CAT:	Welke stalen moeten geweerd worden in de laboratoriumdiagnostiek van Clostridium difficile?
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Clinical bottom line:

Vraagstelling (driedelig):
Moeten bepaalde stalen geweerd worden in de laboratoriumdiagnostiek van Clostridium difficile? Kunnen op deze manier overbodige behandelingen vermeden worden?

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

Weerhouden (valide) evidence:	
Staalrejectie	
Manual of clinical microbiology (7th edition) Murray PR et al.	To lessen the chance of obtaining positive culture results from patients merely colonized with the organism, **we recommend that only liquid or unformed stool specimens be processed**. Submitting **two additional stool specimens** from patients suspected of having CDAD **increases toxin detection by only 10%**.
Guidelines for the diagnosis and management of Clostridium difficile-associated diarrhea and colitis (American College of Gastroenterology) Am J Gastroenterol 1997; Fekety R	If the results of those tests [for the presence of C. difficile and/or its toxins] are negative but diarrhea persists, **one or two additional stools can be sent for testing with the same or different tests.**
Clostridium difficile-associated diarrhea and colitis (SHEA position paper) Infect Control Hosp Epidemiol 1995; Gerding DN et al.	It is recommended that **tests** for C. difficile or its toxins be **performed only on diarrheal (unformed) stool specimens** unless ileus due to C. difficile is suspected [B-III]. **Testing of stools of asymptomatic patients** for C. difficile or its toxins is not clinically useful (including 'tests of cure') and **is not recommended** except for

	epidemiological investigation purposes [B-III]. Clinical illness usually does not correlate with the presence of C. difficile or its toxins in the stools of **infants under 1 year old**; **testing of these patients is discouraged** [B-III]. If the initial stool sample is negative for toxin and C. difficile, **it may be useful to test additional diarrheal specimens**. Testing three stools can increase the likelihood of a positive test by 10%; however, this low increase in yield **does not support routine testing of multiple stools** as a cost-effective diagnostic practice.
Laboratory diagnosis of Clostridium difficile disease (review) Clin Microbiol Infect 2001; Delmée M	For an optimal bacteriological diagnosis, **only liquid stools should be accepted**, except in the case of an epidemiological investigation. **Repeated samples** within 7 days of the initial request **seem to give little useful information**.
Clostridium difficile-associated diarrhea (review) Arch Intern Med 2001; Mylonakis E et al.	If the results are negative and diarrhea persists, **1 or 2 additional stool samples can be sent**. Diagnostic **testing during** or at the end of **treatment or during follow-up is not needed**.
Clostridium difficile (review) *Gastroenterology clinics of North America 2001; Kyne L et al.*	**Testing of nondiarrheal stools** for C. difficile is **not recommended** because many hospitalized patients may be asymptomatic carriers of the organism. For the same reason, **test of cure** of C. difficile in asymptomatic patients with recent episodes of C. difficile diarrhea is **not indicated**.
Clostridium difficile-associated diarrhea and colitis (review) Mayo Clin Proc 2001; Yassin SF et al.	Sensitivity [of ELISAs] is lower, but **performing the test on 2 to 3 separate stool specimens** should increase the sensitivity to the 90% range. The **diagnosis** of CDAD is **difficult to establish in infants** because they commonly carry the organism and toxins.
The diagnosis of Clostridium difficile-associated disease (review) J Antimicrob Chemother 1998; Brazier JS	The Department of Health/Public Health Laboratory Service report stated that **formed stools should not be examined** for C. difficile since free toxin is not usually found in solid stools, and toxigenic and non-toxigenic strains may be carried asymptomatically. Renshaw et al. looked specifically at the value of repeated requests for stool cytotoxin and concluded that **little useful information was gained ordering repeat assays** within 7 days of the initial request. Manabe et al. reported a **97% negative predictive value for the first stool examination**.

Pediatric Clostridium difficile: a phantom menace or clinical reality? J Pediatr Gastroenterol Nutr 2000; McFarland LV et al.	**Neonates** have **high frequencies** (up to 64%) **of C. difficile colonization**, but are **usually asymptomatic carriers**. Although there is a high carriage rate in neonates, **symptomatic disease** is **uncommon**. Dutta et al observed (111) pediatric patients in a hospital in Calcutta, India, and found no incidents of C. difficile disease in children 0 to 6 months of age,… Neonates with toxin A-positive results had more days of diarrhea versus those with toxin negative results. Neonates with toxin A-positive results were smaller and less mature, with longer hospital stays. (Enad et al)

Bespreking (zie ook diagnosis worksheet):

- **Consistentie van het staal**
  Alle auteurs (Manual of clinical microbiology [1999], SHEA position paper [1995], Delmée [2001], Kyne et al [2001], Brazier (Department of Health/Public Health Laboratory Service report) [1998]) zijn het erover eens dat **enkel ongevormde stoelgang** geschikt is voor het opsporen van CDAD, om verwarring met asymptomatisch dragerschap te vermijden.
- **C. difficile of zijn toxines opsporen tijdens of na behandeling ('test of cure'), bij asymptomatische patiënten**
  Alle auteurs (SHEA position paper [1995], Mylonakis et al [2001], Kyne et al [2001]) zijn het erover eens dat het opsporen van C. difficile of zijn toxines tijdens of na behandeling, en bij asymptomatische patiënten **niet zinvol** is.
- **Nut van het herhalen van de diagnostiek bij negatief resultaat**
  Alle auteurs (Manual of clinical microbiology [1999], Fekety [1997], SHEA position paper [1995], Mylonakis et al [2001], Yassin et al [2001]) zijn het erover eens dat herhalen van de diagnostiek na een negatief resultaat **nuttig kan zijn**. Meerdere auteurs (Manual of clinical microbiology [1999], SHEA position paper [1995], Delmée [2001], Brazier (Renshaw et al, Manabe et al [1998]) geven echter aan dat de **meerwaarde** van deze praktijk **beperkt** is.
- **C. difficile of zijn toxines opsporen bij neonaten**
  Enkele auteurs (SHEA position paper [1995], Yassin et al [2001], McFarland et al [2000]) suggereren dat het opsporen van C. difficile of zijn toxines **niet zinvol** is bij neonaten, omwille van de hoge incidentie van asymptomatisch dragerschap.

Opmerkingen:

Uitzonderingen moeten toegestaan worden omwille van **epidemiologische redenen**.
Algemene criteria voor diagnose infectieuze diarree ('3-day rule'):

- 'community acquired' of reizigersdiarree: in de eerste plaats denken aan Salmonella, Shigella, Campylobacter en EHEC
- nosocomiaal (na 3d hospitalisatie): in de eerste plaats denken aan C. difficile

Verdere geplande acties:
LOUK met de clinici op 28/11/2002.