题的处理上,这些章节不仅论及疾病,而且也涉及正常大脑脉管和髓磷脂的衰老改变,并提出这些改变的临床意义。另外的一些章节函盖了衰老怎样影响人类健康的核心问题,例如胰岛素的分泌、肺和心脏功能,以及我们维持体重和体温的能力。这一部分内容对于那些经常观察这些变化,但又不清楚为什么发生的临床医生可能会更感兴趣。有时一个现象有最明显的特点,但却并不为人所关注,所以我们将在最后一章讨论众所公认的男女之间长寿的差异。

事情总是这样,像这样一本书也需要许多人的共同努力,但他们的名字并不出现在目录中。因此,我们感谢这些专业的评审人,他们毫不吝啬地给了我们和读者对于各章的建设性建议。这些评审人包括 Gustavo Barja, James Carey, Richard Cawthon, Hae Young Chung, Karen Cullen, Simon Davis, Anthony Donato, Grigori Enikolopov, Sara Espinoza, Malene Hansen, Jeremiah Herlihy, Peter Hornsby, Ting-Ting Huang, Shin-ichiro Imai, Kazuhiro Ito, Jean-Paul Janssens, Joseph Kemnitz, Kevin Kregel, Christiaan Leeuwenburgh, Roger McCarter, Lawrence Mandarino, Richard Morimoto, James Nelson, Frédéric Picard, David Marcinek, Richard Miller, Charles Mobbs, Florian Muller, Eitaro Nakamura, Peter Rabinovicth, Shane Rea, Deborah Roach, Gary Ruvkun, Christian Sell, David Sharp, Anthony Suave, Edith Sullivan, Marc Tatar, Gary Van Zant, Antonio Vidal-

Puig, Mingyi wang, Walter Ward, Joanna Wardlow, 和 David Waters。我们也感谢作者本人,不仅仅是为他们所撰写的内容,也为他们对其他人所写内容做出的有益评论。

爱德华 J. 马索拉 史蒂文 N. 奥斯塔德

(李 刚 译)

#### 编者介绍

#### 爱德华 J. 马索拉

Masoro 博士是德克萨斯大学圣安东尼奥医学中心(UTHSCSA)退休教授,从1973年9月至1991年5月担任该中心主席。他是UTHSCSA衰老研究和教育中心的创始主任,2004年这一机构改名为Barshop长寿和衰老研究学院,他现在是该学院的成员。

Masoro 博士在 1989 年获得衰老研究的 Allied-Signal 成就奖。1990 年他获得衰老国立学院颁发的 Geriatric 领导学术奖和美国老年学会颁发的 Robert W. Kleemeier 奖。1991 年他获得 Pisa 大学颁发的老年医学成就荣誉勋章,在 1993 年 Masoro 博士获得生理系主席协会颁发的杰出服务奖。此外,他曾获得 1995 衰老研究美国联邦荣誉 IrvingWright 奖和 1995 Glenn 基金会奖。他从 1994 至 1995 年担任美国老年学会主席、衰老国立学院(NIA) 衰老评审委员会主席和 NIA 科学顾问董事会主席。

Masoro 博士是 Queen 大学 (加拿大)、Tufts 大学医学院、华盛顿大学和宾西法尼亚 医学院教授。自 1975 年以来,Masoro 博士的研究集中在食物限制对衰老的影响。他先后担任 10 种期刊的编辑,从 1992 年 1 月至 1995 年 12 月,他曾担任《老年医学杂志:生物科学》的编辑。

#### 史蒂文 N. 奥斯塔德

Austad 博士现在是德克萨斯大学圣安东尼奥医学中心、长寿和衰老研究 Barshop 学院和细胞与结构生物学系教授。他的研究集中在衰老比较生物学、动物健康评价和建立新的衰老研究动物模型。他以前就职于爱达荷大学和哈佛大学,现在是华盛顿大学病理系合聘教授。

Austad 博士 2003 年获得美国老年学会颁发的 Robert W. Kleemeier 奖。他也是美国老年学会会员,也曾任该组织生物科学部主席。他曾获得 Phi Kappa Phi /Idoho 大学校友会杰出职员奖和第五届 Nathan A. Shock 奖,他也与前毕业生 John P. Phelan 分享 Geron Corporation-Samuel Goldstein 杰出发表奖。他曾就职于国家公共电台科学顾问董事会,现在是《老年医学杂志:生物科学》的副编辑,《衰老细胞》的高级编辑,《衰老神经生物学》的责任编辑。他的科普书《我们为什么衰老》(1997 年出版)已经翻译成 8 种文字。他经常就衰老生物学及与医学延长寿命的伦理问题撰写文章,并举办讲座对公众进行讲解。

Masoro 和 Austad 博士以前曾共同编辑了《衰老生物学手册》第五版和第六版。

(李 刚 译)

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# Foreword

Advances in science and technology in the 20<sup>th</sup> century reshaped 21<sup>st</sup> century life in industrialized nations around the world. Living conditions so improved that infant and childhood mortality were profoundly reduced and medical advances in the prevention and treatment of leading causes of death among adults, such as heart disease and cancer, further extended the lives of older individuals. As a result, in the course of a single century, the average life expectancy in developed countries nearly doubled. For the first time in human history, old age became a normative stage in life. Not only are individuals living longer on average, but populations have begun to age as a result of this increase in life expectancy along with a precipitous drop in fertility rates. Countries in the developed world are rapidly reaching the point where there will be more people over 60 than under 15. Thus, the status of older people holds ramifications for the functioning of entire societies.

Even though the near-doubling of life expectancy was a spectacular achievement, there were not concurrent advances in our ability to alleviate the disabling conditions of later life. Nor were there sociological advances to create a world as responsive to the needs of very old people as to the very young. In order to realize the enormous potential of longer life, scientists must come to a more comprehensive understanding of human aging and the social, psychological and biological factors that contribute to optimal outcomes. Along with the phenomenal advances in the genetic determinants of longevity and susceptibility to agerelated diseases has come the awareness of the critical importance of environmental factors that modulate and even supersede genetic predispositions. This series provides a balanced perspective of the interacting factors that contribute to human aging.

The Handbooks of Aging series, comprised of three separate volumes, The Handbook of the Biology of Aging, The Handbook of the Psychology of Aging, and The Handbook of Aging and the Social Sciences, is now in its seventh edition and has provided a foundation for an understanding of the issues of aging that are relevant both to the individual and to societies at large. Because discoveries in these fields have been both rapid and broad, the series has played a uniquely important role for students and scientists. By synthesizing and updating progress, they offer state-of-the-art reviews of the most recent advances. By continually featuring new topics and involving new authors, they have pushed innovation and fostered new ideas. With the explosion of information and research on aging in recent decades, there has been a concomitant increase in the number of college and university courses and programs focused on aging and longevity. The Handbook of Aging series has provided knowledge bases for instruction in these continually changing fields.

Indeed, *The Handbooks* are resources for teachers and students alike, providing information for didactics and inspiration for further research. Given the breadth and depth of the material covered, they serve as both a source of the most current information and as an overview of the various fields. One of the greatest strengths of the chapters in *The Handbooks* is the synthesis afforded by authors who are at the forefront of research and thus provide expert perspectives on the issues that current define and challenge each field. The interdisciplinary nature of aging research is exemplified by the overlap in concepts in chapters ranging from basic biology to sociology.

We express our deepest thanks to the editors of the individual volumes for their incredible dedication and contributions. It is their efforts to which the excellence of the products

#### **Foreword**

is largely credited. We thank Drs. Edward J. Masoro and Steven N. Austad, editors of *The Handbook of the Biology of Aging*; Drs. Sherry L. Willis and K. Warner Schaie, editors of *The Handbook of the Psychology of Aging*; and Drs. Robert II. Binstock and Linda K. George, editors of *The Handbook of Aging and the Social Sciences*. We would also like to express our appreciation to Nikki Levy, our publisher at Elsevier, whose profound interest and dedication has facilitated the publication of *The Handbooks* through their many editions. And, finally, we extend our deepest gratitude to James Birren for establishing and shepherding the series through the first six editions.

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# **Preface**

Jeremiah Herlihy, Peter Hornsby, Ting-Ting Huang, Shin-ichiro Imai, Kazuhiro Ito, Jean-Paul Janssens, Joseph Kemnitz, Kevin Kregel, Christiaan Leeuwenburgh, Roger McCarter, Lawrence Mandarino, Richard Morimoto, James Nelson, Frédéric Picard, David Marcinek, Richard Miller, Charles Mobbs, Florian Muller, Eitaro Nakamura, Peter Rabinovitch, Shane Rea, Deborah Roach, Gary Ruvkun, Christian Sell, David Sharp, Anthony Suave, Edith Sullivan, Marc Tatar, Gary Van Zant, Antonio Vidal-Puig, Mingyi Wang, Walter Ward, Joanna Wardlow, and David Waters. We also thank the authors themselves, not only for their contributed chapters, but also for their helpful comments on one another's work.

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