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Resiliency of the Digestive System During Aging and the Impact of Diet

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Increases in life expectancy are contributing to rapid growth in the aging population around the globe. Aging is accompanied by physiological decline and susceptibility to age-related diseases. To enable healthy aging, it is important to understand the independent effects of aging on biological systems and how comorbidities and lifestyle factors may influence the health of these systems. The digestive system is a multifunctional set of tissues and organs that not only enable the digestion and absorption of nutrients, but also serves as a physical and immunological barrier to the external environment and the primary interface to commensal microbes. This review examined current evidence regarding the effects of aging on gastrointestinal function, including digestion, absorption, motility, microbiome, and barrier function. Overall, the digestive system is quite resilient to the normal aging process with comorbidities and other lifestyle factors contributing to most digestive health issues associated with aging. Emerging research on the gut microbiome and barrier function suggests an important role for the digestive system in the etiology of many age-related diseases and demonstrates how diet may be able to modify the effects of chronic diseases. Nutr Today 2023;58(4):165–174

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INTRODUCTION

Currently, it is estimated that 9% of the global population is 65 years or older, and this percentage is expected to almost double by 2050.[1] Further, if fertility rates continue to decline, it is expected that by 2100 there will be 50% more adults older than 80 years than children younger than 15 years around the globe.[2] Age-related diseases account for more than 50% of the global burden of disease, with a higher prevalence of these diseases in developed countries.[3] Thus, maintaining health during aging is a public health priority with important social and economic consequences.

Of particular importance is the health of the digestive system, as it is critical for the nourishment of the body, serving as the primary site of digestion and absorption of nutrients and water. It also serves as the first line of defense against ingested microbes and toxins by creating a barrier of entry into the body as well as an acidic environment in the upper intestine (eg, stomach pH approximately 1.5–2.0) to neutralize potentially harmful bacteria.

The digestive system is also inhabited by commensal microorganisms, particularly in the large intestine where the pH is higher (eg, 5.4-6.9), which have the potential to influence host physiology and impact the aging process. Although it has long been known that these microbes are capable of digesting food components that humans cannot, results from emerging research suggest these microbes and their functional potential may play an even larger role in host physiology and metabolism than previously considered. Although the line of investigation is still in its infancy, and studies in humans are limited, preclinical models have provided potential mechanistic insights into the ability of the microbiome to influence the aging process through impacts on barrier function, immune function, and cellular metabolism,[4] which will be discussed in more detail in later sections.

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The health of the digestive system is key to the health of the entire body, and it is therefore important to understand how the function and physiology of the digestive system change during aging. This can prove challenging with coexisting conditions associated with aging, such as chronic inflammation or medication use, which can have secondary effects on the digestive system, independent of aging. Furthermore, understanding the role of environmental and lifestyle factors, such as diet, may provide a way to modify the normal progression of aging to favor prolonged health.

Several reviews have been written on the impacts of diet and/or aging on various components within the digestive system, but few reviews examined the intersection of aging and diet on the digestive system as a whole. This review of reviews will discuss physiological and functional changes to the digestive system during healthy aging and the potential impact of diet on these changes.

Multiple factors, including comorbidities and medication use, can put older adults at risk of nutrient insufficiency through negative impacts on digestion and absorption.

Digestion and Absorption in Aging

Current evidence suggests nutrient digestion and absorption are well-maintained during healthy aging with possible small changes that may not be clinically significant (Table 1). However, comorbidities and medication use, common in the aging population, can negatively impact digestion and absorption, placing older adults at risk of nutrient insufficiency. The major factor impacting nutrient adequacy is the decline in food intake that naturally occurs during the aging process, frequently termed the "anorexia of aging."[5] Food intake begins to decline during the fourth decade, and studies suggest energy intake is 16% to 38% lower in healthy individuals in their 70s compared young adults.[6,7] The primary physiological mechanisms driving the reduction in intake are reduced energy requirements, as physical activity and resting metabolic rate decline, and an apparent increased response to inhibitory satiety signals.[5,7] For example, older individuals report greater satiety than younger individuals when provided the same preload.[8] Further, young people who are underfed develop hyperphagia that is not observed in underfed older individuals.[5] As aging progresses, diminished taste and smell reduce the enjoyment of food, further contributing to reduced intake. Poor dentition, swallowing difficulties, medications (including antidepressants and antineoplastics), and comorbidities, such as cancer or dementia, can exacerbate poor food intake in the elderly. Thus, adequate digestion and absorption are critical during aging as food intake declines.

Digestive secretions, such as gastric acids, pancreatic enzymes, and bile acids, do not appear to change substantially with healthy aging.[9–11] Imaging studies suggest the size of the pancreas begins to decline after age 60 years, but this is not necessarily associated with a decline in pancreatic function, particularly for healthy individuals.[10–12] There are also no known age-related impairments in bile acid secretion.[10]

However, comorbidities are more common in the aging population, such as cholelithiasis (gallstones), *Helicobacter pylori* infections, and medications, including proton pump inhibitors, can impact digestive secretions.

TABLE 1 Effects of the Normal Aging Process on Digestion, Absorption, and Gastrointestinal Motility

Gastrointestinal Function	Effect of Aging
Digestive secretions (eg, gastric acids, bile acids)	No change
Carbohydrate digestion and absorption	No change Possible lactase nonpersistence
Protein digestion and absorption	Possible decline in elderly
Lipid digestion and absorption	Possible small decline
Micronutrient digestion and absorption	No change
Esophageal motility	Decreased peristaltic contractility Relaxation of lower esophageal sphincter
Gastric motility	Possible slower gastric emptying
Small intestinal motility	Unchanged
Colonic motility	Possible longer transit time

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The prevalence of cholelithiasis in individuals older than 65 years is 15% to 25% and can lead to complications in bile acid release. Prolonged use of proton pump inhibitors for conditions such as gastroesophageal reflux disease (GERD) has been shown to lead to hypochlorhydria or achlorhydria, which can reduce the bioavailability of micronutrients, such as folic acid, iron, and vitamin B_{12}.[6,9,13] In fact, vitamin B_{12} malabsorption resulting from hypochlorhydria impacts up to 30% of older adults, and B vitamin insufficiency (B_{12} and folate) has been linked to increased risk of stroke and risk of fractures.[13] A reduction in gastric acid can also lead to small intestine bacterial overgrowth (SIBO) as the bacteria are allowed to pass into the small intestine and colonize. Small intestine bacterial overgrowth can further exacerbate vitamin B_{12} deficiency as the bacteria utilize vitamin B_{12}, leaving less for absorption.[14] Small intestine bacterial overgrowth is more prevalent in the elderly, particularly those in long-term care facilities, but even among healthy elderly in the United Kingdom, the prevalence was reported to be 14.5%.[9,13]

Macronutrient digestion and absorption remains fairly stable throughout the healthy aging process.

Absorption of macronutrients also seems to be well maintained during healthy aging. Carbohydrate digestion and absorption do not appear to be altered during aging, even into advanced age,[6] although the research in this area is outdated. While results from some studies have suggested a possible decline, it is unclear if this is truly a function of digestion and absorption or age-related declines in gastric emptying.[5,6]

Older individuals may experience impairments in lactose digestion due to a reduction in lactase activity, also known as lactase nonpersistence.[6,10,15,16] Lactase nonpersistence generally increases in adulthood and may also appear secondary to gastrointestinal infections that disrupt the gut barrier, yet not all individuals will experience digestive symptoms, such as bloating or flatulence, with consumption of lactose. In addition, many adults who self-report lactose intolerance show no evidence of lactose malabsorption when breath hydrogen is measured.[15,16] The amount of lactose consumed may also be important as one study that administered lactose based on body weight did not find a difference in digestive symptoms between young and old individuals with lactase nonpersistence.[16] Some studies have proposed that starch digestion is impaired in the elderly, but these studies have primarily used breath hydrogen tests, which can be influenced by undiagnosed SIBO in elderly subjects; thus, it is unclear if starch digestion is impaired in healthy aging.[6]

There is also little evidence of impaired protein digestion and absorption during the normal aging process. Older studies evaluated nitrogen excretion in the feces as an indirect measure of protein digestion and absorption, and at low to high intakes (0.4-1.6 g/kg per day), no age-related differences were observed.[6] More recent studies, using proteins with intrinsically labeled amino acids, have reported no difference in protein digestion and absorption in young (mean ± SEM, 23 ± 1 years) versus older (64 ± 1 years) men[17]; however, a similar study in elderly men (mean ± SEM, 75 ± 1 years) showed a decrease in protein digestion and absorption compared with young men.[18]

There is a decline in muscle protein synthesis with aging, and the prevalence of sarcopenia increases with age, which can contribute to falls, physical disabilities, and poor quality of life.[19] Thus, adequate dietary protein intake and exercise are critical for the maintenance of muscle mass in the aging population. However, most of the decline in muscle protein synthesis with aging is likely due to anabolic resistance (a lack of muscle protein synthesis even with stimuli such as dietary protein and exercise) rather than inadequate absorption of amino acids.[17] This is supported by data showing an increase in amino acid intake (and consequently absorption) or resistance exercise can improve the anabolic response to dietary protein in aging individuals.[20] Still more studies are needed to evaluate age-related changes in protein digestion and absorption, particularly in the elderly, and if this may contribute to an increased need for protein during aging.

Lipid digestion and absorption appear to be generally well preserved; however, some reports suggest a decline with aging.[6,11] Most studies on lipid absorption in older individuals are dated and used primarily indirect measures of fat absorption, such as fat-soluble vitamin absorption and fecal fat content. Studies analyzing fecal fat show no to small declines in fat absorption in older adults, whereas studies of fat-soluble vitamins show no impact on digestion and absorption, but potential issues with chylomicron clearance and lipoprotein metabolism that could impact vitamin status.[6] For example, older adults clear vitamin A–containing chylomicrons half as quickly as younger adults, suggesting impairments in chylomicron clearance or lipoprotein lipase activity.[21]

Similar to macronutrients, micronutrient absorption is resilient to the effects of age, with most micronutrient insufficiencies resulting from inadequate intake and concurrent diseases or comorbidities.[6,10,13] For example, vitamin B_{12} insufficiency is more frequent in aging individuals, but is primarily driven by hypochlorhydria or achlorhydria secondary to medications or competition from bacteria in SIBO.[6,10,11] Hypochlorhydria may also contribute to declines in mineral absorption, such as iron and calcium, which require acid to maintain these minerals in their most bioavailable form. For example, gastric acid helps keep iron in the ferrous form (Fe^{2+}), which is more bioavailable than the ferric form (Fe^{3+}). There is some evidence that calcium uptake in the intestine may decline with age, particularly

in individuals older than 75 years, but results in humans are inconsistent.[22] Vitamin D deficiency, also common in older individuals, may be due to decreased absorption, but researchers speculate it is likely a decrease in skin cholecalciferol production or reduced conversion that is a more likely factor.[22]

Current research suggests that concurrent disorders or medications may play a bigger role in decreased gastrointestinal motility and transit rate rather than the normal aging process.

Gastrointestinal Motility and Transit

It has long been considered that gastrointestinal motility and transit rate decline during the aging process, primarily because of the increasing prevalence of disorders, such as dysphagia, GERD, dyspepsia, and constipation. However, clinical evidence suggests concurrent disorders or medications may play a bigger role in this pathology than the normal aging process (Table 1).

In the upper intestine, evidence suggests that esophageal motility may be impaired with aging, but data are conflicting and depend on the outcome measured. A recent study in healthy adults ranging in age from 20 to 80 years showed no significant impact of age on total esophageal transit time for thickened foods (eg, nectar and pudding).[23] Others have also shown no differences in overall transit time, but a recent systematic review and meta-analysis showed the most common age-related changes were a decrease in peristaltic contractility in the distal esophagus as well as a reduction in the relaxation of the lower esophageal sphincter,[24] both of which would seem to contribute to GERD. Gastroesophageal reflux disease is more prevalent in the aging population, with estimates ranging from 15% to 40% of individuals 50 years or older.[9,25] However, a recent epidemiologic study in the United States revealed a significant increase in the prevalence of GERD in populations between 30 and 39 years of age, whereas the prevalence remained the same in older individuals.[26] Thus, although physiological changes during aging may contribute to GERD, it seems other factors beyond the normal aging process may also play a role in the development of GERD.

Gastric motility and small intestinal motility do not appear to be independently altered by age.[9,11,27,28] Although results from some studies suggest gastric emptying may be slower in older individuals, the data are conflicting and may depend on the composition of the meal or the methodology used to measure motility. For example, a high-fat meal has been shown to slow gastric emptying in older adults, but other studies with mixed meals or liquids have shown no difference in gastric emptying between healthy older and younger subjects.[9,11,28]

There have also been mixed results on the independent effects of aging on colonic transit, with some studies showing longer transit times in older individuals, whereas others show no significant changes.[9,27–29] However, several factors associated with aging, such as medication use (eg, opioids), low physical activity, and low dietary fiber intake, have been shown to slow transit.[9,27,29,30] These factors, as well as changes in anorectal physiology associated with aging, are proposed to be the primary reasons for increased prevalence of constipation in the aging population. Recent studies have also suggested neurodegenerative changes in the enteric nervous system may contribute to changes in intestinal motility in older individuals, but findings have been inconsistent, and more research is needed.[28,31,32] Endocrine disorders associated with aging, such as type 2 diabetes and hypothyroidism, have been shown to decrease gastric and intestinal motility, which may partially explain changes in gastrointestinal motility with age.[27]

Gut Microbiota Populations and Function

Although older studies evaluated the effects of aging on gastrointestinal digestion, absorption, and motility, recent studies have focused more often on changes to the gut microbiome with aging. Human microbiome research is a rapidly advancing field, and although many studies have evaluated changes in the microbiome with aging, there is still a lack of framework to determine how these changes are associated with overall health. For example, many studies and reviews discuss "age-related dysbiosis," yet there is no accepted characterization of healthy microbiota. Thus, determination of dysbiosis is often predicated upon assumptions of what characterizes a healthy microbiome. Furthermore, if microbiome changes are a result of the natural aging process or if the aging process causes changes in the gut microbiome is also unknown. Therefore, much more research is needed in this area before strong conclusions as to the effects of aging on the microbiome, or vice versa, can be reached.

It is becoming more evident that gut microbiota play an important role in human physiology. The gut microbiota can harvest energy from food components that our digestive enzymes are incapable of degrading, synthesize vitamins, and suppress the colonization of harmful bacteria.[33–36] The microbiota may also play a role in the development of gut immune function and maintenance of the gut barrier.[33,35,37] For example, in germ-free animals, there is a reduction of gut-associated immune cells and impairments in lymphoid structures, which are restored when the animals are treated with commensal microbes.[33] Results from studies suggest that the microbiome in early life is highly dynamic, but a core microbiome is established in childhood, which

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appears to remain stable, with possible subtle changes, into adulthood.[34,35,38] However, as aging continues, some, but not all, studies have shown a loss of microbiota stability, changes in the balance of microbiota populations, and increases in opportunistic pathogens.[4,33–35,37–39] Interestingly, this appears to be highly individualized and may be more related to physiological age than chronological age. Furthermore, geography may be an important factor as studies in different countries have reported different effects on the microbiota in aging individuals.[4,33]

The most frequent changes to the microbiota observed during aging include changes in composition and metabolic function and in the diversity of the microbiota. A recent systematic review evaluated 27 studies in humans that qualitatively compared changes in gut microbes and microbial functions between young and old individuals.[40] In some studies, older individuals could be separated into nonagenarians (90-99 years) and centenarians (100+ years) and "younger-old" adults (60-89 years), whereas young adults were typically 20 to 50 years of age. The authors evaluated changes in alpha diversity (within-sample), beta diversity (between-sample), microbiota composition, and microbial metabolic activity. They concluded that alpha diversity increases with aging; however, several authors reported no change in alpha diversity, and most of the studies finding a significant increase were comparing nonagenarians and centenarians to younger-old or young adults. Indeed, several other reviews have reported an increase in diversity in centenarians, and they are often considered a model of healthy, successful aging, whereas data in frail elderly tend to show a decline in alpha diversity.[38,41] Beta diversity results showed a more consistent difference between younger and older adults, although a few publications reported no significant difference.[40] Changes in microbial populations were less consistent because of differences in taxonomic levels examined between studies.

At the phylum level, several studies showed a decrease in *Firmicutes* and an increase in Proteobacteria in older individuals, but this was not consistent across all studies, and changes in *Firmicutes* appeared to be somewhat dependent on living conditions. At the genus level, more consistent results were observed, with most studies reporting an increase in *Akkermansia* and a decline in *Faecalibacterium* with aging. Increases in *Akkermansia* may be considered beneficial as certain species, such as *Akkermansia muciniphila*, have been associated with improvements in barrier function in animal models.[42]

However, *Faecalibacterium* are well-known producers of the short-chain fatty acid (SCFA), butyrate, an important energy source for the intestinal cells and with potential anti-inflammatory properties; thus, a decline with aging may not be desirable.[4,35] Unsurprisingly, the systematic review also reported a decreased capacity to produce SCFAs in older individuals. Two studies that evaluated centenarians reported an increased functional capacity to produce SCFAs, again suggesting that the oldest-old may be a representation of healthy, successful aging. One of the strengths of the review was the inclusion of studies using high-throughput sequencing methods, which have been shown to be more accurate than older sequencing methodologies.[35,39] However, an important limitation is the inclusion of studies with individuals having comorbidities and recent antibiotic use, which may alter microbiota and microbiota function independently from age. Accordingly, these findings may not be reflective of the natural aging process, but rather associated with comorbidities or medication use during aging. Furthermore, although data from centenarians appear promising for the study of healthy aging, it is unclear if these findings are due to the aging process or an indication of other healthy lifestyle factors, such as physical activity or a prudent diet.

Gut Permeability and Barrier Function

The intestinal tract is the first line of defense against pathogens and toxins encountered in the lumen, while also serving as the site of absorption of nutrients in the diet. Thus, there is a critical balance that must be maintained to ensure optimal nutrient absorption while preventing the translocation of pathogens and toxins. A loss of this balance can lead to an invasion of pathogenic bacteria and toxins across the epithelial barrier triggering an enhanced inflammatory response. Damage to the intestinal barrier has been linked to inflammatory bowel disease, celiac disease, and leaky gut.[34]

The gut barrier is composed of the intestinal epithelial cells and their intercellular junctions, which provide a physical barrier as well as limiting paracellular passage of large molecules (>20 kDa) and bacteria across the epithelial layer.[43–45] Within the epithelium, goblet cells secrete mucus, which forms an additional barrier between the luminal contents and epithelial cell surface. In addition to a physical barrier, the gut-associated lymphoid tissue provides an immune barrier to pathogens.[44,46] Paneth cells in the epithelial layer secrete antimicrobial compounds, and B cells in the lamina propria secrete immunoglobulin A (IgA), both of which prevent adhesion of pathogenic bacteria to the epithelial cells.[44] Emerging evidence suggests the commensal microbiota also play a critical role in the maintenance and health of the gastrointestinal barrier through nourishment of the epithelial cells and the generation of molecules that strengthen the epithelial barrier.[34]

Despite the importance of this barrier, there are relatively few studies in humans evaluating changes in intestinal permeability with aging. Studies in multiple animal models, including nonhuman primates, have shown an increase in intestinal permeability with aging (Table 2).[39,46,47] This may be partially due to intestinal stem cell exhaustion leading to an inability to repair damaged tissue, thus increasing permeability.[45,48] Investigations in nonhuman primates have shown reduced expression of proteins critical for intercellular tight junctions, such as zonulin and occludin, and an increased permeability to larger

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molecules in older animals.[47] However, studies in humans have shown no changes in the expression of these proteins or changes in permeability to large molecules with age.[43,47,49]

An interesting study in mice showed that aging may also impair the ability to recover from a disruption in the intestinal barrier. Young mice were able to recover quickly from an insult to the gastrointestinal barrier, but aged mice did not recover and developed sepsis from bacterial translocation.[49] The inability to repair the intestinal barrier has been linked to inflammatory bowel disease, leaky gut, and celiac disease. The effect of aging on restoration of the intestinal barrier has not been evaluated in humans.

Changes in the thickness of the mucus layer do not seem to occur in older adults, but this has been evaluated only in the small intestine.[47] Similarly, rodent models have shown a small increase in the number of goblet cells in the ileum of aged mice, suggesting an increase in mucus production with age. However, in rodent models of accelerated aging, old animals have been shown to have a thinner colonic mucus layer compared with younger animals.[47] Whether these changes also occur in the human colonic mucus layer has not been confirmed.[39]

Alterations to the secretion of antimicrobial compounds and IgA with aging have also not been well-characterized in humans but have been studied in animal models. Some studies in rodents and nonhuman primates have shown a decline in intestinal IgA with aging in response to an antigen challenge, but other studies have shown no change and even an increase in IgA.[46,47] Rodent models have also shown mixed effects for antimicrobial compounds with a decline in the expression of some proteins, whereas others are increased.[47] Interestingly, studies in germ-free mice have shown an alteration in the maturation of the gut-associated lymphoid tissue with significantly fewer IgA-secreting B cells, suggesting the microbiota may play a critical role in the development and stimulation of immune defenses in the intestine.[50,51] Thus, if there are changes to the intestinal barrier with aging, it may be a consequence of changes in the gut microbiota. However, the directionality of a potential causal relationship may be difficult to tease out in humans.

As noted previously, changes in the intestinal microbiome may occur during aging, and several researchers have suggested that these changes can have a substantial impact on gut barrier function.[4,39,46,51] For example, animal studies have shown the SCFA, butyrate, to reduce paracellular permeability by enhancement of tight junctions, and in vitro studies suggest butyrate can induce the production of mucus by goblet cells and regulate T-cell differentiation.[34,38,44,50,51] Yet, several studies in humans have shown *Faecalibacterium* and other butyrate-producing bacteria to decline with aging.[4,35,40,51] Therefore, it can be hypothesized that a reduction in these bacteria with aging may lead to an increase in gut permeability. In addition, an increase in certain Proteobacteria during aging[40] may lead to an increase in lipopolysaccharide production, which can trigger the expression of inflammatory cytokines in the intestine.[34,51]

Currently, some of the best evidence for the impact of the gut microbiota on barrier function during aging comes from germ-free rodent models. When young, germ-free mice are housed with aged conventional mice, they develop an increase in intestinal permeability and inflammation, which is not seen when cohoused with young mice.[34] Similar results were reported when young germ-free mice were transplanted with microbiota from aged mice.[4] Furthermore, young, germ-free mice transplanted with microbiota from aged mice sometimes show a decline in butyrate and other SCFA production,[52] although this has not been shown consistently.[53] However, these results should be interpreted with caution, and some researchers have advised against overextrapolation of animal data to infer causality.[54]

Further research in humans is needed to confirm changes in intestinal barrier permeability and function seen in animal models.

TABLE 2 Effects of Aging on the Intestinal Barrier in Preclinical Models

Components of the Intestinal Barrier	Effects of Aging in Preclinical Models	Confirmed in Humans
Epithelial cells and intercellular junctions	Increase in paracellular permeability	No
	Reduced expression of tight junction proteins	No
Mucosal layer	Uncertain	No
Antimicrobial compounds and immunoglobulin A	Uncertain	No
Commensal microbiota	Butyrate increases tight junctions	No
	Declines in butyrate-producing bacteria	Yes

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Potential Impact of Diet on Digestive Changes With Aging

As previously discussed, lifestyle factors, such as diet, can play a role in digestive health, so several studies have focused on dietary patterns and components that promote the health of the intestine. This includes plant-based, high-fiber diets, as well as probiotics and prebiotics, targeting the health of the large intestine. Emerging research on plant polyphenols suggests these compounds may also contribute to the health of the intestine.[55]

Dietary fiber and fiber supplements are often the first line of treatment for older individuals experiencing a decline in stool frequency or constipation. Several systematic reviews and meta-analyses have shown certain dietary fibers, such as cereal fibers, beta-fructans, and vegetable fibers, to be moderately effective in the treatment of chronic constipation and to also improve stool frequency and transit time in individuals experiencing slower than normal transit times.[56–60] However, when the etiology of constipation is due to medications or changes in anorectal physiology, there is less likely to be a benefit of fiber. Medications, such as anticholinergics or opioids, reduce peristalsis and colonic propulsion, which is unlikely to be changed by the addition of bulk with fiber.[27,29] In these cases, it is preferred to change the medication, if possible. Changes in anorectal physiology, such as impaired rectal sensation and decreased rectal compliance, are not a result of impaired transit and thus unlikely to be changed with fiber intake.[9,27,29] Some probiotics have also been evaluated for their ability to improve laxation and treat constipation. A systematic review reported probiotics were efficacious for the treatment of constipation in elderly individuals, but the review included only four randomized controlled trials and five observational studies, which varied greatly in populations, probiotic strain, study duration, and study quality, so additional clinical trials are needed on specific probiotics in older populations.[61]

More recent research has evaluated the role of diet on gut microbiota composition and metabolism, as well as the impact to barrier integrity and inflammation. Plant-based diets, particularly a Mediterranean diet pattern, have received considerable attention as studies have shown a reduced risk of chronic diseases and conditions, such as cancer, metabolic syndrome, and cardiovascular disease, and improvements in associated risk factors.[62–64] Because plant-based diets are typically higher in dietary fiber, a major nutrient source for the gut microbes, some have hypothesized that the benefits of plant-based diets may be mediated through changes in the microbiome and impacts on inflammation.[63,65,66] Yet, only a few studies have evaluated this hypothesis. Although initial study results are promising, showing an increase in butyrate-producing bacteria, such as *Faecalibacterium prausnitzii* and *Roseburia*, and increases in fecal SCFAs,[67–72] not all studies with plant-based diets show a change in the microbiota.[70,73]

Furthermore, few studies have evaluated the effects of a plant-based diet in older adults[71,72]; thus, further investigations in this population are needed. Studies on dietary fiber interventions, rather than a plant-based diet per se, are more numerous and show an increase in certain beneficial bacteria and fecal butyrate levels.[74,75] However, most of these studies are on isolated fructans and oligosaccharides (also considered prebiotics); thus, these results may not apply to a diet rich in a variety of fibers from multiple food sources. Dietary polyphenols, contained in a variety of plant foods, may be able to influence the gut microbiota. Findings from recent systematic reviews and clinical trials suggest polyphenols, such as anthocyanins, proanthocyanins, catechins, and isoflavones, may act as prebiotics by selectively stimulating the growth of beneficial microbes and increasing the production of SCFAs.[55,76]

Although most of the work is preclinical, at least one clinical study reported a polyphenol-rich diet (approximately 750 mg polyphenols per day from foods such as blueberries, pomegranate, green tea, and dark chocolate) for 8 weeks, compared with a normal diet, with half the polyphenol content, was able to increase butyrate-producing bacteria and reduce serum zonulin (an indirect marker of intestinal permeability) in elderly individuals diagnosed with "leaky gut" as determined by elevated serum zonulin levels.[76]

Fewer dietary studies have specifically targeted changes in intestinal permeability, choosing more often to focus on changes in microbiota. However, some authors have suggested high-fat or Western-style diets may contribute to a decline in gut barrier function by disrupting tight junctions, generating proinflammatory cytokines, and promoting microbiota that degrade the mucus barrier.[77,78] Although most of the evidence is in *in vitro* and animal models, some studies in humans have shown elevations in gut-derived lipopolysaccharide in the serum during high-fat diets, compared with low-fat diets, indicative of an increase in intestinal permeability.[78] More research is needed in this area, particularly on diets and dietary components that may enhance the intestinal barrier. In addition, studies comparing older and younger individuals are needed to determine the interaction of diet and aging on intestinal permeability.

While a plant-based, high-fiber diet, and the addition of polyphenols, prebiotics, and probiotics may have beneficial health effects, further research in humans is needed to confirm the effect of these dietary factors on the gut microbiota and intestinal permeability.

CONCLUSIONS

As advances in medicine have enabled people to live longer, it is now critical for research to focus on extending the quality and not only the length of life. To do this, it is imperative to distinguish between the physiological effects of aging and senescence and the pathological effects associated with chronic disease, lifestyle factors, or medications. Surprisingly, relatively little is known about the independent effects of aging on gastrointestinal function. However, existing evidence suggests the functions of the digestive system are incredibly resilient to the aging process, and age-related changes are more likely subtle, whereas changes due to lifestyle factors, comorbidities, and medications are likely responsible for most of the digestive issues experienced in the aging population. Thus, digestive health may be a good barometer for overall health during aging. Emerging research on the gut microbiome and barrier function may yield important insights into the etiology of many age-related diseases and enable better understanding of how diet may be able to promote healthy aging and avoid or minimize the effects of chronic disease. Furthermore, studies of gastrointestinal function in healthy individuals of advanced age (eg, centenarians) may provide insight into the healthy aging process as well as lifestyle factors that could contribute to improved quality of life.

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