A lethal side-effect

Ageing

Ageing is bad for us and yet it happens to everyone. So why does it occur at all?

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Industrialized societies throughout the world are greying. Since 1840, maximum life expectancies have increased at a rate of about three months per year and this trend shows no sign of slowing down. The good news is that people are getting healthier. But one downside is the net impact on healthcare. The overall improvement in health is more than countered by the much greater number of individuals reaching ages at which age-related health problems occur. An obvious example is Alzheimer's disease, which was almost unknown a century ago. The same is true of age-related macular degeneration, now the leading cause of blindness. Ageing is bad for us and yet it happens to everyone. So why does it occur at all?

The effects of ageing are particularly obvious in humans, but are not peculiar to us. Ageing occurs in natural populations — as individuals get older they become less fecund and more likely to die. Organisms ranging from yeast to mammals to plants are affected. Cars and washing machines wear out too, which suggests that ageing could be an inevitable consequence of complexity. But at least some things do not age. All organisms living today are descended from lineages that have been going strong for three billion years. Germ lines do not wear out. So if ageing is not inevitable, surely such a universal and ultimately lethal process must have a purpose?

August Weismann suggested that ageing functions to rid the species of worn out and decrepit individuals so as to reduce competition for resources with younger ones. The most obvious problem with this idea is that it is circular because it assumes the existence of the trait whose occurrence it is aiming to explain. The circle could be broken by viewing the inevitable accumulation of damage during a lifetime as an intrinsic trait that has evolved to increase the death rate of the elderly.

But even without the circularity, the claim that a trait has evolved for the benefit of a species requires close inspection. Most traits, such as eyes and digestive systems, evolved because they increase the survival and reproductive success of their bearer or, in a few cases such as mammary glands, the bearer's closest relatives. Fairly restrictive conditions are required for a trait to evolve because it benefits other members of the species. Explanations for the prevalence of ageing based on species-level functions such as increasing the rate of evolution have therefore fallen into disrepute.

Ageing is caused by the accumulation of damage, and no gene has evolved specifically to cause damage and debility. Yet genes do influence the rate of ageing. Birds live longer than comparably sized mammals, which suggests that the rate of ageing evolves. And mutations in single genes can increase the lifespans of laboratory animals. Many of these genes have been identified and are known to encode normal constituents of cells and endocrine systems. So why has natural selection favoured the wild-type form of the gene rather than a mutant trait that extends lifespan?

Genetic effects on ageing can be understood only as a side-effect of something else. Genes that slow ageing could exert these effects because they repress the causes of ageing-related damage. Reproduction seems to be one of these sources of damage, because fecundity is often reduced both during the evolution of slow ageing and by single-gene mutations that extend lifespan. Food seems to be another damage source, because many of the genes that slow ageing are involved in the response to changing nutrient levels. And reducing food intake slows down ageing in organisms ranging from yeast to mammals.

So adaptive, programmed events that are controlled by genes cause damage and therefore lead to ageing as a side-effect. Ageing is not a programmed process like development. No hierarchy of genetic control systems has evolved to ensure that ageing occurs in the right place and at the right time. It is a late-onset genetic disease that affects all of us, a result of damage inflicted by other, adaptive processes earlier in life.

The steady increase in life expectancy in human populations shows that longevity is plastic. Although lifespans are species-specific, they can be greatly modified by the environment as well as by genes. For many human populations, the fixed three score years and ten allotted for human longevity are already but a distant memory. Much of this increase in lifespan has been achieved by improvements in public health, medical care and domestic circumstances. We are beginning to view ageing-related damage as a side-effect of other, adaptive processes. This may allow us to reduce the impact of ageing-related diseases as the limits on human lifespan recede. ■

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"One man in his time plays many parts": the idea of *The Ages of Man* is a familiar one, but is ageing more properly viewed not as a process in its own right, but as a side-effect of accumulated genetic damage?

FURTHER READING

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