Best of en infectiologie
Tube digestif

Laurent Beaugerie
Service de Gastro-entérologie et Nutrition
Hôpital Saint-Antoine
Paris

Best of – Tube digestif

Agents infectieux et cancers
- C. jejuni et lymphome méditerranéen
- H. pylori et lymphome gastrique du MALT
- H. pylori et cancer gastrique
- Cancers gastriques et gènes des cytokines

Agents infectieux et maladie de Crohn
- E. coli adhérents-invasifs
- The « cold chain hypothesis »
- EBV, lymphomes et immunosuppresseurs
- Tuberculose et infliximab

Agents infectieux et diarrhée des antibiotiques
- Réponse immunitaire humorale et C. difficile

Immunoproliferative small intestinal disease (alpha chain disease) associated with Campylobacter jejuni

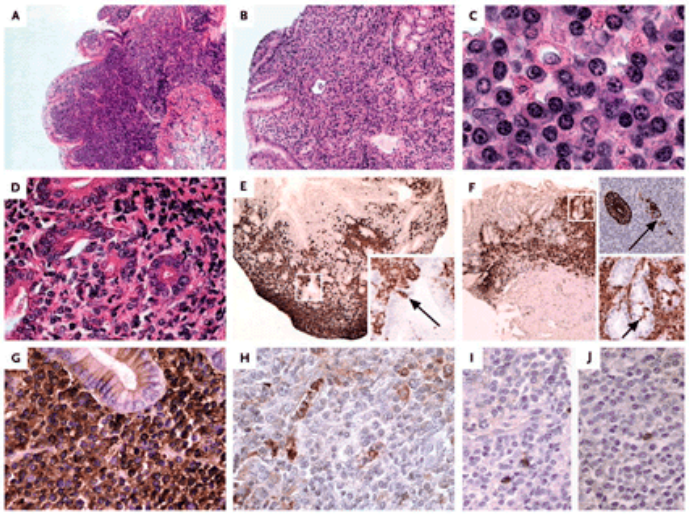
Cas index guéri par antibiotiques (amoxicilline-métronidazole-clarithromycine)

- 12 amplicons séquencés de 16SrDNA
- 8/12 : 99,6 % homologie avec C. jejuni
- 4 autres : flore normale
- C. jejuni présent dans la muqueuse jéjunale du cas index (HIS et immmuno-histochimie)

Présence de C. jejuni (HIS et immuno-histochimie) chez 4/6 cas historiques

Lecuit M et al., N Engl J Med 2004;350:239-48

Immunoproliferative small intestinal disease (alpha chain disease) associated with *Campylobacter jejuni*



Lecuit M et al., N Engl J Med 2004;350:239-48

Identification of a genetic marker of *Helicobacter pylori* strains involved in gastric extranodal marginal zone B cell lymphoma of the MALT-type

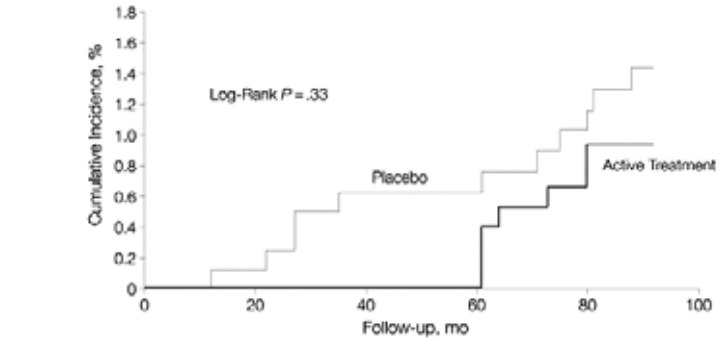
Table 3 Prevalence of JHP950 and JHP1462 open reading frames (ORFs) in *Helicobacter pylori* strains isolated from patients with gastritis, duodenal ulcer, and gastric adenocarcinoma in comparison with strains isolated from patients with gastric MZBL

	Gastritis	Duodenal ulcer	Gastric adenocarcinoma	Gastric MZBL
JHP950	48.7 (p=0.023)*	48.8 (p=0.024)*	39.3 (p=0.006)*	74.4
JHP1462	2.6 (p=0.004)*	16.0 (p=0.545)	35.7 (p=0.429)	25.6

MZBL, marginal zone B cell lymphoma of the MALT-type
p values were determined by Fisher's exact test.
*Significant values versus gastric MZBL strains.

Lehours P et al., Gut 2004;53:931-7

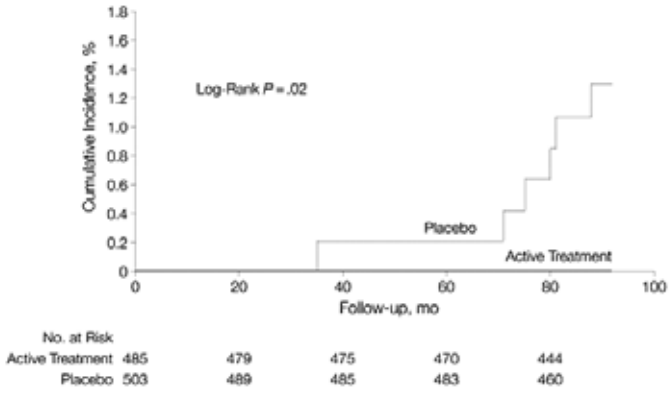
Helicobacter pylori eradication to prevent gastric cancer in a high-risk region of China



No. at Risk					
Active Treatment	817	806	798	790	747
Placebo	813	790	781	774	741

Wong WC et al., JAMA 2004; 291:187-94

Helicobacter pylori eradication to prevent gastric cancer in a high-risk region of China



Sous-groupes des malades sans gastrite atrophique, métaplasie Intestinale ou dysplasie

Wong WC et al., JAMA 2004; 291:187-94

Increased risk of noncardia gastric cancer associated with proinflammatory cytokine gene polymorphisms

Table 5. Multivariate Model-Estimated ORs (and Cornfield 95% CIs) for the Association of Proinflammatory Genotypes With Different Types of Upper Gastrointestinal Cancer

	Esophageal cancer		Gastric cancer	
Genotype	Squamous cell carcinoma (n = 53)	Adenocarcinoma (n = 106)	Cardia (n = 126)	Noncardia (n = 188)
IL-1B-511T+	0.9 (0.4–2.0)	1.0 (0.6–1.7)	1.2 (0.7–1.9)	2.3 (1.4–3.8)
*IL-1RN**2/*2	4.2 (1.3–13.9)	1.0 (0.4–2.8)	1.4 (0.6–3.3)	3.6 (1.7–7.6)
IL-10 ATA/ATA	0.3 (0.1–2.1)	1.5 (0.5–4.4)	1.3 (0.5–3.6)	2.5 (1.1–5.7)
TNFA-308A+	0.8 (0.4–1.7)	1.0 (0.6–1.8)	1.1 (0.6–1.8)	2.2 (1.4–3.7)

El-Omar EM et al., Gastroenterology 2003;124:1193-201

Helicobacter pylori et cancer gastrique

H. Pylori — Gènes bactérien

Inflammation — Gènes de l'hôte

Métaplasie

Dysplasie

Cancer

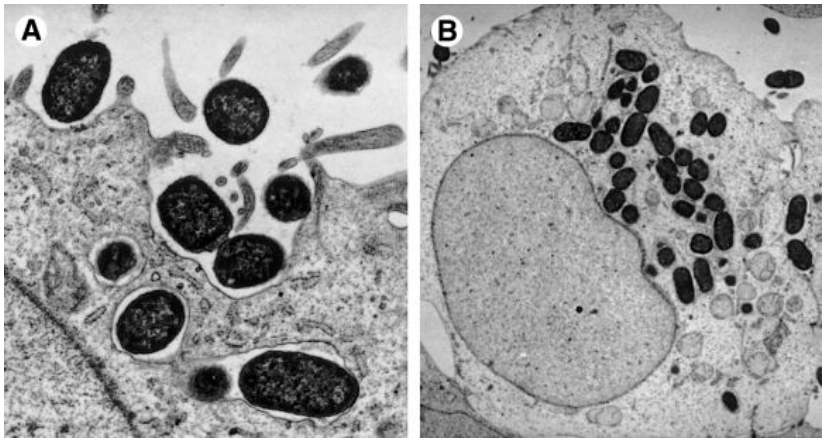
Best of – Tube digestif

Agents infectieux et cancers
- C. jejuni et lymphome méditerranéen
- H. pylori et cancer gastrique
- H. pylori et lymphome gastrique du MALT
- Cancers gastriques et gènes des cytokines

Agents infectieux et maladie de Crohn
- E. coli adhérents-invasifs
- The « cold chain hypothesis »
- EBV, lymphomes et immunosuppresseurs
- Tuberculose et infliximab

Agents infectieux et diarrhée des antibiotiques
- Réponse immunitaire humorale et C. difficile
- C.difficile et diarrhée des antibiotiques en population générale
- Klebsiella oxytoca et colite hémorragique sous antibiotiques

High prevalence of adherent-invasive *Escherichia coli* associated with ileal mucosa in Crohn's disease



Darfeuille-Michaud et al., Gastroenterology 2004;127:412-21

High prevalence of adherent-invasive *Escherichia coli* associated with ileal mucosa in Crohn's disease

Table 3. Prevalence of Invasive *E. coli* Strains Associated With the Ileal and Colonic Mucosa of Patients With CD and of Controls

Origin of the strains	Total no. of subjects	No. of subjects (%) positive		
		Invasive *E. coli*[a]	AIEC[b]	*P* value[c]
Ileal specimens of				
CD patients with chronic lesion	23	7 (30.4)	5 (21.7)	0.196
CD patients with early lesion	22	8 (36.4)	8 (36.4)	0.034[d]
CD patients with healthy mucosa	18	4 (22.2)	4 (22.2)	0.206
Controls	16	1 (6.2)	1 (6.2)	
Colonic specimens of				
CD patients	27	1 (3.7)	1 (3.7)	0.508
UC patients	8	1 (12.5)	0 (0)	0.859
Controls	102	4 (3.9)	2 (1.9)	

[a] *E. coli* strain was defined as invasive when a mean percentage superior or equal to 0.1% of the original inoculum was recovered after 1 hour of gentamicin treatment.
[b] AIEC were defined as described in the Materials and Methods section.
[c] Statistical analysis of the prevalence of AIEC in ileal or colonic specimens of CD patients and in controls.
[d] Significant higher prevalence of AIEC in early ileal lesions of CD patients compared with controls.

Darfeuille-Michaud et al., Gastroenterology 2004;127:412-21

Crohn's disease : the cold chain hypothesis

Réfrigération et maladie de Crohn : même parcours

Bactéries psychrotrophes
- Yersinia enterocolitica
- Listeria monocytogenes
- Pseudomonas fluorescens

Yersinia pestis et NOD2-CARD15

Maladie de Crohn : infection chronique par des bactéries psychotrophes ?

Hugot JP et al., Lancet 2003;362:2012-5

Tuberculosis associated with infliximab, a tumor necrosis factor α-neutralizing agent

USA 1998-2001 :

121 000 pts traités par infliximab
- 76 000 maladie de Crohn
- 45 000 polyarthrite rhumatoïde

70 cas déclarés de tuberculose
- 48 après 1 à 3 perfusions d'infliximab
- 40 avec localisations extra-pulmonaires
- 17 disséminées

Keane J, N Engl J Med 2001;345:1098-104

Epstein-Barr virus load in Crohn's disease : effect of immunosuppressive therapy

TABLE 2. Distribution of Epstein-Barr Virus Virus Load (EBV-VL) Values in Patients with Crohn's Disease (CD) and CD-Free Controls, According to Disease Activity and Immunosuppressive (IS) Therapy

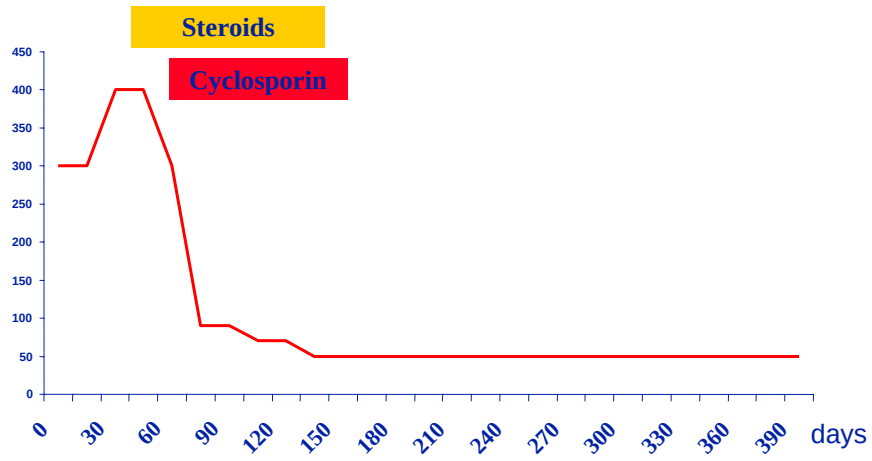
	Blood Samples (n)	Low EBV-VL* (n)	Intermediate EBV-VL* (n)	High EBV-VL* (n)	Statistical Significance
CD-free controls	24	23	1	0	
All CD patients	212	204 (179)†	6	2	NS
Treatment of CD					
No IS therapy	60	58 (52)	2	0	NS
Steroids alone	40	38 (34)	1	1	NS
Azathioprine + steroids	57	54 (48)	2	1	NS
Infliximab within the 3 last months with or without other drugs	55	54 (43)	1	0	NS
CD activity					
Active CD‡	171	165 (144)	4	2	NS
Inactive CD‡	41	39 (35)	2	0	

NS: No difference in EBV-VL values between CD patients and controls.
*EBV-VL values are categorized as low (<400 copies/10^6 mononuclear cells), intermediate (400 to 5000 copies/10^6 mononuclear cells), or high (>5000 copies/10^6 mononuclear cells).
†Values between brackets refer to patients with EBV-VL = 0 copy/10^6 mononuclear cells.
‡CD is defined as active for values of Harvey-Bradshaw index ≥4 or inactive for values of Harvey-Bradshaw index <4.

Reijasse D et al., Inflamm Bowel Dis 2004;10:85-90

Epstein-Barr virus load in Crohn's disease : effect of immunosuppressive therapy

EBV-VL= 5 564 **EBV-VL= 19**



Reijasse D et al., Inflamm Bowel Dis 2004;10:85-90

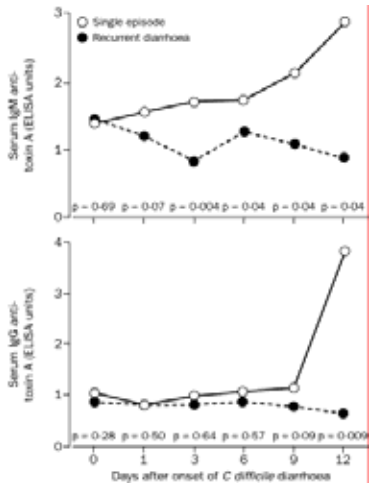
Best of – Tube digestif

Agents infectieux et cancers
- C. jejuni et lymphome méditerranéen
- H. pylori et cancer gastrique
- H. pylori et lymphome gastrique du MALT
- Cancers gastriques et gènes des cytokines

Agents infectieux et maladie de Crohn
- E. coli adhérents-invasifs
- The « cold chain hypothesis »
- EBV, lymphomes et immunosuppresseurs
- Tuberculose et infliximab

Agents infectieux et diarrhée des antibiotiques
- Réponse immunitaire humorale et C. difficile
- C.difficile et diarrhée des antibiotiques en population générale
- Klebsiella oxytoca et colite hémorragique sous antibiotiques

Association between antibody response to toxin A and protection against recurrent *Clostridium difficile*



Kyne L et al., Lancet 2001;357:189

Antibiotic-associated diarrhoea and Clostridium difficile in the community

266 adultes de la région parisienne recevant 5 à 10 jours d'antibiotiques

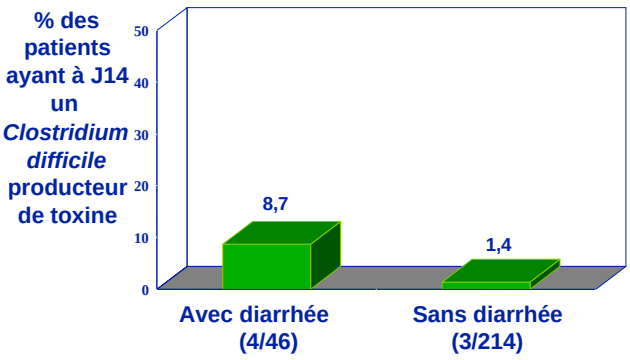
Auto-notification du transit et recherche de C. difficile dans les selles à J1 et J14

17,5 % de diarrhée

- Bénigne et auto-limitée chez tous les patients
- Durée limitée à 24 h dans plus de la moitié des cas

Beaugerie L et al., Aliment Pharmacol Ther 2003;17:905

Antibiotic-associated diarrhoea and *Clostridium difficile* in the community



Beaugerie L et al., Aliment Pharmacol Ther 2003;17:905

Klebsiella oxytoca as an agent of antibiotic-associated hemorragic colitis

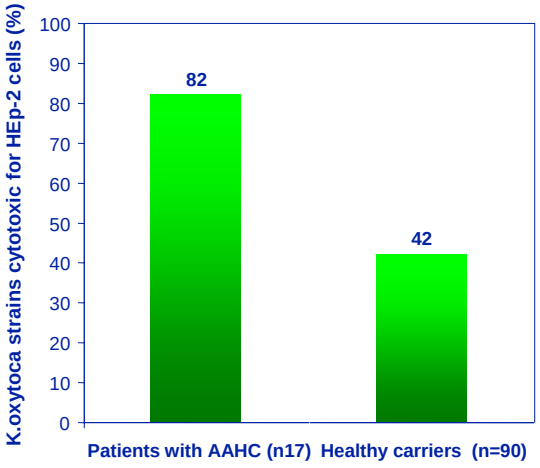
Table 2. Intestinal Bacteria Identified in the Prospective Cohort of 93 Patients With Acute Colitis

	No antibiotic intake within the 2 months preceding the onset of diarrhea (n = 62)		Antibiotic intake within the 2 months preceding the onset of colitis (n = 31)	
	Established pathogen identified (n = 25)	No established pathogen identified (n = 37)	AAHC (n = 4)	Nonhemorrhagic colitis (n = 27)
Salmonella	12 (48.0)		2 (50.0)	2 (7.4)
Shigella	7 (28.0)		0 (0)	0 (0)
Campylobacter	4 (16.0)		0 (0)	0 (0)
C. difficile	3[a] (4.0)		0 (0)	12 (44.4)
Plesiomonas	0 (0)		0 (0)	0 (0)
Aeromonas	0 (0)		0 (0)	0 (0)
Mycobacteria	0 (0)		0 (0)	0 (0)
K. oxytoca	1[b] (4.0)	4 (11.4)	2 (50.0)	1 (3.7)

NOTE. Values are number (% in the subgroup).
AAHC, antibiotic-associated hemorrhagic colitis, clinically defined as sudden occurrence of bloody diarrhea during antibiotic treatment; *C. difficile*, *Clostridium difficile*; *K. oxytoca*, *Klebsiella oxytoca*.
[a]Two cases in the setting of first attack of inflammatory bowel disease and the third in association with Campylobacter.
[b]In association with *Shigella*.

Beaugerie L et al., Clin Gastroenterol Hepatol 2003;1:370-6

Klebsiella oxytoca as an agent of antibiotic-associated hemorragic colitis



Beaugerie L et al., Clin Gastroenterol Hepatol 2003;1:370-6