CLOSTRIDIUM DIFFICILE

Mas Difficile que nunca !

Miguel A. Sierra -Hoffman MD WCC

Diplomate Internal Medicine

Diplomate Infectious disease

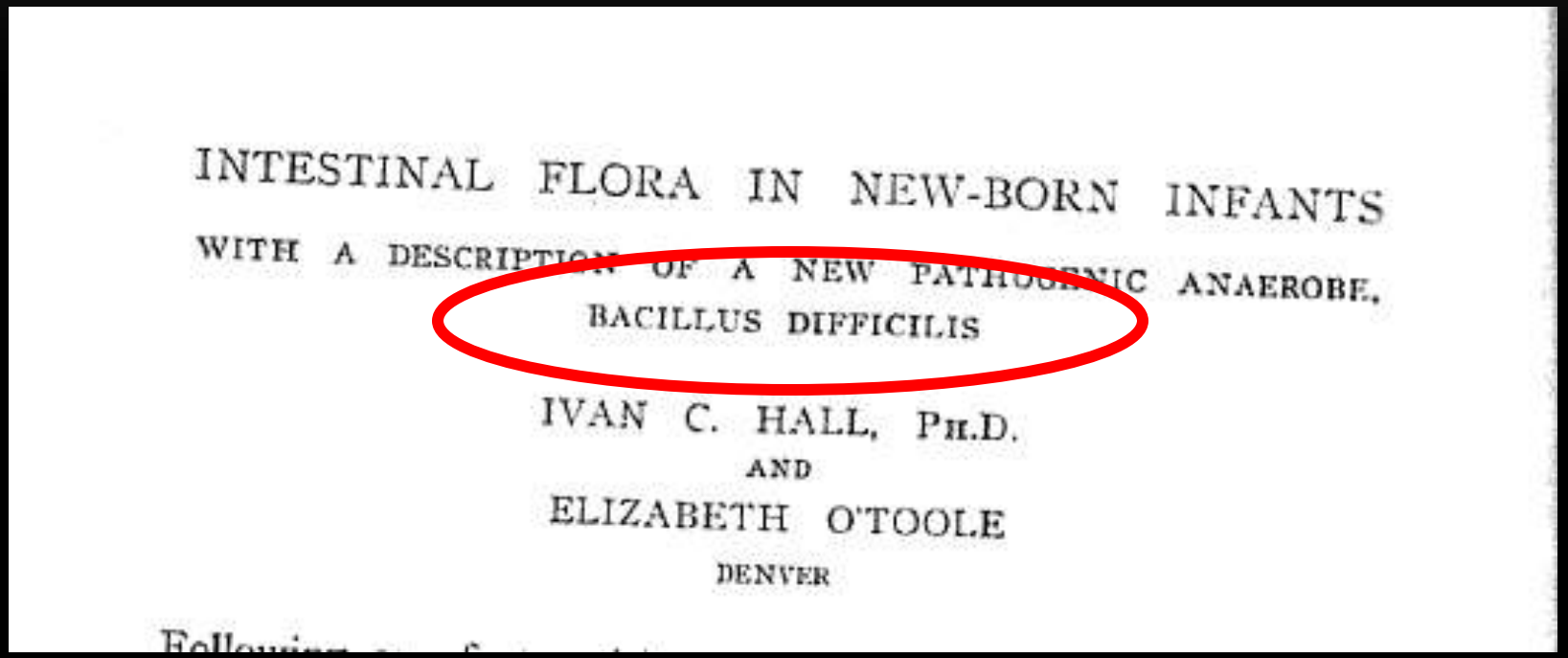
Sub specialist Pulmonary/Critical Care

Complex Wound Care Certfied

OBJETIVOS

- Breve Historia
- Nueva Epidemiologia
- Patofisiologia Molecular
- Patofisiologia Clinica
- Cepa B1/NAP1/027
- Tratamiento Tradicional
- Tratamiento Atipicos
- Rol de inmunidad
- Transplante

1935 DESCUBRIMIENTO



INTESTINAL FLORA IN NEW-BORN INFANTS

WITH A DESCRIPTION OF A NEW PATHOGENIC ANAEROBE,
BACILLUS DIFFICILIS

IVAN C. HALL, PH.D.
AND
ELIZABETH O'TOOLE
DENVER

1935 DESCUBRIMIENTO

- Naturalmente Anaerobico
- Identificaron que Producia una Toxina
- Notaron que NO producia patologia en el recien nacido
- Notaron , que al contrario la toxina producia una colitis en ratas
- Notaron que la toxina era menos potente que la Botulinica

HISTORIA 1935-1970

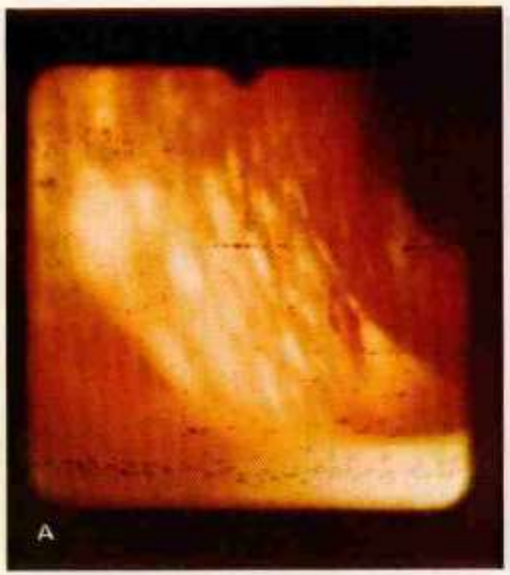
- Hummel RP, Altemeier WA, Hill EO. Iatrogenic staphylococcal enterocolitis. Ann Surg 1964; 160: 551-60
- Altemeier WA, Hummel RP, Hill EO. Staphylococcal enterocolitis following antibiotic theraphy. Ann Surg 1963; 157: 847-58
- ERRONEAMENTE IDENTIFICAN AL *S. Aureus* como el agente causal de la CPM.
- Notan que la CPM responde a VANCOMYCINA

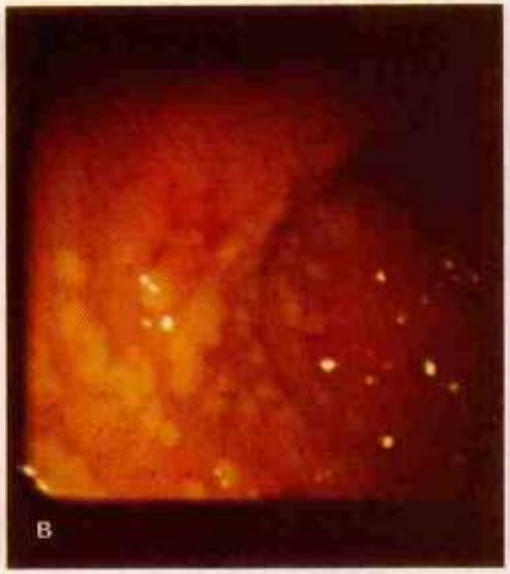
ANNALS of Internal Medicine
OCTOBER 1974 · VOLUME 81 · NUMBER 4
Published Monthly by the American College of Physicians

Clindamycin-Associated Colitis

A Prospective Study

FRANCIS J. TEDESCO, M.D., ROBERT W. BARTON, M.D., and DAVID H. ALPERS, M.D.,
St. Louis, Missouri





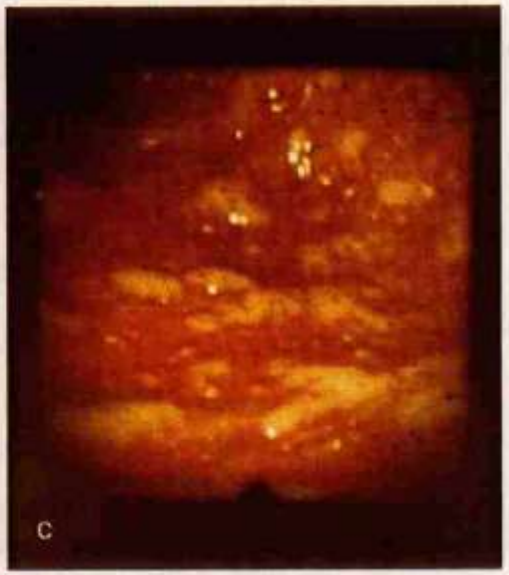
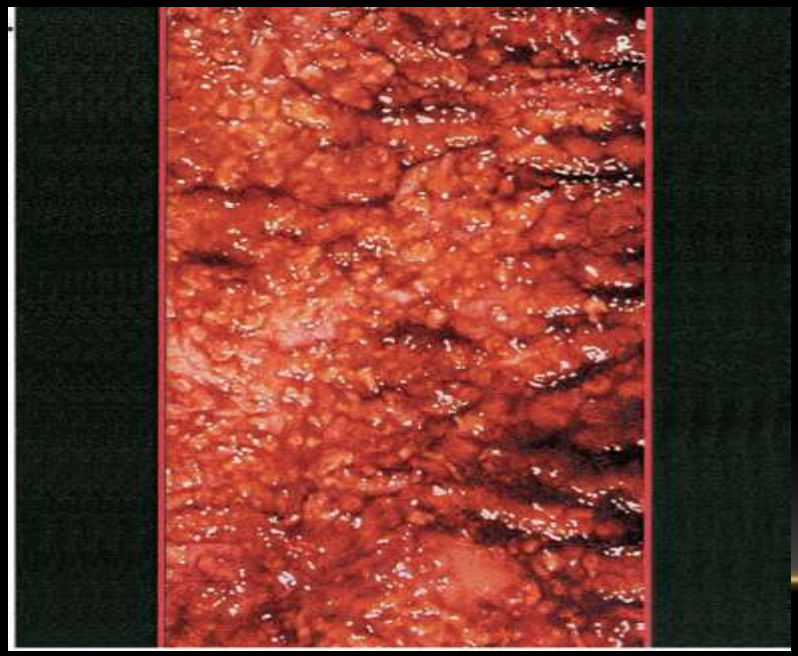


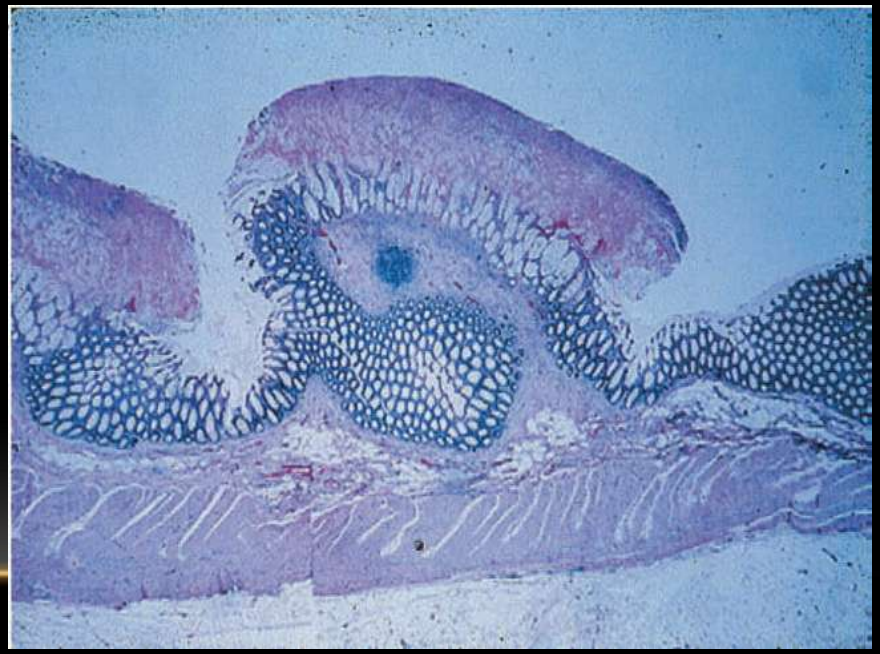
Figure 2. Colonoscopic views of progression of pseudomembranous colitis. Biopsies at all three stages showed pseudomembranes. A.

HISTORIA 1970-1980

ANTIBIOTIC-ASSOCIATED PSEUDOMEMBRANOUS COLITIS DUE TO TOXIN-PRODUCING CLOSTRIDIA

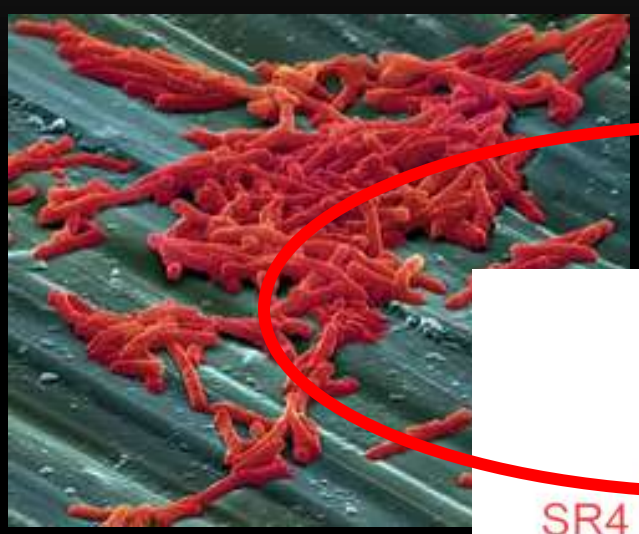
JOHN G. BARTLETT, M.D., TE WEN CHANG, M.D., MARC GURWITH, M.D., SHERWOOD L. GORBACH, M.D., AND ANDREW B. ONDERDONK, PH.D.

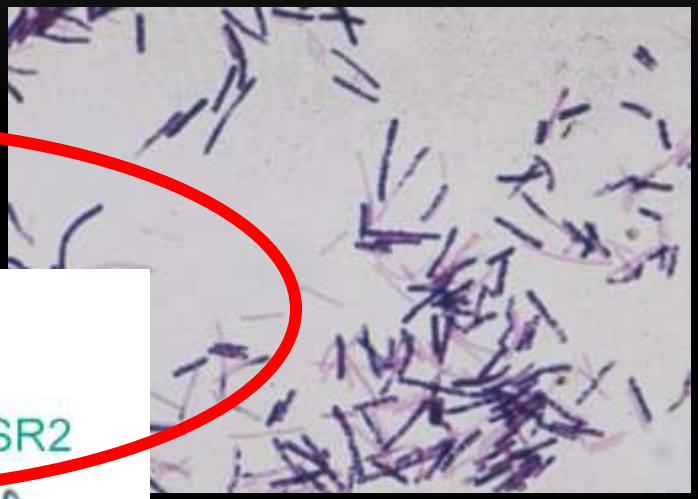


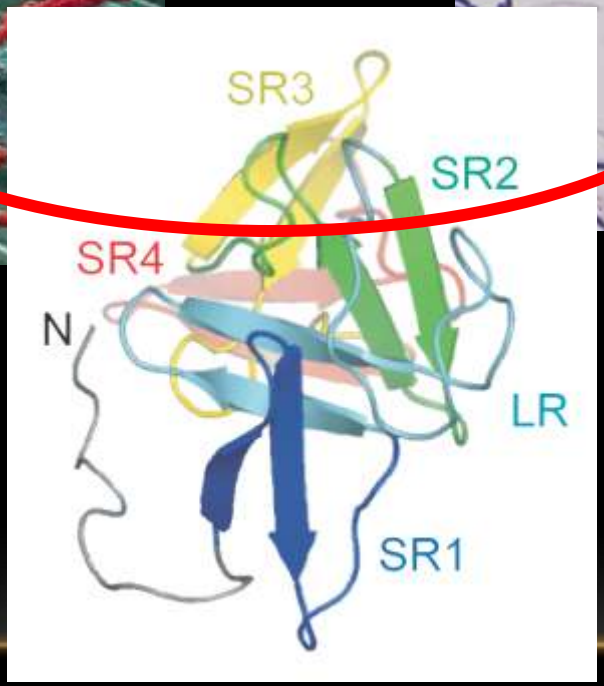


Bartlett JG N Engl J Med **1978**; 298:531–4.

ETIOLOGIA







FACTORES DE RIESGO

- Uso de antibioticos en los ultimos 90 dias
- Edad > 65 anos
- Hospitalizacion reciente
- PPI
- Nutricion Enteral
- Cirugia Gastrointestinal
- Chemotherapia

ANTIBIOTICOS

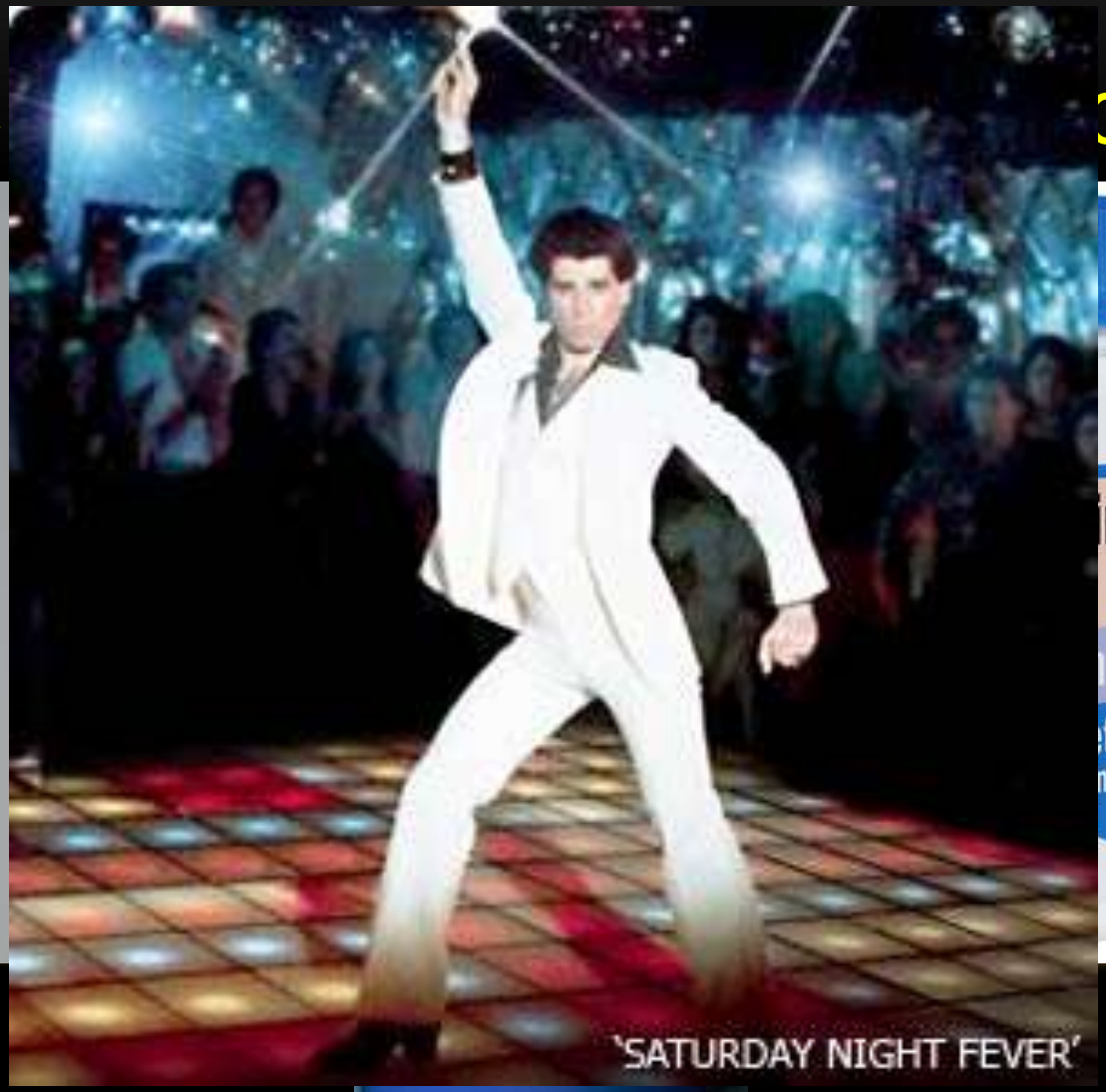
Antimicrobial agents that may induce clostridium difficile diarrhea and colitis

Frequently associated	Occasionally associated	Rarely associated
Fluoroquinolones	Macrolides	Aminoglycosides
Clindamycin	Trimethoprim	Tetracyclines
Penicillins (broad spectrum)	Sulfonamides	Chloramphenicol
Cephalosporins (broad spectrum)		Metronidazole
		Vancomycin

UpToDate

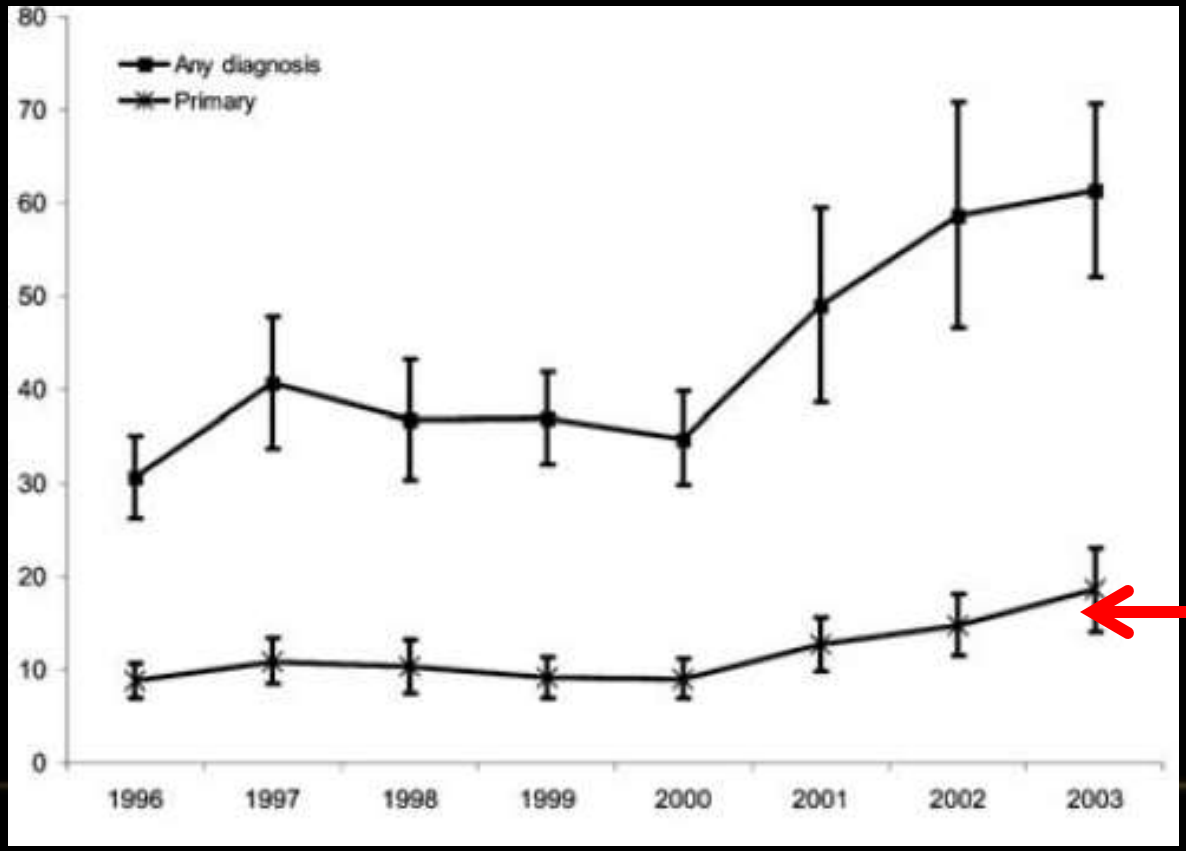
DECADA 80'S

Cepha onas



Clostridium difficile Infection in Patients Discharged from US Short-stay Hospitals, 1996–2003[1]

L. Clifford McDonald,* Maria Owings,* and Daniel B. Jernigan*



Mc Donald LC . Emerg Infect Dis 2006; 12: 409-15

DECADA 90 & 2000

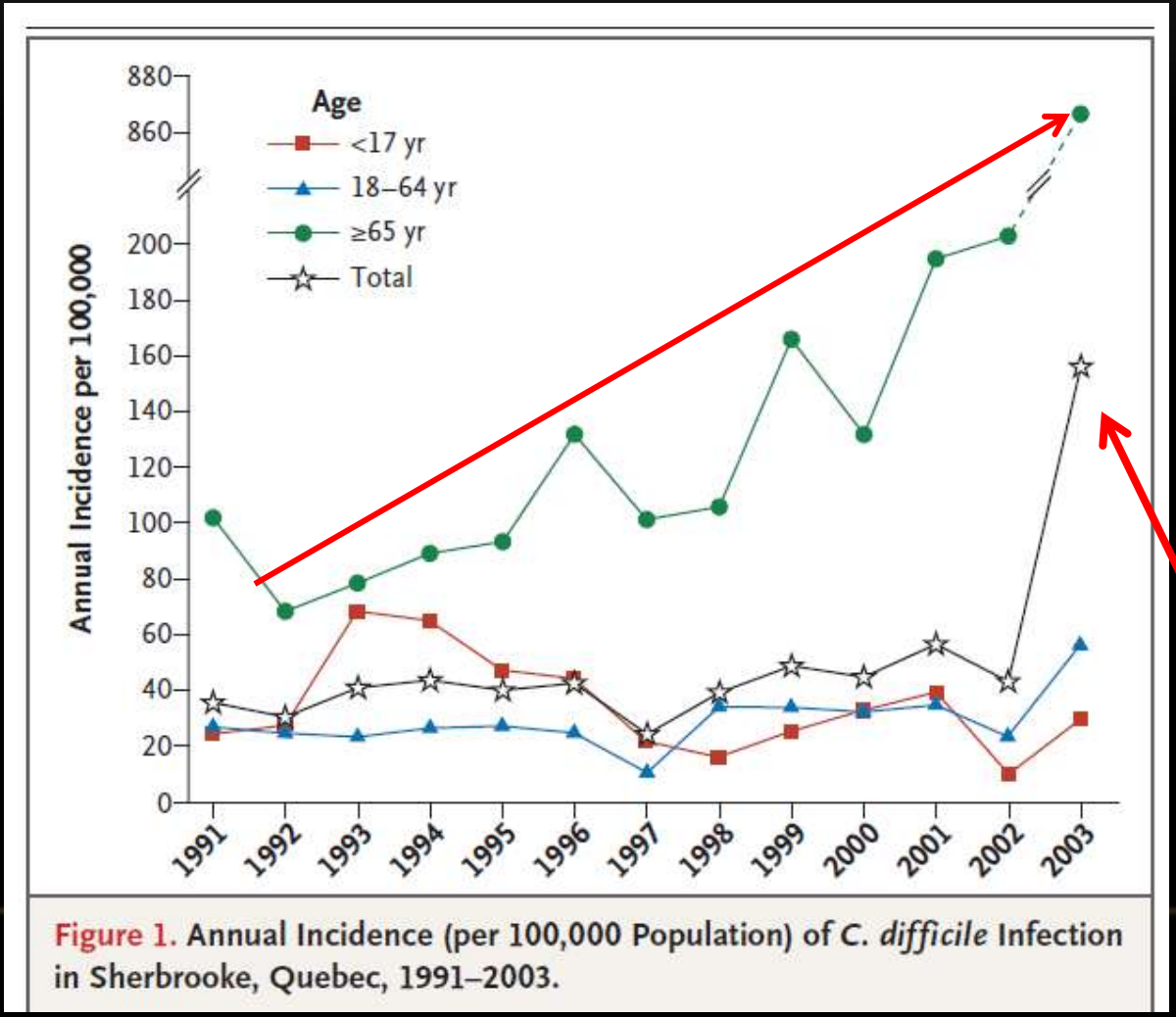
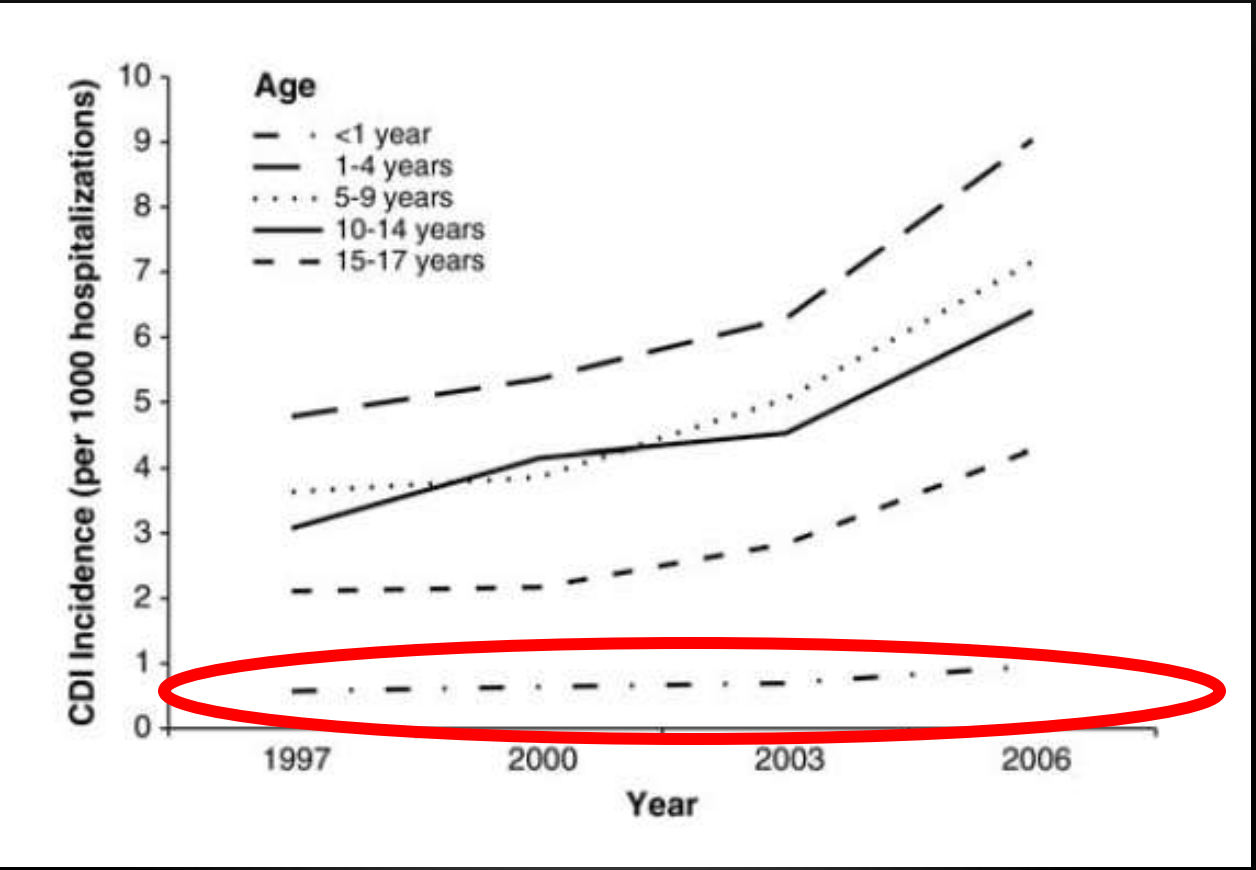


Figure 1. Annual Incidence (per 100,000 Population) of *C. difficile* Infection in Sherbrooke, Quebec, 1991–2003.

CMAJ 2004;171:466-72.

EPIDEMIOLOGIA/ PEDIATRIA



CID 2012:55 (Suppl 2) • Lessa et al

Toxin production by an emerging strain of *Clostridium difficile* associated with outbreaks of severe disease in North America and Europe

Michel Warny, Jacques Pepin, Aiqi Fang, George Killgore, Angela Thompson, Jon Brazier, Eric Frost, L Clifford McDonald

Summary

Interpretation The severity of *C difficile*-associated disease caused by NAP1/027 could result from hyperproduction of toxins A and B. Dissemination of this strain in North America and Europe could lead to important changes in the epidemiology of *C difficile*-associated disease.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*–Associated Diarrhea with High Morbidity and Mortality

Vivian G. Loo, M.D., Louise Poirier, M.D., Mark A. Miller, M.D., Matthew Oughton, M.D., Michael D. Libman, M.D., Sophie Michaud, M.D., M.P.H., Anne-Marie Bourgault, M.D., Tuyen Nguyen, M.D., Charles Frenette, M.D., Mirabelle Kelly, M.D., Anne Vibien, M.D., Paul Brassard, M.D., Susan Fenn, M.L.T., Ken Dewar, Ph.D., Thomas I. Hudson, M.D., Ruth Horn, M.D., Pierre René, M.D., M.D.

Table 2. Age-Specific Incidence and Mortality Attributed to *Clostridium difficile*–Associated Diarrhea.

Age	No. of Cases	No. of Cases/ 1000 Admissions*	Attributable 30-Day Mortality Rate
yr			%†
<40	76	3.5	2.6
41–50	85	11.2	1.2
51–60	191	20.0	3.2
61–70	272	24.4	5.1
71–80	523	38.3	6.2
81–90	458	54.5	10.2
>90	114	74.4	14.0

N Engl J Med 2005;353:2442-9.

An Epidemic, Toxin Gene–Variant Strain of *Clostridium difficile*

L. Clifford McDonald, M.D., George E. Killgore, Dr.P.H., Angela Thompson, M.M.Sc., Robert C. Owens, Jr., Pharm.D., Sophia V. Kazakova, M.D., M.P.H., Ph.D., Susan P. Sambol, M.T., Stuart Johnson, M.D., and Dale N. Gerding, M.D.

Table 1. Isolates of *Clostridium difficile* According to Health Care Facility and the Proportion of Isolates Belonging to the BI/NAP1 Strain.

Health Care Facility	Date of Onset of Outbreak	No. of Isolates Tested	BI/NAP1 Strain
			no. (%)
Georgia	Oct. 2001	46	29 (63)
Illinois	July 2003	14	6 (43)
Maine, Facility A	March 2002	13	9 (69)
Maine, Facility B	July 2003	48	30 (62)
New Jersey	June 2003	12	9 (75)
Oregon*	April 2002	30	3 (10)
Pennsylvania, Facility A	2000–2001	18	7 (39)
Pennsylvania, Facility B	Oct. 2003	6	3 (50)
Total		187	96 (51)

Nejm 2005; 353: 2433-41

EL NACIMIENTO DE UNA ESTRELLA

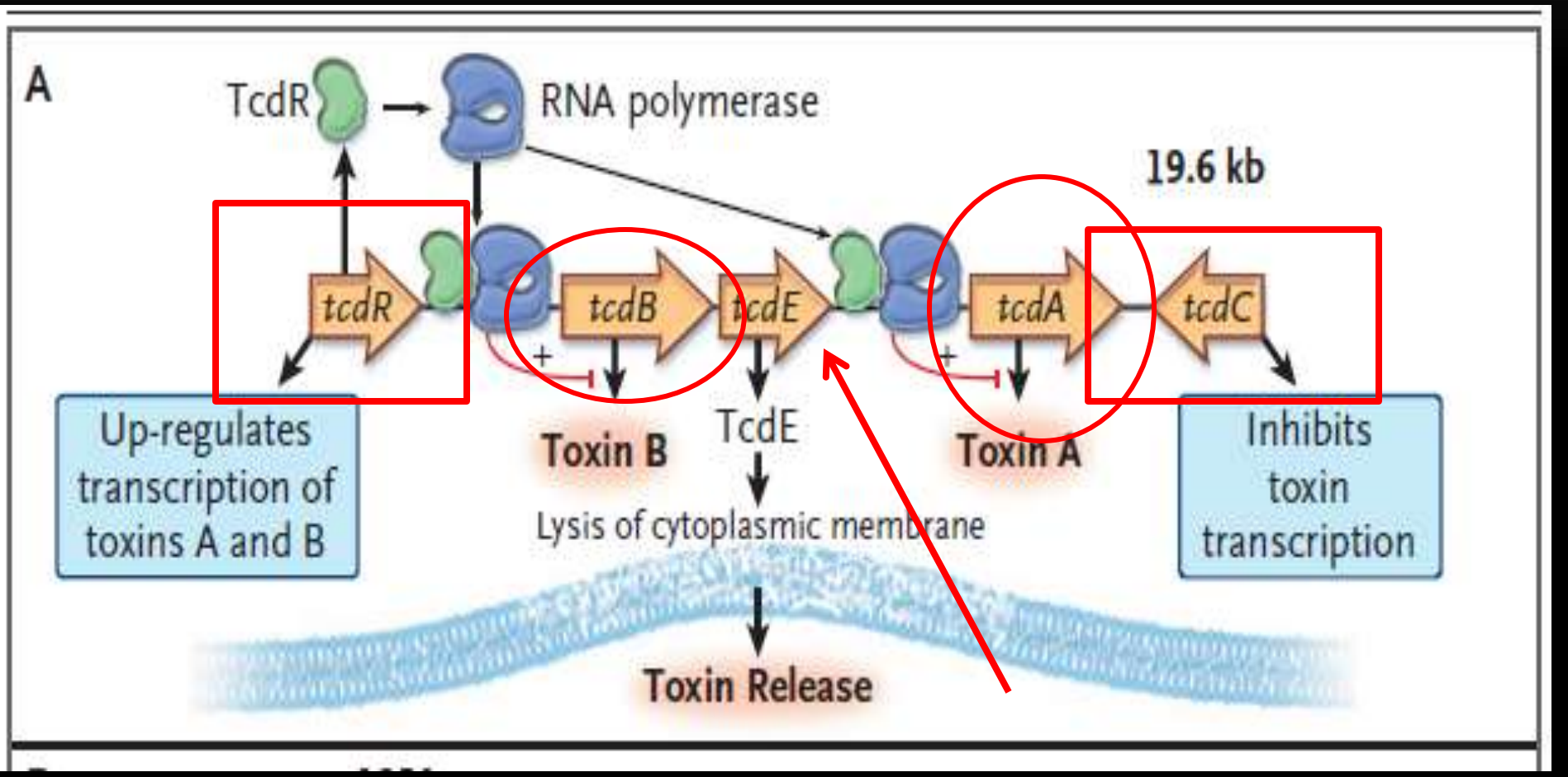
B1/NAP1/027

B1/NORTH AMERICAN PULSE FIELD TYPE 1/ PCR 027

Asociasiones

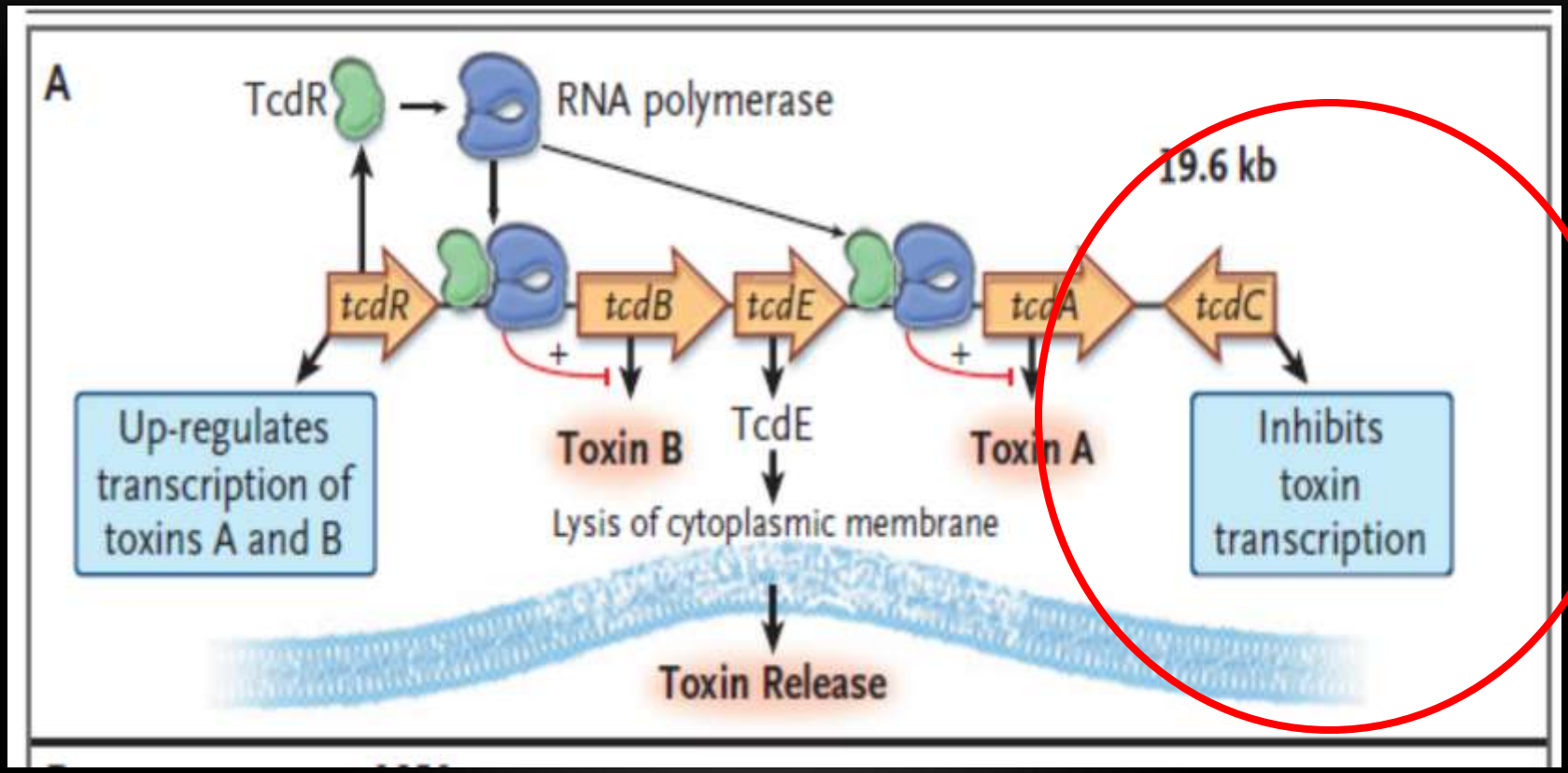
- Hyperproducion de toxina A &B
- Uso de Fluoroquinolonas
- Aparicion de Toxina Binaria

PATOFISIOLOGIA MOLECULAR



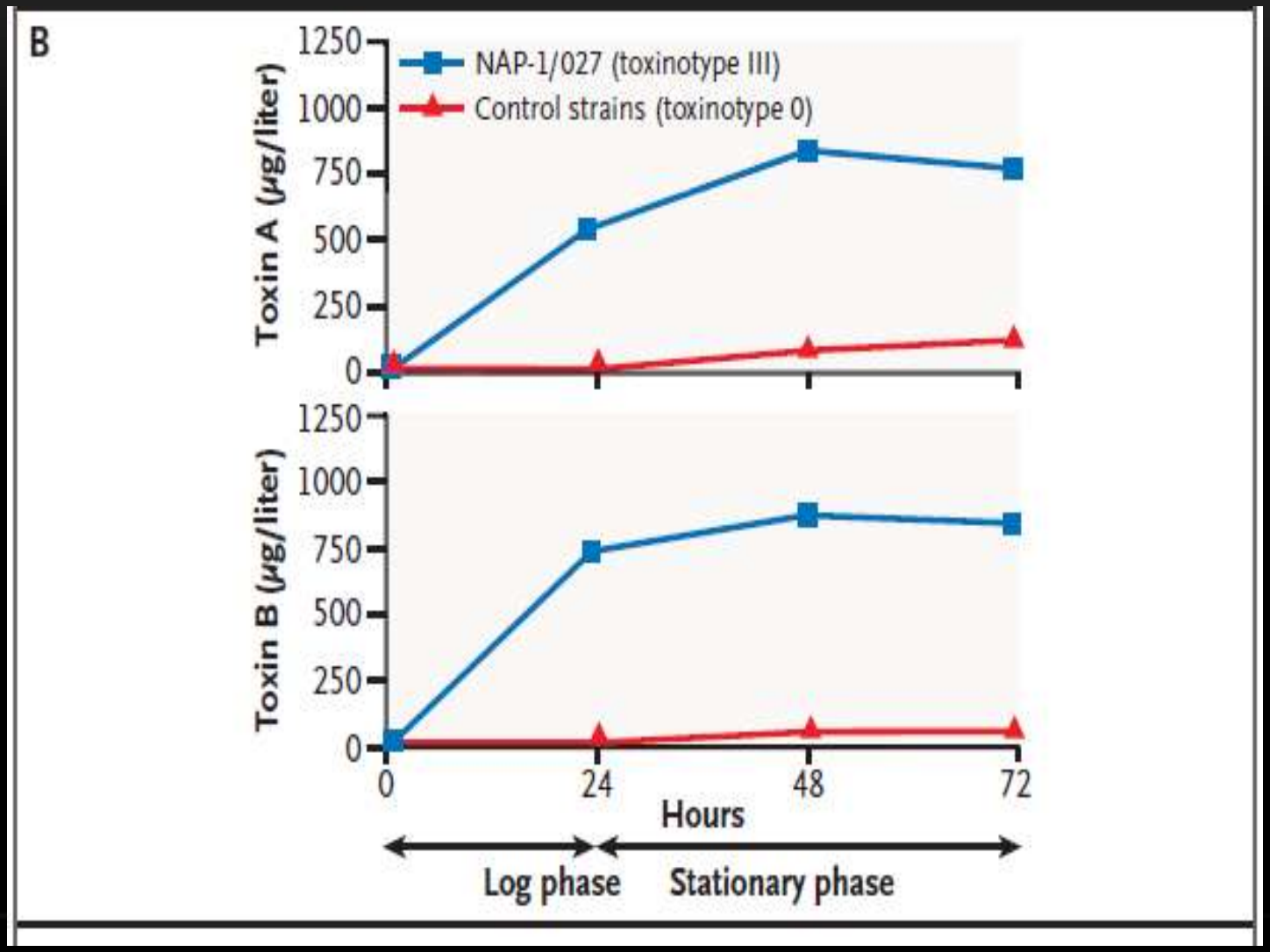
Nejm 359; 18: 1932

MUTACION TCD-C ------- B1/NAP1/027



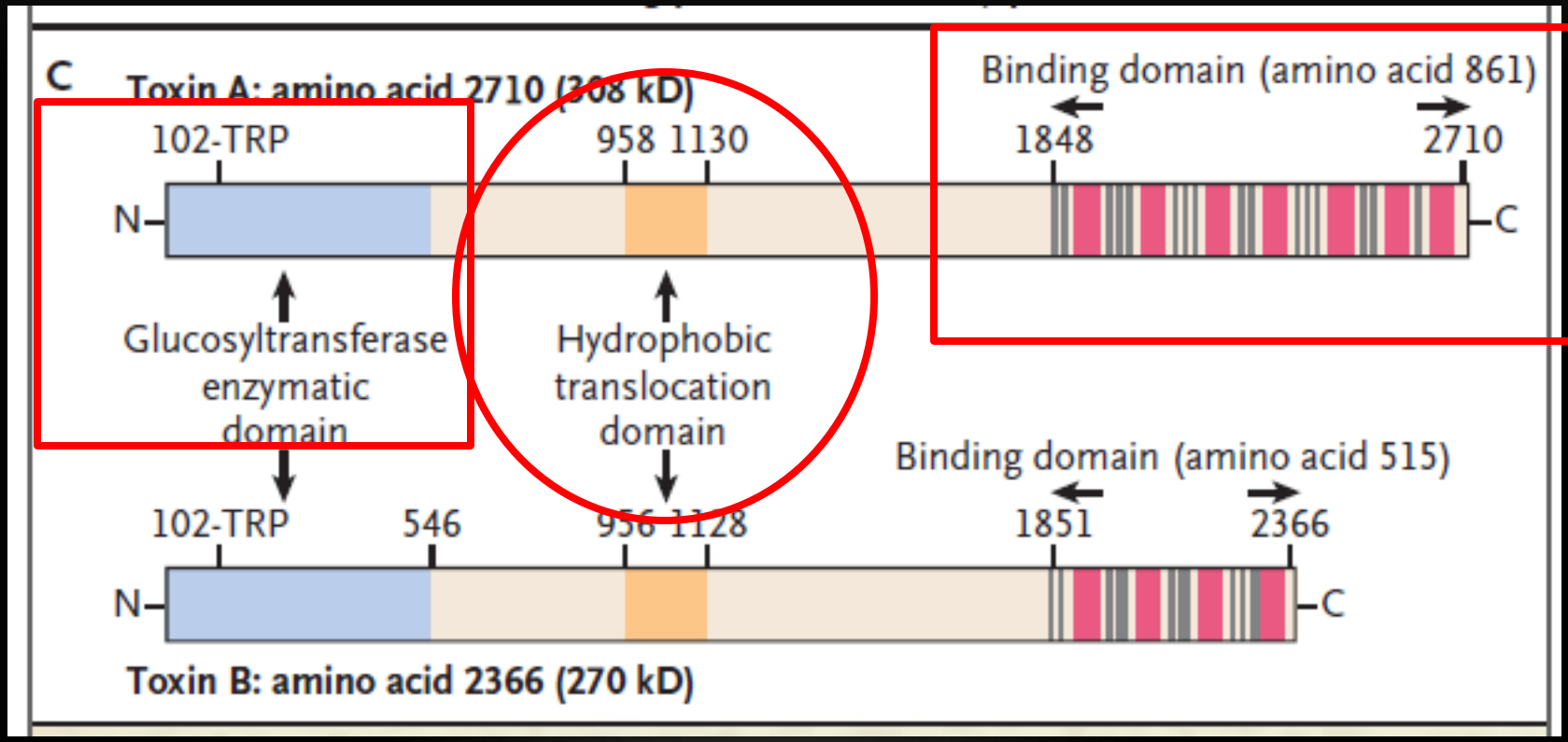
Nejm 359; 18: 1932

PATOFISIOLOGIA MOLECULAR



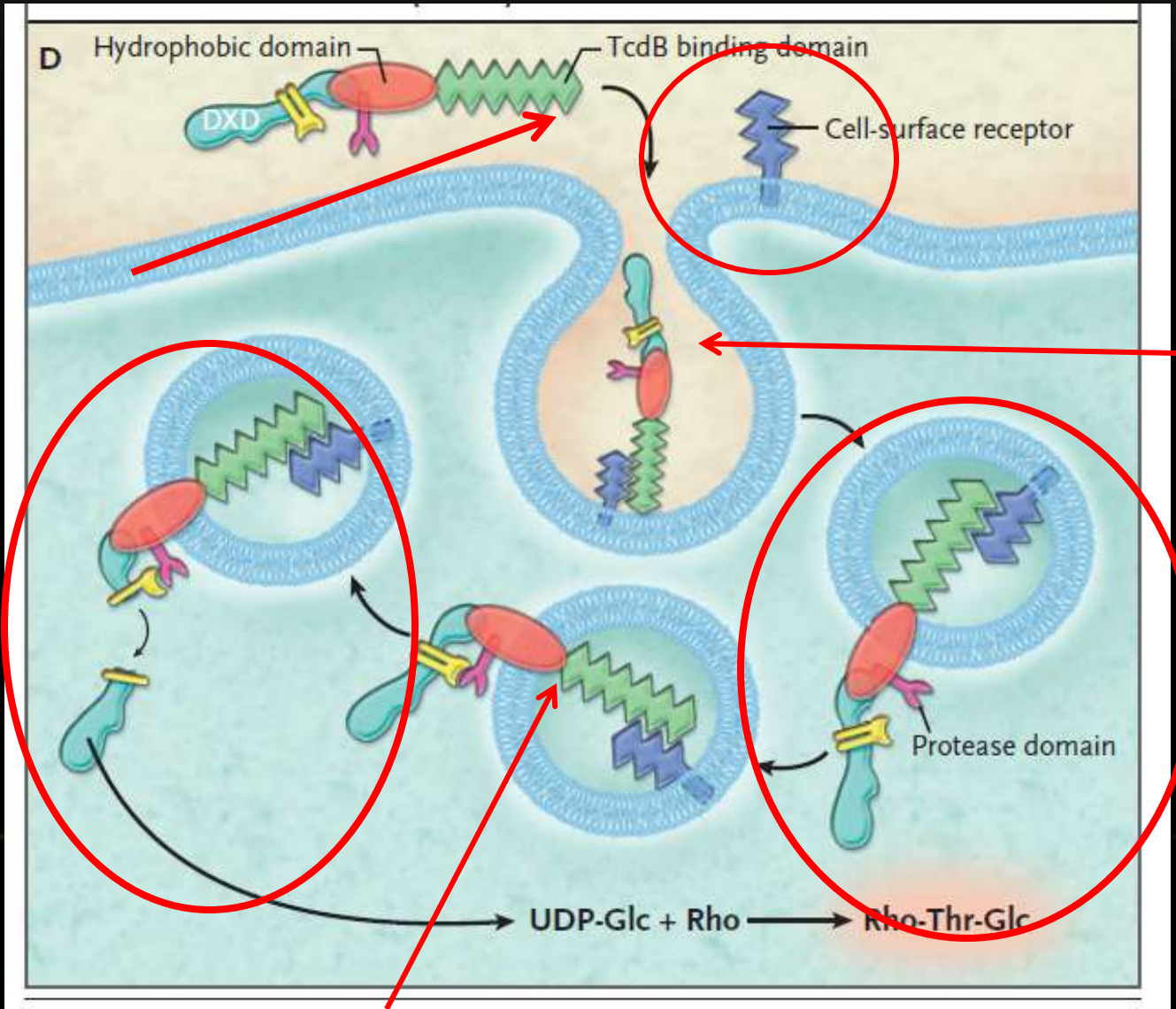
Nejm 359;18:1932

PATOFISIOLOGIA MOLECULAR



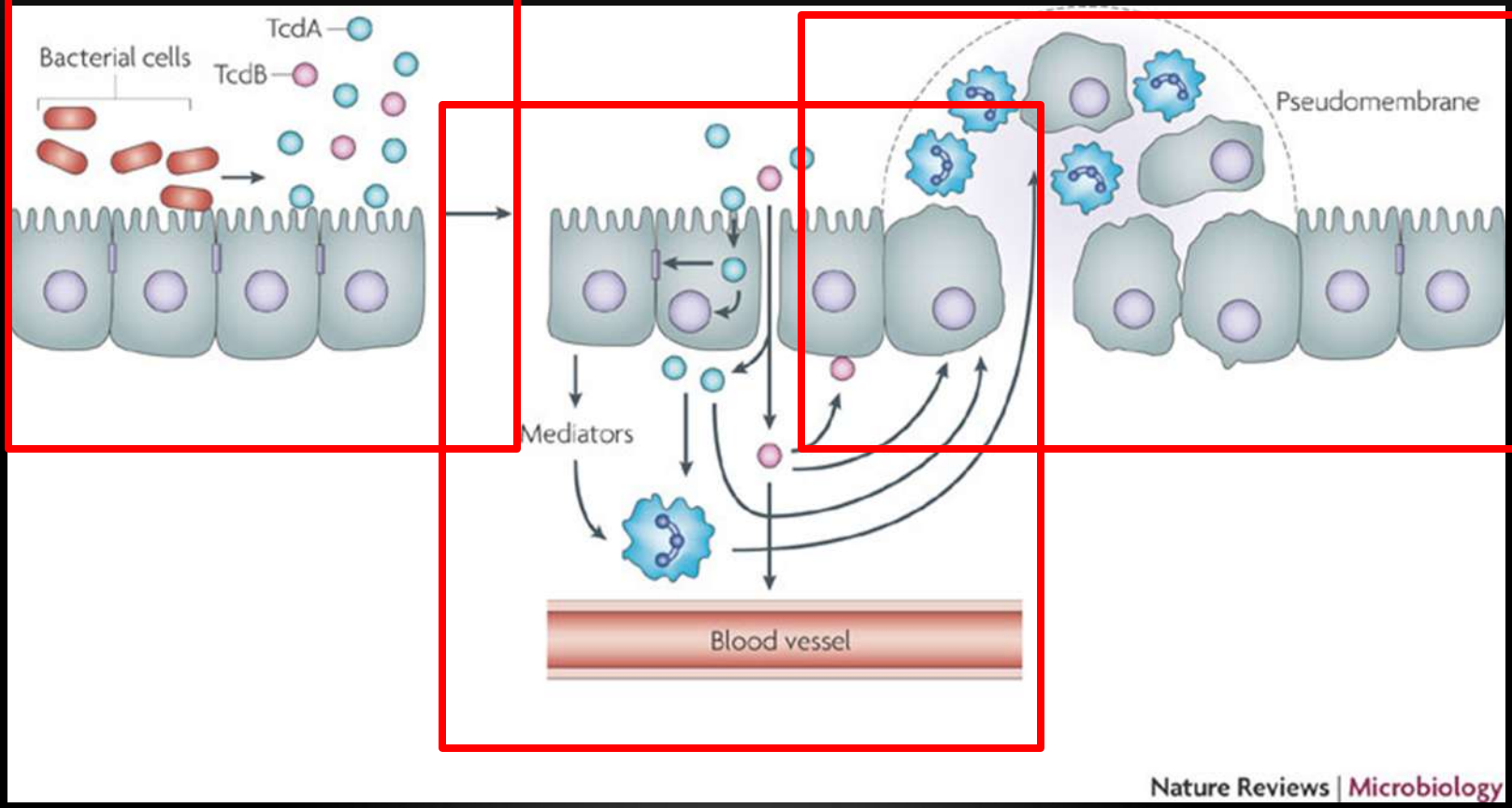
Nejm 359;18:1932

PATOFISIOLOGIA MOLECULAR

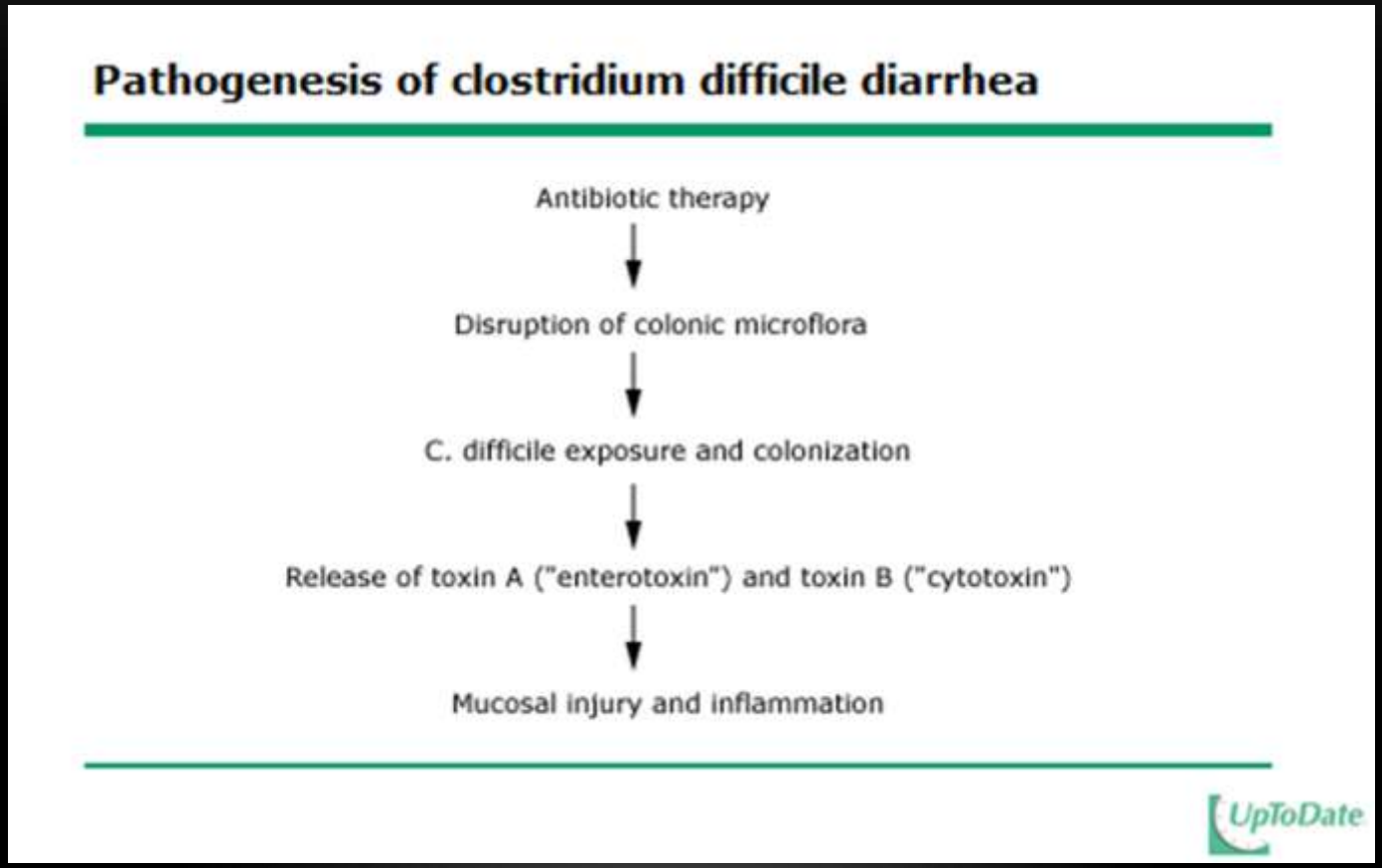


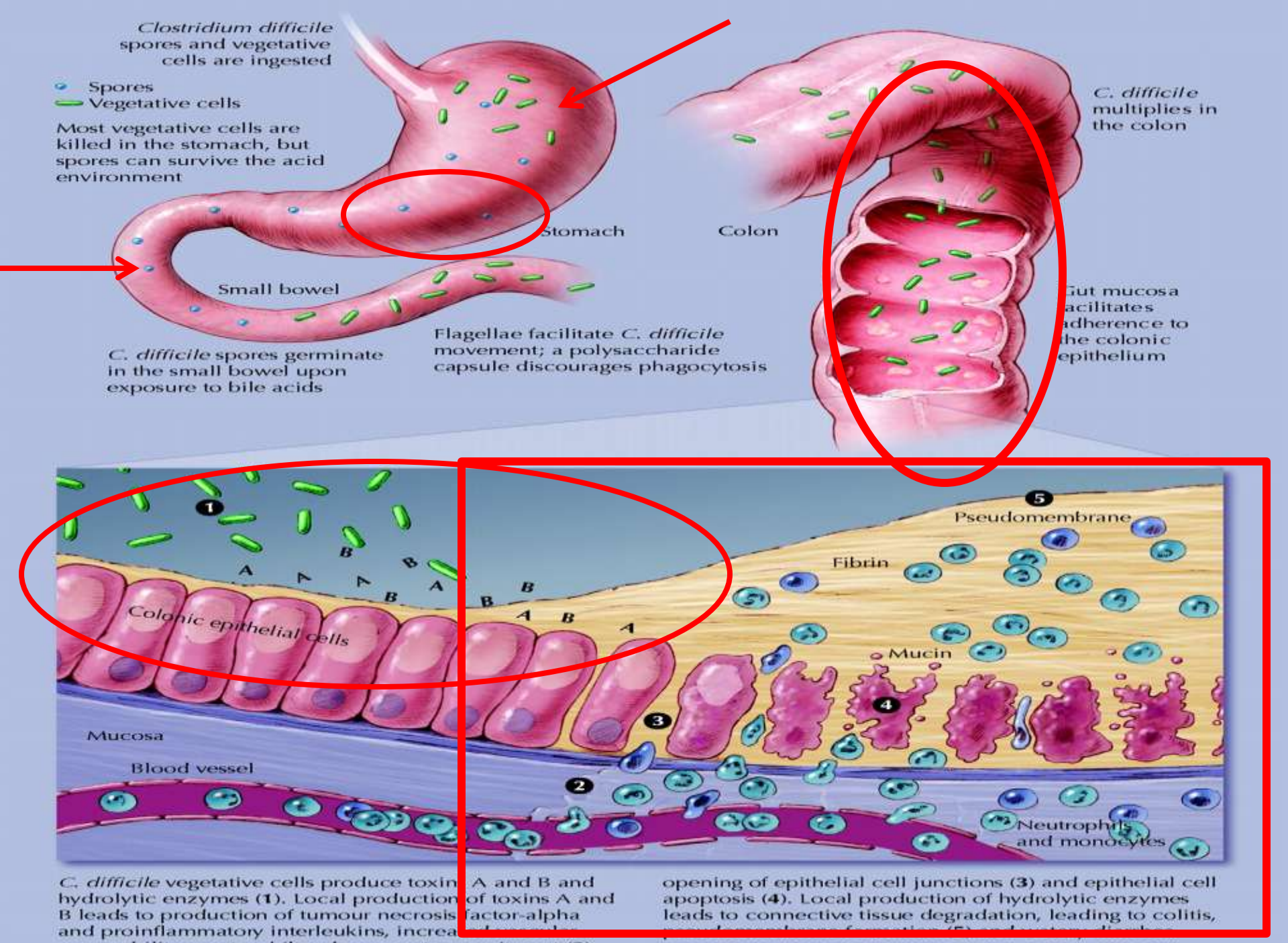
Nejm 359;18:1932

PATOFISIOLOGIA MOLECULAR



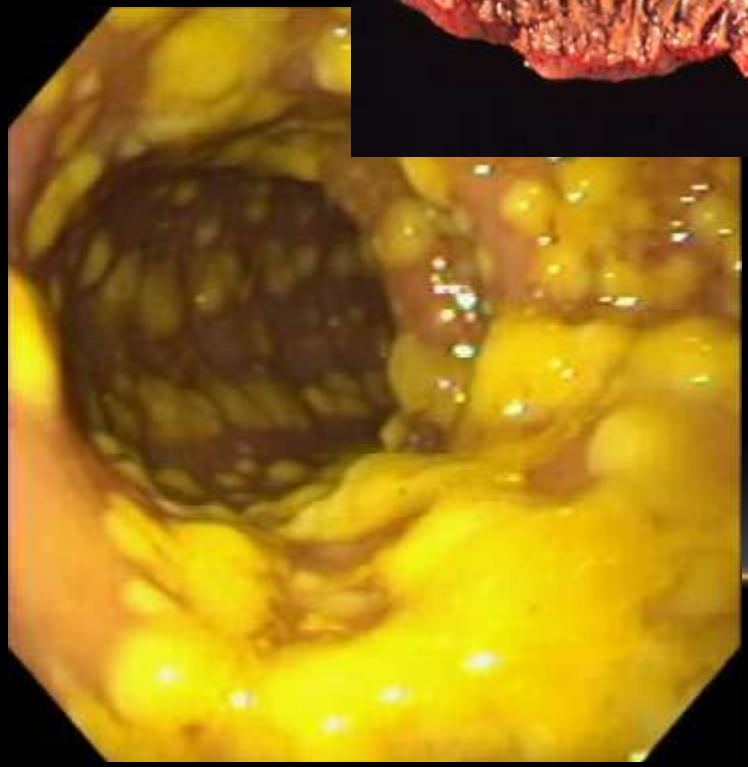
PATHOGENESIS

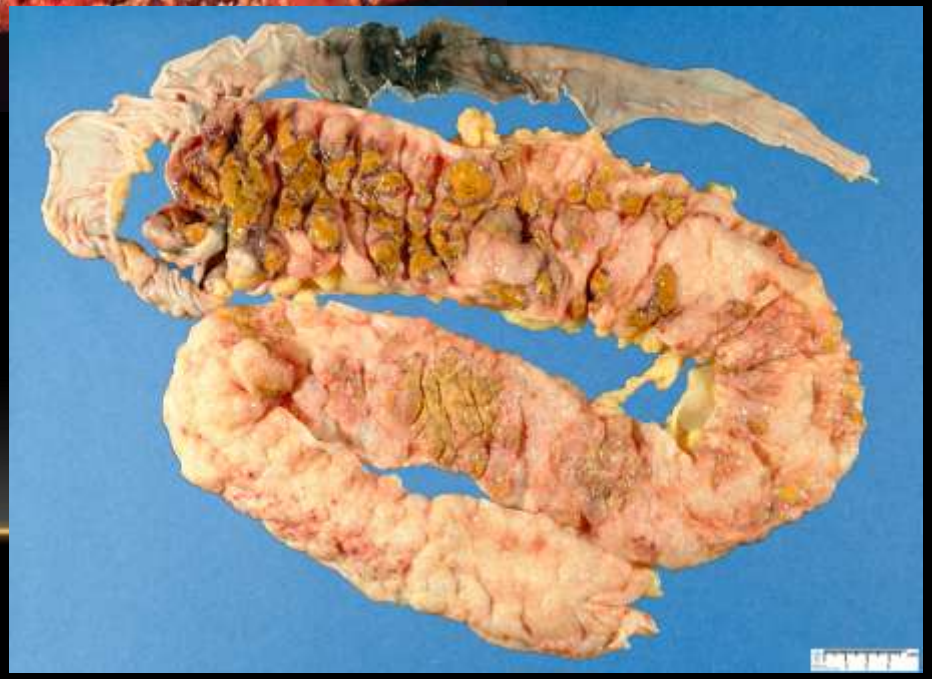




C. difficile vegetative cells produce toxin A and B and hydrolytic enzymes (**1**). Local production of toxins A and B leads to production of tumour necrosis factor-alpha and proinflammatory interleukins, increa permeability, neutrophil and monocyte recruitment (**2**), opening of epithelial cell junctions (**3**) and epithelial cell apoptosis (**4**). Local production of hydrolytic enzymes leads to connective tissue degradation, leading to colitis,

PATOLOGIA CLINICA





PRESENTACION CLINICA

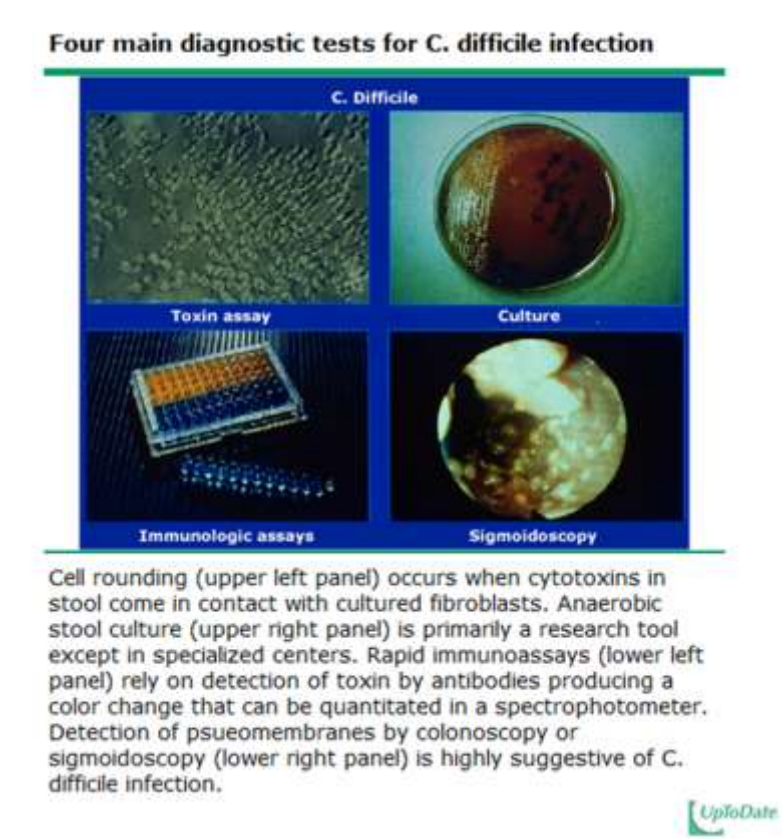
Clinical variants of C. difficile infection

Type of infection	Diarrhea	Other symptoms	Physical examination	Sigmoidoscopic examination
Asymptomatic carriage	Absent	Absent	Normal	Normal
C. difficile associated diarrhea with colitis	• Multiple loose bowel movements per day • Fecal leukocytes present • Occult bleeding may be seen • Hematochezia rare	Nausea, anorexia, fever, malaise, dehydration, leukocytosis with left shift	Abdominal distention, tenderness	Diffuse or patchy nonspecific colitis
Pseudomembranous colitis	• Diarrhea more profuse than in colitis without pseudomembranes • Fecal leukocytes present • Occult bleeding may be seen • Hematochezia rare	Nausea, anorexia, fever, malaise, dehydration, leucocytosiswith left shift; symptoms may be more severe than in colitis without pseudomembranes	Marked abdominal tenderness, distension	Characteristic raised, adherent, yellow plaques, diameter up to 2 cm; rectosigmoid spared in 10 percent of cases; pseudomembranesmay not be noted unless colonoscopy performed
Fulminant colitis	• Diarrhea may be severe OR diminished (due to paralytic ileus and colonic dilatation) • Surgical consult required; colectomy can be life-saving	Lethargy, fever, tachycardia, abdominal pain; dilated colon/paralytic ileus may be demonstrated on plain abdominal film	May present as acute abdomen; peritoneal signs suggest perforation	Sigmoidoscopy and colonoscopy contraindicated; flexible proctoscopy with minimal air insufflation may be diagnostic

PERLAS CLINICAS

- Leucocytosis
- Hypoalbuminemia
- Tenesmo/Diarrea
- “Amebiasis “ sin trofozoitos. !!!!!!

DIAGNOSTICO



- Toxina
- Organismo
- Endoscopia

LABORATORIO DIAGNOSTICO

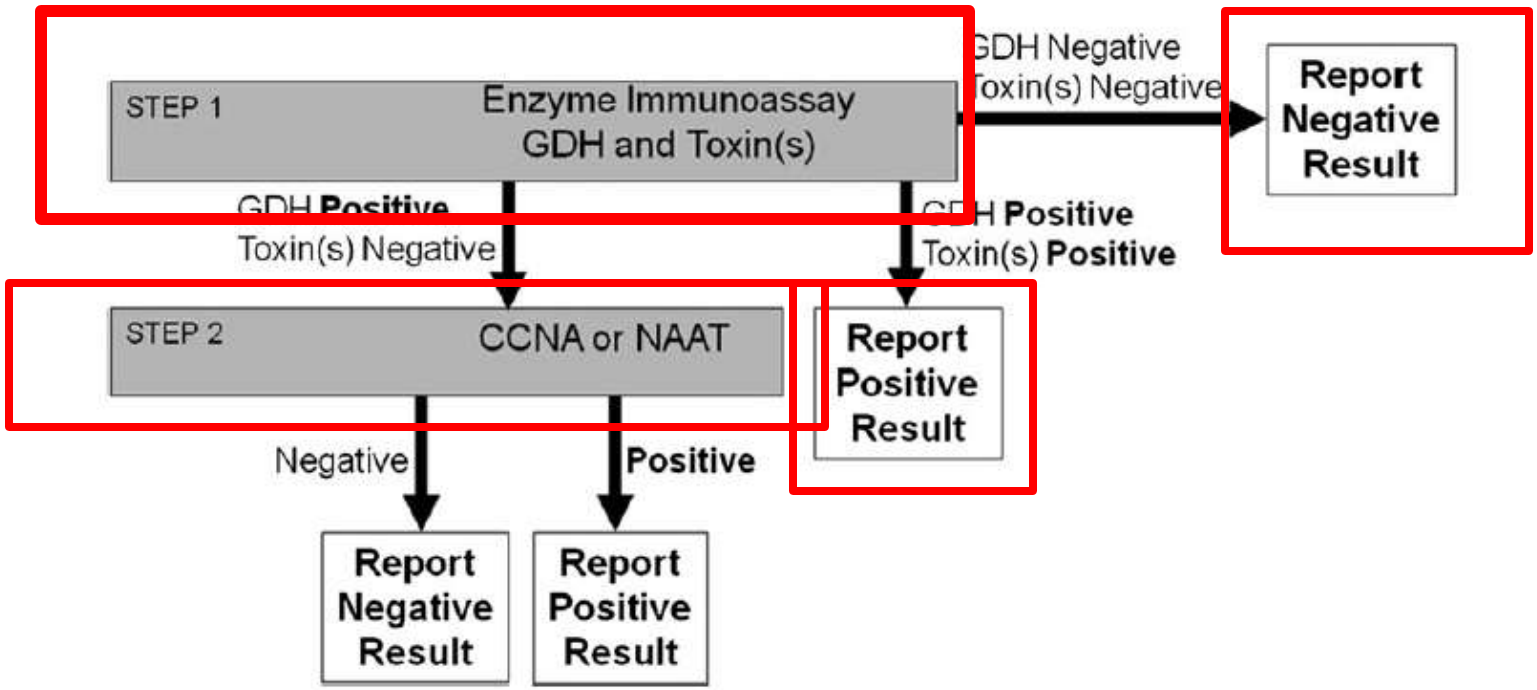
Identificacion de toxina

- EIA
- Citotoxicity *
- PCR

Identificacion del organismo

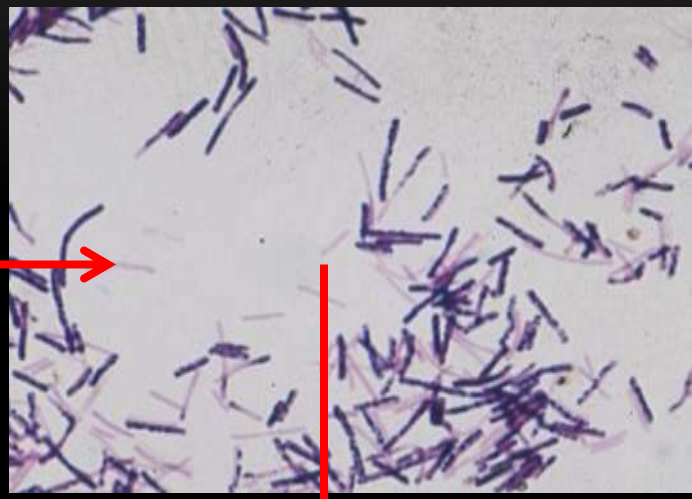
- Antigeno comun GDH
- Cultivo

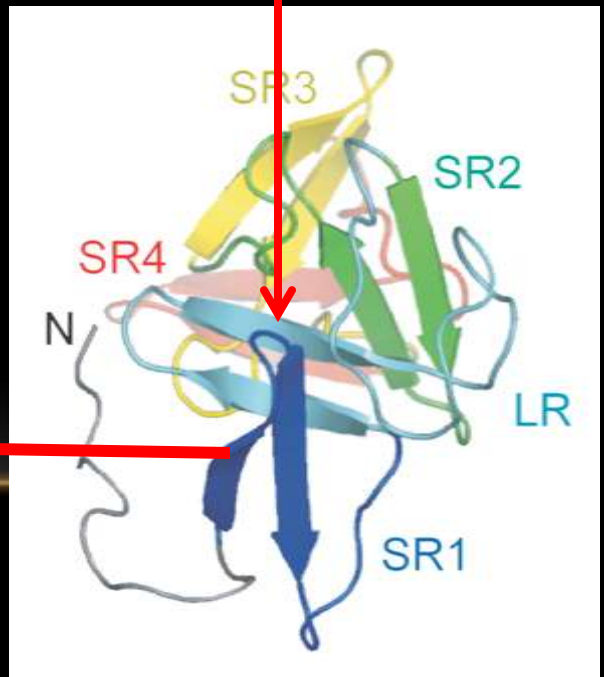
LABORATORIO DIAGNOSTICO

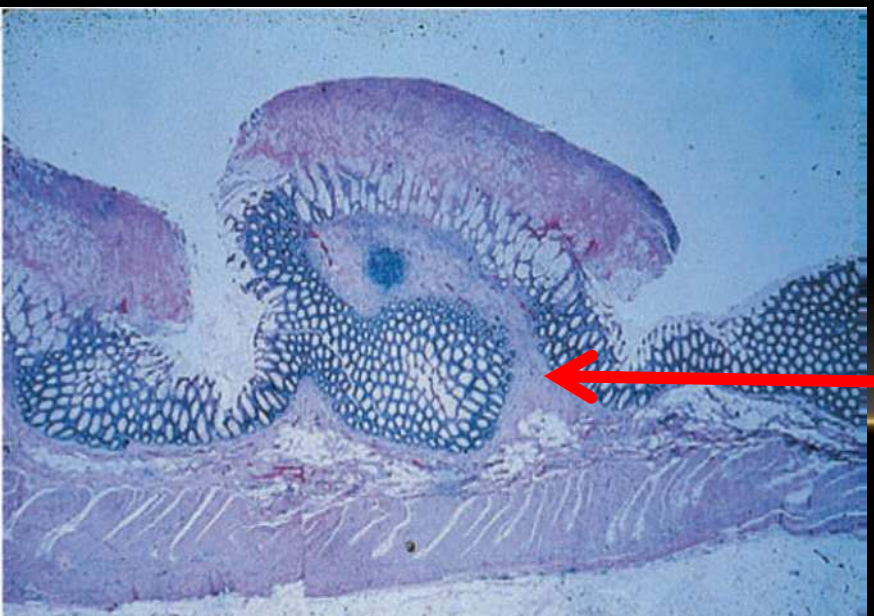


Clinical Infectious Diseases 2011;52(12):1451–1457

TRATAMIENTO



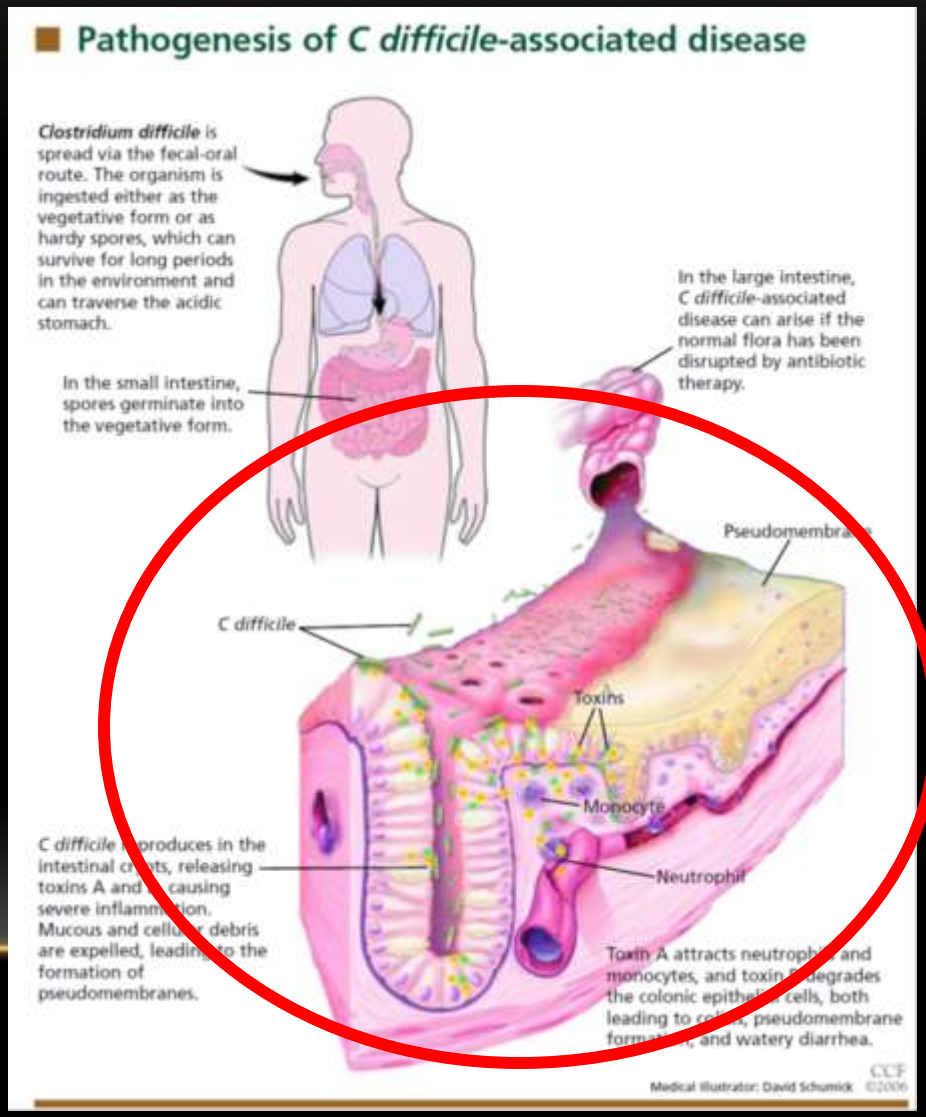




EL ANTIBIOTICO IDEAL

Caracteristicas

- Oral
- No absorbible
- Spectro reducido
- Minima alteracion de la flora
- Alta concentracion en heces



TRATAMIENTO

Table 1. Management of *Clostridium difficile* Infection (CDI)

CID management approaches and agents
"Inside the box" management (antimicrobial agents)
Currently available agents
Vancomycin
Metronidazole
Rifaximin
Nitazoxanide
Tigecycline
Bacitracin
Teicoplanin
Fusidic acid
Agents under clinical development
Fidaxomicin
Ramplanin
CB-183,315 (Cubist)[a]
"Outside the box" management (non-antimicrobial agents)
Currently available agents
Intraluminal toxin neutralizing agents
Biotherapeutic agents
Fecal transplants
Systemic antibody approaches
Intravenous immunoglobulin
Agents under clinical development
Intraluminal toxin neutralizing agents
Bovine whey protein
Tolevamer
Biotherapeutic agents
Nontoxigenic *C. difficile*
Systemic antibody approaches
Monoclonal antibodies
Active vaccines

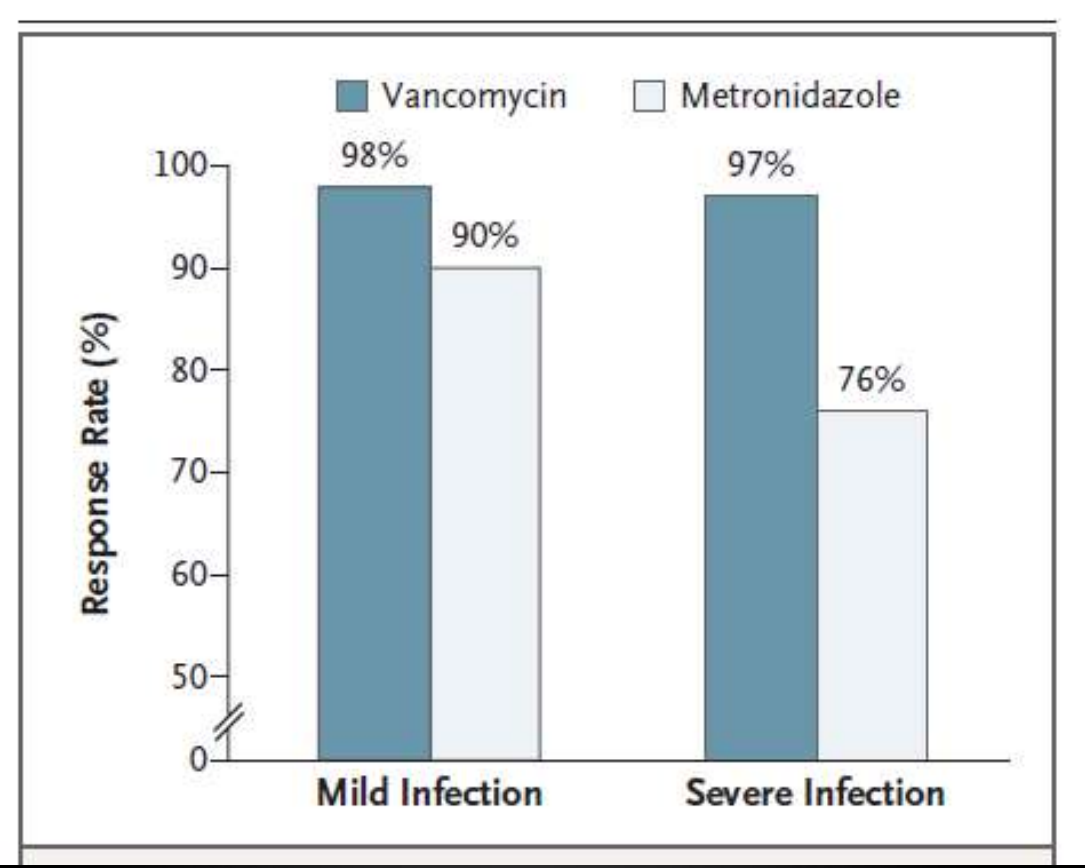
Clinical Infectious Diseases 2010; 51(11):1306–1313

TRATAMIENTO OPCIONES ATYPICAS

Table 1. Limitations of Available Agents Prior to May 2010 for the Treatment of *Clostridium difficile* Infection

Agent/Dose	Cost[a]/Total Treatment Course	Relative Efficacy	Recurrence Risk	Resistance in Clinical Isolates	Adverse Events	Other Comments
Vancomycin: FDA approved for CDI						
Dose: 125 mg po qid × 10 d or "taper/pulse" for recurrence: 125 mg po qid × 10–14 d, then 125 mg po bid per d × 1 wk, then 125 mg po once daily × 1 wk, then 125 mg po every 2 or 3 d for 2–8 wk	$$$$/$$$$	+++	++	Not reported	Not absorbed so systemic symptoms unlikely, nausea	Potential for resistance induction in other clinically important pathogens
Metronidazole: not approved for CDI						
Dose: 500 mg po tid × 10 d or 250 mg po qid × 10 d	$/$	++	++	Increased MICs noted in some studies	Neuropathy, nausea, abnormal taste in mouth	Increasing reports of treatment failures & slow response, less effective in severe CDI
Nitazoxanide: not approved for CDI						
Dose: 500 mg po bid × 10 d	$$	++	++	Not reported	Abdominal pain, diarrhea, nausea	Limited clinical trial data, similar recurrence rate compared with metronidazole
Rifaximin: not approved for CDI						
Dose: 400 mg po tid × 10 d or chaser regimen[b] 400 mg po bid × 14 d	$$$/$$$	++	+?	Potential for development of high-level resistance	Not absorbed, headache, abdominal pain, nausea, flatulence	Used primarily as post–vancomycin treatment in patients with multiple recurrences
Tigecycline: not approved for CDI						
Dose: 50 mg IV every 12 h × 10 d	$$$$	++?	?	Not reported	Nausea, vomiting, diarrhea	Limited case reports of treatment success and failures
Bacitracin: not approved for CDI						
Dose: 25 000 units po qid × 10 d	$$	+	+++	Increasing resistance noted	Minimal absorbed, poor taste	Limited efficacy secondary to resistance
Fusidic acid: not approved for CDI						
Dose: 250 mg po tid × 10 d	N/A in US	++	++	Reported to develop in vivo resistance	Nausea, vomiting, epigastric pain, anorexia	Concern about use as a single agent
Teicoplanin: not approved for CDI						
Dose: 400 mg po bid × 10 d	N/A in US	+++	++	Not reported	Not absorbed so systemic symptoms unlikely	Similar results to vancomycin

METRONIDAZOL VS VANCOMYCINA

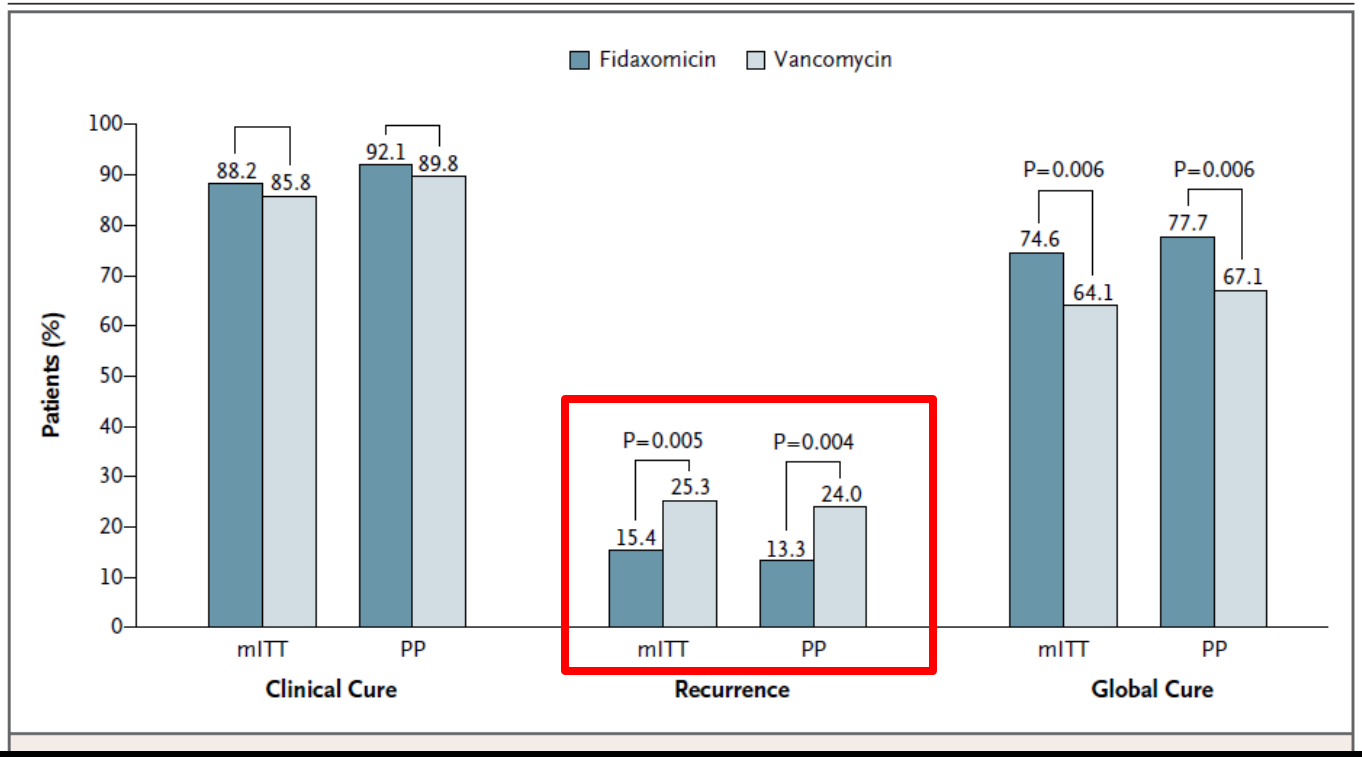


N ENGL J MED 359;18

ORIGINAL ARTICLE

Fidaxomicin versus Vancomycin for *Clostridium difficile* Infection

Thomas J. Louie, M.D., Mark A. Miller, M.D., Kathleen M. Mullane, D.O., Karl Weiss, M.D., Arnold Lentnek, M.D., Yoav Golan, M.D., Sherwood Gorbach, M.D., Pamela Sears, Ph.D., and Youe-Kong Shue, Ph.D., for the OPT-80-003 Clinical Study Group*



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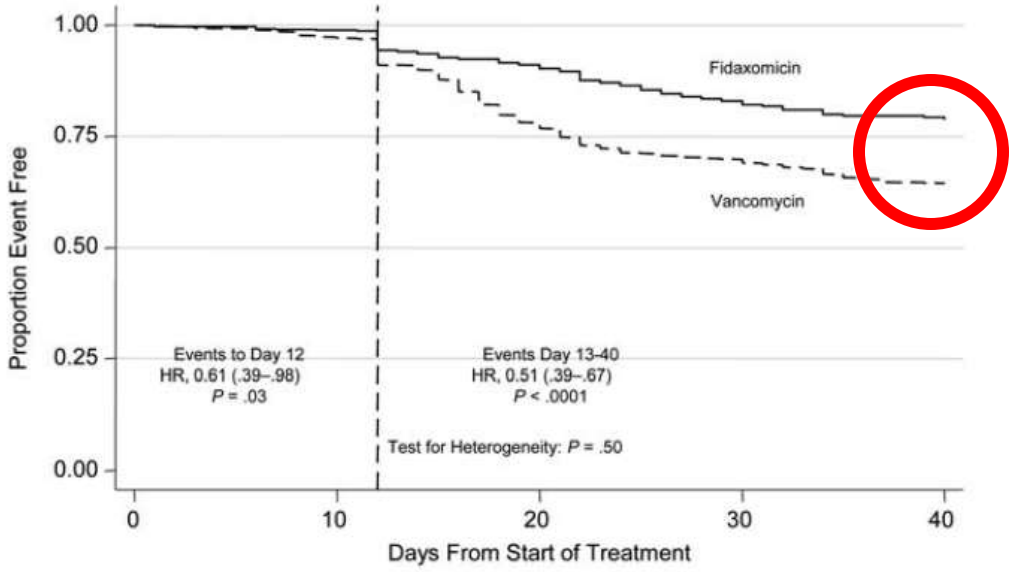
Thomas J. Louie, M.D., Mark A. Miller, M.D., Kathleen M. Mullane, D.O., Karl Weiss, M.D., Arnold Lentnek, M.D., Yoav Golan, M.D., Sherwood Gorbach, M.D., Pamela Sears, Ph.D., and Youe-Kong Shue, Ph.D., for the OPT-80-003 Clinical Study Group*

Subgroup	Modified Intention-to-Treat Population			Per-Protocol Population		
	Fidaxomicin	Vancomycin	P Value	Fidaxomicin	Vancomycin	P Value
	no./total no. (%)			*no./total no. (%)*		
Age						
<65 yr	19/150 (12.7)	27/134 (20.1)	0.09	12/126 (9.5)	22/118 (18.6)	0.04
≥65 yr	20/103 (19.4)	40/131 (30.5)	0.05	16/85 (18.8)	31/103 (30.1)	0.08
Hospital status						
Inpatient	24/136 (17.6)	40/146 (27.4)	0.05	19/106 (17.9)	29/111 (26.1)	0.15
Outpatient	15/117 (12.8)	27/119 (22.7)	0.05	9/105 (8.6)	24/110 (21.8)	0.007
Previous episode of *C. difficile* infection						
No	30/211 (14.2)	52/217 (24.0)	0.01	22/175 (12.6)	41/183 (22.4)	0.02
Yes	9/42 (21.4)	15/48 (31.2)	0.30	6/36 (16.7)	12/38 (31.6)	0.14
Treatment for current episode of *C. difficile* infection in previous 24 hr						
Yes	16/88 (18.2)	25/97 (25.8)	0.22	13/73 (17.8)	19/81 (23.5)	0.39
No	23/165 (13.9)	42/168 (25.0)	0.01	15/138 (10.9)	34/140 (24.3)	0.003
Severity of disease at baseline						
Mild	7/59 (11.9)	20/68 (29.4)	0.02	4/44 (9.1)	13/55 (23.6)	0.06
Moderate	20/102 (19.6)	18/88 (20.5)	0.89	15/90 (16.7)	18/71 (25.4)	0.18
Severe	12/92 (13.0)	29/109 (26.6)	0.02	9/77 (11.7)	22/95 (23.2)	0.05
Strain type						
NAP1/BI/027	16/59 (27.1)	14/67 (20.9)	0.42	11/45 (24.4)	13/55 (23.6)	0.93
Non–NAP1/BI/027	12/117 (10.3)	34/121 (28.1)	<0.001	8/103 (7.8)	27/106 (25.5)	<0.001
Concomitant systemic antimicrobial therapy						
Yes	14/81 (17.3)	25/90 (27.8)	0.10	8/56 (14.3)	20/65 (30.8)	0.03
No	25/172 (14.5)	42/175 (24.0)	0.03	20/155 (12.9)	33/156 (21.2)	0.05

N Engl J Med 2011;364:422-31.

Fidaxomicin Versus Vancomycin for *Clostridium difficile* Infection: Meta-analysis of Pivotal Randomized Controlled Trials

Derrick W. Crook,[1,2] A. Sarah Walker,[1,2] Yin Kean,[3] Karl Weiss,[4] Oliver A. Cornely,[5] Mark A. Miller,[6] Roberto Esposito,[7] Thomas J. Louie,[8,9] Nicole E. Stoesser,[1,2] Bernadette C. Young,[1,2] Brian J. Angus,[1] Sherwood L. Gorbach,[3,10] and Timothy E. A. Peto[1,2] for the Study 003/004 Teams



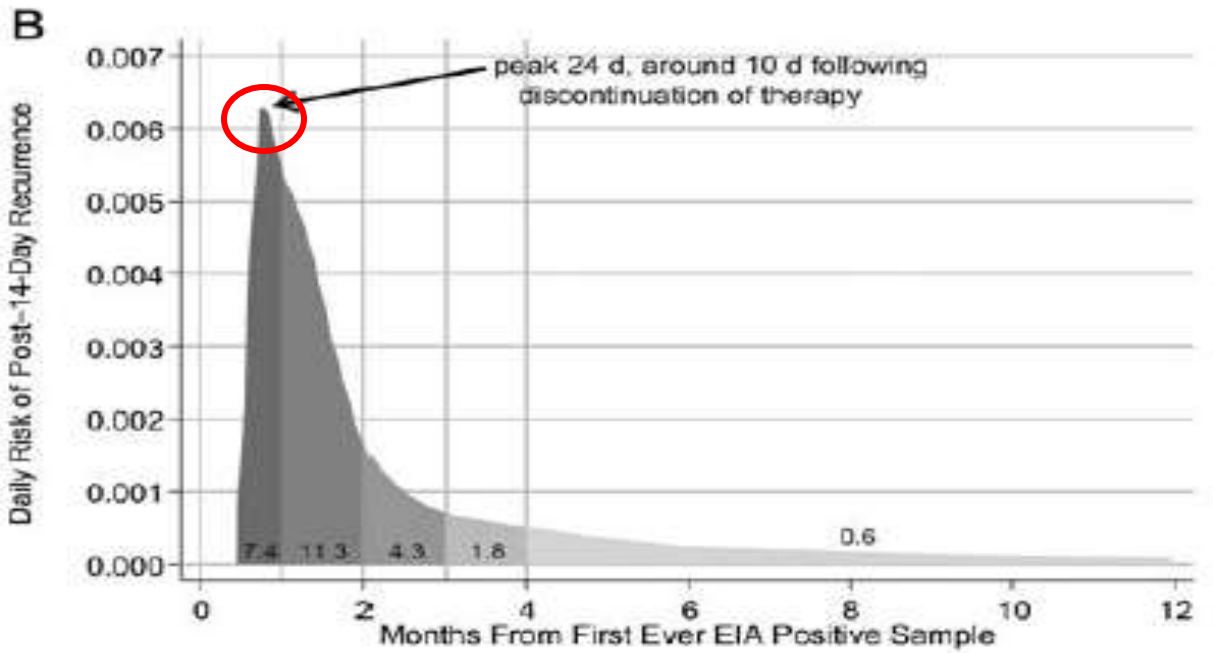
Number at Risk	(events)								
Fidaxomicin	572	(6)	515	(41)	472	(42)	427	(21)	405
Vancomycin	592	(14)	527	(104)	416	(44)	365	(27)	334

Note: Patients first assessed for persistent diarrhea 8 to 12 days after start of treatment: those with diarrhea considered as events on day 12.

Predictors of First Recurrence of *Clostridium difficile* Infection: Implications for Initial Management

David W. Eyre,[1] A. Sarah Walker,[1,2] David Wyllie,[1] Kate E. Dingle,[1,3] David Griffiths,[1,2] John Finney,[1] Lily O'Connor,[1] Alison Vaughan,[1,2] Derrick W. Crook,[1,2] Mark H. Wilcox,[4,5] and Timothy E. A. Peto,[1,2] for the Infections in Oxfordshire Research Database

[1]NIHR Oxford Biomedical Research Centre, John Radcliffe Hospital, [2]Nuffield Department of Clinical Medicine, and [3]Department of Clinical Laboratories Sciences, Oxford University; [4]Department of Microbiology, The General Infirmary, Old Medical School, and [5]Leeds Institute of Molecular Medicine, University of Leeds, United Kingdom



Note: Shaded areas show cumulative rates/100 person-months in each time period. Assuming a log-normal survival distribution with 6df natural cubic splines (best-fitting model on AIC [19]).

Table 3. Score to Predict *Clostridium difficile* Infection (CDI) Recurrence Following First-Ever CDI Diagnosis

Factor		Scoring Criteria			Max	Min
Patient & health status	Age (y)	60–69	70–79	≥80		
	Score	1	2	3	3	0
	Emergency admission	Any emergency admission		1		
		AND previous MRSA+		1		
		AND/OR previous dialysis/chemotherapy		1	3	0
Severity of initial disease	Stool frequency	≥3 unformed stools/d[a]		1		
	Admission with CDI	Sample taken on day of inpatient admission		1		
	C-reactive protein[b] (mg/L)	<35	85–<160	≥160		
	Score	−1	1	2	4	−1
Past health care exposure	Type of past admission	Past gastroenterology admission	No past gastroenterology admission			
	Total inpatient duration before admission	Any past admission	>2–13 wk	>13 wk		
	Score	1	2	3	3	0
Antibiotic selection		(Elective admission OR community sample) AND previous MRSA isolated[c]		−1	0	−1
Susceptibility to diarrhea several wk after hospital exposure	Primary CDI 4–12 wk after hospital discharge[d]	Community sample or sample taken within ≤2 d of inpatient admission AND patient discharged from hospital 4–12 wk previously		2	2	0
Total					15	−2

ESTRATEGIAS TRADICIONALES PARA RECURRENCIAS

Table 2. Suggested Approaches to Therapy.*

Initial episode

Mild-to-moderate infection

- Metronidazole at a dose of 500 mg orally 3 times daily for 10 to 14 days

Severe infection or unresponsiveness to or intolerance of metronidazole

- Vancomycin at a dose of 125 mg orally 4 times daily for 10 to 14 days

First recurrence

Mild-to-moderate infection

- Metronidazole at a dose of 500 mg orally 3 times daily for 10 to 14 days

Severe infection or unresponsiveness to or intolerance of metronidazole

- Vancomycin at a dose of 125 mg orally 4 times daily for 10 to 14 days

Second recurrence†

Vancomycin in tapered and pulsed doses

- 125 mg 4 times daily for 14 days
- 125 mg 2 times daily for 7 days
- 125 mg once daily for 7 days
- 125 mg once every 2 days for 8 days (4 doses)
- 125 mg once every 3 days for 15 days (5 doses)

Third recurrence

Vancomycin at a dose of 125 mg orally 4 times daily for 14 days, followed by rifaximin at a dose of 400 mg twice daily for 14 days

Other options for recurrent infection

Intravenous immune globulin at a dose of 400 mg per kilogram of body weight once every 3 weeks for a total of 2 or 3 doses

Therapy with other microorganisms, including "fecal transplantation"

N ENGL J MED 359;18

Treatment of First Recurrence of *Clostridium difficile* Infection: Fidaxomicin Versus Vancomycin

Oliver A. Cornely,[1] Mark A. Miller,[2] Thomas J. Louie,[3,4] Derrick W. Crook,[5,6] and Sherwood L. Gorbach[7,8]

[1]Department I of Internal Medicine, Clinical Trials Centre Cologne, ZKS Köln, BMBF 01KN1106, Center for Integrated Oncology CIO Köln Bonn, and Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases, University of Cologne, Germany; [2]Division of Infectious Diseases, Jewish General Hospital, McGill University, Montreal, Quebec, Canada; [3]Department of Medicine, and [4]Department of Microbiology-Immunology and Infectious Diseases, University of Calgary, Alberta, Canada; [5]Nuffield Department of Clinical Medicine, Oxford University, [6]NIHR Oxford Biomedical Research Centre, John Radcliffe Hospital, United Kingdom; [7]Optimer Pharmaceuticals, Inc., San Diego, California, and [8]Tufts University School of Medicine, Boston, Massachusetts

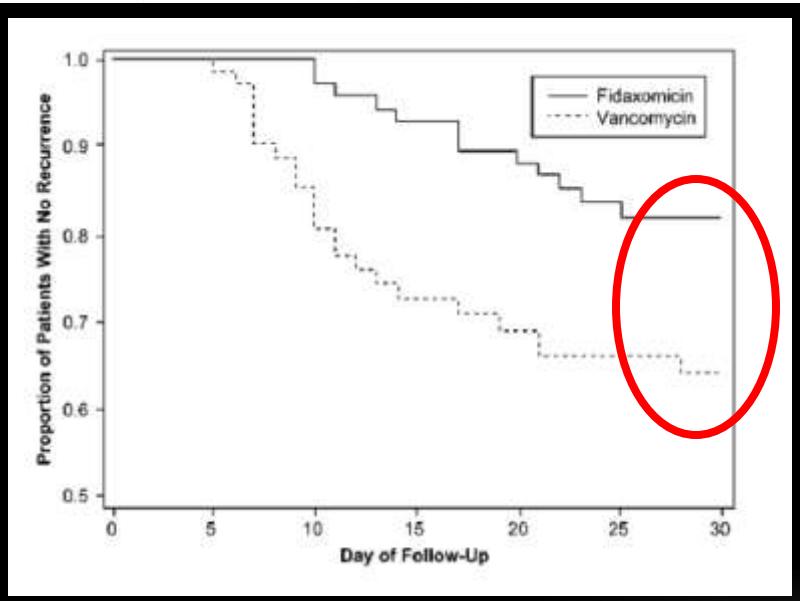


Table 3. Time to Recurrence Following Fidaxomicin vs Vancomycin Treatment in Patients With 1 Prior Episode of *Clostridium difficile* Infection

Endpoint	Fidaxomicin	Vancomycin	*P* Value
Cured and evaluated for recurrence	n = 66	n = 62	
Recurrence within 14 days of follow-up	5/66 (7.6%)	17/62 (27.4%)	.003
No recurrence within 14 days	n = 61	n = 45	
Recurrence from 15 to 28 days	8/61 (13.1%)	5/45 (11.1%)	
Censored at 28 days (no recurrence)	53/66 (80.3%)	40/62 (64.5%)	

AGENTE CB 183-135

- Fase 3 investigacion clinica
- Vanco vs CB-183-135
- Conclusiones 2014

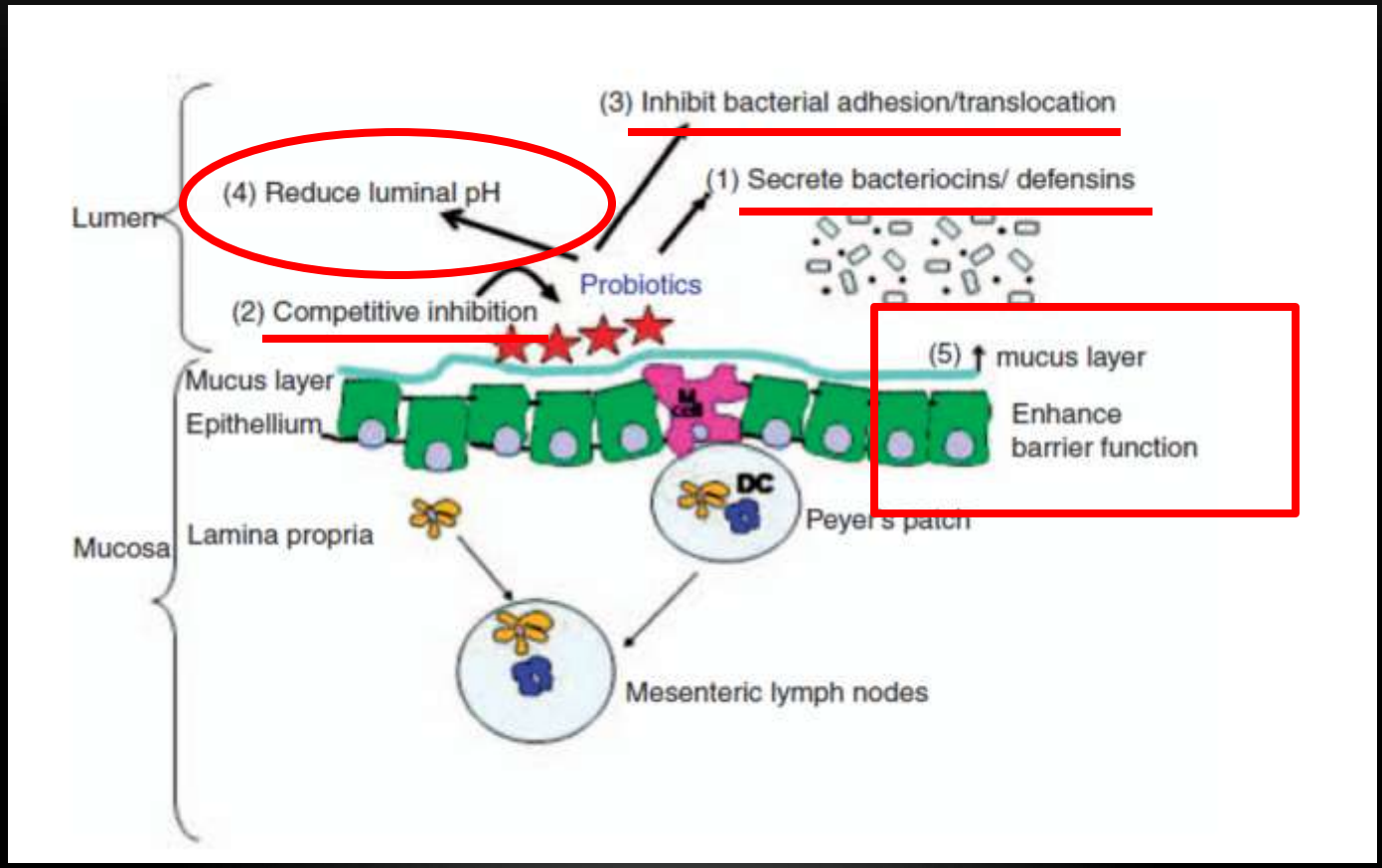
NEUTRALIZACION INTRALUMINAL DE LA TOXINA

- Cholestyramina
- Colestipol
- Tovelamer

PRO-BIOTICOS

- Bacterias no-patogenicas vivas con capacidad de colonizar la mucosa intestinal
- La mayoria son encontrados en productos fermentados o lacteos
- *Lactobacillus, Bifidobacteria y S Boulardi* los mas estudiados

PRO-BIOTICOS



Ther Adv Gastroenterol
(2011) 4(3) 185–197

Probiotics for the Prevention and Treatment of Antibiotic-Associated Diarrhea

A Systematic Review and Meta-analysis

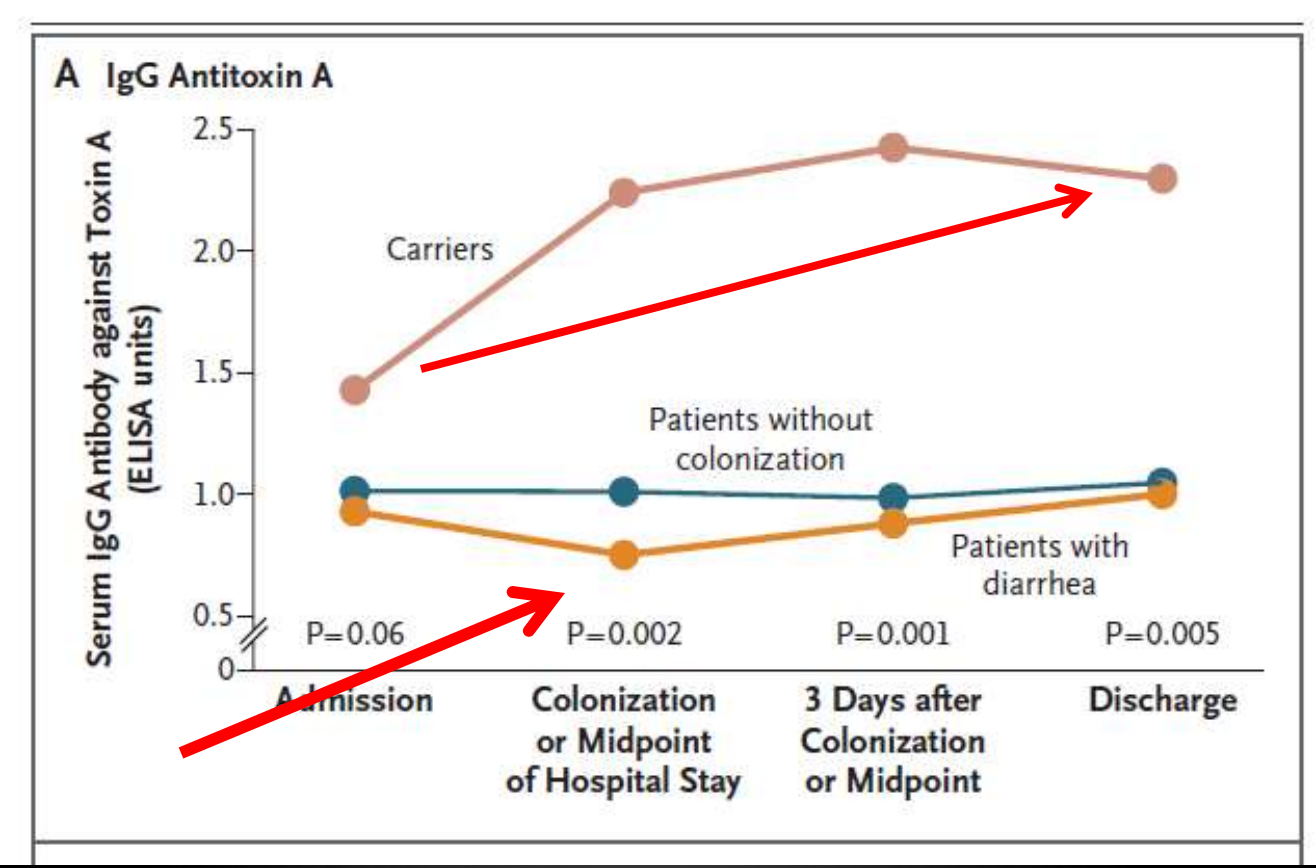
Conclusions The pooled evidence suggests that probiotics are associated with a reduction in AAD. More research is needed to determine which probiotics are associated with the greatest efficacy and for which patients receiving which specific antibiotics.

JAMA. 2012;307(18):1959-1969 www.jama.com

INMUNIDAD Y EL HUESPED

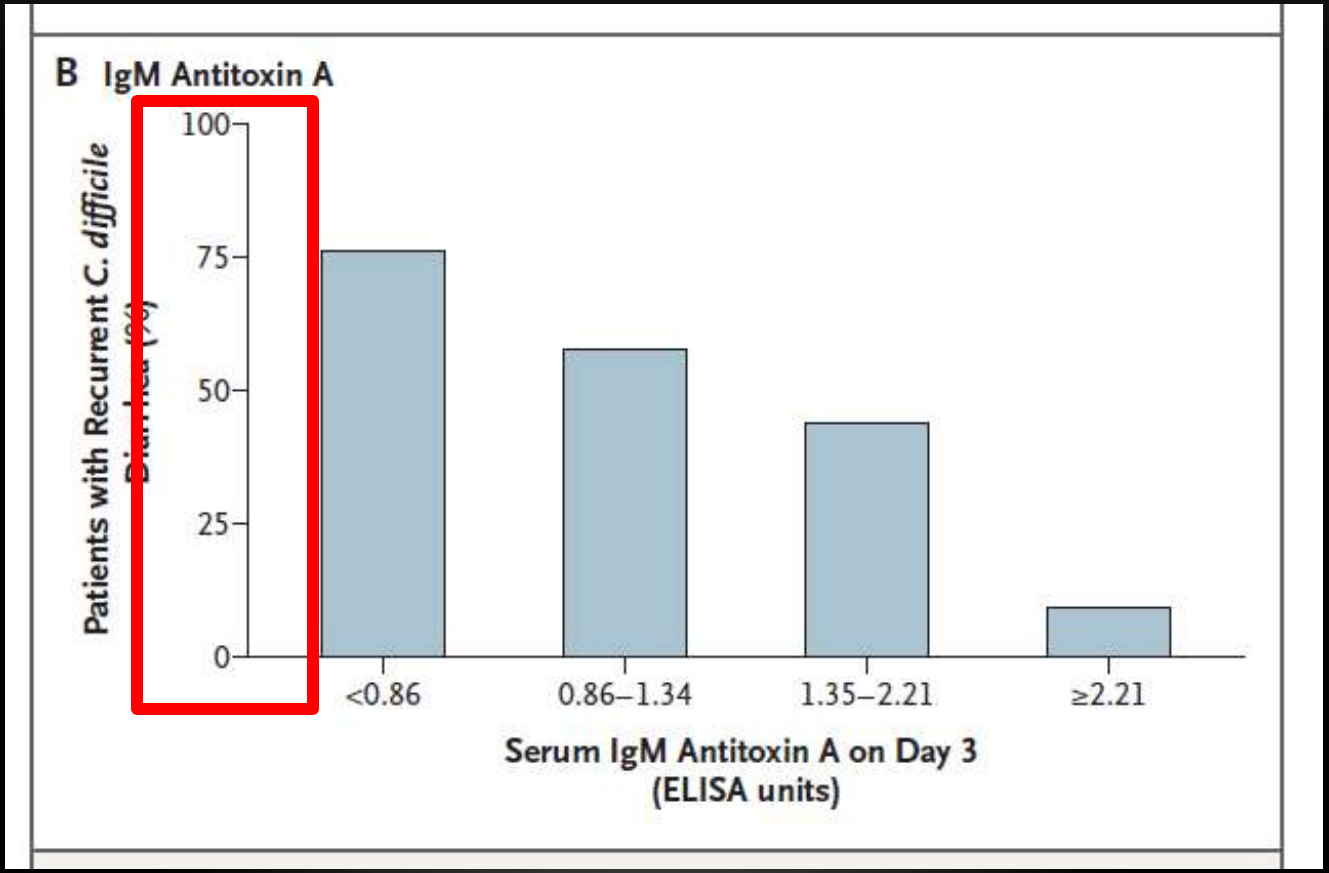
- El riesgo de una recurrencia despues del 1er episodio es un 20%
- Riesgo incrementa a 40 % despues de 1er recurrencia
- 60 % despues del 2da recurrencia

INMUNIDAD E INMUNOTERAPIA



Nejm 359,18: 1932

INMUNIDADA E INMUNOTERAPIA



Nejm 359,18: 1932

INMUNIDAD E INMUNOTERAPIA

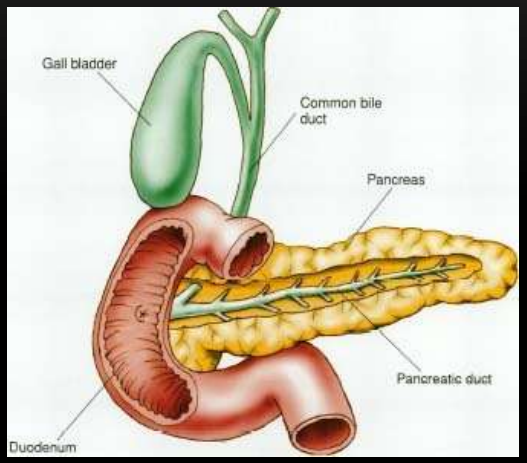
Treatment with Monoclonal Antibodies against *Clostridium difficile* Toxins

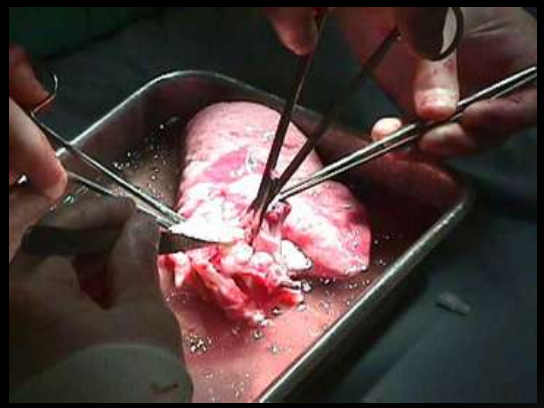
Israel Lowy, M.D., Ph.D., Deborah C. Molrine, M.D., M.P.H., Brett A. Leav, M.D., Barbra M. Blair, M.D., Roger Baxter, M.D., Dale N. Gerding, M.D., Geoffrey Nichol, M.B., Ch.B., William D. Thomas, Jr., Ph.D., Mark Leney, Ph.D., Susan Sloan, Ph.D., Catherine A. Hay, Ph.D., and Donna M. Ambrosino, M.D.

The addition of monoclonal antibodies against *C. difficile* toxins to antibiotic agents significantly reduced the recurrence of *C. difficile* infection. (ClinicalTrials.gov number, NCT00350298.)

Nejm 2010; 362: 197-205

TRANSPLANTES





DONANTES

Recurrent *Clostridium difficile* Colitis: Case Series Involving 18 Patients Treated with Donor Stool Administered via a Nasogastric Tube

Johannes Aas,[1] Charles E. Gessert,[2] and Johan S. Bakken[3]

[1]Department of Gastroenterology, [2]Division of Education and Research, and [3]Department of Infectious Diseases, St. Mary's/Duluth Clinic Health System, Duluth, Minnesota

Table 4. Demographic and clinical information for 18 patients treated for *Clostridium difficile* colitis with stool transplantation (ST).

Patient	Year	Age, years	Sex	Predisposing infection	Antimicrobial agents used before *C. difficile* infection	Antimicrobial courses before ST[a]	*C. difficile* test results before ST, negative/positive[b]	Days from diagnosis to ST	*C. difficile* test results after ST, negative/positive[c]	Outcome
1	1994	61	M	Pneumonia	Cpfx, Clm	3	1/2	73	4/[illegible]	Resolution
2	1994	76	F	SBO	Ctri	4	0/3	128	1/[illegible]	Resolution
3	1996	76	F	Postoperative wound infection	Amp, Gm	3	1/3	80	0/[illegible]	Resolution
4	1996	72	F	Infected BKA	Clex, Cpfx	3	0/3	83	1/[illegible]	Resolution
5	1997	58	F	Postoperative wound infection	Cpfx	4	1/3	77	1/[illegible]	Resolution
6	1997	65	M	Septic bursitis	Cm, Pen	4	1/4	85	1/[illegible]	Resolution
7	1997	88	M	Pneumonia	Ctox	3	1/3	41	0/[illegible]	Death
8	1998	79	M	SBO	Amox, Pip	2	0/2	87	0/[illegible]	Treatment failure[f]
9	1998	82	F	Pneumonia	Ctri	5	0/5	126	1/[illegible]	Resolution
10	1999	83	F	Bronchitis	Clex	2	0/2	25	0/[illegible]	Death
11	1999	71	F	Cellulitis	Cpfx, Cm, Pip, TMP-SMZ	3	0/3	57	0/[illegible]	Resolution
12	1999	69	F	Chronic osteomyelitis	Ala	3	2/2	81	2/[illegible]	Resolution
13	2000	80	F	Urosepsis	Cpfx, Pip	4	0/3	87	1/[illegible]	Resolution
14	2000	77	F	Pneumonia	Cpfx	4	0/3	48	1/[illegible]	Resolution
15	2000	70	F	Pneumonia	Lev	2	0/2	76	2/[illegible]	Resolution
16	2001	71	F	*Helicobacter pylori* gastritis	Tet	7	0/7	497	2/[illegible]	Resolution
17	2002	77	M	Leukemia	Vm, Atm, Mtz	6	2/5	114	1/[illegible]	Resolution
18	2002	51	F	Crohn colitis	Clex, Pip, Taz	3	0/3	66	1/[illegible]	Resolution

FIN