- For constipation, increase dietary fiber intake to 10–25 g/d and fluid intake to 1500 mL/d. A bulk laxative (methylcellulose or psyllium) can be added.

Novel Interventions to Modify Aging Processes Aging is a complex process with multiple manifestations at the molecular, cellular, organ, and whole-organism level. The nature of the aging process is still not fully understood, but aging and its effects may be modulated by appropriate interventions. Dietary and genetic alterations can increase healthy life span and prevent the development of dysregulated systems and the aging phenotype in laboratory model organisms. The mechanisms responsible for life span expansion are "food" sensors typically activated in situations of food shortage, such as IGF/insulin and the TOR (target of rapamycin) pathways. Accordingly, a reduction in food intake without malnutrition extends the life span by 10–50% in diverse organisms, from yeasts to rhesus monkeys. Mechanisms that mediate the effects of caloric restriction are under intensive study because they are potential targets for interventions aimed at counteracting the emergence of the aging phenotype and its deleterious effects in humans. For example, resveratrol, a natural compound found in grape skin that mimics some of the effects of dietary restriction, increases longevity and improves health in mice fed a high-fat diet but has little effect on mice fed a standard diet. Other compounds that potentially mimic caloric restriction are being developed and tested. A high prevalence of IGF-1 receptor gene mutation has been found in Ashkenazi Jewish centenarians and in other long-lived individuals, suggesting that the downregulation of IGF-1 signaling may promote human longevity. A 20-year period of 30% dietary restriction applied to adult rhesus monkeys was associated with reduced cardiovascular and cancer morbidity, reduced signs of aging, and greater longevity, although a second such study did not find increased longevity. In humans, dietary restriction is effective against obesity and reduces insulin resistance, inflammation, blood pressure, CRP level, and intima-media thickness of the carotid arteries. However, the beneficial effects of dietary restriction in humans are still controversial, and some potential negative effects have not been sufficiently studied. An interesting effect of caloric restriction in humans is mitochondrial biogenesis. Mitochondrial dysfunction has emerged as a potentially important underlying contributor to aging. Reduced expression of mitochondrial genes is a strongly conserved feature of aging across different species. Mitochondria are the machinery for chemical energy production, and brain and muscle are particularly susceptible to defective mitochondrial function. Thus, declining mitochondrial function may be a direct cause of at least three of the main dysregulated systems contributing to the phenotype of aging.

OTHER ASPECTS OF AGING

This chapter has touched on some of the fundamental aspects of human aging, focusing mostly on those that are relevant to the care of older patients. Many aspects of geriatric medicine have not been addressed because of space limitations. Valuable topics not considered include details of comprehensive geriatric assessment, depression and anxiety, hypertension, orthostatic hypotension, dementia, vision and hearing impairment, osteoporosis, palliative care, prostate disorders, foot problems, and women's health. Some of these topics are treated extensively elsewhere in this text, sometimes with comments on age-specific issues.

CONCLUSIONS

The universal process of aging is becoming better understood. There appear to be shared underlying cellular and molecular processes that induce widespread dysregulation in key systems. This dysregulation contributes to clinical manifestations of a frailty phenotype and can be used to understand how to evaluate and manage the older patient.

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