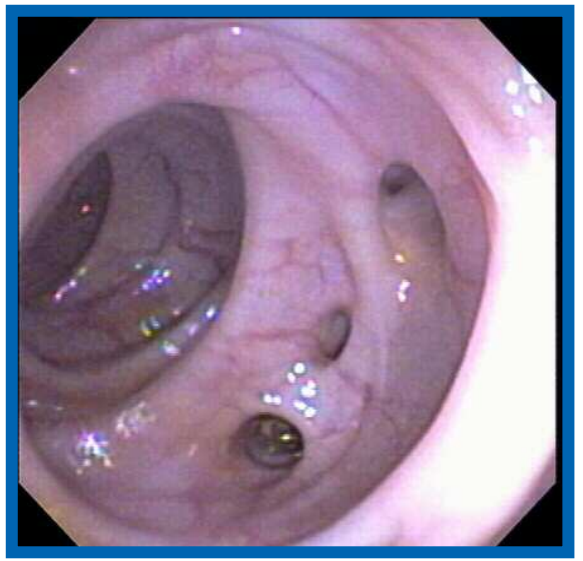
La patologia diverticolare

- impatto sulla popolazione anziana -



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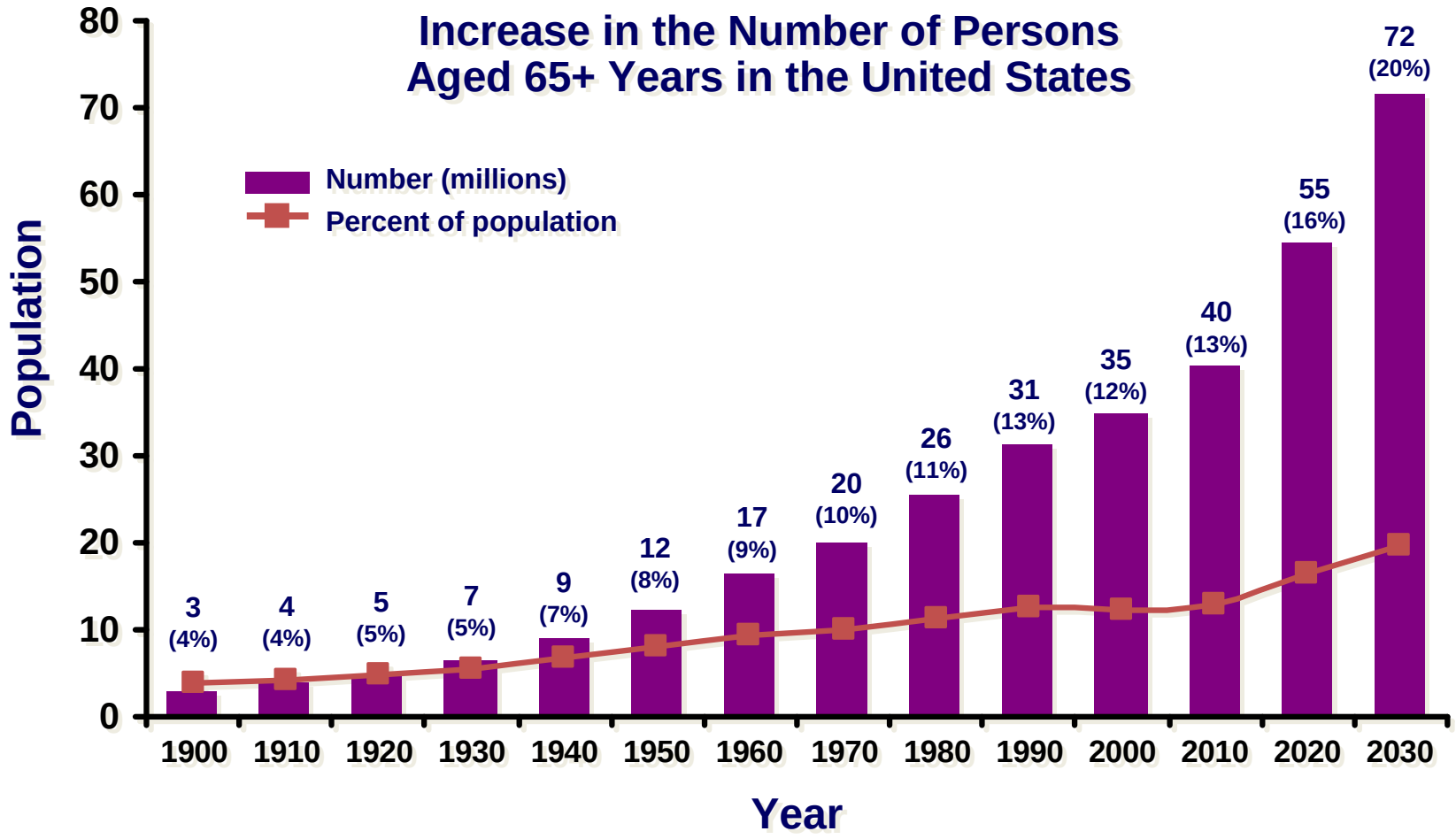
The “Age Wave”



He W, et al. 65+ in the US: 2005. US Census Bureau Web site.

CLINICAL PRESENTATION

1. **Diverticulosis:** anatomic presence of diverticula

2. **Diverticular disease:** any clinical manifestation of diverticula

3. **Painful diverticular disease:** symptomatic diverticulosis without diverticulitis

4. **Acute diverticulitis:** symptomatic inflammation or perforation of diverticula

WR Hazard. Principles of Geriatric Medicine and Gerontology. Mc Graw Hill Ed. 4th Edition

HINT OF HISTORY

- In 1849 Cruveilhier first described the colonic involvement by diverticular disease.
- The term “diverticulosis” was first used in 1914.
- Acute diverticulitis was recognized at the turn of the 20th century.
- Burkitt & Painter described the geographic distribution of diverticular disease (Western countries vs third world) due to industrialization of milling of flour.
- Diverticulosis defined as a “deficiency” disease

Aging-Associated Changes in Colonic Motility

- Common disorders observed ***in the ELDERLY*** that are correlated with colonic motility:
  - **Constipation**
  - **Diverticular disease**
  - **Diarrhea**
  - **Fecal incontinence**
- There are age-associated **reductions in myenteric neurons, calcium influx, and tensile strength of the collagen and muscle fiber**

Hall KE et al. *Gastroenterology.* 2005; Petruzziello L et al. *Aliment Pharmacol Ther*. 2006

La diverticolosi del colon

L'erniazione della mucosa attraverso la parete colica ha una eziologia multifattoriale. Oltre ad una eventuale **predisposizione individuale** su base anatomico-genetica, diversi fattori possono contribuire allo sviluppo della patologia; ***molti di essi sono correlati all'invecchiamento:***

- Mutamenti qualitativi della parete colica
- Disordini della motilità intestinale
- **Alterazioni della microflora residente**
- **Carenza di fibre alimentari nella dieta**
- **Abitudini sedentarie**
- **Infiammazione colica prolungata**

Jasim M Radhi, Jennifer A Ramsay and Odette Boutross-Tadross. Diverticular disease of the right colon. BMC Research Notes 2011

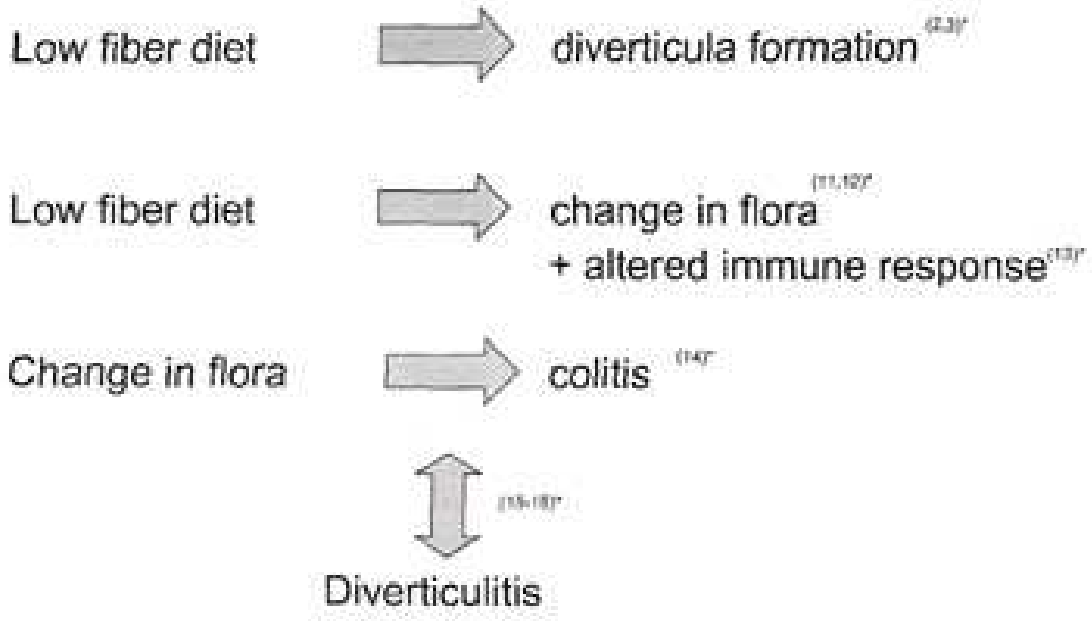
Aetiology of diverticulosis

- Precise aetiology unknown.
- **High intraluminal pressure and a weak colonic wall** (where blood vessels penetrate the muscularis) may predispose to herniation of the mucosa and sub-mucosa.
- **Abnormal colonic motility, defective muscular structure and defects in collagen consistency, *usually due to AGING*** may also be causes.

- **L-sided** diverticular disease predominates in industrialised western societies. **R-sided** disease more common in Asians.
- Affects males and females equall

Diverticulosis/tis development

Theoretical Progression from Diverticula Formation to Diverticulitis



*References suggesting each step

Theoretical progression from diverticula formation to diverticulitis.

Diverticular Disease

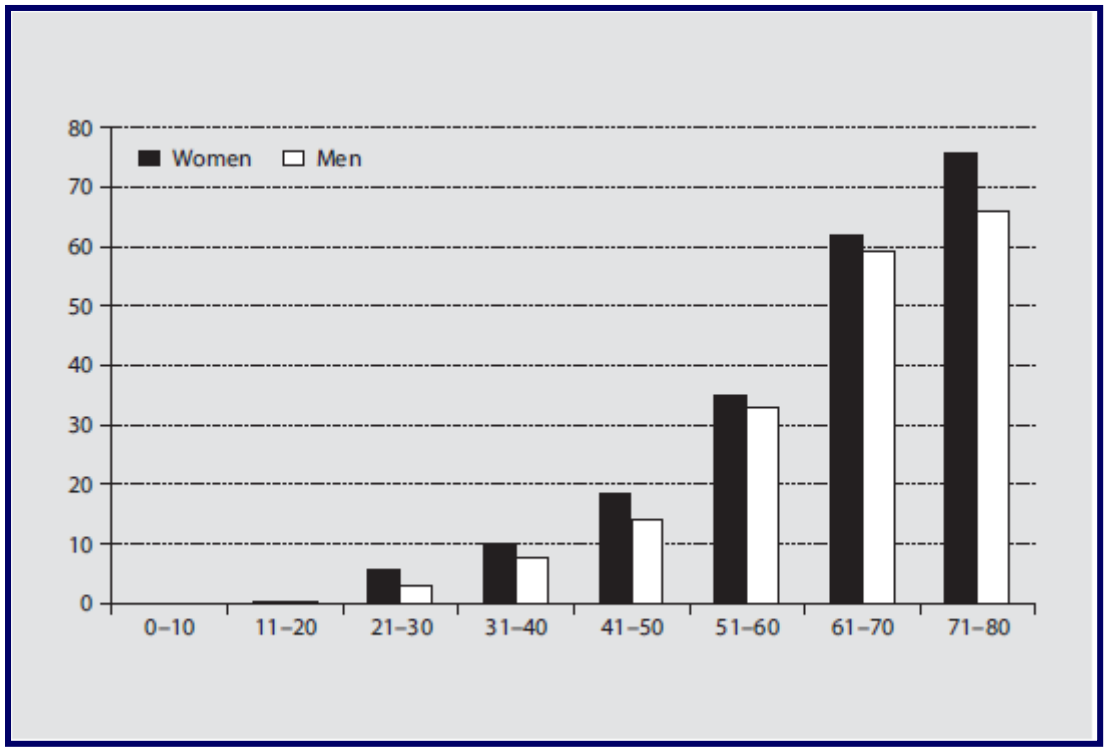
According to data from the National Demographic and Health Survey (NDHS) between **1997** and **2002:**

- Hospital admissions: increased by 14% (to 261.180)
- Office visits: increased by 14% (to 1.493.865)
- Emergency department visits: increased by 84% (to 161.364).

Hall KE, et al. *Gastroenterology.* 2005;129:1305-1338.

Prevalenza

È una patologia asintomatica per anni, fatto che rende molto difficile stimare la prevalenza nella popolazione generale.



Di fatto è di riscontro poco comune nei giovani adulti

Progressivo aumento dell'incidenza con l'avanzare dell'ETA'

Comparato, Pilotto, Franzè, Franceschi, Di Mario. ***Diverticular Disease in the Elderly.*** *Dig Dis 2007;25:151–159*

Diverticular Disease

- By age 50 years, ***one third*** of Americans have diverticulosis coli; by age 80 years, ***two thirds*** will be affected
  - Incidence less than 5% among those aged < 40 years
  - Incidence greater than 60% by age 85 years
  - Mean age at clinical presentation: ***60 years***
- The majority of those affected are **asymptomatic**

Hall KE, et al. *Gastroenterology.* 2005;129:1305-1338.
Cooperman A, et al. *Diverticulitis.* eMedicine Web Site. Available at: www.emedicine.com/MED/topic578.htm. Accessed 11/3/06.

NUMBERS AND PATHOPHYSYOLOGY

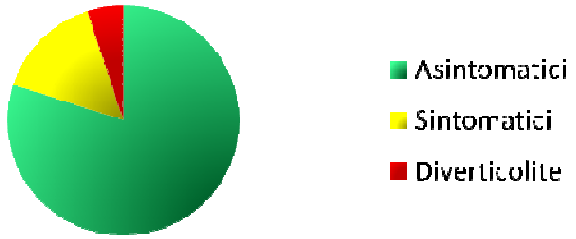
- Up to 5%, life long, will develop complications; if considered by symptoms - up to 25%.
- 2%, life long, will need hospitalization; of them, about 50% will require surgery.
- 30% persistence of symptoms or recurrent diverticulitis in 5 years after the first attack.

Sintomatologia

Come già detto, in alcune casistiche fino all'80-85% dei pazienti rimane esente da sintomi.

Del restante 15-20% (pazienti sintomatici) solo un quarto (5%) ha chiari segni di diverticolite (comprese complicanze come ascessi, fistole o emorragie).

Nei **pazienti sintomatici senza diverticolite conclamata** sembrano comunque riconoscersi segni anatomo-patologici di infiammazione della mucosa.



Comparato, Pilotto, Franzè, Franceschi, Di Mario. ***Diverticular Disease in the Elderly.*** *Dig Dis 2007;25:151–159*

Malattia diverticolare sintomatica

Si presenta come un attacco di ***dolore colico o costante nel quadrante inferiore sinistro*** (fossa iliaca sn), solitamente esacerbato dalla ingestione di cibo e che migliora dopo l'emissione di aria.

Nel 33-46% dei casi si osserva una ***alterazione dell'alvo***: più spesso stipsi, oppure diarrea o alternanza di stipsi e diarrea.

L'esame obiettivo è spesso negativo.

NB: La presenza di questa sintomatologia assieme al riscontro di diverticolosi non significa necessariamente la presenza di una malattia diverticolare sintomatica.

Diverticolite

La diverticolite, infiammazione di uno o più diverticoli e del tessuto pericolico, è espressione di **micro/macro perforazioni** della parete colica. E' quasi sempre localizzata a livello del ***SIGMA.***

Il processo eziopatogenetico sembra consistere nell'***erosione della parete diverticolare secondaria a flogosi cronica o ad aumento della pressione intraluminale.***

Una piccola perforazione può essere tamponata dal grasso pericolico o dal mesentere risultando in ascessi o fistole con eventuale coinvolgimento degli organi viciniori.

La sua incidenza ***aumenta progressivamente con l'ETA'*** e quindi con la durata della malattia diverticolare

http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-colonic-diverticular-disease?

Diverticolite

I sintomi classici sono:

- **Dolore profondo** al quadrante inferiore di sn (70%); il dolore ha esordio acuto è persistente e peggiora nel tempo
- **Febbre e leucocitosi**
- **Nausea e vomito** (20-62%)
- **Addome disteso, timpanico, peristalsi ridotta**
- **Stipsi** (50%) o **Diarrea** (25-35%)
- **Sintomi urinari**: disuria, urgenza minzionale, pollachiuria (10-15%)

http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-colonic-diverticular-disease?

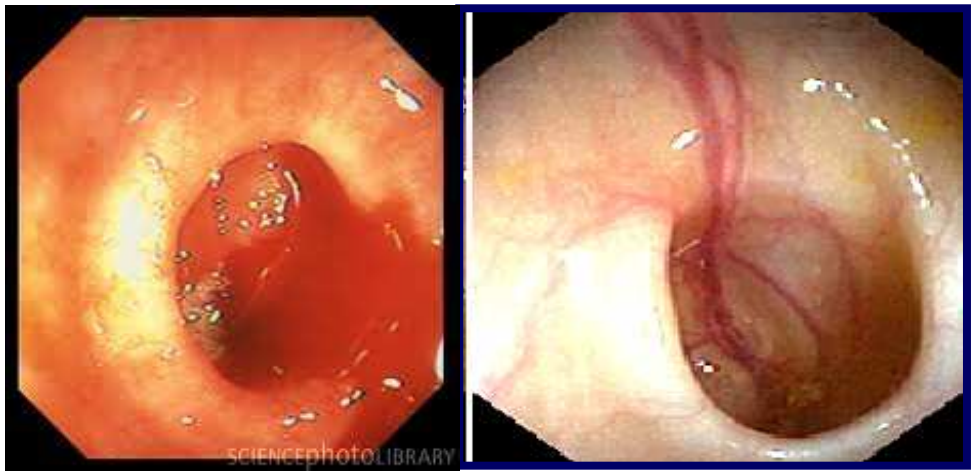
Sanguinamento diverticolare

Un sanguinamento occorre in quasi il **20% dei pazienti affetti da diverticolosi** e in un terzo dei casi è massivo.

In una review (1559 pazienti) su pazienti con sanguinamento GI acuto del tratto inferiore, la patologia diverticolare risultava responsabile nel **5-42%** dei casi.

Si tratta della conseguenza di erosione di un vaso a localizzazione intra o peri-diverticolare

La frequenza di una concomitante **terapia antiaggregante o anticoagulante nel paziente ANZIANO** lo espone a manifestazioni più frequenti e di maggior entità, condizionando l'indicazione alla terapia stessa



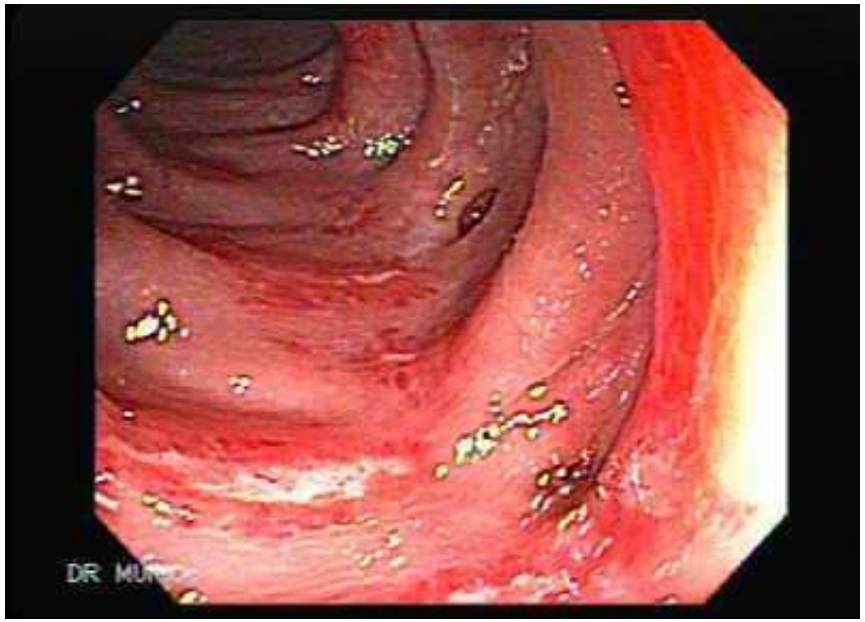
http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-colonic-diverticular-disease
http://www.uptodate.com/contents/etiology-of-lower-gastrointestinal-bleeding-in-adults
http://www.uptodate.com/contents/colonic-diverticular-bleeding

Presentazioni cliniche atipiche

La ***colite diverticolare*** è un evento che occorre in un piccolo sottogruppo di pazienti.

Si tratta di un interessamento flogistico esteso di un intero segmento colico.

Le manifestazioni endoscopiche vanno da modesta flogosi di parete con emorragie sub-mucosali a quadri floridi che riproducono un danno simile a quello delle malattie infiammatorie intestinali.



http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-colonic-diverticular-disease?

Profilassi

Il trattamento del paziente asintomatico è mirato a ridurre l'evenienza di eventi acuti. Nella pratica clinica la prevenzione verte su:

- ***Dieta ricca in fibre***
- ***Cicli di disinfezione intestinale con antibiotici***
- ***Uso di probiotici***

ma con quali evidenze ?

Salzman H, Lillie D. ***Diverticular disease: diagnosis and treatment.*** *Am Fam Physician. 2005 Oct 1;72(7):1229-34.*

Profilassi

Mentre è ben consolidato il fatto che una dieta ricca in fibre è un fattore protettivo per l'insorgenza di diverticolosi, non altrettanto robusta è l'evidenza che, a condizione conclamata, essa riduca l'incidenza di diverticolite.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*
Patients with asymptomatic diverticulosis should eat a high-fiber diet to prevent symptomatic diverticular disease	C

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1154 or http://www.aafp.org/afpsort.xml.

Diete ricche di semi ***non*** sembrano influire sulla flogosi diverticolare o sull'evenienza di sanguinamento.

Salzman H, Lillie D. ***Diverticular disease: diagnosis and treatment.*** *Am Fam Physician. 2005 Oct 1;72(7):1229-34.*
Uptodate: *http://www.uptodate.com.ospfe.cilea.it/contents/treatment-of-acute-diverticulitis*
http://www.uptodate.com.ospfe.cilea.it/contents/probiotics-for-gastrointestinal-diseases

Terapia conservativa della diverticolosi

- Fibre (dieta o supplementi)
- Antibiotici a cicli per OS (rifaximina)
- Probiotici
- Mesalazina
- Miscellanea: Ca-antagonisti, antispastici

Probiotici e diverticolosi

Table 1. Probiotics Evaluated for Treatment of Diverticular Disease

Probiotic	Manufacturer	Bacterial sp.	Dose Used (# Bacteria/Day)
Escherichia coli (Nissle 1917)	Ardeypharm (Herdecke, Germany)	Nonpathogenic *E. coli*	5.0×10^{10}
Lactobacillus casei	Enterolactis (Trezzano Rosa, Italy)	*Lactobacillus casei*	1.6×10^{10}
VSL #3	Sigma Tau (Rome, Italy)	*Lactobacillus casei*, *Lactobacillus plantarum*, *Lactobacillus acidophilus*, and *Lactobacillus delbrueckii* subsp. *Bulgaricus*; *Bifidobacterium longum*, *Bifidobacterium breve*, and *Bifidobacterium infantis*; *Streptococcus thermophilus*	4.5×10^{10}

Probiotici e diverticolosi

Table 2. Studies Evaluating the Effectiveness of Probiotics for the Treatment of Diverticular Disease

Author	Number of Participants	Probiotic	Diverticular Disease	Follow-Up	Outcome
Giaccari et al[26]	79	*Lactobacillus* sp.	Diverticulitis with colonic stenosis	12 months	Prevention of recurrence, improved symptoms
Fric and Zavoral[27]	15	*Escherichia coli* (Nissle 1917)	Uncomplicated diverticulitis	8-40 months	Prolonged remission, improved symptoms
Tursi et al[28]	90	*Lactobacillus casei* (+ mesalazine)	Uncomplicated	12 months	Increased rates of clinical remission
Tursi et al[29]	30	VSL #3 (+ balsalazide)	Uncomplicated	12 months	Increased rates of clinical remission

Conclusion

The potential role of altered bacterial flora in the pathogenesis of diverticular inflammation suggests that probiotic therapy may prove effective in the management of this disorder. Small, uncontrolled studies, many of which combine probiotics with other therapies, appear promising, but randomized, placebo-controlled studies are needed before probiotics can be recommended in the management of diverticular disease. Furthermore, the diversity of diverticular disease warrants specific studies to evaluate probiotic efficacy in a variety of clinical settings, including treatment of acute diverticulitis, prevention of recurrent diverticulitis, and management of chronic symptoms.

Probiotics in Diverticular Disease of the Colon: an Open Label Study

Pepu Lamiki[1], Junji Tsuchiya[1], Surajit Pathak[2], Ruichi Okura[1], Umberto Solimene[3], Shalini Jain[4], Shichiro Kawakita[1], Francesco Marotta[5]

1) TMC Hospital, Shizuoka, Japan; 2) Cytogenetics & Molecular Biology Lab, University of Kalyani, India; 3) WHO-cnt for Bioclimatology, Biotechnology & Traditional Medicine, University of Milano, Italy; 4) Department of Food Science and Human Nutrition, University of Illinois, USA; 5) Hepato-GI Department, S. Giuseppe Hospital, Milano, Italy

Abstract

Aim: To investigate the effectiveness and safety of a symbiotic mixture in preventing recurrence of constipation-related abdominal pain in patients with uncomplicated diverticular disease of the colon. **Methods**: Forty-six consecutive patients (10 men, 36 women, mean age 62.5 years, range 49 to 77 years), previously affected by symptomatic uncomplicated diverticular disease of the colon, were enrolled in a 6-month follow-up study in a prospective, randomized, open-label study. The following symptoms were assessed at entry and through follow-up by using a quantitative scale: constipation, diarrhoea and abdominal pain. After recruitment, the patients were assigned to the following treatment: SCM-III symbiotic mixture, 10ml three times a day. The colonization of ingested Lactobacillus acidophilus 145 and *Bifidobacterium* spp. 420 was assessed by specie-specific PCR. Forty-five patients completed the study (97%). **Results**: Thirty-one patients (68%) were still symptom free after the 6th month of treatment. Treatment with SCM-III was regarded as "effective" or "very effective" in more than 78% of the patients altogether ($p<0.01$ vs baseline values). The microbiological study showed that, as compared to baseline values, SCM-III enabled a significant increase of the lactobacilli and bifidobacteria counting and a trend decrease of clostridia. Genomic analysis confirmed the survivability of the ingested strain as long as treatment was given. **Conclusions**: The present symbiotic mixture seems to be effective in preventing recurrence of symptomatic uncomplicated diverticular disease of the colon, especially in those patients with constipation-predominant features.

Introduction

Diverticular disease of the colon is very common in developed countries and its prevalence increases with age and up to an estimated 20% of patients may manifest clinically-relevant illness in their lives [1]. The treatment of uncomplicated diverticulitis (characterized by lower abdominal pain, fever, and bowel movement alterations) is generally non surgical whereas the latter option is usually required when serious complications supervene. In uncomplicated diverticular disease, treatment is aimed at relieving symptoms which may remarkably affect the quality of life of these patients requiring poorly absorbable antibiotics or anti-inflammatory drugs [2]. Nonetheless, despite the high prevalence of this disease, literature data on the treatment for maintaining remission in symptomatic diverticular disease is still a matter of debate. Stasis of luminal contents may occur within colonic diverticula, and it is probably associated with changes in the spectrum of intestinal microflora although such assumption has not been fully demonstrated yet. However, it is likely that faecal stasis and dysbiosis may trigger the formation and topical release of abnormal metabolites eventually causing those inflammatory/functional changes leading to abdominal symptoms. A recent study has showed that only less than 60% of patients using rifaximin for tentative maintenance treatment were symptom free at the 12th month of follow up [3]. On the other hand, concomitant constipation might represent a causative factor in the occurrence of symptomatic flare up. Dietary changes and disaccharides are among the most common prescriptions in such cases but their effective clinical benefit is not entirely established.

Received: 24.08.2009 Accepted: 08.12.2009
J Gastrointestin Liver Dis
March 2010 Vol.19 No 1, 31-36
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COLON

Do calcium channel blockers and antimuscarinics protect against perforated colonic diverticular disease? A case control study

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Gut 2003;**52**:1734–1737

See end of article for authors' affiliations

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Accepted for publication 23 July 2003

Background: The aetiology of perforated colonic diverticular disease (PCDD) remains largely unknown. Perforation may result from a combination of high intracolonic pressures, secondary to excessive colonic segmentation, and impairment of the mucosal barrier. Calcium channel blockers and antimuscarinic drugs, which reduce colonic contractility and tone, could potentially protect against perforation. The aim of this study was to test this hypothesis using a case control design.

Methods: All cases of acute PCDD were identified over a five year period in two hospitals in Norfolk, UK. Each case was matched for age, sex, and date of admission to two controls groups: (1) patients undergoing cataract surgery and (2) patients with basal cell carcinoma. Data on drug use prior to hospital admission were obtained from medical and nursing records and compared between cases and controls.

Results: A total of 120 cases of PCDD were identified and matched to 240 controls in each group. A statistically significant protective association was seen between calcium channel blocker use and PCDD using both control groups. The odds ratios were 0.41 (95% confidence interval (CI) 0.18–0.93) using the ophthalmology control group and 0.36 (95% CI 0.16–0.82) using the dermatology control group.

Conclusions: This study has shown for the first time that a protective association exists between calcium channel blockers and PCDD. The validity of this association is supported by the consistent finding in both control groups and the plausible biological mechanisms. Further studies are required to confirm this association but calcium channel blockers may represent a potential preventive therapy in PCDD.

Int J Colorectal Dis (2008) 23:1193–1197
DOI 10.1007/s00384-008-0555-4

ORIGINAL ARTICLE

Perforated colonic diverticular disease: the importance of NSAIDs, opioids, corticosteroids, and calcium channel blockers

Kristoffer Piekarek · Leif A. Israelsson

Accepted: 17 July 2008 / Published online: 5 August 2008

Abstract
Purpose Perforated colonic diverticular disease is associated with a high rate of late sequel and mortality. The risk of colonic perforation may relate to intracolonic pressure and mucosal barrier function in the wall of diverticula. The use of substances affecting these parameters may therefore be associated with the risk of developing a perforation. The

Conclusions The administration of NSAIDs, opioids, and corticosteroids are associated with an increased risk of colonic diverticular perforation. Acetylsalicylic acid in cardiologic dose does not affect the risk of perforation. Calcium channel blockers are associated with a reduced risk of perforation.

Trattamento della patologia acuta

Il trattamento della patologia acuta prevede un iniziale **approccio conservativo** se si tratta di un caso **non complicato:**

- ***Antibiotici*** ad ampio spettro con copertura di gram-negativi ed anaerobi

- ***Reidratazione*** *e* ***alimentazione liquida o nutrizione parenterale*** a seconda dei casi

- la ***Mesalazina*** sembra essere efficace nel ridurre la durata della fase acuta.

Tutti i pazienti sono uguali? NO

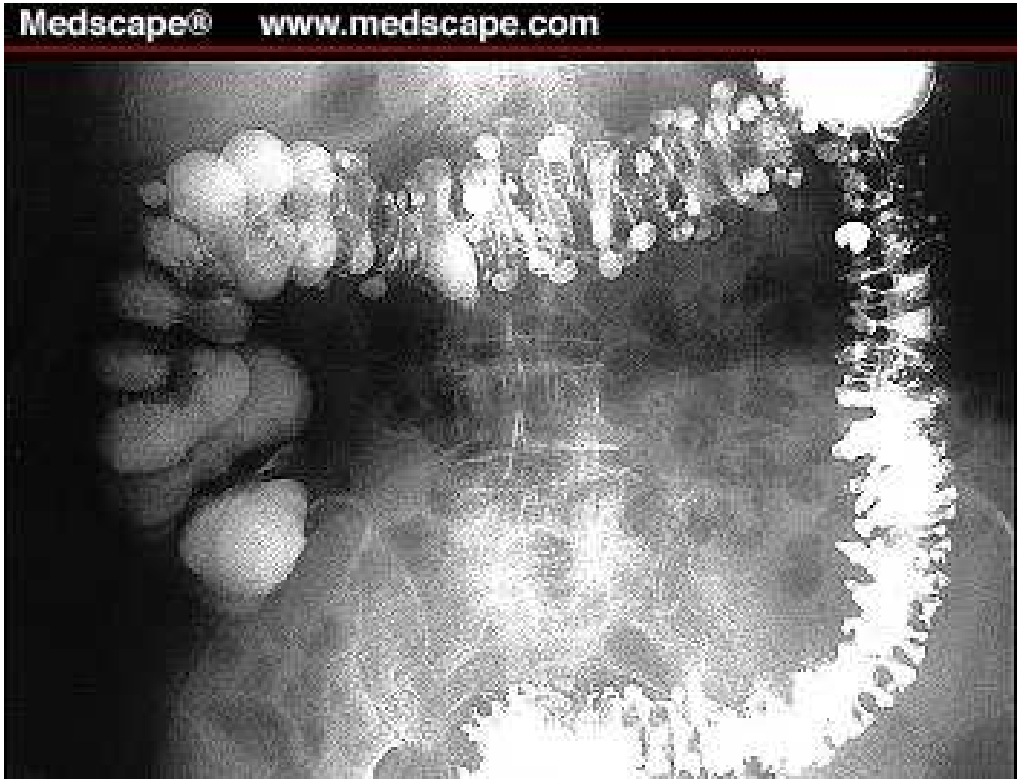
Il paziente ANZIANO oppure critico merita una maggior attenzione a parità di sintomi: deve essere abbassata la soglia decisionale per l'ospedalizzazione.

TABLE 1
Comparison of Diverticular Syndromes

Disease	*Features*	*Treatment*
Asymptomatic	Diverticula in the absence of clinical symptoms	High-fiber diet
Symptomatic	Diverticula and abdominal pain, with or without change in bowel habits; no inflammation	High-fiber diet
Diverticulitis: uncomplicated (in stable patients)	Abdominal pain, fever, leukocytosis; able to tolerate oral fluids	Oral antibiotics (to cover anaerobes and gram-negative rods); clear liquid diet; avoid morphine (Duramorph) if possible because of risk of increasing intracolonic pressure
Diverticulitis: uncomplicated (in older or ill patients)	Abdominal pain, fever, leukocytosis; able to tolerate oral fluids, or patient is older than 85 years	IV antibiotics (to cover anaerobes and gram-negative rods); IV fluids; bowel rest, nothing by mouth; meperidine (Demerol)
Diverticulitis: complicated	Abdominal pain, fever, leukocytosis; with or without sepsis, perforation, abscess, fistula, obstruction	Stabilization with fluids and antibiotics; surgical consultation; percutaneous drainage

IV = intravenous.

Salzman H, Lillie D. **Diverticular disease: diagnosis and treatment.** Am Fam Physician. 2005;72:1229-34



Grazie per l’attenzione …