Annals of Gastroenterology (2012) **25,** 371-375

The role of probiotics in pouchitis

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In their invited narrative review article, Gionchetti *et al* (April-June issue) [1] report 6 studies in which probiotics were used for maintenance of remission in pouchitis or induction of remission in acute pouchitis. In all but one studies VSL#3 probiotic was used. In 4 studies treatment group (VSL#3 regimen was used in 3 studies) was compared to a control group [2-5]. [Q1. references are missing]. The studies of VSL#3 may form a coherent group, although the duration of treatment varied between 9 and 12 months. A recent meta-analysis of probiotic efficacy for gastrointestinal diseases synthesized data of 4 studies of pouchitis treatment [6]. In this systematic review the relative risk ratio for the probiotic group was 0.17 [95% Confidence Interval (CI) 0.10-0.30]. However, most of the studies cited by the article of Gionchetti *et al* were not included in this meta-analysis. The heterogeneity among the 3 probiotic-control studies referred by Gionchetti *et al* is not statistically significant (Cochrane's Q for Odds Ratio, Risk Ratio and Risk Difference is 3.435, 0.040 and 4.730, with 2 degrees of freedom, and P value of 0.178, 0.980 and 0.094, respectively). Using a fixed-effect meta-analysis model (NCSS 2007 software) the combined Odds Ratio for the disease is 0.036 (95% CI 0.011-0.113), the Risk Ratio for the disease is 0.182 (95% CI 0.100-0.328) and Risk Difference is -0.718 (95% CI -0.835 - -0.602) in favor of the probiotic group (Fig. 1). These results are in accordance with the findings of the systematic review [6]. Statistically significant heterogeneity will be detected if the study of Kuisma (*Lactobacillus rhamnosus* GG was used for 3 months) is included in the meta-analysis model.

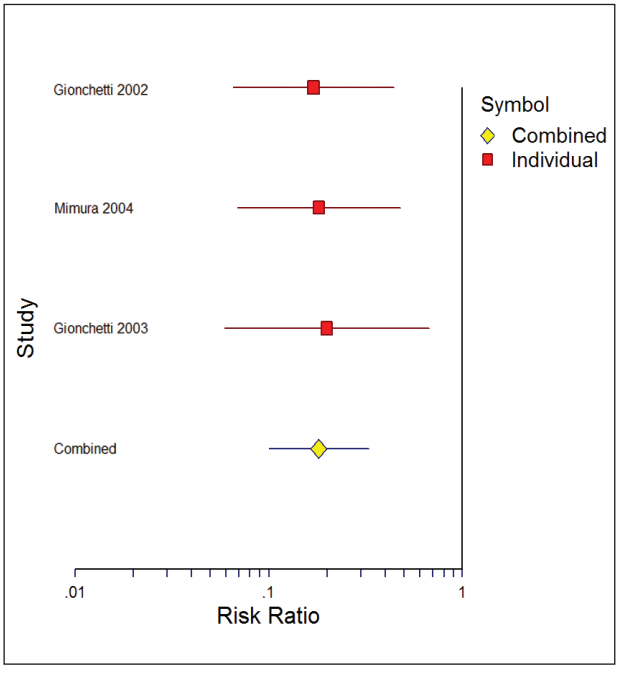

Figure 1 Forest plot of Risk Ratio of pouchitis in patients receiving VSL#3

It is of interest that a case report of 2 patients suggested that another type of probiotic, *Escherichia coli* Nissle 917, might be beneficial for the treatment of active pouchitis and for maintenance therapy [7].

The results of small clinical trials and anecdotal reports indicate the urgent need for large-scale, randomized, placebo-control trials.

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Conflict of Interest: None

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Received 29 May 2012; accepted 2 July 2012

Author's reply

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In their letter to the Editor about our review article (and not "narrative article") Nalmpantidis and Maris mention a meta-analysis [1] in which results with probiotic preparation VSL#3 in pouchitis are not included [2-4], suggesting their limited value. The authors concluded that there is an urgent need for a large, placebo-controlled trial on this topic.

The authors have probably chosen the wrong meta-analysis, because it was a non-specific meta-analysis on the treatment of pouchitis.

They should have considered the Cochrane meta-analysis on treatment and prevention of pouchitis [5], in which all studies, where VSL#3 was used, were included and were considered the most appropriate and the best performed with clear evidence of the efficacy of VSL#3 both in the prevention of pouchitis onset and in the maintenance treatment of remission.

Furthermore, based on the results of these studies, the ECCO Consensus has suggested the use of VSL#3 in both indications [6].

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Conflict of Interest: None

Received 2 July 2012; accepted 2 July 2012

Intestinal spirochetosis: a "fuzzy" entity

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The presence of spirochetes in the human bowel has been recognized for over a century. Harland in 1967 described spirochetes on electron microscopy of rectal biopsies in a man with chronic diarrhea, and coined the term intestinal spirochetosis (IS) [1]. We report two cases of IS followed by review of literature.

A 23-year-old male homosexual presented with diarrhea for 9 months but no blood. The routine hematology, biochemistry and inflammatory markers were normal. A rigid sigmoidoscopy showed normal mucosa. The biopsies revealed mucosa covered with fuzzy brush border, 2-3 μm thick and staining blue with hematoxylin (Fig. 1). His symptoms improved with a course of metronidazole.

A 16-year-old girl presented with sudden onset pain, fever, vomiting associated with tenderness and guarding in right iliac fossa. The white cell count was 12800 /mm^3 (normal 4-11,000) and a C-reactive protein of 36 mg/dL (normal less than 6). She underwent laparoscopic appendicectomy. The resected specimen showed inflamed appendix with neutrophilic infiltrates. The mucosa was covered with hematoxylin-stained fuzzy border.

IS is a well-recognized entity. Prevalence rates are highly variable but in general, the rates are inversely related to standards of living. Incidence varies throughout the world from 2-10% in Western Europe to 30% in Chicago to nearly 100% in western Africa [2]. It is also more common in homosexuals and HIV-infected patients and prevalence of up to 54% has been observed in homosexual men [3].

Human IS is mainly caused by two species of spirochetes named *Brachyspira aalborgi* (*B. aalborgi*) and *Brachyspira pilosicoli*.

The clinical presentation in humans varies from being asymptomatic to common symptoms of abdominal pain (46%), diarrhea (51%), alternating diarrhea and constipation (13%) and rectal bleeding [4]. Abdominal pain can mimic acute appendicitis. The invasive disease is very rare unless the patient is immunocompromised [3]. The diagnosis of IS is by histological examination of the biopsy specimens. The characteristic appearance of a dense basophilic band, 2-3 μm thick, along the colonic surface is diagnostic. The organisms can be demonstrated by electron microscopy. It is difficult to culture the organisms due to fastidious and slow growth, especially *B. aalborgi* [5].

IS can involve the entire colon, appendix and even terminal ileum. In a large study spirochetes were found in 12.3% of appendices removed from patients clinically suspected to have acute appendicitis but whose appendices were histologically

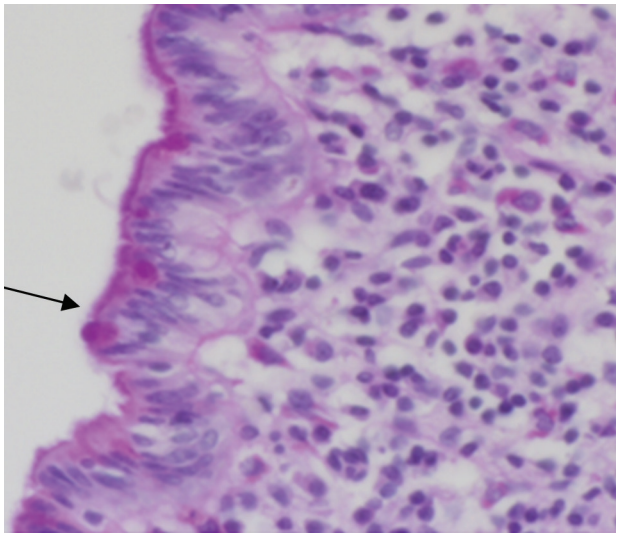

Figure 1 Colonic biopsy showing 2-3 μm thick hematoxylin stained spirochetes lining the mucosa forming a false brush border

normal. However, only 0.7% with histologically confirmed appendicitis did show spirochetes in their appendices (P<0.05) [6]. Our second case belongs to this group.

The clinical importance of IS remains unclear and controversial. Symptoms do not seem to correlate with the extent of colonic involvement or even clearance or persistence of the organisms. There is inadequacy of evidence based information regarding this clinical entity. The management consensus seems to lean towards a 'wait and watch' approach with the antibiotic treatment reserved for patients with persistent symptoms without other demonstrable pathology, especially in high-risk groups.

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Conflict of Interest: None

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Received 10 May 2012; accepted 11 May 2012

Adult intussusception

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In their study of adult intussusception, Sarma et al reported that, over a 6-year period, 15 patients with the disease were identified in a tertiary hospital in South India [1]. It would be of interest to know the total number of admissions or patients in the same hospital during the study period to be reported by the authors, so that estimates of the frequency rates of the disease could have been calculated. A cross-sectional study from Glasgow, UK, estimated the annual incidence of the disease to be 2-3 cases/10^6 population (accounted for <0.1% of hospital admissions) [2]. In a study from Switzerland, over a 17-year period, 10 adults with intussusception were recorded in three hospitals [3]. In this study, only 3 patients were diagnosed as ileocolic intussusceptions and 2 of them suffered from lymphoma. In another recently published study of 20 adult patients from Turkey, conducted over 8 years, 5 cases of jejunojejunal intussuception were identified, most of them due to Peutz-Jeghers hamartomatous polyps. In the same case-series study, rectal bleeding was reported only in 1 patient (5%) and acute symptoms (<4 days) in 6 patients (30%) [4]. These numbers are slightly different than those reported by Sarma et al and may indicate the diversity of the disease in different source populations. Finally, in the study of Sarma et al, no case of small bowel adenocarcinoma was diagnosed in 12 patients who underwent laparotomy, indicating the rarity of this type of tumor in the adult intussusception population. This finding is in accordance with the results of another retrospective review of 41 cases from China [5].

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Received 5 May 2012; accepted 7 August 2012

Management of obstructive cholangiocarcinoma with metallic stents, implanted in a Y-shaped pattern, in one session

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Most patients with unresectable, malignant, obstructive, cholangiocarcinoma are candidates for palliation. Biliary

drainage by endoscopic interventions (ERCP), with implantation of self-expandable metallic stents (SEMSs), plays a major role in improving liver function and managing or avoiding cholangitis [1].

We present two cases (a 78-year-old man and a 65-year-old woman) with advanced, unresectable, cholangiocarcinoma (Bismuth, Type IV). They were treated with, a ¨*one-step*¨ implantation of SEMSs (Wallstent stents – Uncovered Nitilol stents), by ERCP, in a *Y-shaped* pattern. The biliary decompression was successful and significant reduction in jaundice was achieved, in both cases. The *male patient* had bilateral hilar strictures in both the right and left hepatic duct, in the common hepatic duct and in the middle of the common bile duct (Fig. 1A). Endoscopic sphincterotomy and balloon dilatation (distal stenosis) were performed. Then we inserted an uncovered SEMS 8 cm (with window) in the left hepatic bile duct and a second uncovered SEMS 10 cm (intact gallbladder) in the right hepatic bile duct and in the common bile duct, through the first SEMS (Fig. 1B). The total serum bilirubin level (TSBL) dropped from a mean of 27 mg/dL to 2.5 mg/dL, within the first 20 days. The *female patient* had an inoperable cholangiocarcinoma that involved the confluence and both (right and left) hepatic bile ducts (Fig. 1C). We inserted an uncovered SEMS 10 cm (with window) in the right hepatic bile duct and a second uncovered SEMS 10 cm in the left hepatic bile duct and in the common bile duct, through the first SEMS (Fig. 1D). The TSBL dropped (13.5 mg/dL to 1.5 mg/dL), within the first 5 days.

The use of unilateral or bilateral SEMSs, in patients with unresectable malignant obstructive cholangiocarcinoma, is debatable [1-5]. In some cases, the placement of unilateral SEMSs is adequate, because only 30% of the liver needs to be drained in order to reduce jaundice [3]. Inversely, unilateral drainage alone may not completely relieve jaundice and may increase the risk of cholangitis. Most endoscopists prefer to place bilateral SEMSs when possible, in an attempt to maximize biliary drainage, avoiding cholangitis [1,4,5].

Endoscopic SEMSs, are the treatment of choice in patients with malignant biliary obstruction [1,2]. In the unresectable cholangiocarcinomas (Bismuth, Type III + IV), bilateral drainage, with uncovered SEMSs (to avoid occluding drainage from the contralateral biliary system), in one session, is the optimal palliative treatment [1,4,5].

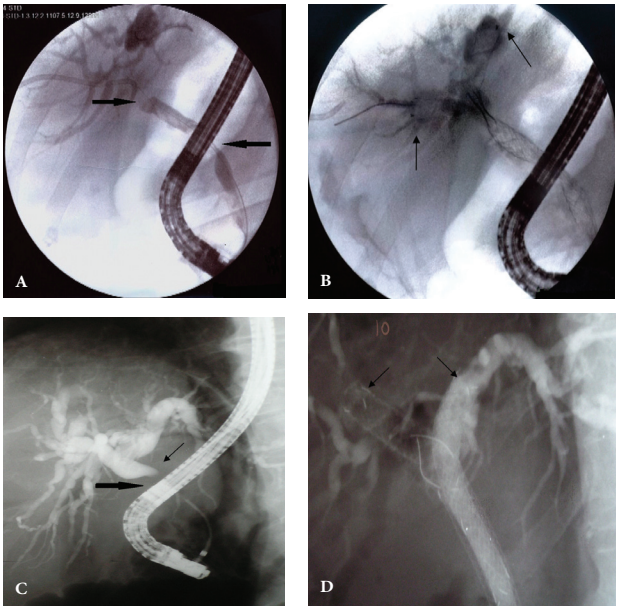

Figure 1 Unresectable obstructive cholangiocarcinomas (Bismuth Type IV). Malignant strictures (A,C, arrows). Two uncovered self-expandable metallic stents implanted in a Y-shaped pattern (B,D, arrows). Biliary drainage (B,D)

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Received 11 May 2012; accepted 28 May 2012

Acute constipation due to abdominal herpes zoster: an unusual association

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The association of herpes zoster and acute constipation, or even colonic pseudo-obstruction, has received only scant attention in the published literature. Since 1950, twenty studies

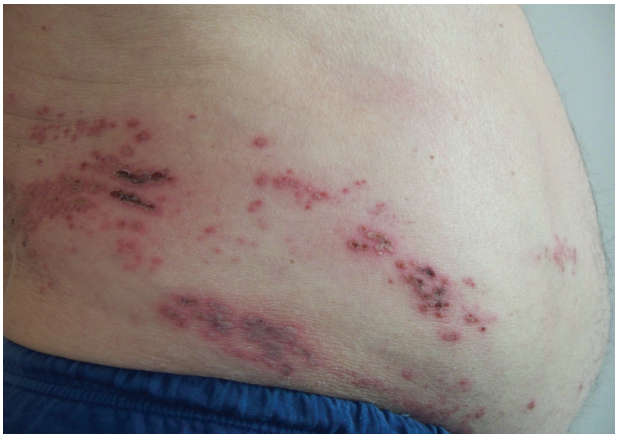

Figure 1 A cutaneous vesicular eruption involving the area of the T8-T12 dermatomes on the right

have been published with 28 patients reviewed. Significant co-morbidities were present in half of the patients while the time of skin eruption was variable when compared with the onset of the abdominal symptoms. The majority of patients was observed and treated conservatively [1].

Herein we present a male patient with acute severe constipation and a concomitant painful skin eruption due to herpes zoster.

An 80-year-old diabetic man was admitted to our Department for abdominal distention, discomfort and severe constipation for a week. He previously had regular bowel habits. One day before presentation he noticed erythema with the appearance of small grouped vesicles involving the area of the T10-T12 dermatomes on the right abdominal wall (Fig.1). Physical examination revealed scarce bowel sounds and abdominal distention. Laboratory testing was normal with the exception of a mild hyperglycemia (207 mg/dL). Neurological examination revealed no evidence of myelopathy that might cause severe bowel dysfunction. He had no bladder dysfunction. Abdominal roentgenogram did not show a pattern of ileus and a colonoscopy was unremarkable. The patient was diagnosed as having visceral neuropathy associated with herpes zoster infection. He was treated with Vancyclovir 1000 mg t.i.d. with gradual resolution of symptoms during the next two weeks.

The pathogenesis of herpes zoster-associated intestinal pseudo-obstruction has not yet been fully elucidated. Direct viral involvement of the colonic intrinsic autonomic nervous system has been thought to result in local inflammatory reaction, thus causing segmental spasm and proximal dilatation [2]. Another theory has been proposed to explain pseudo-obstruction with prominent colonic dilatation. The theory includes spread of the virus from the dorsal root ganglia to the thoracolumbal or sacral lateral columns resulting in autonomic balance, interruption of sacral parasympathetic nerves, and resultant decrease in segmental colonic contractions [3]. Finally, direct involvement of the intrinsic colonic autonomic nerves (submucosal and myenteric plexuses) has also been discussed [4].

Herpetic neuralgia in a dermatomal distribution preceding the rash has long been recognized and noted to antedate the rash by up to 100 days, thereby creating significant diagnostic confusion [5]. The viral spread can involve not just the colon, but also the diaphragm, urinary tract, anus, and abdominal wall, and affect their motor activity [6].

The prognosis is generally good. The need for antiviral therapy should be based on immune status of the patient, the dermatome involved and the likelihood of visceral dissemination. Conservative management can achieve complete resolution of symptoms [7].

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Conflict of Interest: None

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Received 1 June 2012; accepted 2 June 2012