CAT:	Kan de laboratoriumdiagnostiek van Clostridium difficile gebeuren met toxine-bepaling alleen?
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Clinical bottom line:

Vraagstelling (driedelig):
Kan men voor patienten met vermoeden van Clostridium difficile diarree zich beperken tot de detectie van toxines, zonder bijkomende kweek van de bacterie? Heeft deze benadering geen nadelige invloed op de behandeling en prognose van de patient?

Zoekactie/ Zoektermen:
Zoektermen: 'Clostridium difficile + diagnosis' PubMed: (systematic) reviews SumSearch Cochrane Library National Guideline Clearinghouse CDC-website Manual of clinical microbiology (7th ed; 1999) Murray et al.

Weerhouden (valide) evidence:	
Methode: nut van kweek?	
Manual of clinical microbiology (7th edition; 1999) Allen SD et al.	There are multiple methods for the detection of C. difficile and its toxins. **Controversy exists about which detection method or combination of methods is optimal**.
Practice guidelines for the management of infectious diarrhea (IDSA guidelines) Clin Infect Dis 2001; Guerrant RL et al.	**Test for C. difficile toxins A ± B** (Figure 1)
Guidelines for the diagnosis and management of Clostridium difficile-associated diarrhea and colitis (American College of Gastroenterology) Am J Gastroenterol 1997; Fekety R	When the diagnosis of C. difficile diarrhea is suspected, a single stool specimen should be sent to the laboratory for **testing for the presence of C. difficile and/or its toxins**.
Clostridium difficile-associated diarrhea and colitis (SHEA position paper) Infect Control Hosp Epidemiol	**Stool culture** is the most sensitive test for CDAD, whereas stool **cell cytotoxicity** is the most specific; for maximal diagnostic sensitivity and specificity, **performance of both tests is recommended**. [A-II]

1995; Gerding DN et al.	Enzyme immunoassays for toxin A are rapid but may be less sensitive or less specific than cell cytotoxin assays; **use of EIA in place of cytotoxin assay is recommended as an acceptable alternative** to the cell cytotoxin assay. [B-II]
Laboratory diagnosis of Clostridium difficile disease (review) Clin Microbiol Infect 2001; Delmée M	In our viewpoint, these observations justify the following scheme for the routine bacteriological diagnosis of CDAD (Table 1); **culture and toxin detection (by cytotoxicity or by EIA) should be performed** on every specimen.
Clostridium difficile-associated diarrhea (review) *Arch Intern Med 2001; Mylonakis E et al*	Confirm the diagnosis with a **test for C. difficile toxin**.
Clostridium difficile (review) *Gastroenterology clinics of North America 2001; Kyne L et al.*	The diagnosis of C. difficile diarrhea or colitis is based on a history of recent or current antibiotic therapy; development of diarrhea or other evidence of acute colitis; and **demonstration of infection by toxigenic C. difficile, usually by detection of toxin A or toxin B** in a stool sample.
Clostridium difficile-associated diarrhea and colitis (review) *Mayo Clin Proc 2001; Yassin SF et al.*	NA
The diagnosis of Clostridium difficile-associated disease (review) J Antimicrob Chemother 1998; Brazier JS	The value of isolating C. difficile from stool specimens as a means of diagnosis irrespective of method, has been the topic of much debate in the literature. There can be little question therefore, that the **optimum laboratory investigations should include the ability to culture the bacteria when the need arises**.
Clostridium difficile-associated diarrhea and colitis: clinical manifestations, diagnosis, and treatment (review) Dis Colon Rectum 1998; Cleary RK	Stool for **ELISA**: negative → 1) **tissue culture cytotoxicity**; 2) sigmoidoscopy (Figure 1)
Usefulness of culture in the diagnosis of Clostridium difficile infection Eur J Clin Microbiol Infect Dis 1995; Bond F et al.	**Culture of 500 specimens (405 patients) for Clostridium difficile yielded an additional four patients with possible Clostridium difficile infection which would not have been diagnosed with faecal cytotoxin detection alone.**

Bespreking (zie ook diagnosis worksheet):
Er zijn **verschillende opinies** terug te vinden in de literatuur. Meerdere auteurs van recente publicaties (IDSA guidelines [2001], Mylonakis et al

[2001], Kyne et al [2001], Cleary [1998]) stellen dat de **detectie van toxines volstaat**.
Maar enkele andere auteurs (SHEA position paper [1995], Delmée [2001]) stellen dat de **combinatie van kweek en toxinedetectie** nog steeds **vereist** is. Brazier [1998] pleit voor het behoud van de expertise vereist voor de kweek van C. difficile. De aanbevelingen van de SHEA en Brazier worden vooral ingegeven vanuit **epidemiologische overwegingen** (controle van outbreaks, surveillance voor resistentie).

Opmerkingen:

Terugbetaling via het **RIZIV** vereist gecombineerde kweek en toxinedetectie.
Expertise met betrekking tot de **kweek** van C. difficile mag niet verloren gaan in het kader van efficiënte **controle van nosocomiale 'outbreaks'**.
In de **praktijk** worden sommige patiënten met negatieve toxinetest maar positieve kweek bij (sterk) vermoeden van CDAD toch **(empirisch) behandeld**. Om deze aanpak te evalueren willen wij aan de clinici een voorstel doen voor een studie.

Verdere geplande acties:

LOUK met de clinici op 28/11/2002.
Voorstel voor een studie om de empirische behandeling van CDAD te evalueren.