BRITISH JOURNAL OF HOSPITAL MEDICINE

REVIEW

The Ageing of the Human Lower Bowel

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Abstract

Older people suffer a greater number of disorders of the gastrointestinal tract, including chronic constipation and faecal incontinence. In this review, we examine the age-related degenerative changes that have been identified in the lower bowel of humans. Firstly, older individuals may experience less abdominal pain and a lower incidence of gut-brain disorders that are defined partly by abdominal pain (e.g., irritable bowel syndrome); the causes are unclear. Secondly, an age-dependent reduction in mucosal barrier functions may follow a decline in intestinal stem cell activity, a reduced density of tight junction proteins linking epithelial cells and a decline in mucus layer thickness. This allows antigenic and toxic material to enter the wall of the colon. Thirdly, degenerative changes within the wall of the colon occur in both the ascending and descending regions, but the ascending colon appears most vulnerable. Here, there is reduced cholinergic neuromuscular function (potentially reducing colonic motility), perhaps because of dysfunctional nerve axon transport, and associated senescence-like activity. These changes lower the 'intestinal reserve', that is the capacity of neuromuscular functions to absorb other 'life events' that affect bowel motility (e.g., changes in lifestyle or eating habits, medications that affect neuromuscular functions and diseases such as diverticulosis) without generating symptoms such as constipation. When combined, symptoms are more likely to develop.

Key words: ageing; human colon; nociception; mucosal barrier; enteric nervous system; senescence; inflammageing; microbiome

Submitted: 9 October 2024 Revised: 7 November 2024 Accepted: 29 November 2024

Introduction

Cellular, tissue and physiological functions decline over time, and as a result, we experience bodily disorders as we grow old. This includes disorders of the gastrointestinal tract (Goldberg and Jhurani, 2020). For example, older people within the community may experience chronic constipation, with an estimated prevalence of 7% to more than 42% (e.g., Vazquez Roque and Bouras, 2015), rising to over 50% within nursing homes (Tariq, 2007). Faecal incontinence is more common and may encourage institutionalisation. If constipation is poorly treated, older patients develop a significant risk of faecal impaction, which affects nearly 50% of this population (Rey et al, 2014), reducing the quality of life and the ability to live independently (Wald et al, 2007). However, older people also experience less abdominal pain (e.g., Beckers et al, 2021) and may have a smaller incidence of certain gut-brain disorders, including irritable bowel syndrome, dyspepsia and functional constipation (Sperber et al, 2022).

How to cite this article:
Baidoo N, Sanger GJ. The Ageing of the Human Lower Bowel. Br J Hosp Med. 2025. https://doi.org/10.12968/hmed.2024.0734

To understand these clinical observations and what happens to lower bowel functions as we grow older, we examine the age-related degenerative changes that have been identified in human cells and tissues within the colon. The concept of 'intestinal reserve' is introduced. This hypothesises that despite an age-dependent decline in cellular and acellular functions of the intestine, for many people there remains sufficient cellular and tissue reserve capacity to allow the bowel to function in an approximately normal manner. However, if bowel functions are further reduced by 'life events', then because of the smaller reserve capacity, these individuals are now more likely to experience symptoms such as those described briefly above. Examples of 'life events' include disease, changes in diet and exercise, and increasing use of medications affecting bowel functions.

Degenerative Changes in the Colon

This region of the intestine has been most often used when investigating how ageing affects the structures and functions of the human large bowel, comparing older and younger adults (e.g., Gomes et al, 1997; Hanani et al, 2004; Bernard et al, 2009; Hetz et al, 2014; Broad et al, 2019). The former are usually aged around 65–70 years and above. Here, changes across the broader lifespan are not included, to avoid confusion between ageing among adults and the developmental changes of juveniles and children. In addition, and where possible, the different regions of colon are considered separately, because they have distinct and separate functions, blood supplies, extrinsic innervation, gene expression and embryonic origin (de Santa Barbara et al, 2003; Glebov et al, 2003).

Before discussing the mechanisms of change with ageing, we describe the changes that have been identified for different cell types within the human colon, including those playing key roles in functions of the mucosa/submucosa and the neuromuscular layers, the enteric glial cells and transmission of visceral pain. Fig. 1 provides a summary of changes in structures and functions within the human colon.

Mucosal and Submucosal Functions

The Mucosal Barrier

This prevents leakage of solutes from the lumen through the paracellular spaces, including bacterial toxins (and perhaps the bacteria themselves), the products of digested food and any undigested food material, while still allowing nutrients, electrolytes and water to be absorbed from the lumen and into the blood circulation. Major players in mucosal barrier function include the epithelial layer of the intestine and the adhering mucus layer, in addition to the presence of antimicrobial peptides and the immune system of the mucosa (Branca et al, 2019).

The epithelial cell layer is maintained by continual replenishment of the epithelial cells by intestinal stem cells and by tight junction proteins (TJPs). The latter facilitates epithelial cell-to-cell adhesion and thereby limits paracellular transport between the cells (they include the Junctional Adhesion Molecule-A (JAM-A), occludin and Zonula Occludens-1 (ZO-1)), whereas others (e.g., claudin-2) have the ability to form small cation-permeable pores (Horowitz et al, 2023). During age-

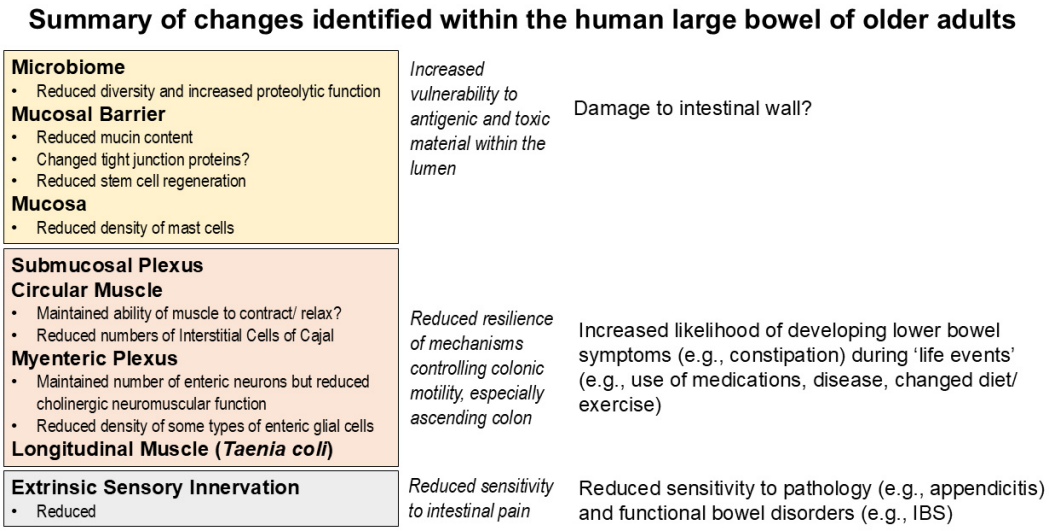

Fig. 1. Extrapolation of the known changes in structures and functions of the adult human intestine during natural ageing, to the potential physiological and clinical consequences. Changes have been identified in the microbiome diversity, as well as specific key cellular structures within the mucosa, submucosa, and muscularis externa of the intestinal wall. Additionally, older individuals exhibit diminished sensitivity to intestinal pain, attributed to a reduction in extrinsic sensory innervation. IBS, irritable bowel syndrome.

ing there is evidence for a decline in the capacity of the stem cells to regenerate epithelial cells (Nalapareddy et al, 2022) and among older adults, TJPs can break down (Kelly et al, 2015). For the human colon, an immunohistochemistry study found a significantly reduced density of JAM-A, occludin, ZO-1 within the mucosal epithelial layer of the ascending colon from older individuals, along with an increased density of claudin-2 (30–52 years vs. 70–89 years, n = 6 and 12, respectively; Baidoo, Dahiri & Sanger, unpublished observations). Another study used biopsies from the transverse colon of baboons using an immunohistochemistry approach and found that the older animals exhibited significant decreases in densities of JAM-A, occludin and ZO-1, in comparison with younger baboons. The authors linked these changes to increased mucosal permeability (4–10 years = young; 18+ years = old; n = 10 each; Tran and Greenwood-Van Meerveld, 2013). Finally, in biopsies from the human terminal ileum a decrease in transepithelial electric resistance was recorded for the older individuals (67–77 years, n = 32; compared with younger adults aged 20–40 years, n = 31), implying reduced integrity of the epithelia; permeability to macromolecules was unchanged. The authors also found elevated expression of IL-6, but no differences in mRNA expression of JAM-A, occludin and ZO-1 (Man et al, 2015).

The mucosal barrier is also maintained by the mucus layer, formed by mucin secreted by the goblet cells in the epithelial layer. In both the ascending and descending colon of older people, the density of mucin (measured per mucosal area) was smaller compared to younger adults (Baidoo and Sanger, 2024a). Interestingly, this reduction was not accompanied by a similar reduction in the numbers of goblet cells per mucosal area (although several empty mucin-vesicles could be identified) suggesting a loss of ability to synthesise mucin.

In conclusion, the evidence points to some loss of mucosal barrier integrity within the intestine of older people, but the mechanisms, the degree of loss and the possibility of region-dependency remain unclear.

Secretory Functions

A large study (n = 435 patients, using Ussing chamber and immunohistochemistry techniques) found an absence of age-related changes in small and large intestinal mucosal epithelial secretory functions; this included the basal resistance and short-circuit current, in addition to the current that was evoked by neuronal stimulation of the epithelia (Krueger et al, 2016). Another study on the submucosal plexus (Bernard et al, 2009) reported no changes in the numbers of nerve cell bodies (n = 16; 33–99 years).

Collagen

Using histochemical and biochemical methods, on ageing human ascending colon samples, Baidoo and Sanger (2024b) found that the total amount of collagen within the mucosa was comparable with younger adults; this was argued to be consistent with the absence of marked inflammation within the mucosa of the older people.

Mast and Enterochromaffin Cells

The density of mast cells (as assessed by tinctorial and immunohistochemistry methods) in the mucosa of the human distal ileum and the ascending colon was shown to be increased among older adults. In addition, the number of enterochromaffin cells was increased in the terminal ileum, but not in the colon (n = 59 patients; 24–88 years; Yu et al, 2016). In older adults, mast cells were more often found closely aligned to the extrinsic nerve terminals embedded within the mucosa, suggested by the authors to represent a possible mechanism by which sensory neurodegeneration could be at least partly compensated by greater access to the products of mast cells (see below; Yu et al, 2016). By contrast, in forty subjects (n = 20 below and n = 20 above 55 years), mast cell counts within rectal biopsies were smaller in older individuals, with the enteroendocrine cell numbers (containing 5-hydroxytryptamine and peptide YY) remaining unchanged (Dunlop et al, 2004).

Neuromuscular Functions

Smooth Muscle

An increase in the presence of collagen (e.g., Baidoo and Sanger, 2024b) is likely to increase muscle ‘stiffness’ and for at least some people, this may reflect diverticulosis that has not developed as diverticulitis. However, for others the consequences of increased collagen on the ability of the smooth muscle to relax or contract are unclear. For example, in circular muscle preparations from the ascending and descending colon of patients without diagnosis of diverticulitis, there were no differences between the older and younger adults in terms of the tension generated by the muscle when contracting and relaxing (Broad et al, 2019; Baidoo and Sanger, 2024b).

Interstitial Cells of Cajal

Movements of the smooth muscle of the intestine are orchestrated, facilitated and directly controlled by interstitial cells of Cajal (ICCs), working together with the enteric and extrinsic nervous systems (Huizinga et al, 2021). These specialised cells exist as groups of connected cells (syncytia) and are found in association with the myenteric and submuscular plexus, within the longitudinal and circular muscle and the sub-serosa (Rumessen, 1994). They interact with platelet-derived growth factor receptor-positive fibroblast-like cells, the fibroblasts, and glial cells, in addition to enteric and extrinsic neurons. In the colon, ICCs depolarise spontaneously and/or in response to neuronal stimulation. This generates slow waves of electrical activity which because of the syncytial organisation propagates around and along the length of the colon at frequencies which differ according to whether the depolarisation is spontaneous or neuronally evoked (Sanders et al, 2023). The electrical activity is transmitted to the smooth muscle via gap junctions, influencing the patterns of muscle contractions by facilitating action potential generation in response to neuronal stimulation. Thus, the ICCs are 'pacemaker cells', helping to orchestrate the propulsive, segmental and retropulsive movements of the large bowel caused by enteric and extrinsic neurons (Huizinga et al, 2021).

In the adult colon, increasing age has been found to reduce the number of ICCs and their network volume in the myenteric plexus and also the circular muscle (n = 23; 36–92 years; Gomez-Pinilla et al, 2011). It was speculated by the authors that this decline might have occurred because of increased oxidative stress leading to cellular apoptosis, together with a reduced ability of intestinal stem cells to replenish the ICCs. The consequences are unclear. It is not known, for example, if any loss of ICCs—in a uniform or 'ectopic' manner—will have an immediate impact on the generation of symptoms or if the colon can tolerate some loss of ICCs before symptoms develop (see later for a discussion on 'functional reserve').

Myenteric Neurons

The myenteric plexus is part of the enteric nervous system (ENS), where the cell bodies are located between the outer longitudinal muscle and the inner circular muscle. It contains many ganglia which are found in the enteric nerve cell bodies. These can be interneurons, motor neurons (largely projecting to the muscle) and intrinsic primary afferent neurons (Furness, 2012). The latter function as sensory neurones, with dendrites projecting into the mucosa that are mechanosensitive and chemosensitive (e.g., responding to substances released by mucosal endocrine cells). Responses are then elicited by other dendrites which project from the cell body to enteric inter- and motor-neurons (see Wade, 2002).

Compared with younger adults, both the ascending and descending colon of older people have similar numbers of myenteric ganglia (although a number of ganglia have been observed by some authors to contain empty spaces), nerve cell bodies, volume of neuronal structures within the myenteric plexus, and volume of nerve fibres within the musculature. Broad et al (2019) have conducted the largest

study yet, and in addition, they discussed other, smaller studies. Thus, ageing does not appear to affect the number of myenteric neurons or the total penetration of nerve terminals into the muscle.

Neurons of the ENS have different neurotransmitters. The dominant myenteric motor neurons are nitrergic, causing muscle relaxation by releasing nitric oxide, and also cholinergic, which release acetylcholine (ACh) to cause muscle contraction. For the human colon of adults, ageing does not appear to change the numbers of inhibitory nitrergic neurons, and in addition, changes in different peptide neurotransmitters have not been observed (vasoactive intestinal peptide, substance P, met-enkephalin, neuropeptide Y, somatostatin) (see Baidoo and Sanger (2024b), for discussion and references). However, age-related changes are reported for the cholinergic neurons. Thus, in the ascending colon of older adults, cholinergic neurons have been shown to have a reduced ability to cause muscle contraction; interestingly a similar loss of function was not found for the descending colon (Broad et al, 2019). The authors hypothesised that the decline in function was caused by a compromised ability of cholinergic neurons to transport a key enzyme, choline acetyltransferase (ChAT), from the nerve cell body to its nerve terminals. There it catalyses the formation of ACh from choline and acetyl-CoA (acetyl coenzyme A). Such changes have previously been seen in other neurodegenerative disorders, with reduced cholinergic functions. Finally, and perhaps consistent with a region-dependent reduction in enteric cholinergic function with increasing age, other work suggests that the ascending colon becomes more susceptible to stool retention. Thus, Gau et al (2022) found that a majority (52.1%) of older adults (65+ years; n = 120) had high faecal load scores in ascending colon (interpreted as significant retention of faeces), with the transverse and descending colon and rectosigmoid area containing approximately equal amounts of the remainder.

Enteric Glial Cells (EGCs)

Enteric glial cells (EGCs) have an important role to play in the provision of metabolic, structural, and trophic support to enteric neurons (Rodrigues et al, 2011). Additionally, they are involved in neurotransmission and hence, help regulate gastrointestinal motility (Grubišić et al, 2018). EGCs also provide immunological support and possess the potential to differentiate into new neurons (Guyer et al, 2023). These cells are strategically located, surrounding myenteric and submucosal nerve cell bodies and nerve processes, residing within muscle layers and the mucosa, and interacting with both enteroendocrine cells and the epithelial layer. This multifaceted involvement underscores the essential functions of EGCs in maintaining gastrointestinal health and function. Loss of EGCs have been associated with enteric neurodegenerative disorders and neuroplasticity (see Seguella and Gulbransen, 2021).

There are no pan-glial cell markers for EGCs. Nevertheless, within myenteric ganglia and the circular muscle of adult human colon, an age-dependent loss in density has been shown for EGCs expressing one marker (the S100 calcium binding

protein β; Baidoo et al, 2023). The functional consequences are unclear but trophic support may be unlikely since the overall numbers of enteric neurons are largely maintained in the colon of older people.

Reduced Sensitivity to Visceral Pain

This has been demonstrated in the healthy older individuals (n = 12; 70–94 years) by means of balloon distention in the rectum (Lagier et al, 1999), by consumption of a standard enteral feeding solution, in which sensitivity to both pain and nausea were less among the older subjects (Gururatsakul et al, 2010), and in a reduced occurrence of abdominal pain among older people (e.g., Beckers et al, 2021). The latter includes a lower occurrence of irritable bowel syndrome (IBS; characterised by abdominal pain with diarrhoea and/or constipation, without organic cause) among older people. Further, a quality-of-life study on IBS patients found that those aged over 65 years experienced milder pain before they consulted clinicians when compared to younger adults (Tang et al, 2012). Perhaps a downside is a reduced ability to sense pain during appendicitis, reducing the urgency of seeking medical care (Cibert-Goton et al, 2020; Beckers et al, 2021).

Studies with adult human isolated ascending and descending/sigmoid colon have demonstrated a reduced response of the extrinsic afferent innervation to noxious chemical stimulation among older individuals. This reduced sensitivity may, at least partly be caused by loss of sensory afferent innervation (Yu et al, 2016; Cibert-Goton et al, 2020). In addition, responses to noxious mechanical stimuli are reduced in aged mice (Cibert-Goton et al, 2020). Consistent with these observations, sigmoid colon biopsies showed reduced immunoreactivity for ion channels expressed by extrinsic neurons, namely the transient receptor potential ankyrin-1 (TRPA1) and vanilloid-1 ligand-gated channels, together with reduced *TRPA1* gene expression within older people compared with younger adults (Beckers et al, 2021). To more fully understand the consequences of age-dependent degeneration on human visceral pain (and perhaps an ability to sense the need for defecation), similar experiments must now be conducted and extended to study human pelvic afferent nerves.

Mechanisms of Damage

Inflammageing

During advancing age many tissues exhibit ‘inflammageing’ or persistent low-level inflammation. This includes the gastrointestinal tract (Franceschi et al, 2000). Inflammaging may involve the actions of, for example, interleukin (IL)-6, IL-1β, and tumor necrosis factor alpha (TNFα) (Tylutka et al, 2024), potentially affecting immune and neuronal functions. One hypothesis is that macrophages are continually stimulated because of ‘molecular waste’ during ageing (from dead/damaged cells and organelles), leading to inflammation.

Oxidative Stress and Senescence

During advanced ageing, inflammation can be exacerbated by reduced autophagy, reduced mitophagy and increased oxidative stress (Liguori et al, 2018). Combined, this can lead to senescence. In cells, the latter is characterised by an exit from the cell cycle and the development of a senescence-associated secretory phenotype, or the generation of proinflammatory cytokines and other agents. Normally, the immune system rapidly clears senescent cells, but with increasing age this may become less efficient. Consequently, the senescence becomes chronic and continues to generate pro-inflammatory molecules, further contributing to inflammageing (Bhatia-Dey et al, 2016). Recently, a molecular and immunohistochemistry study found an increased presence of the cell cycle regulator and chronic senescence marker, p16, within the cytoplasm of myenteric neurons of ascending, but not the descending colon of older adults (Palmer et al, 2021). Interestingly, a reduced cholinergic function in the same region of the colon from older adults (Broad et al, 2019; see above) suggests a linked mechanism. Nevertheless, the findings were surprising. Thus, enteric neurons are post-mitotic (unlike proliferative glial cells, for example). Further, p16 (a regulator of the cell cycle) is not usually present in the cell cytoplasm but in the nucleus. Nevertheless, these apparent anomalies have been noted for other cell types. At present, it is necessary to define such changes as 'senescence-like'.

The Microbiome and Mucosal Permeability: A Key Weakness?

The ascending and descending colons differ in their composition of microbiota (Biagi et al, 2010). Further, a reduced diversity of microbiota species and phyla has been found within older individuals. For example, a small genomic study with faecal samples from centenarians demonstrated a loss of genes for the bacteria which help generate short-chain fatty acids (SCFAs) by fermenting polysaccharides eaten as part of our diet (Rampelli et al, 2013). SCFAs are a source of energy for both the microbiota and the epithelial cells lining the intestine, with additional regulatory and signalling functions (e.g., anti-inflammatory activity, ability to enhance intestinal barrier integrity and increased mucin production by goblet cells). Consequently, reduced SCFAs can promote gut inflammation and possibly compromise the integrity of the mucosal barrier.

Rampelli et al (2013) also found that proteolytic functions of the intestinal metagenome were more abundant than in younger adults. Thus, the aged-type microbiota had moved from a saccharolytic to a putrefactive metabolism. These changes coincided with the enrichment of genes belonging to pathobionts or minor microbiota opportunists which thrive in inflamed conditions, sustaining the inflammation and potentially worsening the health status of older people. Other changes included an age-dependent increase in the abundance of genes involved in tryptophan metabolism, generating the hypothesis that increased 'consumption' of tryptophan by the gut microbiota may affect its bioavailability and perhaps, a role in inflammatory immune and cognitive disorders (Reyes Ocampo et al, 2014).

Functional Reserve and Disruptive Life Events

Some studies have found an age-related reduction in the motility patterns of the small and large intestines. These include the contractile activity of isolated tissues, the migrating motor complex, the rates of colonic and rectosigmoid transit and prolonged small intestine and oro-caecum transit times (Anuras and Sutherland, 1984; Pilotto et al, 1995; Graff et al, 2001; Firth and Prather, 2002; Madsen and Graff, 2004). However, many others have found that the motility of the intestine is largely unchanged during normal adult working lives (Fich et al, 1989), including healthy older people (Loening-Baucke and Anuras, 1984; Loening-Baucke and Anuras, 1985). In addition, rectal sensitivity to mechanical distension may be either unchanged or in other studies impaired but without a change in muscle tone or compliance (see Madsen and Graff, 2004; Baidoo and Sanger, 2024b, for references). Thus, the greater prevalence of lower bowel disorders among older people, such as chronic constipation, does not appear to be matched by clear and consistent disruptions of physiological functions of the bowel in healthy-aged individuals. Conversely, age-related degenerative changes in cellular structures and functions are usually identified in 'macroscopically normal' colon (often from patients with non-obstructive bowel cancer without a diagnosis of chronic constipation; Broad et al, 2019). How then, can these apparently conflicting observations be reconciled?

In laboratory animals, the ENS is thought to have a high reserve capacity (Wade, 2002). This means that some degeneration can be tolerated without necessarily causing symptoms. The human ENS and perhaps other cellular systems of the gastrointestinal tract are also hypothesised to possess a high functional reserve (Camilleri et al, 2000; Gomez-Pinilla et al, 2011; Broad et al, 2019). Table 1 illustrates this concept and provides illustrative examples. These suggest that the bowel, and its gross physiological functions may be largely maintained during ageing even though there is a decline in cellular functions, unless impacted by a secondary disorder. When combined, a 'tipping point' is reached and symptoms develop. Additional secondary factors may include the use of medications by the elderly, such as opioid receptor agonists (for pain relief), antagonists at muscarinic ACh and other receptors affecting bowel functions (e.g., antidepressants), and inhibitors of Cav1 voltage-gated calcium channels (for high blood pressure). Each drug class, and others, can potentially disrupt GI motility and/or extrinsic afferent nerve sensitivity. Among the elderly, constipation may also be associated with disease (e.g., long-term survival from colorectal or anal carcinoma, clinical depression, hypothyroidism), and altered lifestyle (e.g., impaired mobility and reduced calorie and fluid intake) (Baidoo and Sanger, 2024b).

Future Perspectives

Further studies are now warranted to elucidate the underlying biological mechanisms driving age-related alterations in the colonic wall, including the role of inflammation, changes in gut microbiota, and the molecular pathways involved. An example of the latter may be the need to examine for age-related epigenetic changes in key genes involved in bowel functions, potentially increasing the probability of

Table 1. The intestinal reserve.

What is it?	The human enteric nervous system (ENS) is estimated to contain 200–600 million neurons. It is thought that the ENS can tolerate some loss of functions or reduced numbers of neurons without generating symptoms.
What is unclear?	Is there a reserve capacity for other cell types within the wall of the large bowel (e.g., interstitial cells of Cajal, smooth muscle with collagen), including the mucosa, and also for extrinsic nerve mechanosensitive, chemosensitive, or nociceptive functions?
What might this mean for older people?	A reduced functional reserve lowers the tolerance to other factors which reduce intestinal functions and which are more common among older people (e.g., use of medications, occurrence of disease), increasing the likelihood that symptoms such as constipation will develop.
Suggested clinical examples	• A small loss of innervation of anal sphincter musculature during increasing ageing may reduce its functional reserve, increasing the likelihood that incontinence occurs when there is also loose stool or depressed cerebral function (Percy et al, 1982). • Long-term complications following childbirth may become more apparent following age-related changes in how the functions of the anal sphincter are modulated by the pudendal nerve (Ryhammer et al, 1997). • A reduced mucosal barrier (increased intestinal permeability) among older people may only have clinical significance when compromised by type-2 diabetes or other 'minor disease' (Valentini et al, 2014).

developing cancer or other disorders (e.g., Horii et al, 2008). Additionally, conducting longitudinal studies on potentially diverse populations (e.g., race, ethnicity, etc.) can provide insights into how age-related changes in colonic function progress over time, as well as the factors influencing variations within different demographic groups. Research into dietary interventions, probiotics, and prebiotics could be explored to determine their efficacy in ameliorating the effects of ageing on colon function. Further, identifying specific dietary components that promote the health of the colonic environment could have significant implications. For example, caloric restriction prevents neuronal loss (Pereira et al, 2014; Mari et al, 2018) whereas a high-fat diet may decrease acetylcholine synthesis and increase oxidative stress (Almeida et al, 2022). Other future research may focus on developing pharmacological therapies aimed at modulating inflammation or enhancing mucosal barrier function to mitigate the adverse effects of ageing of the intestine. Investigating multidisciplinary approaches that incorporate lifestyle modifications, physical activity, and stress management techniques could be vital in enhancing the quality of life and colon health for older adults.

Interestingly, an analysis of gut-brain disorders among the elderly highlighted a decline in the occurrence of irritable bowel syndrome, functional dyspepsia and functional constipation (Sperber et al, 2022). To some extent, this may be explained by an age-dependent fall in sensitivity to visceral pain (a major symptom for patients with irritable bowel syndrome, for example). However, the decline in num-

ber of patients with functional constipation appears to conflict with the increased occurrence of chronic constipation among older people. Perhaps, the mismatch is explained by differences between constipation that is 'functional' and that which is caused by degenerative changes. Further work is needed to clarify these differences.

Conclusion

In summary, the degenerative changes associated with ageing in the human lower bowel are multifaceted and not yet fully understood. They include a reduced mucosal barrier function, altered nerve activity, and variations in cellular structures and functions across different segments of the colon, particularly in the ascending colon. While some conditions such as irritable bowel syndrome display a decline in prevalence among the elderly, other phenomena—like chronic constipation—continue to pose challenges. The interplay between these degenerative changes and their clinical manifestations highlights the importance of further investigation to determine their impact on intestinal reserve and overall bowel function. Future research efforts should aim to clarify these complex relationships and inform potential therapeutic strategies to enhance intestinal health in ageing populations.

Key Points

- A reduction in abdominal pain experienced by older adults may be explained by a reduced nociceptor innervation.
- Among older people, a reduction in the mucosal barrier may follow a decline in intestinal stem cell activity, a reduced density of tight junction proteins linking epithelial cells and a decline in the mucus layer.
- Among older adults, the degenerative changes that have been identified involve the muscle, the enteric nervous system, and the mucosa/submucosa. This can involve both the ascending and descending colon, but the ascending colon may be more vulnerable. Potential mechanisms leading to degeneration include inflammageing and 'senescent-like' states.
- The concept of a 'functional intestinal reserve' means that the enteric nervous system can tolerate some degeneration without generating symptoms such as constipation.
- It follows that constipation and other bowel disorders among older people are more likely to develop during age-related challenges (e.g., changes to lifestyle, the development of disorders/disease, and the use of medications), each influencing bowel functions that now have a smaller capacity to absorb these changes without developing symptoms.

Availability of Data and Materials

All data of this study are included in this article.

Author Contributions

NB and GJS made substantial contributions to the conception and design of this research. GJS wrote the first draft and then both authors contributed to important editorial changes of important content in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgement

We thank all our previous colleagues and many collaborators for the generation of data and for their thoughtful insights into some of the mechanisms discussed within this manuscript.

Funding

For age-related research, GJS has previously received funding from the research into aging fund, set up and managed by AgeUK, by Dunhill Medical Trust for research into Ageing and the Human Bowel (grant number R382/1114), by the Bowel and Cancer research charity and by Takeda Pharmaceuticals.

Conflict of Interest

The authors declare no conflict of interest.

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