

The Clock of Ages

Why we age, how we age,
winding back the clock

JOHN J. MEDINA

岁月之钟

剑桥英语科普注释读物系列



上海外语教育出版社

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出版说明

随着我国改革开放的深入和对外科技交流的发展,广大科技工作者迫切需要通过英语媒介获取专业科技知识,了解相关学科领域的最新发展动态;而有一定英语基础的普通读者则亟须通过阅读大量英语版的科普文章来扩大知识面,获取信息,同时提高英语水平。所以,引进一批国外原版的优秀科普读物满足读者的需要是改革开放进一步深化的需要,是当务之急。

我社从英国剑桥大学出版社引进的这本《生命之钟》(*The Clock of Ages: Why we age · how we age · winding back the clock*)就是这样一部优秀的科普作品。它阐述了人体衰老的过程和原因,帮助人们了解其内在因素。它所包含的一些分子生物学知识属于深奥的前沿学科。但是,作者以他非凡的写作技巧、通俗易懂的语言,不但吸引了诸多专业人员的注意力,而且也引起了一般读者的兴趣。

本书可作为大专院校生物、医学专业学生的专业英语教材或课外读物,也可供广大英语爱好者用作提高科普英语水平的读物。

上海外语教育出版社

Preface

It was time to say my last words to my mother.

She was dying. Not much had changed since I had last seen her. She still had a full head of hair, making her look much younger than her 64 years. Her voice betrayed some of her tenure, though. It was almost half an octave higher than the one I had heard as a little boy, the product of a natural stiffening of the vocal cords. The lines on her face spoke of her years too, already sculpted by the finger of time, greatly deepened by decades of loving laughter. These marks always concerned her, though she had once read that wrinkles were a natural, unstoppable part of growing older. She often looked in the bathroom mirror — even as a young mother — to examine their progression. ‘The Clock of Ages’, I would sing to her at the top of my lungs, making a pun from a hymn she loved to hear at church. She paused. ‘But not cleft for me, unfortunately,’ she sighed, tilting her head for the hundredth time, still looking in the mirror.

When I came to see her, she was lying in her bed. It was a darkened room, lit only by the soundless snow from an unwatched TV. I turned off the attached video tape machine. She had fallen asleep watching an old black and white movie from Hollywood.

‘They liked young faces, you know,’ she told me once in high school. In the days when the wrinkles did not exist, Mom had been a promising young actress at the University of Michigan. And much more. She was on the diving team, in the choir, inducted into the honors society, one of those people that kind of make you sick at graduation because they get all these awards. And impressive all the more because she was so nice, always laughing, always giving away a smile you’d remember all day, as effervescent as a can of soda pop.

Where she truly shone, however, was in the talent of her chosen major, the dramatic arts. Her gift was of sufficient quality that she began starring in stage productions with the likes of Fernando Llamas and Ricardo Montalban. She started a correspondence with Basil Rathbone and eventually with Jane Wyman and Ronald Reagan. In going through her things I found a number of

letters and a ream of publicity photos I didn't know existed. She was so *young*.

'They told me that I should go to Hollywood before I got too old.' Her eyes twinkled as she related an earlier time for me. Now I was going off to college and she wanted to give me some advice. 'That's because there were almost no parts for women over the age of 30. To be honest, John, there are still no parts for older women!' Taking the advice of her coach and a few famous friends, she went to Hollywood before *The Clock of Ages* took its toll.

Mom was immediately successful, of course. Her connections on the stage got her a screen test for a part in an upcoming movie, and she outdid all her competition. 'The day I found I was going to get the part was the happiest day of my life.' Mom said, 'And then also the saddest.' The young starlet was called into one of the executive's offices to talk about negotiating a contract. He wasn't well known to the outside world, but he was a power broker in the feudal star system of the early 1950s. And when he began to talk about the problems he and his wife were having and how beautifully youthful Mom looked and how this contract would be so easy to offer if Mom would be nice to him and how smooth life would be for future projects if she remained friendly to him and how awful it would be if she said no . . .

'I knew inside what he was doing, John. I also knew that if I refused his offer, that would be the end of my career,' she told me. 'I was shocked, of course. This kind of thing did not happen in Michigan. And I was raised in a different time. So I thought about it there in his office. In the end, it was more important that I be able to look at my image in the mirror every morning than gaze at my image on the silver screen every night.' With a sinking feeling that only comes when you are watching life-long hopes and dreams die at your own hand, she refused his offer.

The executive told her that she was a fool, that for every young girl in her position there were ten waiting in line to take her place. Mom said that this was fine, and told him to give the other ten a phone call, because she was walking out the door. 'Now I have these photographs, and a couple of letters,' she said as she gathered them into an envelope. And then wearing a slight smile, she gave some of them to me before I went off to college. And then she left the room.

But that was a long time ago. And also several worlds away. Now I am an adult and I am watching this would-be movie star and life-long friend sputter

against a Clock she declared war on many years ago. The doctors had told us she was dying. But we knew long before. She didn't talk very much at the end, except to whisper for an occasional glass of water. And when we gave it to her she said thank-you and smiled.

Try as I might, I wasn't there to recollect old memories with her. I was there to say my last words and then leave, because I am a research professor at a medical school and I will have to drive all night to get back to the laboratory. I draw near to the side of her bed and pray in the dark she cannot see me crying. I can see her, however, her gaunt face outlined in the flicker of the unwatched TV. I manage to stammer 'Tell Jesus I said hi, okay?' and I touch her hand and I hear her waken. 'Okay,' she whispers hoarsely and then she pauses. In a slightly louder voice, she asks:

'Will you please turn off the television?'

Mom slipped into unconsciousness shortly after that and died seven days later.

The purpose of this book

No laboratory experience can ever prepare you for the death of a loved one. You can anticipate and plan and rehearse your feelings for an Oscar-winning performance, and then when death comes, you mostly just stammer. The impending sense of loss is extreme, the helplessness in the face of biological processes you can't control is frustrating and terrifying.

The death of relatives and friends is powerful for another reason too. Lying in the back of your mind, like a sleeping dog, is the raw fact of your own mortality. If someone close to you can age and die, then you can too. As the years pass, certain immutable changes occur in our bodies, which do nothing but remind us of this strange terminal outcome. Such a sense of timed fragility is one of the most profound feelings I have ever experienced. It is the persistent ticking of *The Clock of Ages*.

The book you have in your hands describes a personal tour. Not through a strange country, or even a foreign concept. It is a tour through a biological time piece, this amazing *Clock of Ages*, which is the aging process in human beings. The tour is informational. It will be filled with various stops around the world and, eventually, around our bodies. We will pause to consider

questions at specific times to enlighten us on the aging process, questions like ‘Why do different animals have different life spans?’, ‘Why does my hair turn gray?’ and ‘Am I really losing my memory?’ Because I am a scientist as well as the tour guide, we will approach the answer to these questions from a reductionist’s point of view; that is, we will look closely at the unimaginable complex world of our tissues and cells and even genes. These are the objects, of course, that make up the screws and gears and springs of the Clock. We will certainly observe the machine in operation, and we will even speculate on work that may have found a way to extend its operation. Or in a few cases, even wind it back.

The first stop on our tour is a historical one. We will attempt to place aging and death into an evolutionary context. Why do organisms age at all? Is our ability to reproduce tied to our life span? Are there creatures that never die? To answer these questions, we will first have to outline some operating definitions of death in the general and human death in the specific. As we’ll see, that may not be very easy to do.

The second stop on our tour is a description of the various components of the Clock. We will describe how the divers tissues and organs of the human body change over time. Why does my skin wrinkle as I get older? What happens to my thinking processes as I age? Why must I place books farther from my eyes in order to see the text? By individually examining these disparate systems, we will discover the effects of the years on our capabilities — and to what we have to look forward as we age.

The last stop on our tour is a description of how the components work together to make the Clock tick. Instead of examining whole tissue and organs, we will observe individual cells and the lilliputian genes they contain. Are there genes that deliberately cause cells to die? Are there genes that can extend their life span? What can I do to arrest or even turn back the effects of aging on my body? To answer these questions, we will discuss how various genes work inside cells and creatures. We will discuss some exciting new frontiers in the effort to rewind *The Clock of Ages*.

It is fully realized by this reductionist scientist that aging and dying have more components than just test tubes and petri dishes. These processes are a shared experience that in many ways fertilizes our religions and causes entire societies to behave in certain ways. The reason, of course, is that *The Clock of Ages* possesses a ticking heard by everyone. Included in this tour package, then, is a description of how other historically familiar human beings have

experienced aging and death. We will learn about the attitudes of writers like Jane Austen and painters like Francisco Goya, nurses like Florence Nightingale and generals like Napoleon Bonaparte, lovers like Casanova and criminals like Billy the Kid. They have in common the fact of facing this Clock head on, even as we do today. They have in addition the fact that they experienced its final ticking, even as we have not.

A quick word about expertise

Even though this text is about science and biology, please don't let that fact be frightening. The tour guide is well aware that even if we share a similar biological fate, we do not similarly share biological backgrounds. You can have flunked most of your grade school biology and still understand everything written in these pages — in fact, you can read this book like you read a newspaper. There are plenty of drawings to help explain certain processes and the chapters are well delineated by subject. The intent is to communicate clearly the changes with which you are already in various stages of being familiar. The purpose of this book is to find out exactly what those changes are.

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PART ONE

Who ages?

INTRODUCTION

Our first task in the beginning of this book is to attempt to define the process of aging. By the end, you will find this task will be mostly unaccomplished.

The reason for this ambiguity is manifold^①, and perhaps surprising. The problem is that there are so many ways to look at the roots of biological maturity. Some look to aging's final obligation, death, and attempt to work backwards from the event to describe what aging means. But even death can be difficult to define absolutely, in an it-makes-sense-to-the-biologist language. We will understand this ambiguity best by attempting a definition of our own. And we will do so in the same backwards style, first examining the process of death and then working our way in reverse.

A working^② definition

At first blush,^③ the inability to define death, and the body's prior preoccupation with survival, might sound odd. We have no ambiguities, for example, surrounding the material facts of such notable nonagenarians^④ as the playwright George Bernard Shaw. Not only do we know when and how he expired^⑤(at the age of 94, after suffering a 108-degree fever), we have a general idea of what happened. He *died*, and from this event a corpse and a funeral were created.

And so it is for most of us. Death appears to be a definable, monolithic, biologically irreversible fact of life. Quibbling with its consistency seems a strange exercise, even an irrelevant one. We are forced, for better or worse, to link the words 'inexorable'^⑥ and 'death' in a strong bond. Such a linkage

① manifold; various

② working; acceptable

③ at first blush; without the knowledge before; at first glance

④ nonagenarian; a person in his/her nineties

⑤ expire; die

⑥ inexorable; irreversible; inevitable

is true, however, only if you don't look too closely.

Overarching definitions run into semantic and conceptual obstacles quite easily. Automobiles and aunts both age, for example. But then, so do wine and cheese. We surely don't imply the same physical process — or outcome — is occurring in each. The only commonality is a certain time-dependent^① physical change, even a deterioration.

Because of this ambiguity, many researchers tether^② the process of aging to an event that appears more definable, at least to biological organisms. That event is 'natural causes'. Scientists think of aging in terms of probabilities, with mounting tenure increasing the likelihood of expiration. Aging, in their minds, is a decrease in the chance of survival. Death is a cessation^③ of that decrease.

Though it leaves any explicit consideration of reproduction out of the picture, this definition of aging is not a bad start. Everything fated to have a beginning is also doomed to have an ending. We share, along with light bulbs and fan belts, an extinction so predictable that it almost appears planned. Focusing on death as the end point of this planned obsolescence^④ gives a comforting linearity to our definition. But we deteriorate to what? 'Cessation of a decrease' has to *mean* something. Since all living things seem to undergo it, there must be some common thread to their experience of death. We ask a single question: Is there an overarching, universal definition of the biological process of death? This question lies at the heart of our ability to understand the aging process in biological life. It is the purpose of the chapters in this section to answer it.

To accomplish this task, we will first discuss the world of non-human biology, exploring the process of death in a variety of vertebrate^⑤ and invertebrate organisms. Second, we will consider the mechanisms of human expiration, looking both biologically and historically for an explanation of our 'moment of death.' Finally, we will explore the evolutionary context of aging and death. By examining the force of natural selection on senescence^⑥,

① time-dependent: as a result of the passage of time

② tether . . . to . . . ; confine . . . to . . .

③ cessation: termination

④ obsolescence: extinction

⑤ vertebrate: (animal, bird, etc.) having a backbone

⑥ senescence: aging

we will attempt to find a biological reason for its existence. Once a context is established, understanding the purpose may help us also understand the substance.

A few ground^① rules

Several issues need clarifying before we begin. I will be using the terms 'aging' and 'senescence' interchangeably. This has its hazards, whether we consider multi-cellular organisms or simple single cells. Botanists, for example, use the term 'senescence' when they describe deciduous trees shedding their leaves; that does not mean the tree is 'aging' in the traditional sense. Certain cells in our body undergo the process of senescence. This is a fairly well established series of specific internal biochemical events not necessarily leading to death, and not part of common definitions. Some cells age and die in living things — even in developing embryos — but leave the rest of the organism youthful and growing. It is important to distinguish between whole organismal aging processes and mechanisms occurring within individual cells. When considering evolutionary theory, we must distinguish between the forces exerted on an individual and those exerted on a group.

In addition to the terms 'aging' and 'senescence', I will soon be using words like 'cells' and 'cell cycle.' Although more formal definitions will follow as these pages unfold^②, I will give a brief description here. You remember from grade school that all human beings are composed of cells, those small, grease-lined objects that look like beach balls (Figure 1). A typical human has 60 trillion of these structures. Each cell has a nucleus, which is a glorified storage container for human genetic information. As you may recall, this information is locked up in structures called chromosomes, and is made of DNA.

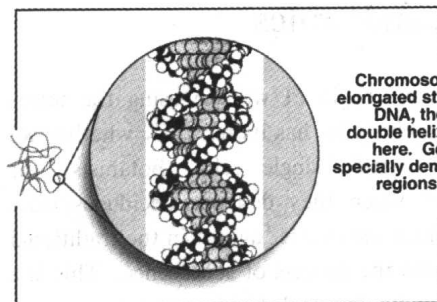
In order to keep us healthy, these cells must make copies of themselves. To do that, they simply copy their genetic information and then split in two. This process, a highly controlled and very complex event, is called mitosis

① ground: basic, governing

② as these pages unfold; as we proceed with / continue our discussion

Animal cell architecture

A 'typical' animal cell, drawn below, looks something like a fried egg.



Chromosomes are elongated strands of DNA, the typical double helix shown here. Genes are specially demarcated regions of DNA.

THE 'YOLK' is termed the nucleus, the 'white' termed the cytoplasm. The nucleus is the command and control center for the cell. It contains the genetic information (housed in structures named chromosomes) necessary to run the day-to-day operations of the cell. Chromosomes are really long strands of DNA, the double helix pictured on the left.

The cytoplasm has very few control functions. Instead, it contains the power supplies, manufacturing base, and much of the transportation infrastructure. In order to issue commands, the genetic information in the nucleus has to send out 'messages' to the cytoplasm, a topic we will consider in a later chapter.

