

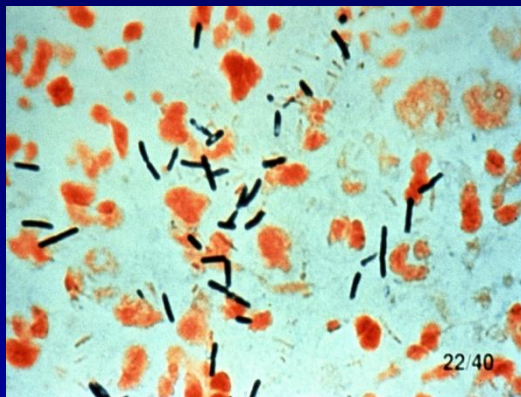


Clostridium difficile Infection (CDI) Guideline Update

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Faculty of medicine-Damascus-Syria**





If you prescribe too much antibiotics you
are as a terrorist or a pollutant

ANTIBIOTIC-ASSOCIATED DIARRHEA

TABLE 112-1 Differences between Antibiotic-Associated Diarrhea from *Clostridium difficile* Infection and from Other Causes

Characteristic	<i>C. difficile</i> Infection	Other Causes
Most commonly implicated antibiotics History	Clindamycin, cephalosporins, penicillins, fluoroquinolones Usually no history of antibiotic intolerance	Clindamycin, cephalosporins, ampicillin, or amoxicillin-clavulanic acid History of diarrhea with antibiotic therapy is common
Clinical Features		
Epidemiologic pattern	May be epidemic or endemic in hospitals or long-term care facilities	Sporadic
Diarrhea	May be florid; evidence of colitis with cramps, fever, and fecal leukocytes is common	Usually mild-moderate in severity ("nuisance diarrhea") without evidence of colitis
Findings on CT or colonoscopy	Evidence of colitis is common; pseudomembranes often are present	Usually normal
Complications	Hypoalbuminemia, anasarca, toxic megacolon; relapse can occur after treatment with metronidazole or vancomycin	Usually none; occasional cases of volume depletion
Results of assay for <i>C. difficile</i> toxin	Positive	Negative
Treatment		
Withdrawal of implicated antibiotic	Condition can resolve but often persists or progresses	Condition usually resolves
Antiperistaltic agents Oral metronidazole or vancomycin	Contraindicated Prompt response	Often useful Not indicated

**Antibiotic-Associated
Diarrhea and
Clostridium Difficile Infection**

Confusing terminology

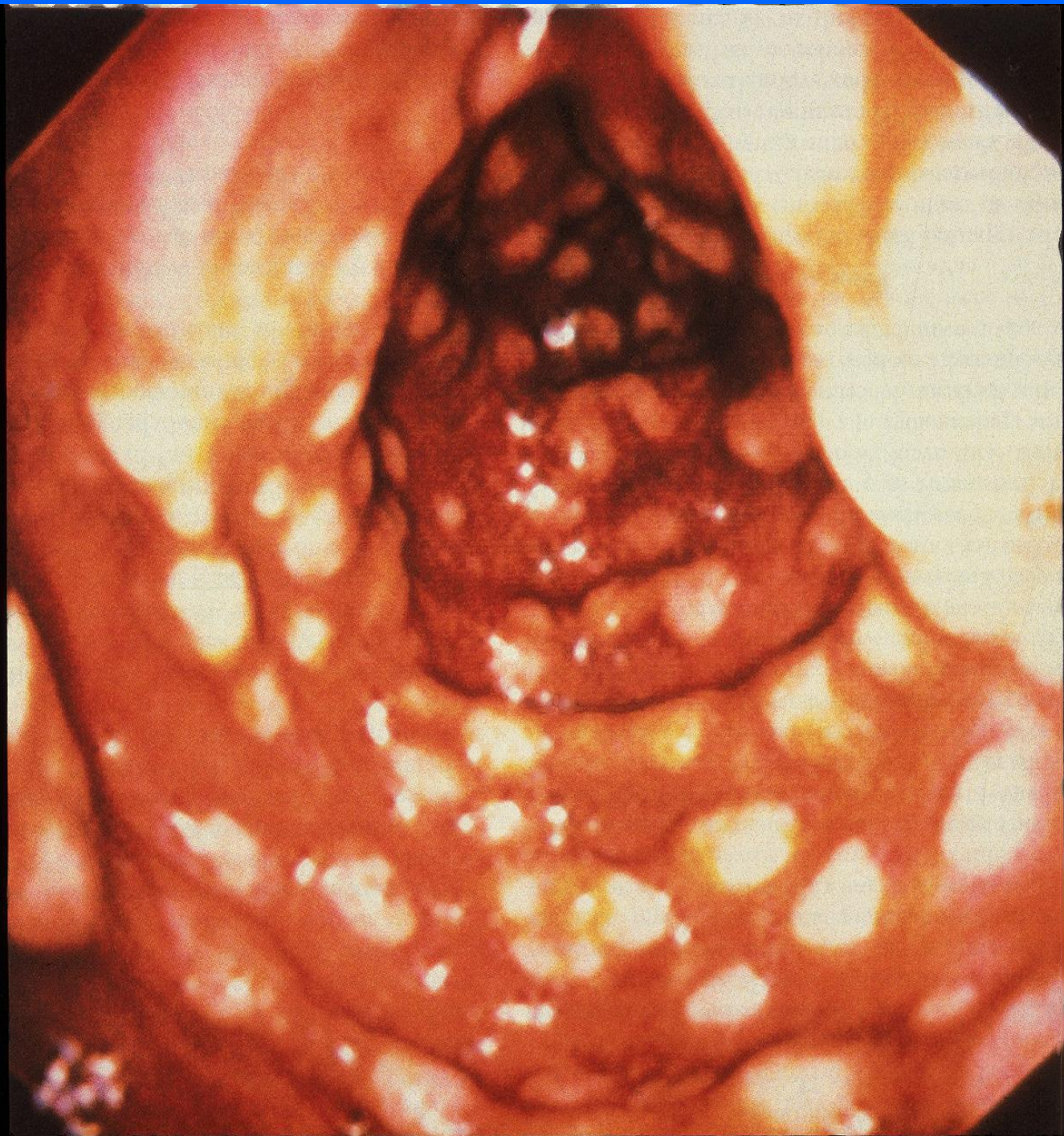
- Antibiotic-associated diarrhea
 - *C. difficile* is one of many causes (approx 20-30%)
- *Clostridium difficile*-associated diarrhea
 - diarrhea + positive stool test
- *Clostridium difficile* colitis
 - underlying pathologic process
- Pseudomembranous colitis
 - endoscopic demonstration of exudative lesions
- Toxic megacolon
 - radiologic and surgical diagnosis

Antibiotic-Associated Diarrhea and *Clostridium difficile* Infection

Très Difficile



22/40



Historical Perspective

- In the 1960s it was noted that patients on antibiotics developed diarrhea¹
 - “staphylococcal colitis”
 - Originally thought to be caused by *S. aureus* and treated with oral bacitracin
 - Stool cultures routinely ordered for *S. aureus*
- Early 1970s, a new explanation
 - “clindamycin colitis”
 - Severe diarrhea, pseudomembranous colitis, and occasional deaths documented in patients on clindamycin

1. Gorbach SL. *NEJM*. 1999;341:1689-1691.

“Antibiotic Associated Pseudomembranous Colitis Due to Toxin-Producing Bacteria”

- Bartlett and co-workers¹ demonstrated cytotoxicity in tissue culture and enterocolitis in hamsters from stool isolates from patients with pseudomembranous colitis
 - Isolate was *C. difficile*
- *Bacillus difficilis* (now confirmed as *C. difficile*) was cultured from healthy neonates (with difficulty, hence the name) in 1935²

1. Bartlett JG, et al. *NEJM*. 1978;298: 531-534.

2. Hall JC and O'Toole E. *Am J Dis Child*. 1935;49:390-402.

Clostridium difficile

- Gram-positive, anaerobic, spore-forming bacillus
- Vegetative cells die quickly in an aerobic environment
- Spores are a survival form and live for a very long time in the environment
- Grows on selective media in 2 days and smells like horse manure (p-cresol)

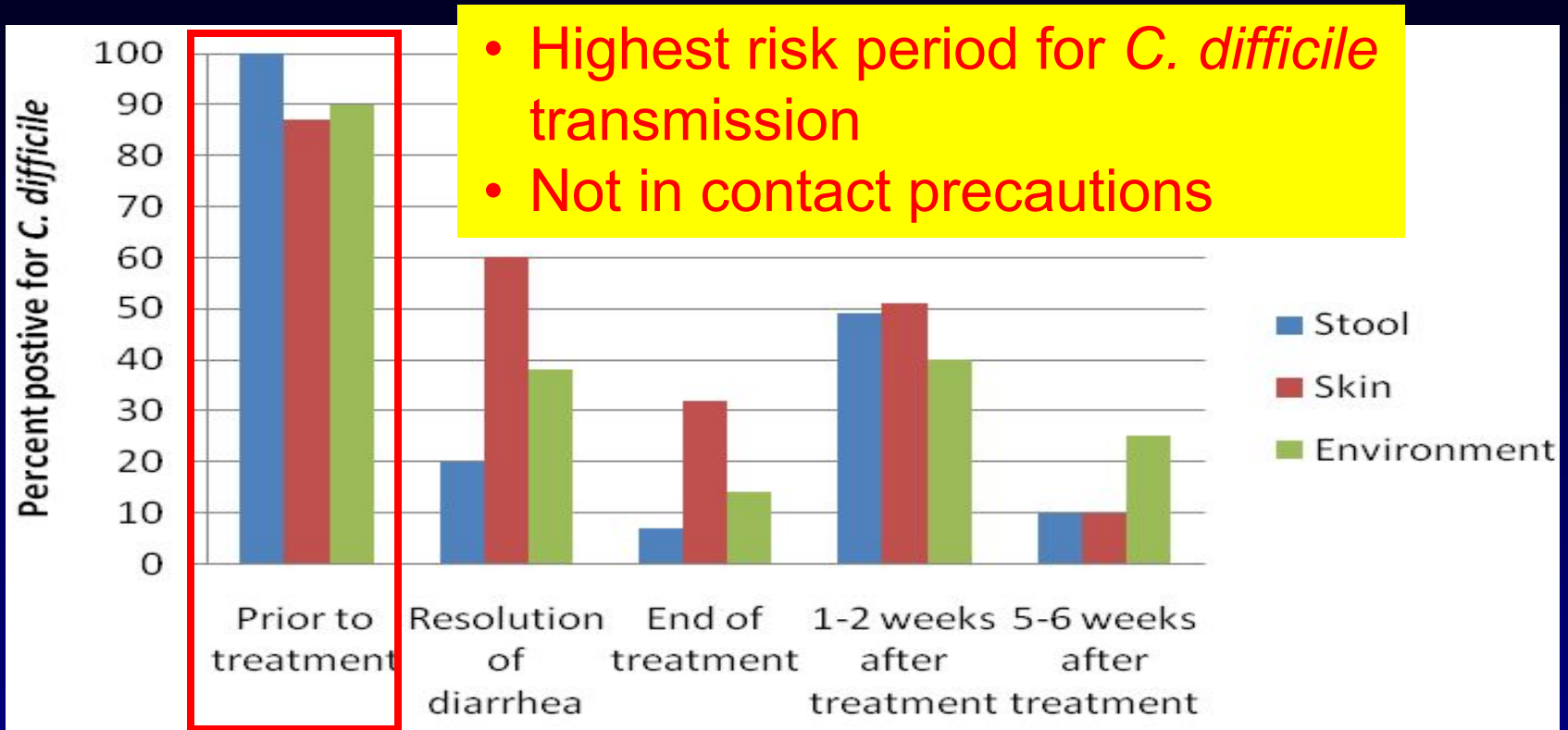
Importance of Spores

- Resistant to heat, drying, pressure, and many disinfectants
- Resistant to all antibiotics because antibiotics only kill or inhibit actively growing bacteria
- Spores survive well in hospital environment
- Spores are not a reproductive form, they represent a survival strategy

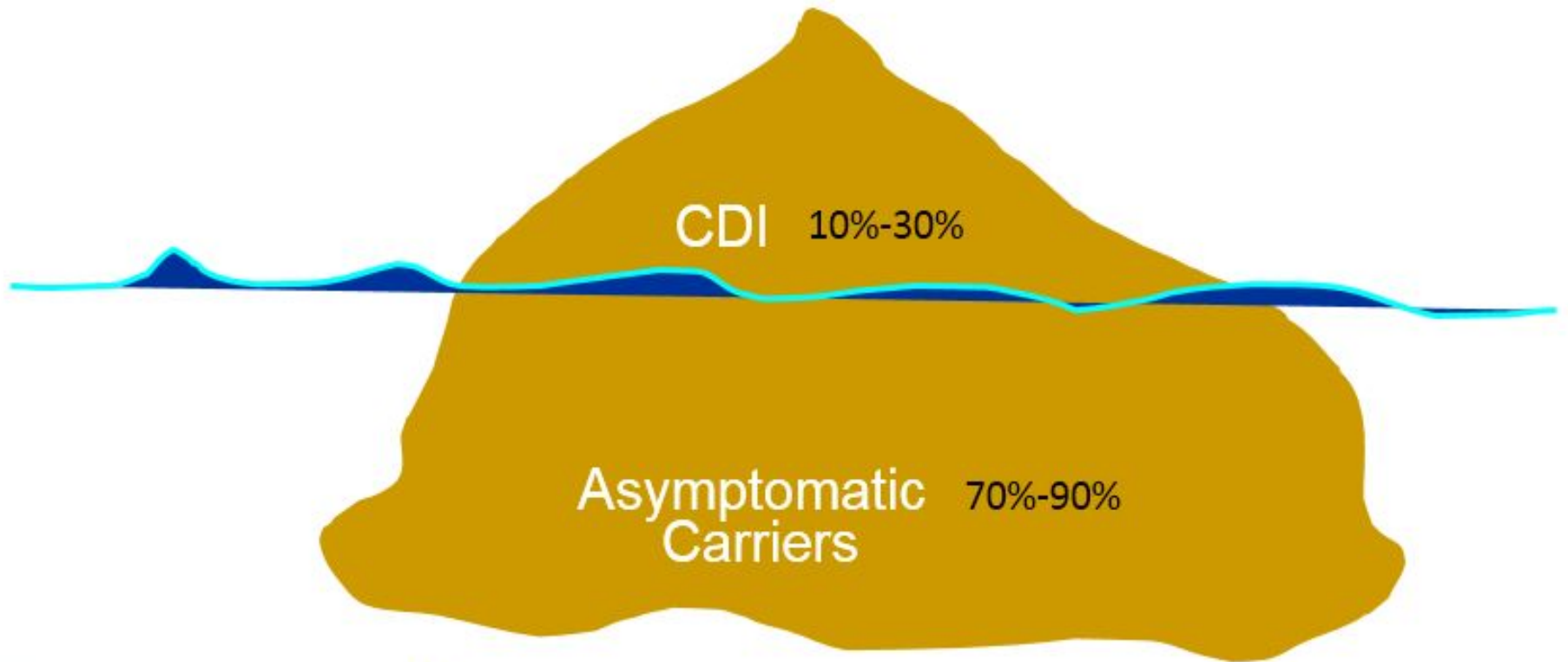
Source of Infections

- Spores in hospital, nursing home, or long-term care environment associated with ill patients
 - Large numbers of spores on beds, bed-rails, chairs, curtains, medical instruments, ceiling, etc.
- Asymptomatic carriers in those same environments

Greatest Risk of Transmission Early



The *C. difficile* “Iceberg”



Role of Antibiotics

- All antibiotics (including metronidazole and vancomycin) are associated with CDI
- High-risk group
 - Clindamycin
 - Cephalosporins/penicillins/beta-lactams
 - Fluoroquinolones
- Alteration of normal colonic flora thought to favor growth of *C. difficile*
 - Antibiotics do not know they are suppose to kill/inhibit only the “bad guys”

Role of Antibiotics

TABLE 112-2 Antimicrobial Agents That Predispose to *Clostridium difficile* Infection

Frequently	Sometimes	Rarely
Amoxicillin Ampicillin Cephalosporins Clindamycin Fluoroquinolones	Macrolides Other penicillins Sulfonamides Trimethoprim Trimethoprim ± Sulfamethoxazole	Aminoglycosides Bacitracin Carbapenems Chloramphenicol Daptomycin Metronidazole Rifampin Rifaximin Teicoplanin Tetracyclines Tigecycline

Adapted from Kelly C, Lamont J. Treatment of *Clostridium difficile* diarrhea and colitis. In: Wolfe MM, editor. *Gastrointestinal pharmacotherapy*. Philadelphia: WB Saunders; 1993. p 199.

Role of Antibiotics

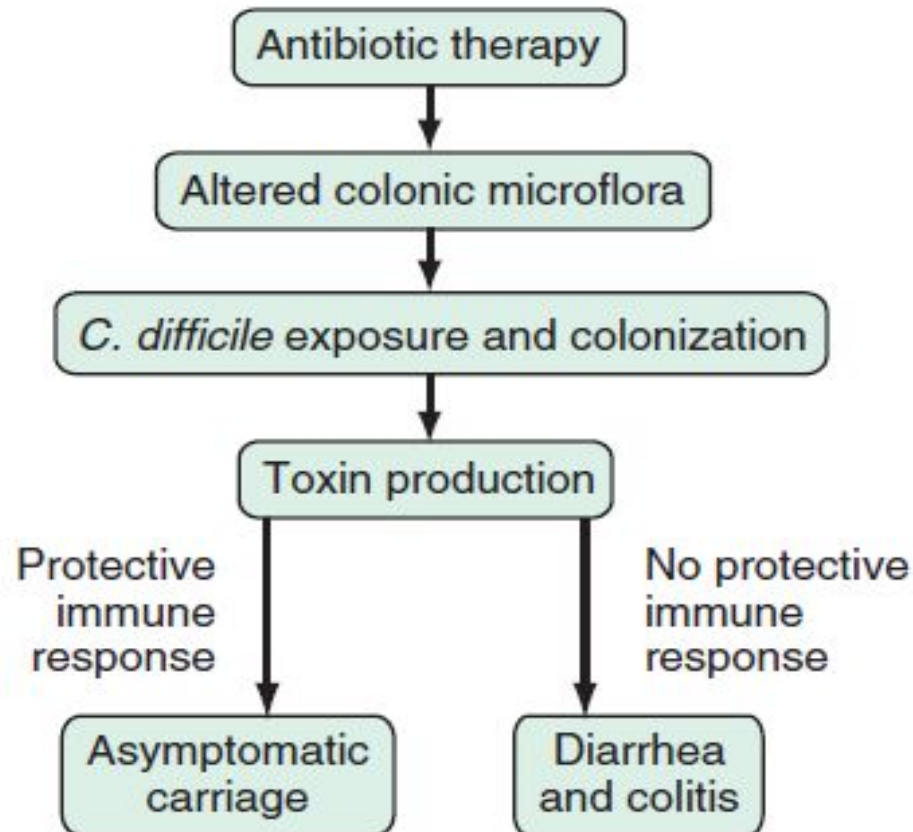
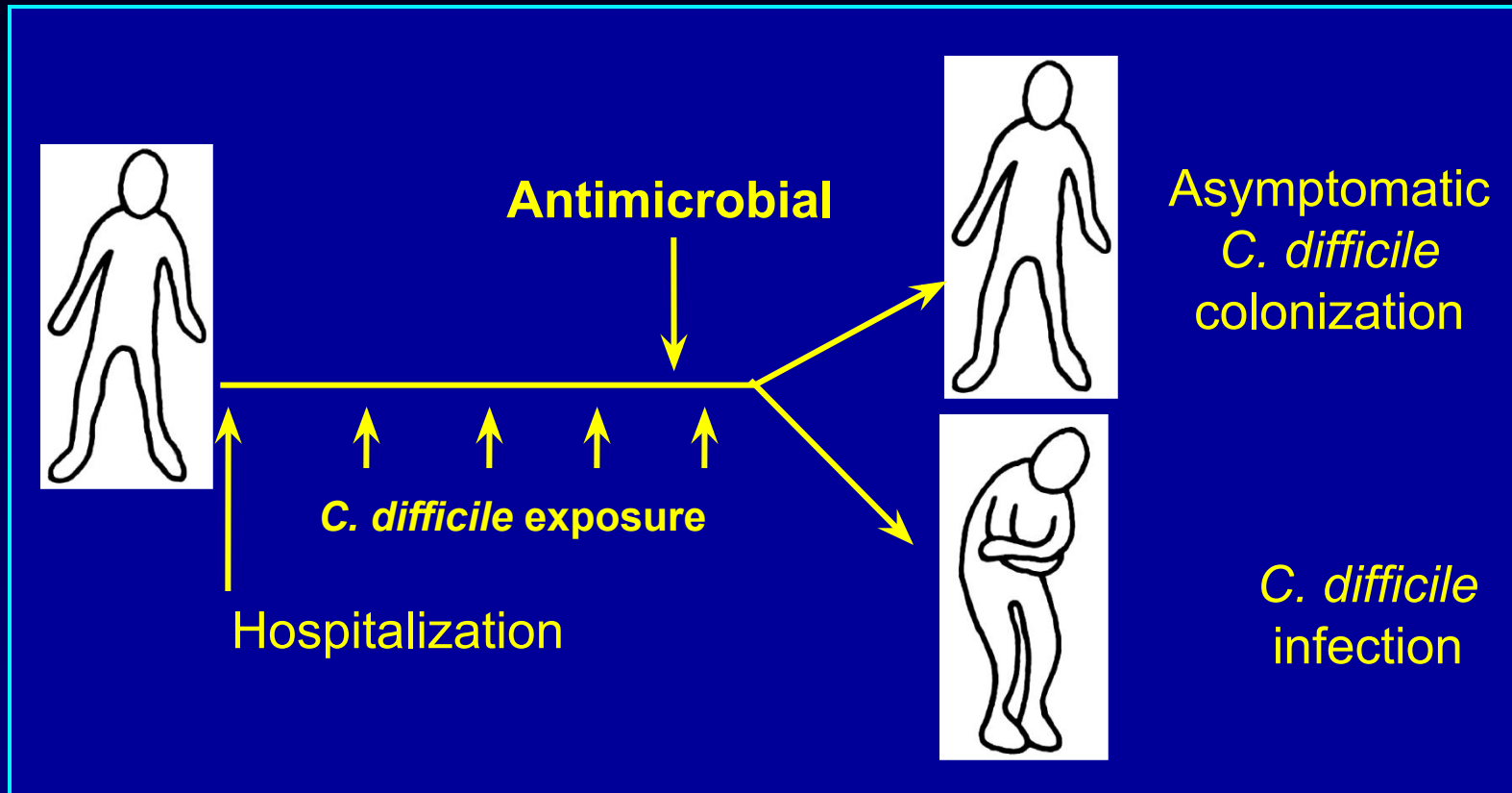
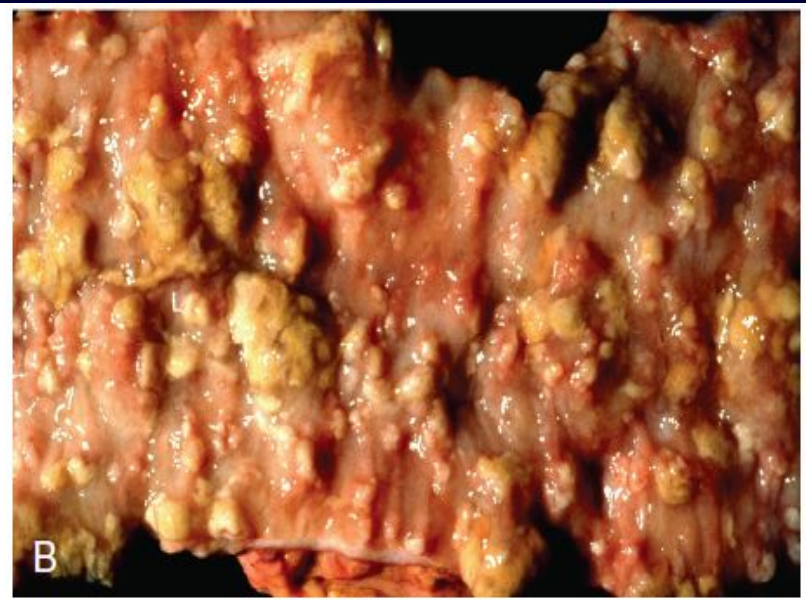
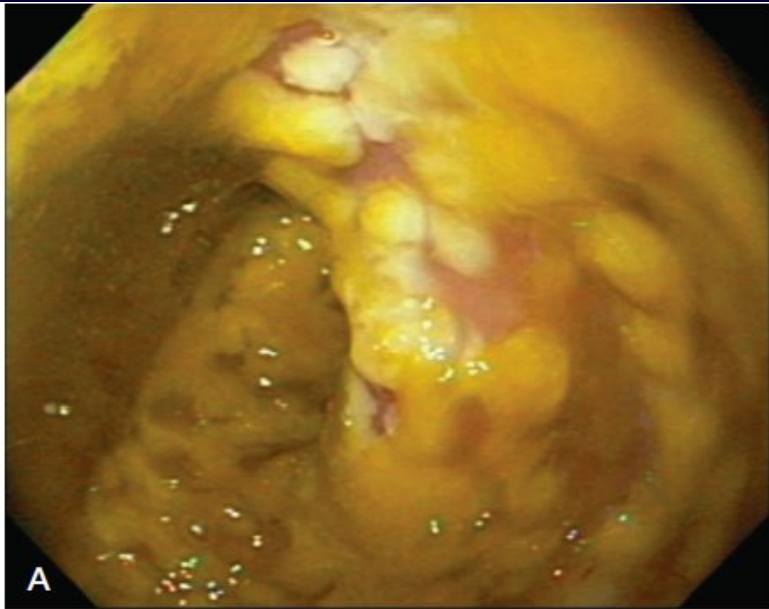


FIGURE 112-1. Pathogenesis of *Clostridium difficile*-associated diarrhea and colitis.

Pathogenesis of CDI



Antibiotic Associated Pseudomembranous Colitis Due to Toxin-Producing Bacteria

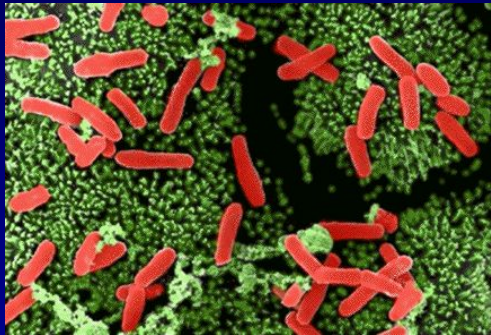


Growing problem of pseudomembranous colitis

- "...incidence, deaths, and excess health care costs are at historic highs" +/- 1 billion dollars/yr
- 3x increase in decade- now 500,000 infections and 29,000 deaths per year. More deaths than even MRSA infections.
- **#1 cause** of increase- over use of antibiotics
- **#2 cause** – appearance of a more virulent *C.diff* strain associated with risk of greater mortality
- **#3 cause**- increased relapse rate – 20% of cases have at least one relapse- difficult to treat
- **#4 cause**- overdiagnosis???



***Clostridium Difficile* colitis-
more virulent than ever**



Pathogenesis

- Toxigenic strains produce 2 large protein exotoxins that are associated with virulence
 - Toxins A and B
 - Mutants strains that do not make toxins A and B are not virulent
 - Some strains make a third toxin known as Binary Toxin
 - By itself, not pathogenic
 - May act synergistically with toxins A and B in severe colitis
 - More common in animal strains

Clostridium difficile spores and vegetative cells are ingested

- Spores
- Vegetative cells

Most vegetative cells are killed in the stomach, but spores can survive the acid environment

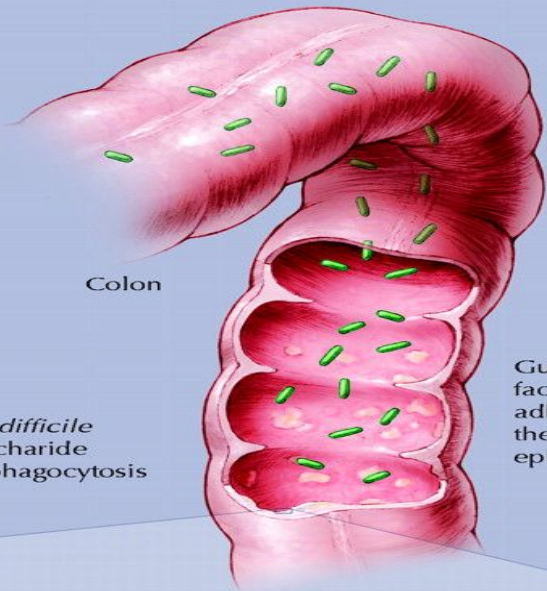


Stomach

Small bowel

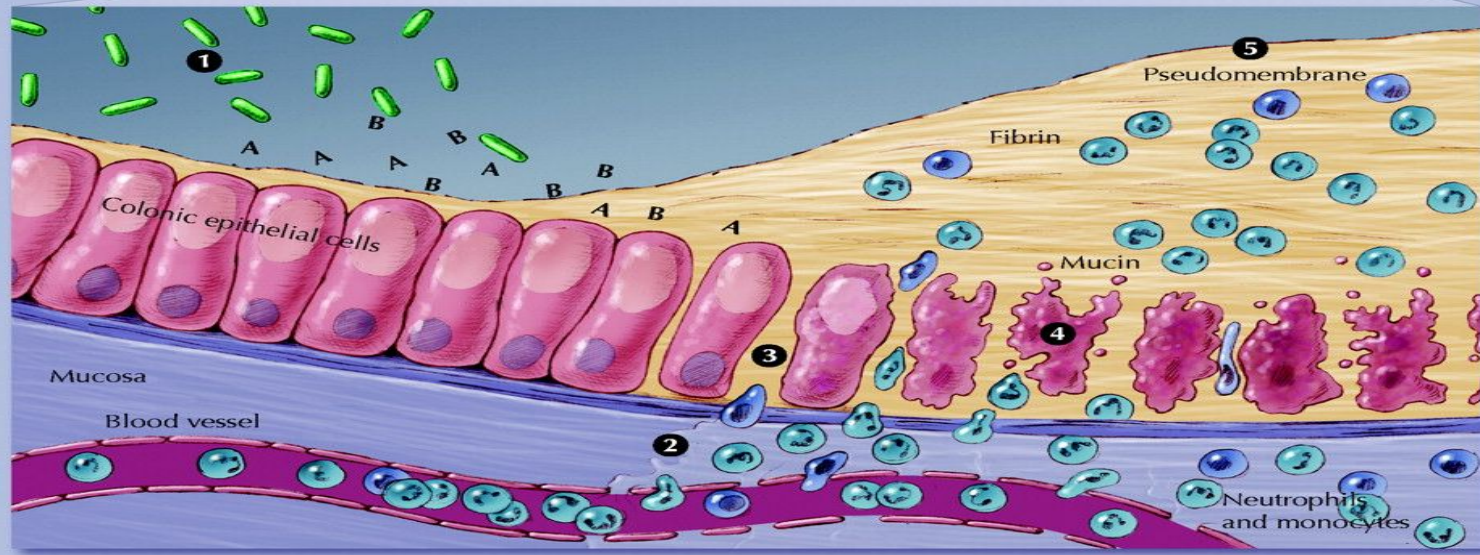
C. difficile spores germinate in the small bowel upon exposure to bile acids

Flagellae facilitate *C. difficile* movement; a polysaccharide capsule discourages phagocytosis



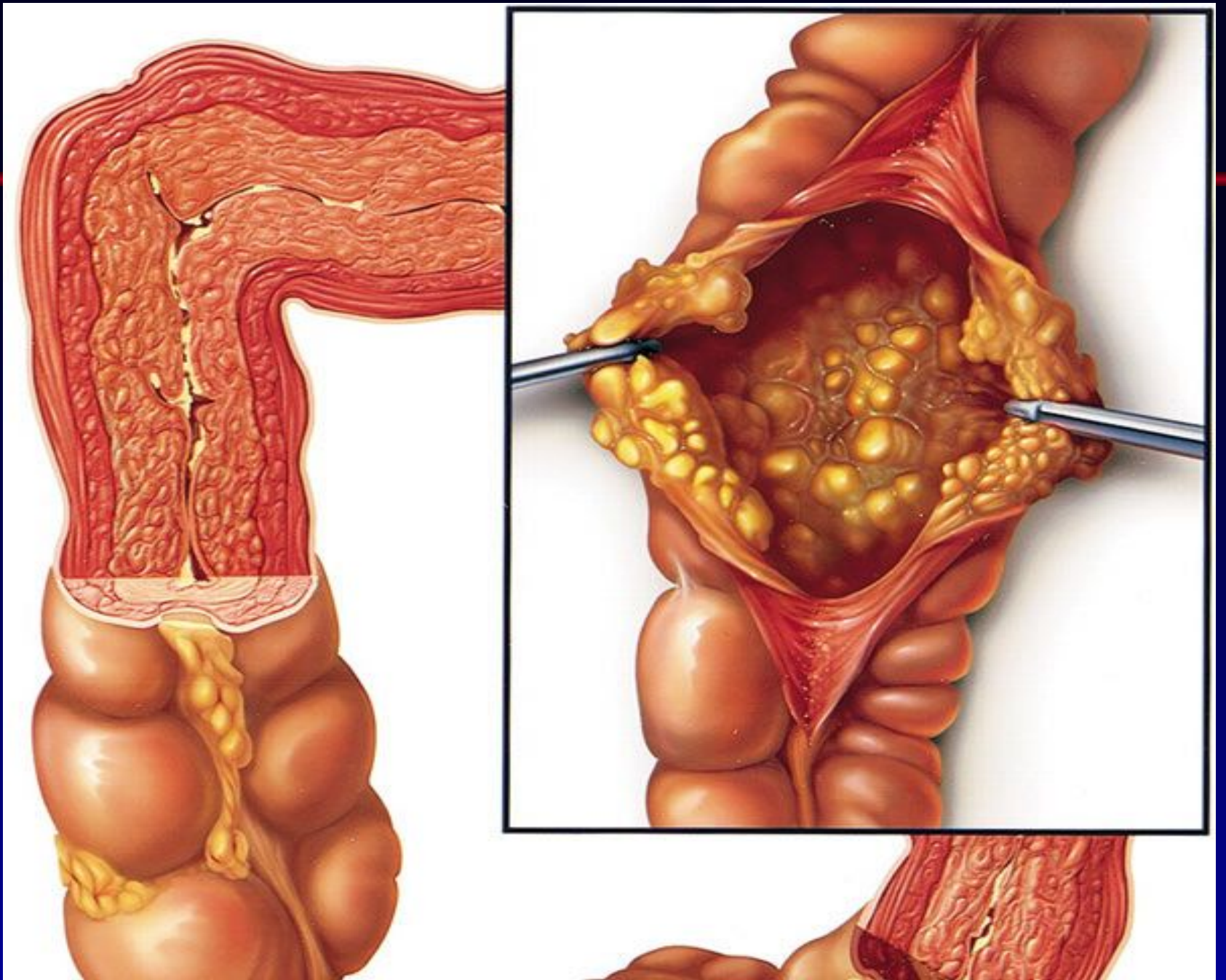
C. difficile multiplies in the colon

Gut mucosa facilitates adherence to the colonic epithelium



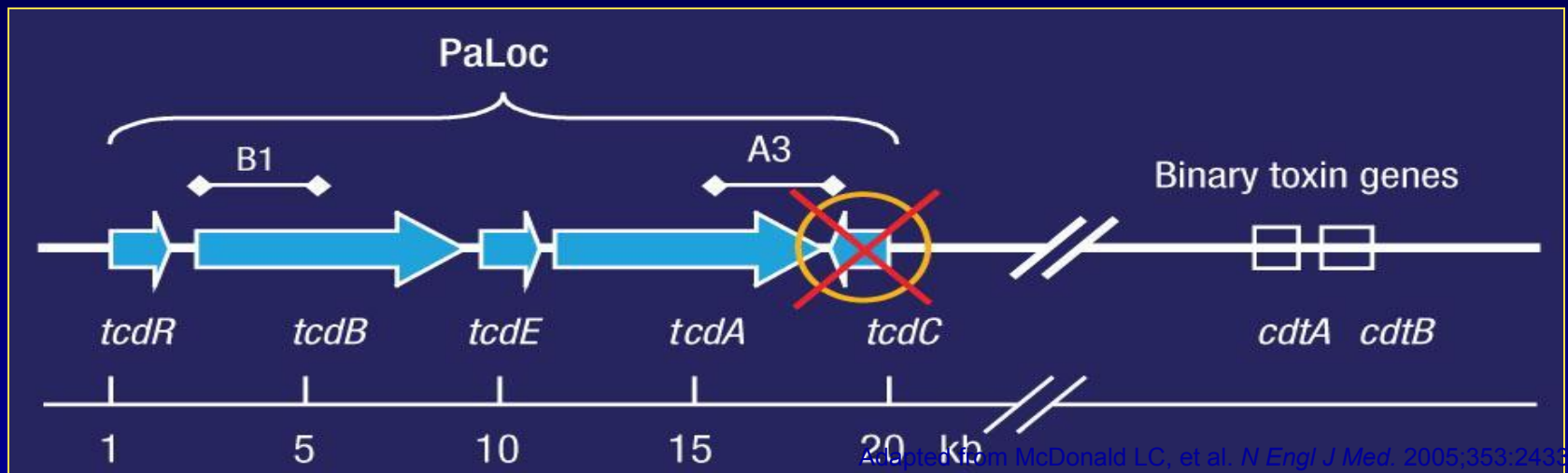
C. difficile vegetative cells produce toxins A and B and hydrolytic enzymes (1). Local production of toxins A and B leads to production of tumour necrosis factor-alpha and proinflammatory interleukins, increased vascular permeability, neutrophil and monocyte recruitment (2),

opening of epithelial cell junctions (3) and epithelial cell apoptosis (4). Local production of hydrolytic enzymes leads to connective tissue degradation, leading to colitis, pseudomembrane formation (5) and watery diarrhea.



Epidemic Strain

- Strain typed BI/NAP1/027^{1,2}
- Is highly resistant to fluoroquinolones^{2,4}
- Binary toxin genes are present
- Produces large quantities of toxins A and B^{1,3}
- Has a *tcdC* gene deletion¹



Declines in 027 since 2011

	2011	2012	2013	2014	2015
Incidence (per 100,000)	147.2	145.8	141.8	141.7	148.6
027: Healthcare associated (%)	31%	21%	24%	14%	19%
027: Community associated (%)	19%	17%	12%	7%*	8%*

*not most common strain

<https://www.cdc.gov/hai/eip/clostridium-difficile.html>

Symptoms of CDI

- Asymptomatic colonization
- Diarrhea
 - mild → moderate → severe
- Abdominal pain and distension
- Fever
- Pseudomembranous colitis
- Toxic megacolon
- Perforated colon → sepsis → death

Host factors

- Age \geq 65 year
- Immunosuppression
 - recipients of organ transplants (3-11%), chemotherapy, corticosteroids, HIV, IBD, ESRD, ESLD
- PPI use \geq 3-fold
- Hospitalization, long-term care facilities
 - After 1 week 13%, after 4 weeks $>$ 50% colonization rate
- Previous CDI

Laboratory Diagnosis of *C. difficile* Infection (CDI)








What Should I do First?

Make some rules

- **Rule 1:** Accept only liquid stools or soft stools
- **Rule 2:** Limit repeat testing once a patient is positive

The Specimen

- Fresh is best (test within 2 hours)
- Liquid or loose, not solid
- If unable to test within 2 hours, refrigerate at 4°C for up to 3 days
- Freeze at -70°C (not -20°C) if testing will be delayed
- Specimen quality will influence test results

Bristol Stool Chart		
Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

Guidelines: Diagnosis

Clinical question: What is the preferred population for *C. difficile* testing, and

Take home messages:

- **If clinical judgement used: 65% did not need to be tested**

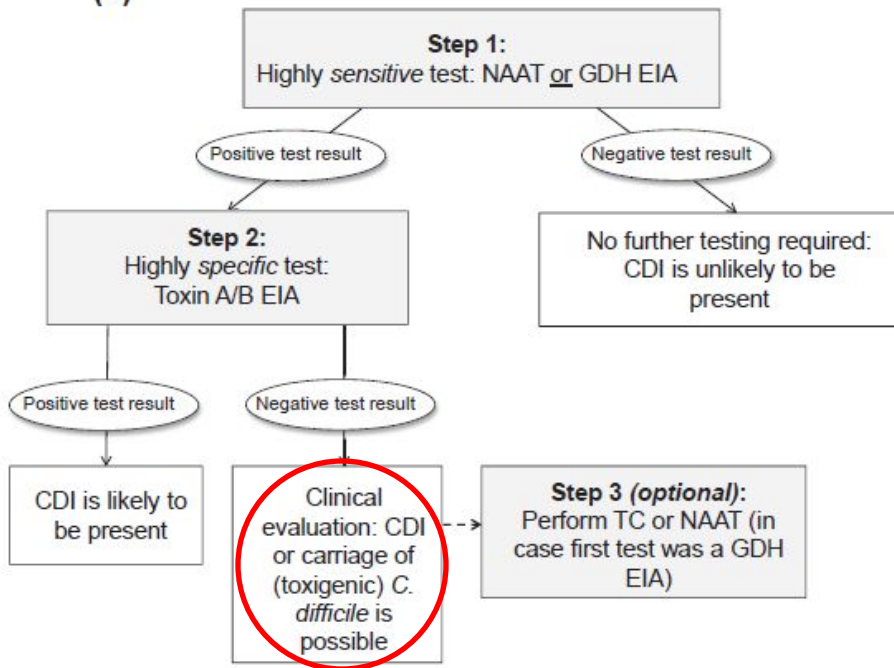
unformed stools in 24 hours are the preferred target population for testing for CDI (weak recommendation, very low quality of evidence)

Diagnosics Available

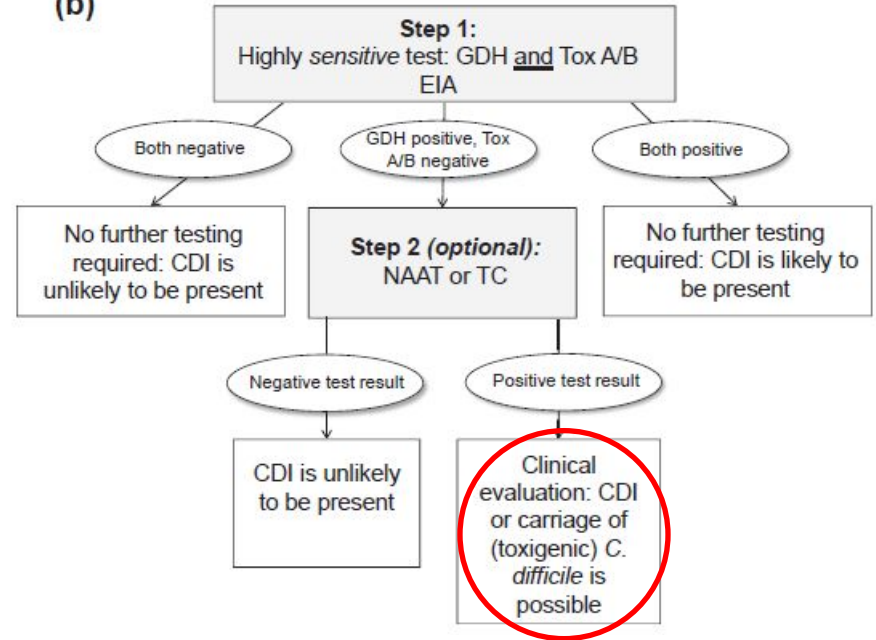
Test	Advantage(s)	Disadvantage(s)
Toxin testing		
Toxin Enzyme immunoassay (EIA)	Rapid, simple, inexpensive	Least sensitive method, assay variability
Tissue culture cytotoxicity	More sensitive than toxin EIA, associated with outcomes	Labor intensive; requires 24–48 hours for a final result, special equipment;
Organism identification		
Glutamate dehydrogenase (GDH) EIA	Rapid, sensitive	Non-toxigenic and toxigenic <i>C. difficile</i> detected;
Nucleic acid amplification tests (NAAT) (PCR)	Rapid, sensitive, detects presence of toxin gene	Cost, special equipment, may be “too” sensitive
Stool culture	Most sensitive test available when performed appropriately	Non-toxigenic and toxigenic <i>C. difficile</i> detected; labor-intensive; requires 48–96 hours for results

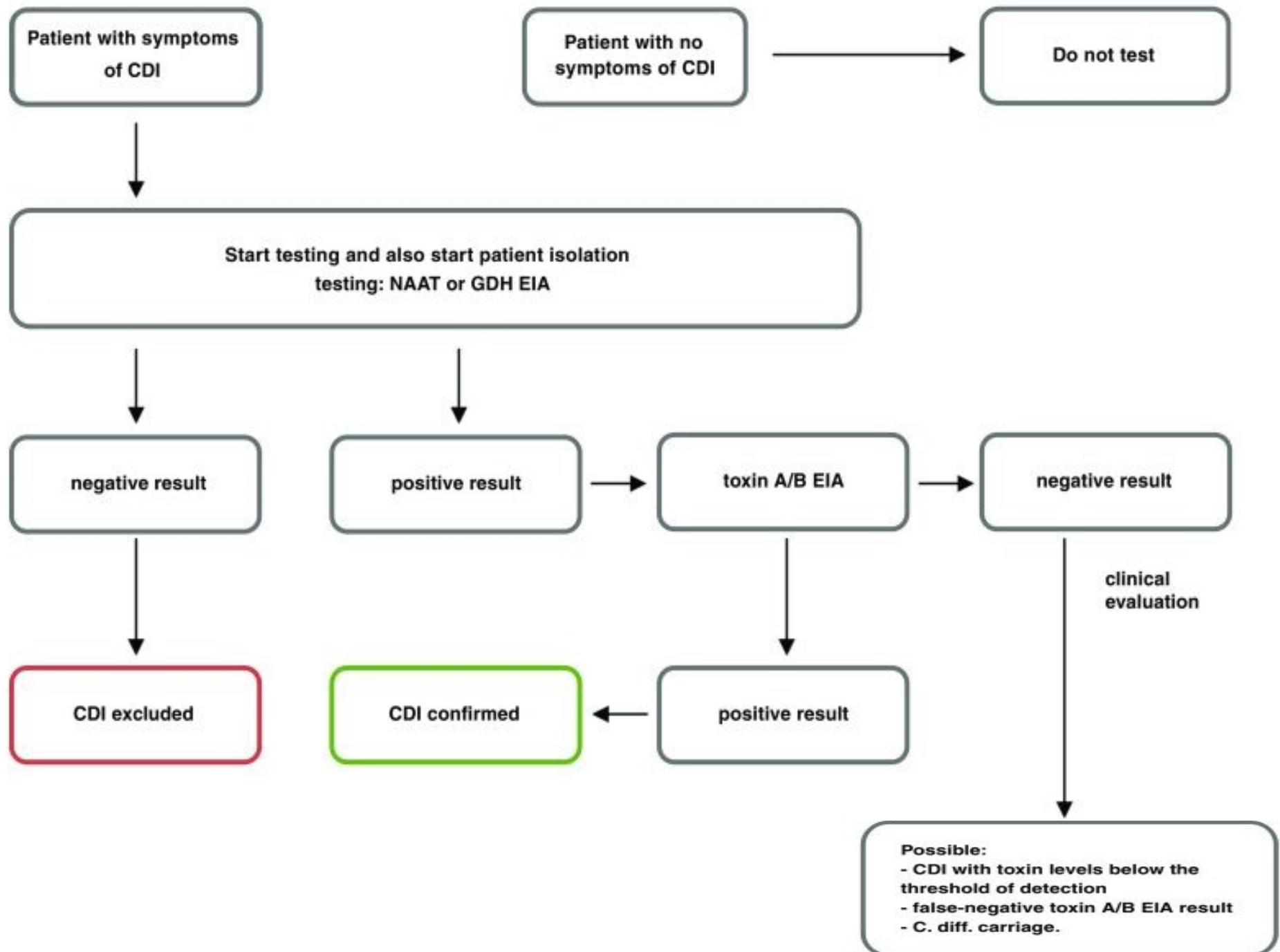
European Recommendations: Importance of Toxin Detection and Clinical Evaluation

(a)



(b)





Treatment

Treatment: supportive care

- Any inciting antimicrobial agent should be discontinued
- Maintain enteral nutrition
- Fluid resuscitation, electrolyte replacement
- DVT prophylaxis
- Anti-motility agents are allowed but only in combination with medical therapy

Should You Treat the Patient or Treat the Strain?

- Routine diagnostics laboratory tests do not provide strain type
- Routine tests not always reliable
- Always treat the patient based symptoms, history, risk factors and markers of severe disease

Guidelines: Treatment

Clinical Definition	Supportive Clinical Data	Recommended Treatment ^a	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of ≤ 15000 cells/mL and a serum creatinine level < 1.5 mg/dL	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days, OR • FDX 200 mg given twice daily for 10 days • Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days 	<p>Strong/High</p> <p>Strong/High</p> <p>Weak/High</p>
Initial episode, severe ^b	Leukocytosis with a white blood cell count of ≥ 15000 cells/mL or a serum creatinine level > 1.5 mg/dL	<ul style="list-style-type: none"> • VAN, 125 mg 4 times per day by mouth for 10 days, OR • FDX 200 mg given twice daily for 10 days 	<p>Strong/High</p> <p>Strong/High</p>
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> • VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present. 	<p>Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)</p>
First recurrence	...	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR • Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR • FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode 	<p>Weak/Low</p> <p>Weak/Low</p> <p>Weak/Moderate</p>
Second or subsequent recurrence	...	<ul style="list-style-type: none"> • VAN in a tapered and pulsed regimen, OR • VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR • FDX 200 mg given twice daily for 10 days, OR • Fecal microbiota transplantation^c 	<p>Weak/Low</p> <p>Weak/Low</p> <p>Weak/Low</p> <p>Strong/Moderate</p>

Initial episode

Clinical Definition	Supportive Clinical Data	Recommended Treatment (Strength of Recommendation/ Quality of Evidence)
Initial episode, non-severe	WBC \leq 15,000 cells/ml, serum Cr \leq 1.5 mg/dL	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days (Strong/High), OR • FDX 200 mg given twice daily for 10 days (Strong/High) • Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days (Weak/Low)
Initial episode, severe	WBC $>$ 15,000 cells/ml, serum Cr $>$ 1.5 mg/dL	<ul style="list-style-type: none"> • VAN, 125 mg 4 times per day by mouth for 10 days (Strong/High), OR • FDX 200 mg given twice daily for 10 days (Strong/High)
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> • VAN, 500 mg 4 times per day by mouth or by nasogastric tube (Strong/Moderate). If ileus, consider adding rectal instillation of VAN. IV metronidazole (500 mg every 8 hours) (Strong/Moderate) should be considered if oral therapy is not possible.

Fidaxomicin now first-line agent

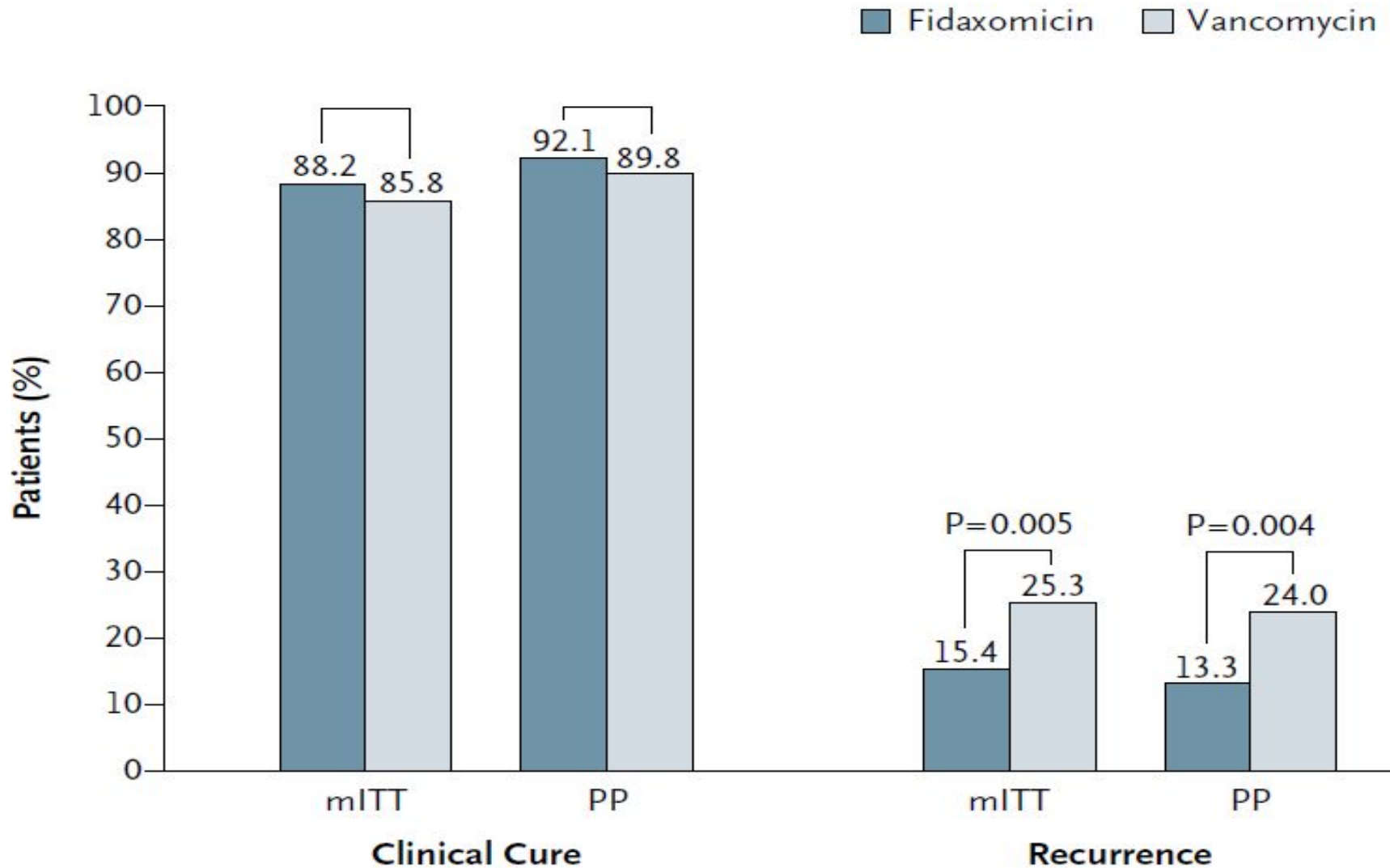
Minor change to serum creatinine cut-off

Major change: metronidazole is no longer first line agent for non-severe CDI in settings where access to VAN/FDX is not limited

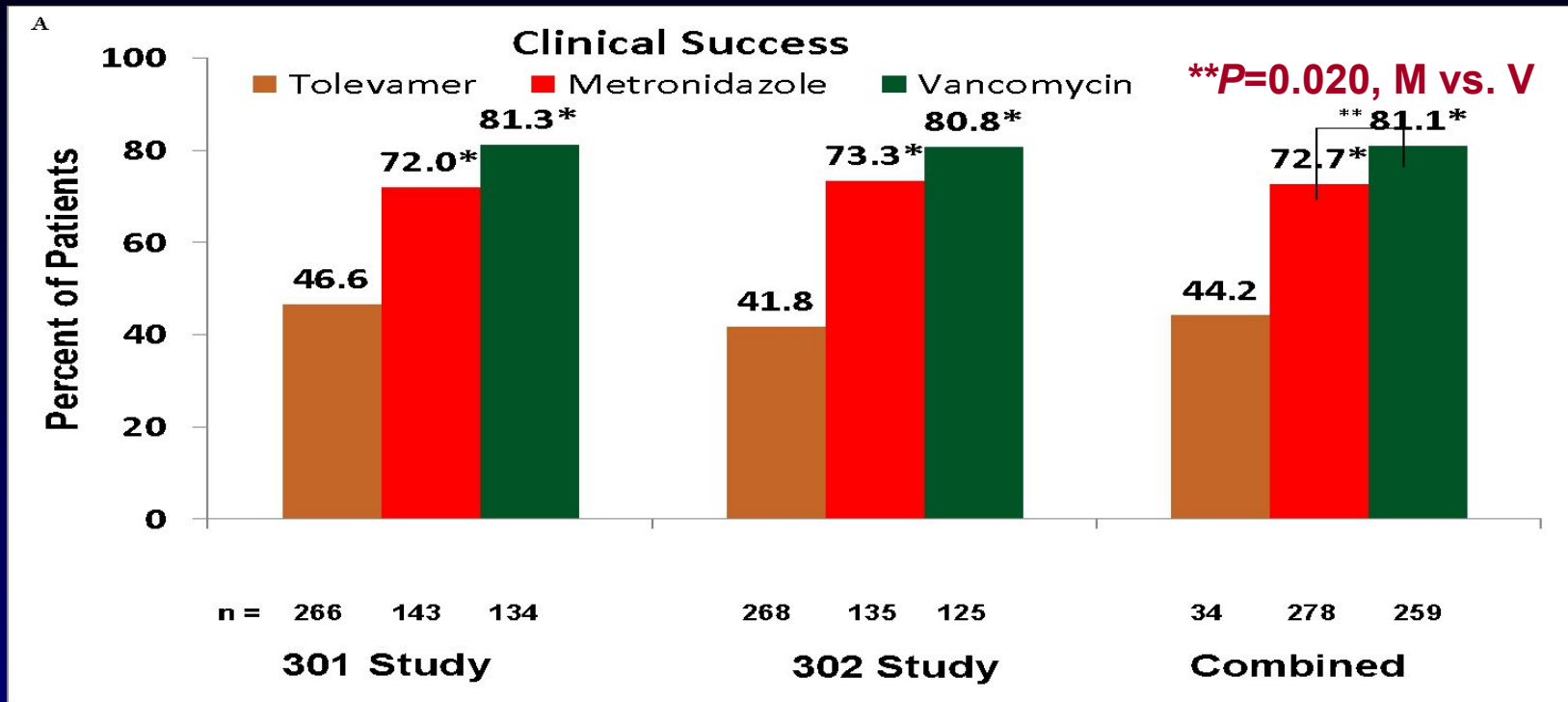
Fidaxomicin

- New bacteriocidal antibiotic
- Poorly absorbed narrow-spectrum macrolide
- FDA approval for CDI in 2011

Fidaxomicin vs. Vancomycin



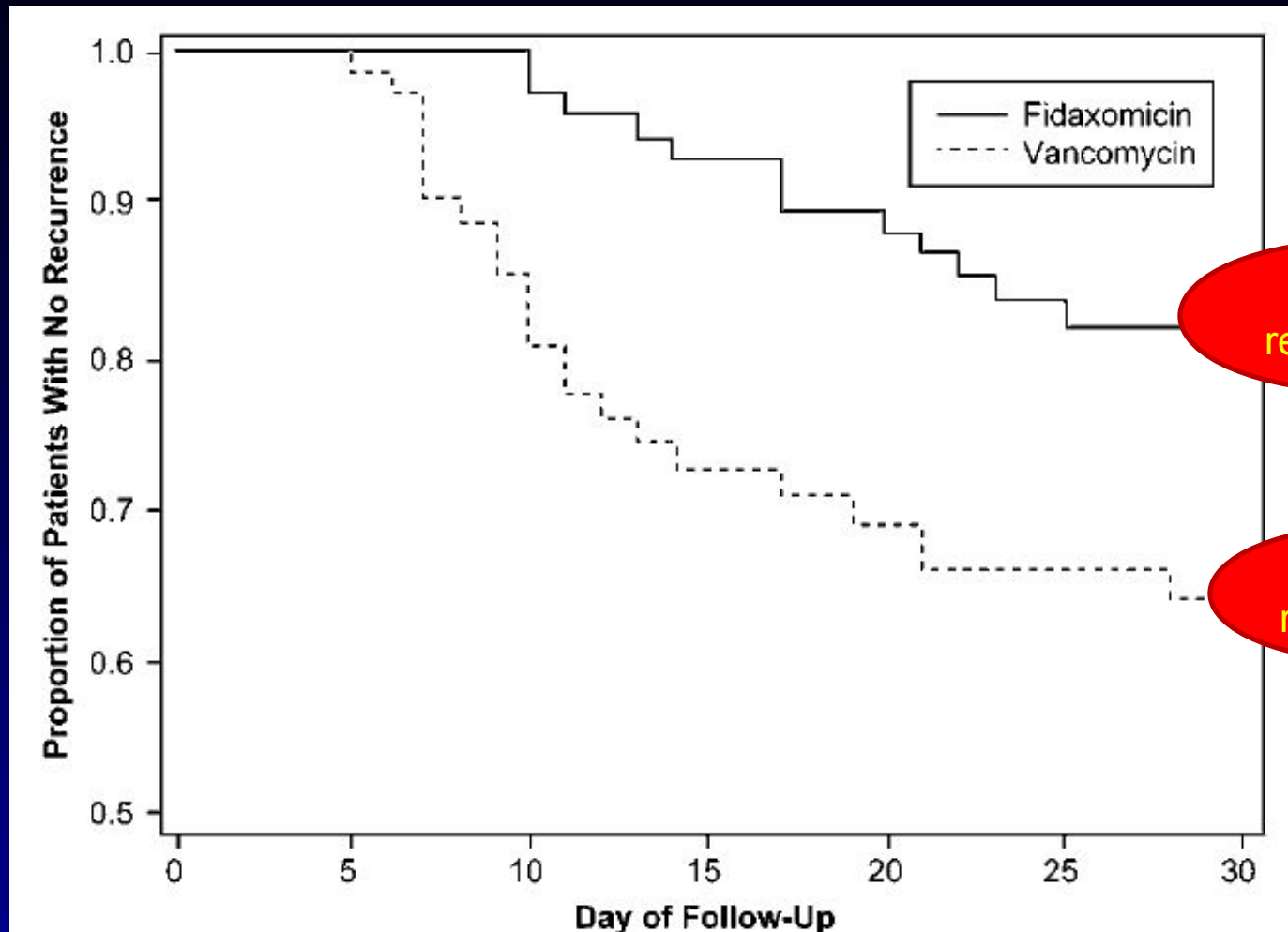
Metronidazole Inferior For Severe and Non-Severe CDI



Vancomycin superior to metronidazole on multivariable analysis, including controlling for clinical severity (p=0.013)

Johnson S, et al. *Clin Infect Dis*. 2014;59:345-354.

Vancomycin vs. fidaxomicin for the first recurrence of CDI



20%
recurrence

36%
recurrence

Recurrence CDI

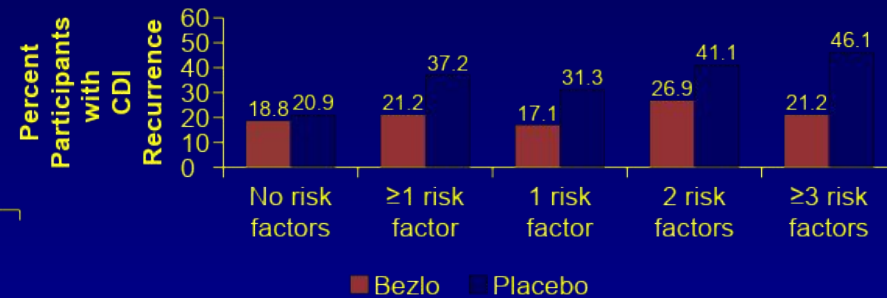
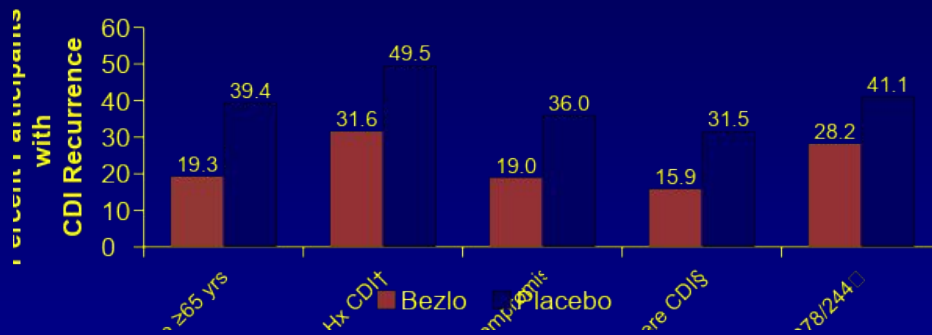
Clinical Definition	Recommended Treatment (Strength of Recommendation/ Quality of Evidence)
First recurrence	<ul style="list-style-type: none">• VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode (Weak/Low), OR• Use a prolonged tapered and pulsed VAN regimen if a was used for the initial episode (Weak/Low), OR• FDX 200 mg given twice daily for 10 days if VAN was used for the initial Episode (Weak/Moderate)
Second or subsequent recurrence	<ul style="list-style-type: none">• VAN in a tapered and pulsed regimen (Weak/Low), OR• VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days (Weak/Low), OR• FDX 200 mg given twice daily for 10 days (Weak/Low), OR• Fecal microbiota transplantation (Strong/Moderate) (appropriate antibiotic treatments for at least 2 recurrences (ie, 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation)

Do not give same regimen a second time

More options provided for second or subsequent recurrence

What about Bezlotoxumab?

- Monoclonal antibody against *C. difficile* toxin B
 - Administered as single IV infusion in addition to standard of care CDI treatment antibiotics
 - Indication: prevention of recurrent CDI
- Results not available early enough to be included



Patients with ileostomy, Hartman's pouch, or colon diversion

- Vancomycin via enema should be included in the treatment
- Oral vancomycin can't reach the disconnected segments
- Metronidazole as adjunctive therapy: colonic excretion is high across the inflamed mucosa but drops dramatically once mucosa starts to heal

Markers of Severe Disease

- Leukocytosis
 - Prominent feature of severe disease
 - Rapidly elevating WBC
- >10 BM/day
- Albumin < 2.5
- Creatinine 2x baseline
- Pseudomembranous colitis
- Toxic megacolon
- Severe distension and abdominal pain

Severe and Complicated CDI

- Vancomycin 500 mg po qid plus metronidazole 500 mg iv q 8 hrs, and vancomycin per rectum (500 mg in 500ml saline as enema) qid (patients with ileus)
- Consult surgery: colectomy vs. loop ileostomy with lavage and vancomycin flushes
- Fidaxomicin po and tigecycline iv.
- ((Fecal transplant?))

ACG guidelines 2013

Special situations

- Pregnancy and breastfeeding: Oral Vancomycin
- IBD
 - All patients with IBD flare need testing for c.diff – empirical therapy
 - Highest risk with corticosteroid use > 3-fold
 - Reduced dosing of corticosteroids
 - Immunosuppression can be maintained but escalation should be avoided
 - Initiation of anti-TNF 72-hrs after starting therapy for CDI
- C. diff can cause enteritis and pouchitis!

The New Kid on the block: Stool

- FMT(Fecal Microbiota Transplant) is placement of suspension of fresh stool harvested from healthy individual into the gastrointestinal tract of an individual with CDI
 - Through standard colonoscopy
 - Rectal enema
 - NJ and NG tube
- Alternative therapy, but by no means new...

A 1,700-year-old method

- 4th century China: human fecal suspension by mouth “yellow soup” for food poisoning, severe diarrhea



Fecal transplantation in veterinary medicine since the 17th century

- Transfaunation
- Horses with diarrhoea per rectum
- Cattle per os as rumen



Modern history of human fecal transplantation

- 1958 Ben Eiseman reported “miraculous cure” with FMT in 4 patients with fulminant pseudomembranous colitis
- “re-establish the balance of nature”
- “immediate and dramatic” responses

Donor's badge



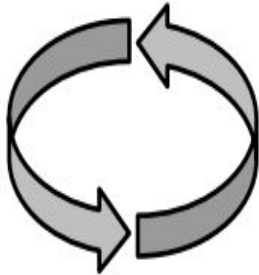
Sélection du donneurs
(cf recommandations GFTF)



50-150g selles

→ sérum physiologique

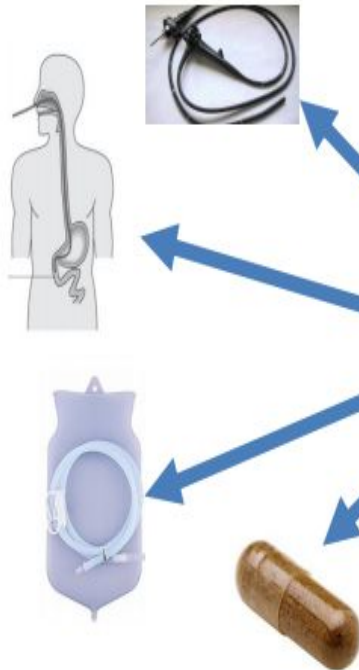
Homogénéisation



Bilan
donneur



TMF



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ESTABLISHED IN 1812

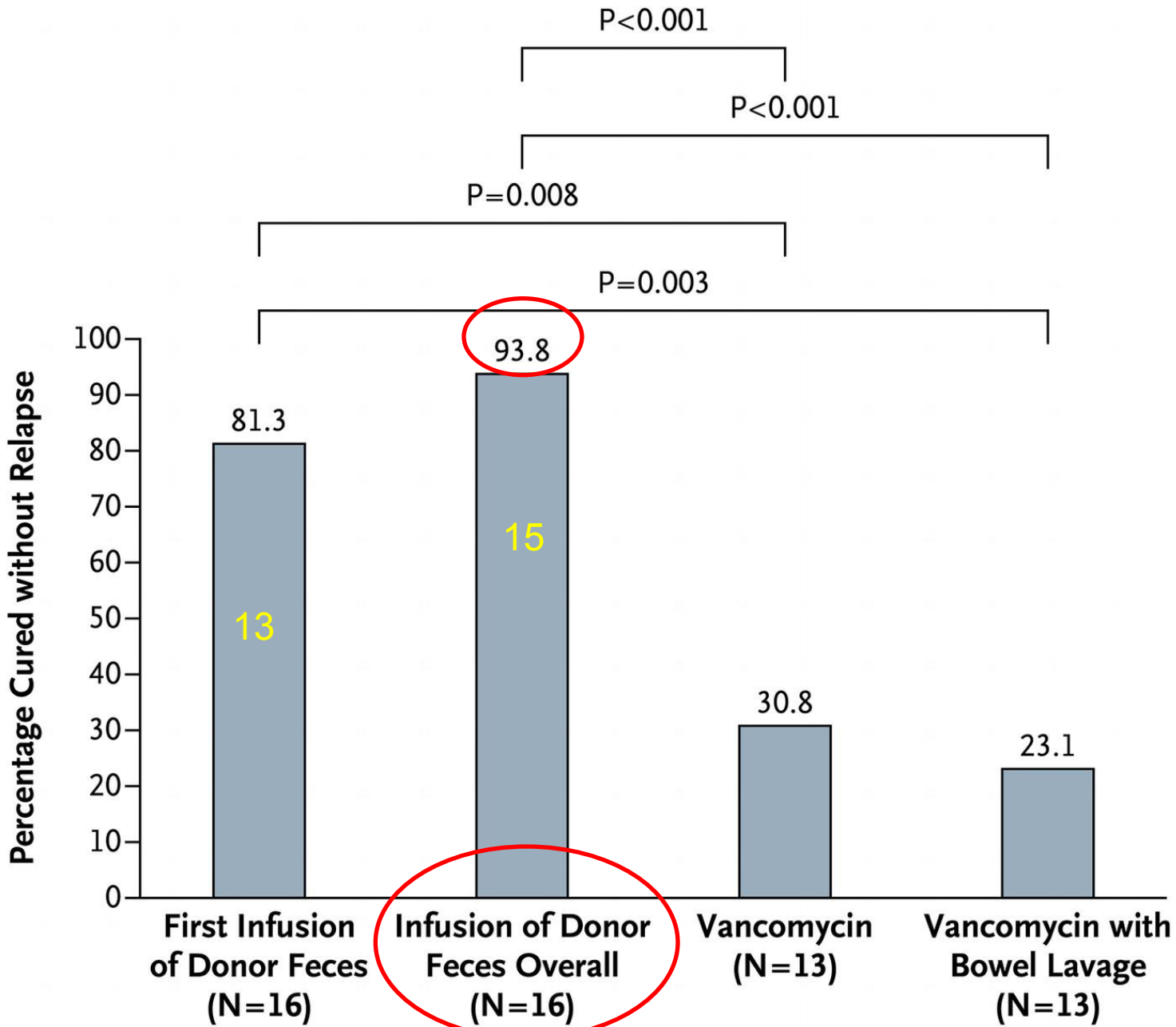
JANUARY 31, 2013

VOL. 368 NO. 5

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

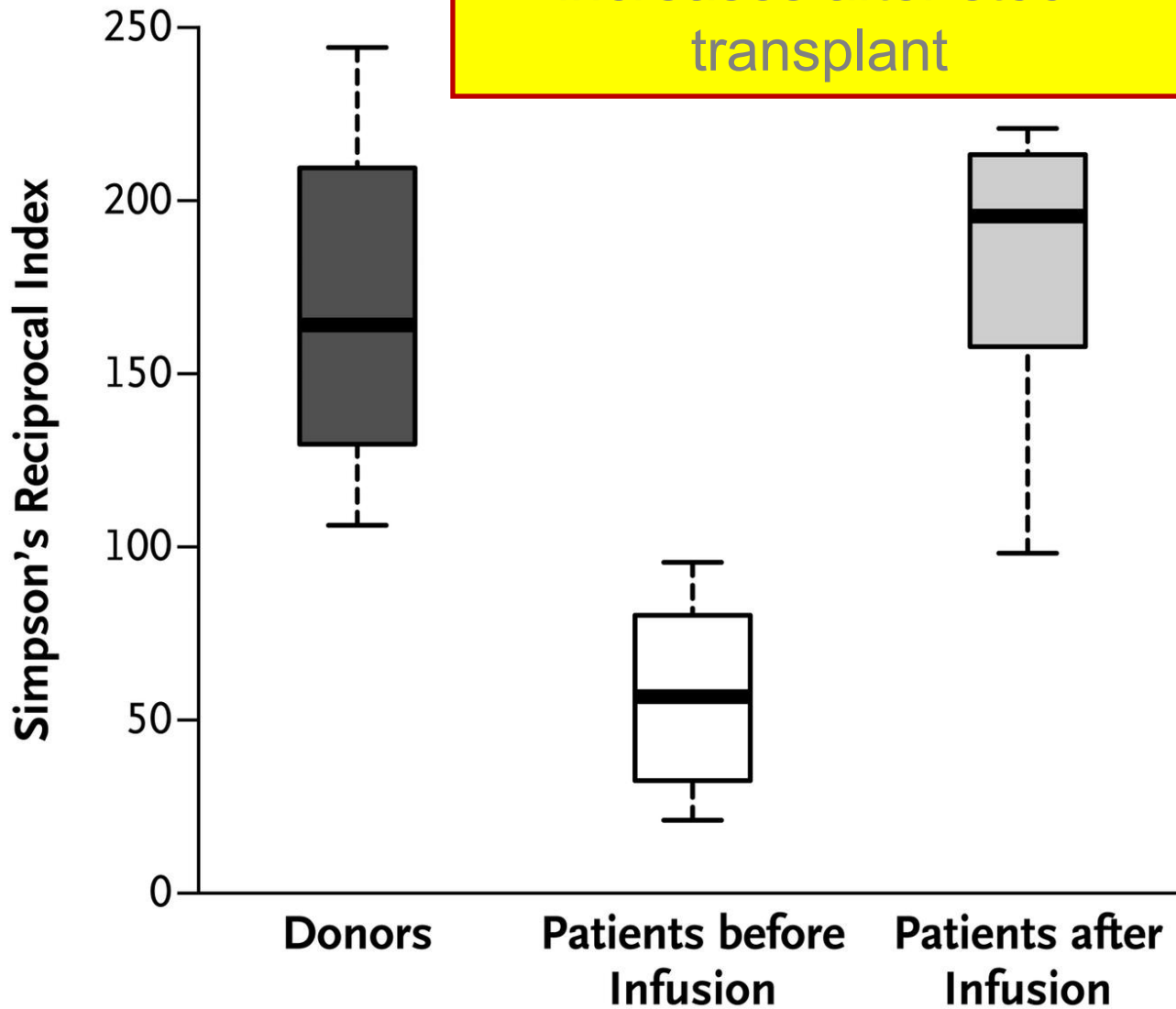
Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D.,
Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D.,
Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D.,
Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

- Duodenal infusion of donor feces after vancomycin for 4 days
- Vancomycin therapy for 14 days

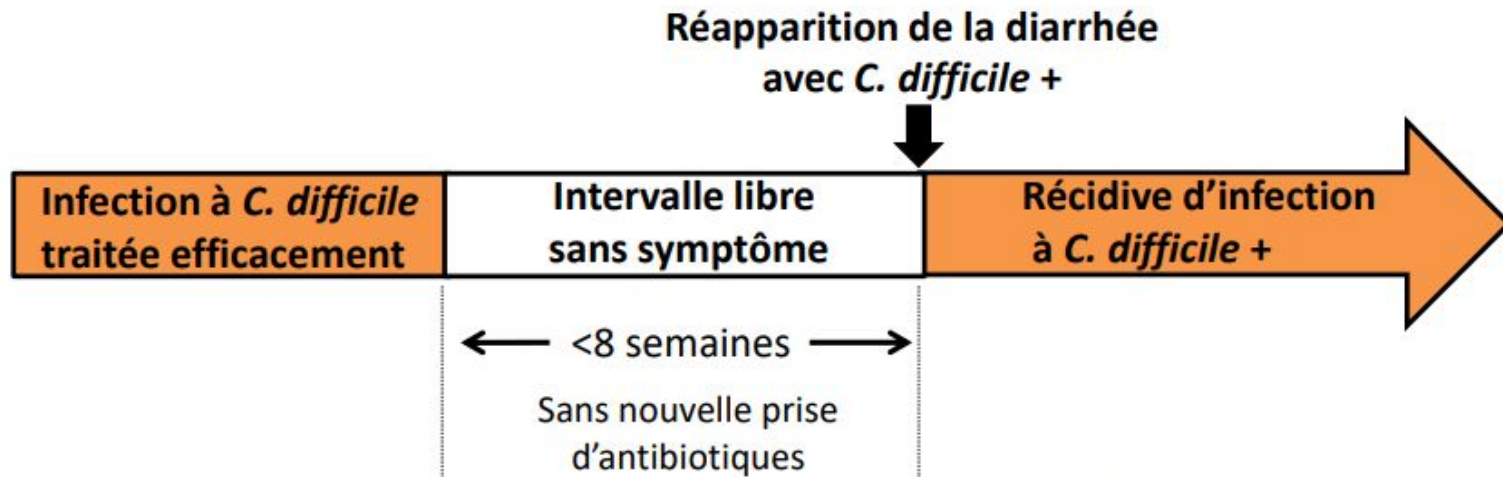


Nood et al
NEJM.
Jan. 2013

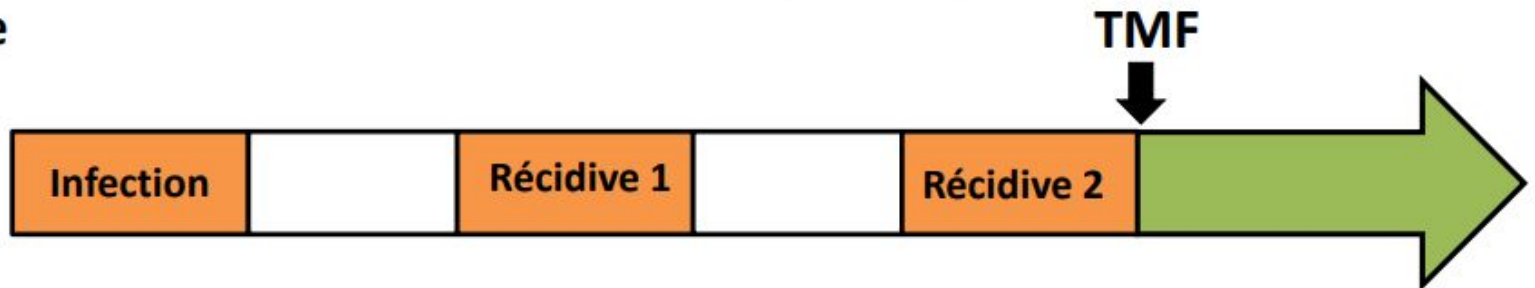
Microbiota diversity increases after stool transplant



Récidive



Multi-Récidive



Who should be treated with FMT?

- After 3 episodes or after failure of vancomycin pulse regimen (ACG guidelines)
- L. Brandt recommendations:
 - First line therapy in severely ill patients
 - FMT may be preferred for the first episode of CDI because antibiotic perturbs the microbiota and may lead to antibiotic resistance

Which route of administration is the best?

Nasogastric
Nasoenteric tube
EGD

Quick
Convenient
Inexpensive
Avoid colonoscopy

Fecal enemas

Easy to administer
Cheap
Can be performed at home

Via colonoscopy

Highest patient acceptance

Ability to assess disease severity and colonic mucosa

- SER 1: colonoscopy and enema (required repeated infusions) with superior cure rate > 85% vs. 76% upper GI route
- SER 2: colonoscopy superior 93% vs. 85% nasogastric tube

Risks of FMT

- Colonoscopic perforation
- Transmission of infections and other diseases
- Long-term risk?
 - Increased incidence of autoimmune conditions: 4 out of 77 patients developed peripheral neuropathy, Sjögren syndrome, RA, ITP within median 17 months f/u

Summary of FMT

- FMT is a simple, acceptable and currently the most efficacious treatment for recurrent CDI--- may play a role in the treatment of variety of GI and non-GI diseases
- FMT via the upper tract seems to be less efficacious than via the lower tract
- Long-term safety remains unknown
- The Future... “Artificial stool” or targeted bacteriotherapy

Questions non résolues

Questions Pratiques	Sélection du donneur: dépistage - Habitus - Antécédents - Infection transmissible	Préparation de selles - En aérobie ou en anaérobie? - Frais ou congelé?	Préparation du receveur - Préparation colique? - Antibiotiques ?	Voie d'administration? Haute ou basse	Sécurité à long terme Maladies infectieuses?
	Avant la TMF		TMF		Après la TMF
Questions Conceptuelles	Sélection du donneur : critère d'efficacité - Diversité du microbiote ? - Composition ? - Présence de métabolites ? - Compatibilité avec le receveur?		Timing de la TMF Poussée ou rémission ?		Sécurité à long terme Transmission de pathologies chroniques?



Fewer Bloodstream Infections With Fecal Transplantation in Recurrent C Diff

Reuters Health Information | November 7, 2019

Fecal Transplant Transmits Fatal Drug-Resistant E coli Infection



Medscape Medical News | October 31, 2019 |  13

Some new C. diff Developments

- Tigecycline looks to be an effective antibiotic in fulminant C.diff combined with oral vanco and iv metronidazole
- Enthusiasm for stool transplant, now available in (Jelly Belly Diarrhea Flavored ?) gelatin capsules!





TMF

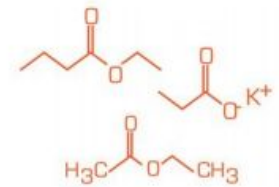
Traitements disponibles
dans 5 à 10 ans



Consortium



Souche unique



Probiotiques de nouvelle génération

Postbiotiques

C. difficile Infection: Case

- 79-year-old woman with multiple medical problems admitted to hospital for treatment of community-acquired pneumonia
- Responds slowly to levofloxacin 750 mg daily
- After 6 days
 - Develops diarrhea (9 loose BMs)
 - WBC count: 11,500/mm³
- Day 7–14 loose BMs, WBC count rises to 19,500/mm³
- Stool testing for *C. difficile* toxins A and B is requested
- Continued antibiotic therapy for pneumonia is deemed necessary

- How would you manage her care?
 - A. Await stool test results and monitor her progress
 - B. Empirically start metronidazole PO
 - C. Empirically start metronidazole IV
 - D. Empirically start vancomycin PO

C. difficile Infection: Case 3

- 79-year-old woman with multiple medical problems admitted to hospital for treatment of community-acquired pneumonia
- Responds slowly to levofloxacin 750 mg daily
- After 6 days
 - Develops diarrhea (9 loose BMs)
 - WBC count: 11,500/mm³
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- How would you manage her care?
 - A. Await stool test results and monitor her progress
 - B. Empirically start metronidazole PO
 - C. Empirically start metronidazole IV
 - D. Empirically start vancomycin PO

Infection Control

Prevention: infection control

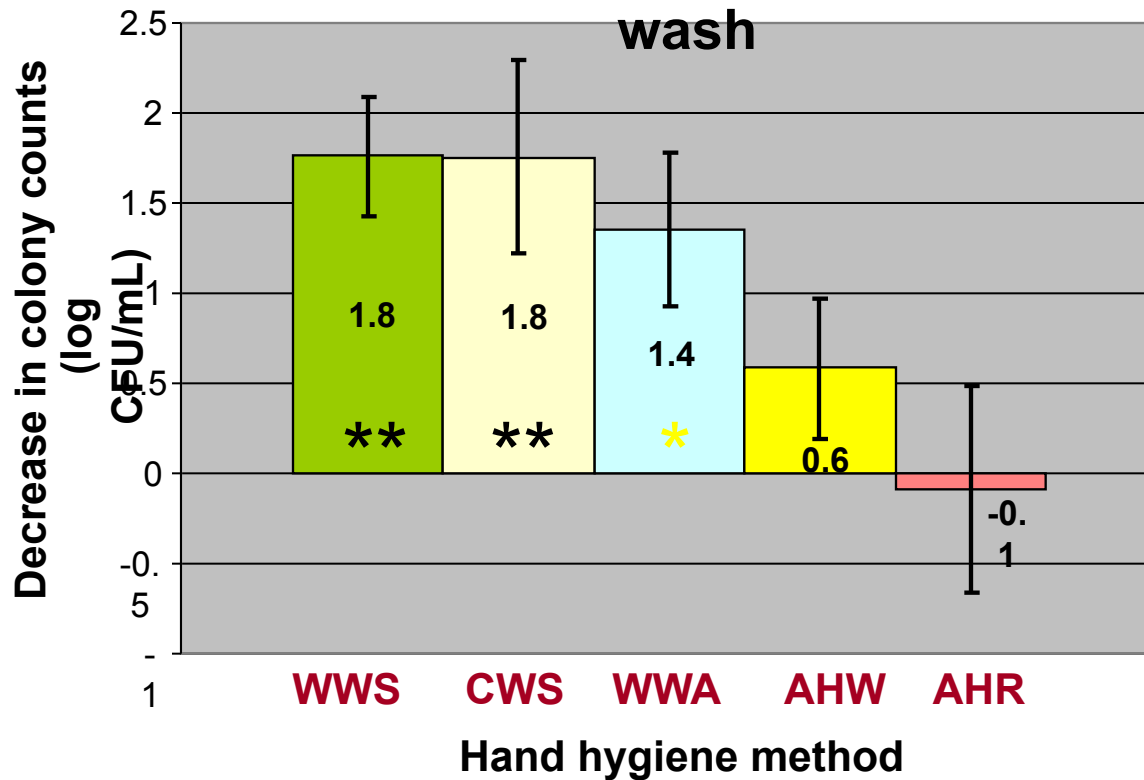
- Early detection
 - High index of suspicion in patients with risk factors
 - Empiric therapy should be started regardless of laboratory testing
 - Repeat stool testing is discouraged
 - < 5% chance for positive test
- Routine screening in hospitalized patients without diarrhea is not recommended

Hospital-based infection control program

- Antibiotic stewardship
- Contact precautions should be maintained at a minimum until the resolution of the diarrhea
 - Private rooms
 - Hand hygiene: soap (preferably 4% chlorhexidine) & water. Alcohol based antiseptic does not kill C.diff spores!
 - Barrier precautions (gloves & gowns)

Efficacy of Hand Hygiene Methods for Removal of *C. difficile* Contamination from Hands

Decrease in colony counts compared with no wash



WWS = warm water and soap

CWS = cold water and soap

WWA = warm water and antibacterial

AHW = alcohol hand wipe

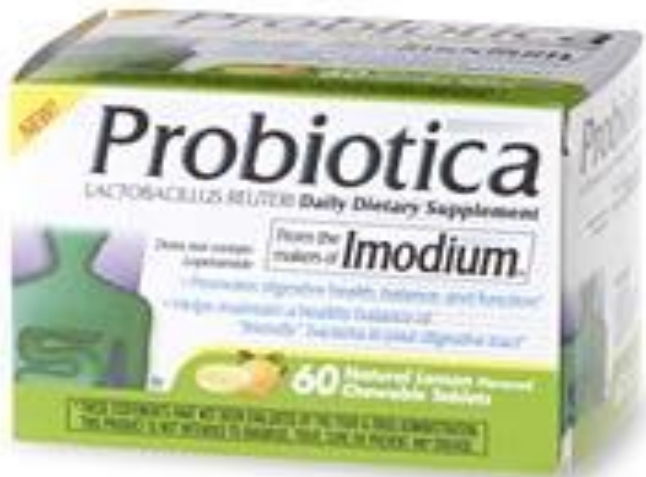
AHR = alcohol hand rub

Isolation and Barrier Precautions

- Patients with CDI and incontinence should be in private rooms or cohorted if private rooms are not available
- Contact precautions and isolation
 - Gloves and gowns required for direct contact and contact with environment
 - Discontinuation of isolation when diarrhea resolves

Prevention: Probiotics

- Annals 2012 SER and Meta-analysis of 20 trials: Probiotics given for the duration of the antibiotic therapy or up to 2 weeks after reduced the incidence of CDI by 66%
- No difference in outcome
 - Between species: Bifidobacterium, Lactobacillus, Saccharomyces, or Streptococcus
 - Single species vs. mixture
 - Adults vs. children



Conclusions: 2017 Guideline Update

- CDI epidemiology is changing
 - 027 strain may be declining
- Testing recommendations still with weak supportive data
 - Improve patient selection
 - In most scenarios, toxin testing helpful
- Antimicrobial stewardship best available CDI prevention intervention
 - Screening for asymptomatic carriage: research for now
- Major changes to treatment recommendations
 - Metronidazole no longer first-line agent
 - Fidaxomicin is a first-line agent
- The microbiology lab is a key component to CDI prevention efforts



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