Aging

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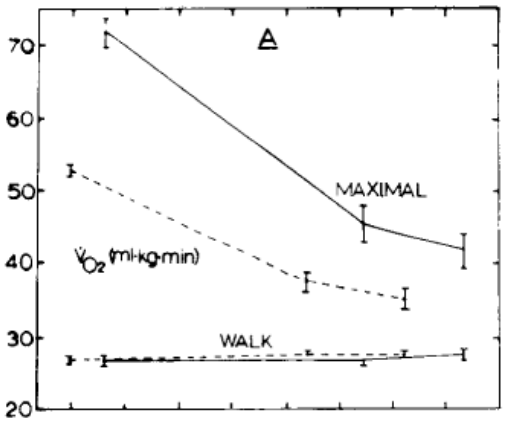
November 11, 2010

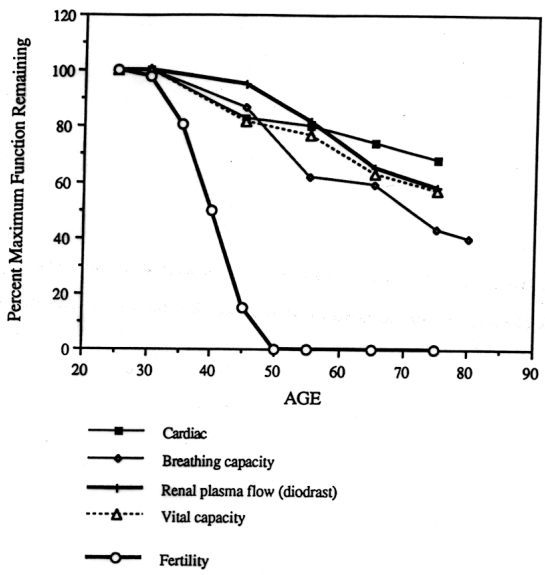
Outline

- The problem
- How selection affects genes with age-specific effects
- The theory of mutation-selection balance
- The theory of antagonistic pleiotropy
- Evidence from selection experiments
- Evidence from natural history

- Why can't old people run as fast or see as well as they used to?
- Why do they develop heart disease and cancer?



Vital capacity declines with age
solid: atheletes
dashed: others

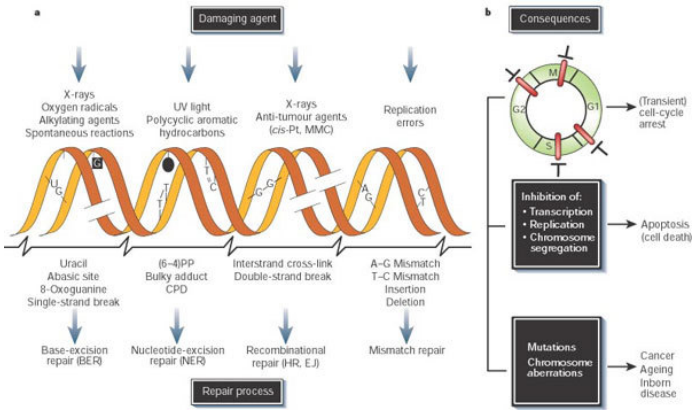


Physiological aging

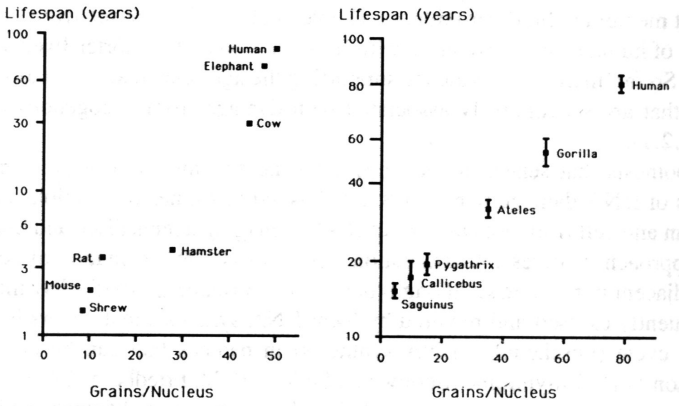
What happens during aging?

Part of the story involves ongoing damage to DNA...

DNA: constant damage and repair



More DNA repair in long-lived species



DNA repair

A Puzzle

- More DNA repair means fewer damaged cells.
- Lets you live longer.
- Some species (humans, elephants) do a lot.
- Others (mice, shrews) do much less.
- Why the difference?

Theories of senescence

1. Wear and tear. *(But why do fruit flies wear out in a few weeks, humans in 70 years?)*
2. Limits on cell proliferation. *(But why are they different in different organisms?)*
3. Evolutionary theories
   - 3.1 Antagonistic pleiotropy.
   - 3.2 Mutation-selection balance.

How selection affects genes with age-specific effects

Principle 1. If a gene is not expressed until late in life, few will live long enough to express it. Selection is therefore weak.
Principle 2. A gene that kills you at age 40 deprives the world of the children you might have had at ages 41, 42, and so on. If fertility is low after age 40, then the force of selection against such genes is weak.
Principle 3. Evolution favors early reproduction in growing populations but late reproduction is shrinking ones.

The theory of mutation-selection balance

Alleles that act late in life are only occasionally exposed to selection. Therefore, selection will be less effective in removing harmful mutations that are expressed in old age. Consequently, harmful mutations with late effects may accumulate.

The theory of antagonistic pleiotropy

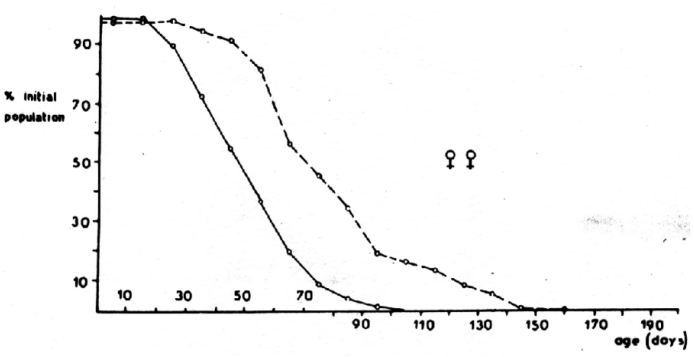
Pleiotropic gene: one with multiple effects. In the present context, a pleiotropic gene is one that acts at two or more ages.
Antagonistic pleiotropy: Refers to a gene that helps at one age but harms at another.
Theory: Many genes are helpful early in life but harmful later on. Selection may favor such genes, because it is more sensitive to effects early in life.

One cause of antagonistic pleiotropy

Any decrease in maintenance or repair at age 20 has an immediate beneficial effect and a delayed detrimental effect:

- It allows resources to be used for other purposes at age 20. This may allow the 20-year-old to have higher fertility or to increase the probability of surviving to age 21.
- It increases the probability that the organism will break down at (say) age 30.

Outline



In fruit flies, selecting for early fertility (solid line) reduces life span; selecting for late fertility (dashed) increases it.

Predictions of theory

- Senescence only when germ line is separate from soma.
- Senescence $\nearrow$ with externally-caused mortality.
- Senescence $\searrow$ when fertility grows throughout life.
- The sex with higher mortality should senesce faster.
- Little or no post-reproductive life.
- Senescence should begin at maturation.

Senescence should not occur unless the germ line is separate from the soma.

Does not occur in protozoan clones.

Senescence ↗ with externally-caused mortality.

First compare very different taxa:

Group	Death Rate	Senescence
Insects	10% per day	Rapid
Humans	1% per yr	Slow

In the right direction, but not convincing because of the grossly different body plans of these organisms. Therefore, let us seek better comparisons.

- Birds have lower mortality than mammals of similar size (because they can fly to escape predators) and senesce more slowly.
- Flightless birds (ostrich & emu) have high mortality and rapid senescence in spite of their large size.
- Bats live longer than mammals of similar size.
- Turtles are long-lived, presumably because their shell protects them from predation.

Sustained growth in fertility should slow senescence.

Many fish have indeterminate growth and increase in fecundity throughout life. They also senesce slowly.

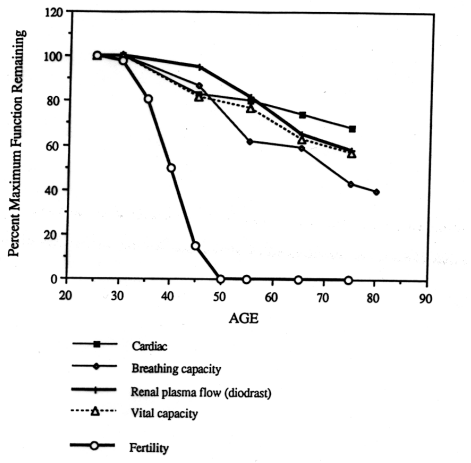
Within species, the sex with higher mortality should senesce faster.

Males of many species take more risks. They also senesce faster.

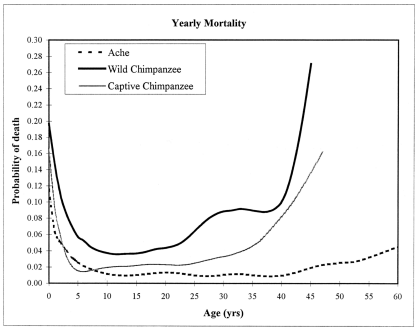
There should be little or no post-reproductive life.

True of nearly all species, but not of human females. (Why?)

Senescence should begin at maturation.



Mortality of chimps and human hunter-gatherers (Ache)



- Chimps die faster at every age. Why?
- Perhaps human reciprocity acts like workman's comp, reducing mortality.
- Result: slow senescence in humans (Kim Hill).

Review of main points

- Theories of senescence (Non-evolutionary theories fail to account for different rates of aging in different species.)
- How selection affects genes with age-specific effects
- The theory of mutation-selection balance
- The theory of antagonistic pleiotropy
- Evidence from selection experiments (In fruit flies, there is evidence for both evolutionary theories of aging.)

Evidence from natural history

- Separation of germ line and soma
- Exogeneous causes of mortality
- Sustained growth in fertility
- Absence of post-reproductive life
- Senescence begins at maturation

Comparison btw chimp and human mortality

- Chimps die faster.
- Perhaps because human reciprocity allows us to survive accidents.
- Immediate effect: lower human mortality.
- Delayed effect: selection removes harmful human genes that act late in life.
- Result: reciprocity extends life span (Kim Hill).