Clinical Significance of Bacterial Overgrowth in Elderly People

The normal concentration of bacteria in the upper small bowel is less than $1 \times 10^4$ to $10^5$ organisms per ml of contents, which compares with a concentration of $1 \times 10^{12-14}$ per ml in the colon. There is an oral–aboral concentration gradient in the number of bacteria and, furthermore, upper gut bacteria generally consist of aerobic Gram-positive organisms whereas bacteria found in the ileum and colon generally are Gram-negative strict or facultative anaerobes [1]. Thus, small-intestinal bacterial overgrowth is defined as the presence of more than $1 \times 10^6$ bacteria per ml of duodenal or jejunal contents.

Three differing factors prevent the accumulation of enteric bacteria in the upper small intestinal lumen—propulsive intestinal motility, gastric acid secretion and intestinal bacteriostatic and immune secretions. Under normal conditions, the major factor that limits the concentration of bacteria in the upper small intestine is intestinal motility sweeping gut contents aborally [2]. The phase 3 migrating interdigestive motor complex, which functions between meals and particularly at night, often termed the 'housekeeping complex', is the most important gut motor activity that limits intraluminal bacterial accumulation [3]. In addition, a high gastric acid concentration helps to reduce proximal intestinal bacterial numbers, and immune and bacteriostatic secretions from the gut may also play a role.

Upper small-intestinal bacterial overgrowth usually occurs in the presence of stasis of intestinal contents, a condition which is classically mimicked in experimental rodent models by isoperistaltic, self-filling, non-emptying blind loops [4]. In man, intestinal strictures, surgical resections that lead to stasis, such as Bilroth II gastrectomy, jejunal diverticulosis and intrinsic diseases of the small-gut wall that interfere with propulsion, i.e. intestinal pseudo-obstruction syndromes, including diabetes mellitus [5], can lead to bacterial overgrowth.

Bacterial colonization of the upper small intestine may have a number of clinical consequences. Dietary carbohydrate or protein (or micronutrients such as vitamin B12) may be utilized by bacteria, reducing their availability for intestinal absorption. Conjugated bile salts passed into the duodenum in bile are readily deconjugated by gut bacteria, the unconjugated bile acids then are absorbed or precipitated in the upper small intestine, resulting in bile acid deficiency, fat malabsorption and malnutrition. In addition, intestinal mucosal damage may occur, reducing absorption of all nutrients [6, 7]. Micronutrient depletion or deficiency states also may develop [8]. Thus, there are major clinical and nutritional consequences of small-bowel bacterial overgrowth [9].

In this issue of Age and Ageing, two papers focus on the question of small-bowel bacterial overgrowth in elderly subjects in the absence of the usual structural causes of intestinal stasis [10, 11]. Since these two studies come to essentially opposite conclusions, it is necessary to evaluate their approach and methods critically and put the data from each study in perspective. Since 1977, studies of small numbers of selected elderly patients have described bacterial contamination of anatomically normal small bowel [12–14]. Some of the subjects of these studies were malnourished, and it was suggested that the bacterial overgrowth was responsible for the poor nutrition [15].

On the other hand, using non-invasive indirect tests, investigators have frequently
demonstrated abnormalities that suggest intestinal bacterial overgrowth in elderly control subjects, including residents of nursing homes [16]. As a result of these observations, several clinical questions that are important for the health of elderly people became apparent: (a) how frequently does bacterial overgrowth occur in elderly subjects? (b) if bacterial overgrowth occurs frequently in elderly people, does it cause malabsorption or/and does it cause malnutrition? (c) what is the best method for detecting possible bacterial overgrowth in elderly subjects at risk for this abnormality?

In order to understand the data of the two recent reports and other studies in the literature, it is necessary briefly to review the methods that have been used to assess proximal intestinal bacterial overgrowth in humans. Initially, the 'gold standard' was finding more than $1 \times 10^6$ organisms per ml in intestinal fluid collected anaerobically. This test required the passage of a fine-bore tube into the distal duodenum or proximal jejunum, and expert bacteriologic measurements, using strictly anaerobic as well as aerobic, culture conditions [16]. Since this method cannot be used as a screening test, several indirect diagnostic approaches to intestinal bacterial overgrowth have been used. The $^{14}$C-cholylglycine breath test [17] is based upon the concept that the $^{14}$C-glycocholate is rapidly deconjugated by small-intestinal bacteria, the $^{14}$C-glycine is then absorbed, metabolized and appears as $^{14}$CO$_2$ in the breath. $^{14}$C-Cholylglycine also is hydrolysed by colonic bacteria if the substrate reaches the caecum. Therefore, to diagnose bacterial overgrowth, excess breath $^{14}$CO$_2$ must appear in the initial period after ingestion. Because of this limitation, a 1 g $^{14}$C-xylose test was devised and was advocated as a 'gold standard' for bacterial overgrowth [18]. However, this test recently has been disparaged [19]. To avoid using isotopically labelled substrates, breath hydrogen (H$_2$) analysis was introduced based on the hypothesis that small doses of either glucose or lactulose would rapidly be metabolized if excess bacteria were present in the upper small intestine and that breath H$_2$ concentrations would increase early after ingestion [20]. The timing of breath H$_2$ tests also is critical [21], and the substrate used alters the amount of H$_2$ that appears in the breath [22]. Postprandial serum unconjugated bile acid concentrations [23] and jejunal short-chain fatty acid measurement [24] also have been suggested as being useful. The reports by Lipsky and co-workers [10] and by Haboubi and Montgomery [11] exemplify differing methods to evaluate subjects for bacterial overgrowth.

Lipsky et al. [10] studied a large number of fit young control volunteers, fit ambulatory elderly volunteers and elderly long-stay hospitalized patients and sought the presence of bacterial overgrowth by using a combination of $^{14}$C-glycocholate and a 15 or 25 g lactulose breath test. These workers also evaluated the nutritional status of their subject groups. The lactulose breath test that they used appears to be flawed since up to 20 to 40% of normal young volunteers had positive tests and up to 35% were non-hydrogen producers. Approximately 20% of the elderly long-term-stay patients and fit ambulatory elderly subjects showed a positive glycocholate breath test compared with only 3% of younger controls. Since the glycocholate and lactulose were administered simultaneously, this raises questions about the validity of the data. Only 'minor abnormalities' in anthropometric and nutritional measurements were detected in each group but there was no indication whether nutritional differences occurred between elderly subjects with normal or abnormal glycocholate breath tests. Thus, the conclusion reached that "bacterial contamination of the small bowel may be common in normal, fit elderly people and in elderly long-stay hospital patients and may be a concomitant of 'normal' ageing, not necessarily leading to ill health", is premature.

Haboubi and Montgomery [11] evaluated 16 community dwellers aged 71–88 years who were selected for study on the basis of an abnormal lactulose breath H$_2$ test. These patients represented about 60% of those who, on clinical grounds and after basic laboratory tests, were suspected of having a small-bowel disorder. The breath H$_2$ test performed by this group used only a 10 g (50%) lactulose test solution, analysed breath samples more frequently than Lipsky et al. [10] and deemed the test positive with a rise of 20 parts/10$^6$ H$_2$ over fasting, occurring at least 30 min before the
COMMENTARY

The diagnosis of bacterial overgrowth is suspected and an abnormal 10 g lactulose H₂ breath test is found, malnutrition may well be present and can frequently respond to antibiotic therapy. Since most of the subjects had normal acid secretion, achlorhydria was not responsible for gut colonization. Instead, they suggest that a possible mechanism for bacterial overgrowth is a change in intestinal propulsive motility.

It is clear that further studies need to be done in this field. The simple 10 g lactulose breath test used by Haboubi and Montgomery might be suitable for screening larger numbers of otherwise normal subjects and appears to be superior to the 15 or 25 g undiluted lactulose test used by Lipsky et al. It is not unexpected that some individuals demonstrating bacterial overgrowth also will have evidence of malnutrition and that such individuals subjected to antibiotic treatment and intensive medical supervision will improve. Further studies with a suitable control group are necessary before one concludes that malnutrition is a frequent concomitant of intestinal bacterial overgrowth in elderly people and may respond to antibiotics. On the other hand, with the available data at present, I would treat an elderly malnourished patient with bacterial overgrowth with antibiotics in the hope of improving his or her nutritional state. Finally, if Haboubi and Montgomery are correct that a prolongation of intestinal transit occurs in elderly subjects with bacterial overgrowth, similar to the suggestion of Vantrappen et al. [3], prokinetic agents that increase small-bowel motility may be an important therapeutic measure to try in these patients.

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References
2. Kellow JE, Gill RC, Wingate DL, Calam JE.


