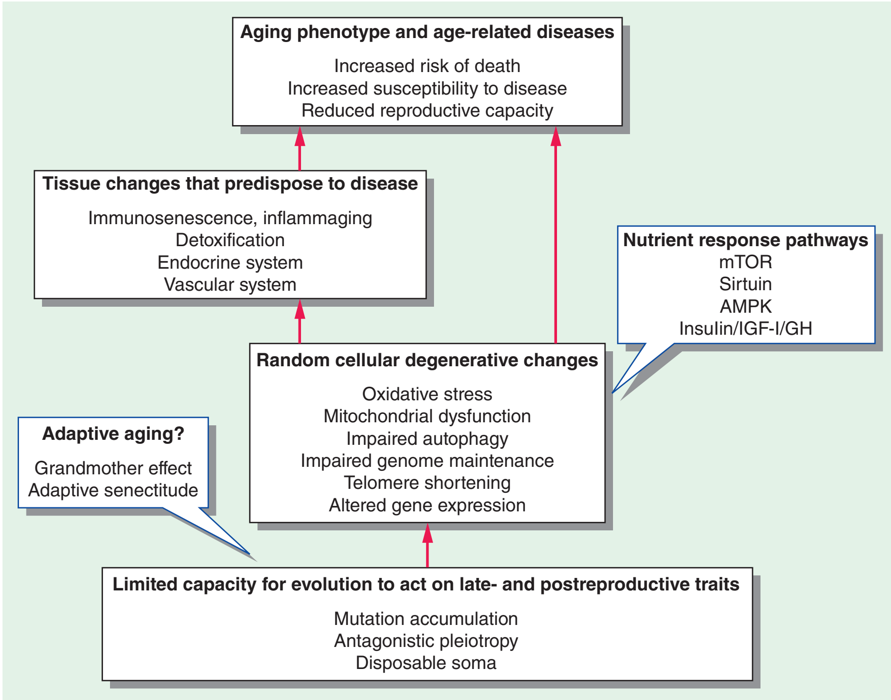

FIGURE 94e-3 Schema linking evolution and cellular and tissue changes with aging. The call-out blue boxes indicate factors that might delay the aging process including nutrient response pathways and, possibly, adaptive evolutionary effects.

survival. Aging is seen as the random degeneration resulting from the inability of evolution to prevent it, i.e., the nonadaptive consequence of evolutionary "neglect." This conclusion is supported by studies that restricted reproduction to later life in the fruit fly, *Drosophila melanogaster*, thus permitting natural selection to operate on later life traits and leading to an increase in longevity. There are some species of plants and animals that do not appear to age, or at least they undergo an extremely slow aging process, termed "negligible senescence." The mortality rates of these species are relatively constant with time, and they do not display any obvious phenotypic changes of aging. Conversely, there are some living things that undergo programmed death immediately after reproduction, such as annual plants and semelparous animals (Fig. 94e-4). However, many other living things from yeast to humans undergo a gradual aging process leading to death

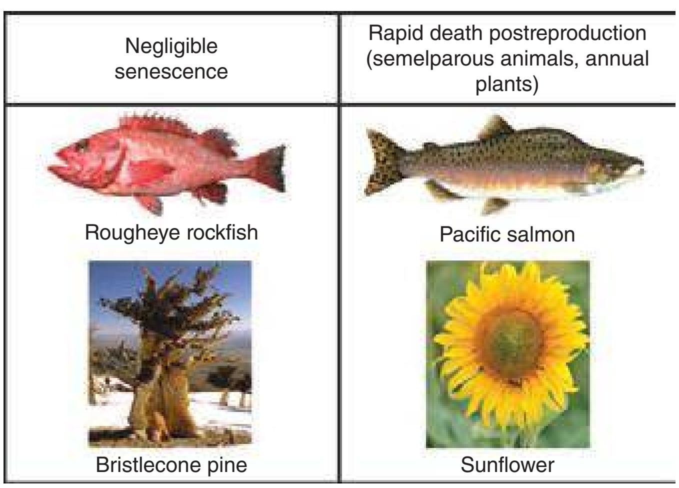

FIGURE 94e-4 The typical features of aging (aging phenotype and exponential increase in risk of death) are not universal findings in living things. Some living things (e.g., rockfish and the bristlecone pine, sometimes called the Methuselah tree) undergo negligible senescence, whereas others die almost immediately after reproduction is completed (e.g., semelparous animals and annual plants).

that is surprisingly similar at the cellular and biochemical level across taxa. Some of the major classical evolutionary theories of aging include the following:

- *Programmed death.* The first evolutionary theory of aging was proposed by Weissman in 1882. This theory states that aging and death are programmed and have evolved to remove older animals from the population so that environmental resources such as food and water are freed up for younger members of the species.
- *Mutation accumulation.* This theory was proposed by Medawar in 1952. Natural selection is most powerful for those traits that influence reproduction in early life, and therefore, the ability of evolution to shape our biology declines with age. Germline mutations that are deleterious in later life can accumulate simply because natural selection cannot act to prevent them.
- *Antagonistic pleiotropy.* George C. Williams extended Medawar's theory when he proposed that evolution can allow for the selection of genes that are pleiotropic, i.e., beneficial for survival and reproduction in early life, but harmful in old age. For example, genes for sex hormones are necessary for reproduction in early life but contribute to the risk of cancer in old age.
- *Life history theory.* Evolution is influenced by the way that limited resources are allocated to all aspects of life including development, sexual maturation, reproduction, number of offspring, and senescence and death. Therefore, "trade-offs" occur between these phases of life. For example, in a hostile environment, survival is highest for those species that have large numbers of offspring and short lifespan, whereas in a safe and abundant environment, survival is highest for those species that invest resources in a smaller number of offspring and a longer life.
- *Disposable soma theory.* Kirkwood and Holliday in 1979 combined many of these ideas in the disposable soma theory of aging. There are finite resources available for the maintenance and repair of both germ and soma cells, so there must be a trade-off between germ cells (i.e., reproduction) and soma cells (i.e., longevity and aging). The soma cells are disposable from an evolutionary perspective, so they accumulate damage that causes aging while resources are preferentially diverted to the maintenance and repair of the germ cells. For example, the longevity of the nematode worm, *Caenorhabditis elegans*, is increased when its germ cells are ablated early in life.