Frequently asked questions for users of the recommended protocol for testing for *Clostridium difficile* and subsequent culture

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1. Why do we need to switch to a new testing algorithm (available from: http://www.hps.scot.nhs.uk/haiic/sshaip/guidelinedetail.aspx?id=53536)?

It was stated in the previous recommended protocol (2009) that emerging evidence would be reviewed and used to revise the advice.

The latest scientific evidence shows that the most effective testing protocol was a combination of two tests, one of which should be a glutamate dehydrogenase (GDH) EIA or toxin gene test (PCR) followed by a sensitive toxin EIA test. The new recommended protocol draws on this scientific evidence. We expect NHS boards/laboratories to review their approach in the light of the new guidance, and alter their practices accordingly.

2. Reporting – When should a result be reported to the requester – and what should be reported?

A report, oral or written, should not be issued until both tests of the algorithm have been performed.

It is good practice for laboratories to inform ward staff orally of any positive result, and it is good practice for written reports to provide both the test result and its interpretation.

3. How should samples be transported and stored?

Samples should be transported to the laboratory promptly and stored at 4 degrees Celsius prior to testing. When toxin testing has been completed the faecal sample should be frozen at -80 degrees Celsius for at least 3 months in order to allow culture at a later time for typing if required.

4. Will reporting after performing both algorithm tests prolong the turn-around time?

The technologies involved lend themselves to rapid testing, and all labs in Scotland should already have been using a two-step algorithm, so this should not introduce further delay beyond what was already in place. Releasing a result on the basis of the initial screen would potentially result in overtreatment, overuse of antibiotics, and possible increase risk of CDI as a result.

5. If reports are not issued before the results of both algorithm tests are available, does this conflict with the rationale that using a more sensitive test first would allow earlier treatment and implementation of additional IPC measures?

The issue of IPC management would be for those patients who were toxin-negative after the second test is performed (especially those who have already had a previous recent stool sample that was toxin-negative), who are unlikely to have significant CDI, but have diarrhoea due to another cause and may nonetheless be shedding *C. difficile* in their stool. Clearly if they have significant ongoing diarrhoea this may cause potential issues in terms of environmental contamination. The management of such patients is not clear cut. It has been suggested that nursing such patients in single rooms to reduce environmental contamination may prevent infection of other patients. However, it is regarded as good practice to place patients who present a cross-infection risk, e.g. diarrhoea, in single rooms in any case.

There are no studies to date that have demonstrated that there is a reduction in infection rates associated with such a practice. Antibiotic treatment, if the patient is not considered to have CDI, could theoretically increase their risk of developing CDI. Such patients will require careful evaluation on a case by case basis by the IPCT and the clinicians involved in their care.

6. How should a patient with an equivocal algorithm test result be managed?

A clinical assessment should be undertaken and if the patient remains symptomatic a further sample should be submitted for testing.

Even if toxin is not detected in the stool sample, *C. difficile* may be present in the sample and the patient could be a potential *C. difficile* excretor. This may be the case, even if ongoing diarrhoeal symptoms are thought to be due to another cause. Any patient with continuing undiagnosed diarrhoea will require clinical review with regards the requirement for therapeutic or supportive interventions, and an infection control risk assessment with regards to potential for nosocomial transmission of enteric pathogens.

7. When and for how long is isolation necessary?

Any patient with unexplained diarrhoea should be quickly assessed and placed in the most appropriate care setting, i.e. a single room with en suite facilities (or with a commode allocated for their sole use), unless there is clear clinical reason not to do so (e.g. it is unsafe for the patient to be isolated). Contact precautions should be followed.

A positive test result should not be awaited before placing the patient in isolation.

Patients should remain in isolation until they have been symptom-free for at least 48 hours. A negative CDI result is not in itself sufficient to discontinue isolation.

8. Should clearance testing be performed?

Clearance testing is not recommended. Individuals can remain toxin positive for some weeks after symptoms have settled.

Repeat testing in confirmed positive cases should only be undertaken where symptoms have recurred after initial successful treatment.

9. When should CDI testing be available?
Laboratories need to make testing available 7 days a week (including public holidays).

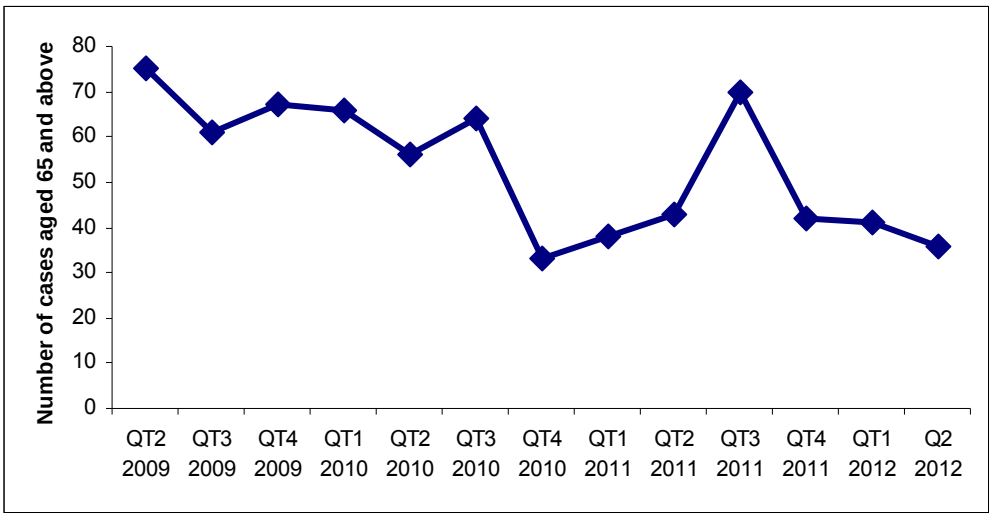
10. Will there be an impact of the new testing algorithm on numbers of reported cases and meeting the HEAT target for CDI reduction?

In England it has been estimated by HPA that introduction of a similar revised two-step algorithm will yield a reduction of 17% in the number of cases of CDI (in a population with a true prevalence of 2.5%). However the majority of English laboratories were still using standalone toxin EIA tests prior to the latest guidance. This suggests that the major impact of the new algorithm is primarily in reducing the number of false positives.

In Scotland the majority of laboratories introduced a two-step algorithm shortly after the first recommended protocol for testing was issued in 2009. As the previous Scottish algorithm and the revised algorithm are both dependent on a positive toxin-EIA result for the purposes of national surveillance reporting, there should be no net impact. This assumes that laboratories continue to use the same test for the toxin testing component of the algorithm.

This is supported by the results of two separate diagnostic studies performed in one Health Board area, which looked at a combined total of almost 500 faecal samples tested by a range of methods, including GDH and toxin EIA tests. These studies showed that the number of cases that would have been reportable to national surveillance based on a two-step algorithm (i.e. which were positive in both tests) was identical, regardless of the order in which the tests were performed. One of the studies included a commercial toxin gene PCR test. Again, based upon a two step algorithm including PCR and a toxin EIA, the number that would have been eligible for reporting to national surveillance was identical, regardless of the order in which the two tests were performed (references available).

One board (see figure below) introduced the new testing algorithm in May 2012 (prior to the issue of the new algorithm), and despite the report of more than one outbreak in this period the average of identified new cases has continued to decrease from 43 cases to 36 cases per quarter (when omitting quarter 3 2011 containing a large outbreak) corresponding to a 16% decrease in total cases (or 13% decrease in incidence per total OCBDs).



11. What will happen if a NHS board nonetheless feels it has failed to meet its HEAT target because of the new algorithm?

Although this is regarded as unlikely for the reasons explained above (Q. 10), the board will be asked to complete an exception report, including a summary of the change in numbers and the estimated change (in relative terms) due to the algorithm along with a summary of changes in clinical practice and IPC.

12. What is the potential cost implication of switching to the new testing algorithm?

The overall costs of implementation will vary from laboratory to laboratory depending upon which combinations of tests have been previously used, and which tests will be used in future.

Those laboratories that have previously used a less sensitive initial screening test will see an increase in the number of samples that require a second test as part of the algorithm. In the studies referred to above, the relative increase in initial positive screens was of the order of 2.5 times.

Assuming a true prevalence of 2.5%, this would result in approximately 4 extra second tests having to be performed for every 100 stool samples tested for CDI. Clearly, this only applies to laboratories that previously performed the less sensitive assay first, otherwise there is no increase in tests performed.

This very modest increase in laboratory tests must be balanced against benefits and/or savings in clinical care, diagnostic accuracy and improvements in patient safety that will accrue.

13. What about using GDH followed by PCR testing for *C. difficile*?

PCR kits are included in the guidance, i.e. GDH (or NAAT) followed by toxin test. But a testing algorithm comprising GDH followed by PCR is not supported by the latest research.

14. Is it acceptable to use a cytotoxin test instead of a sensitive toxin EIA?

Yes, it is acceptable to use a neutralised cell cytotoxin test instead of a sensitive toxin EIA as part of the recommended two-stage algorithm. In DH/HPA evaluations, the cytotoxin test was more sensitive than the toxin EIAs. Clearly, the cytotoxin assay yields slower results than the toxin EIA, and this needs to be accounted for when making management and infection prevention decisions regarding suspected CDI cases.

15. What stools should be tested for CDI?

If a patient has diarrhoea that is not clearly attributable to an underlying condition then it is necessary to determine if this is due to *C. difficile*. The stool sample must take the shape of the container. All diarrhoeal samples from patients aged ≥15 years should be tested as a minimum.

In suspected cases of 'silent CDI' such as ileus, toxic megacolon or pseudomembranous colitis without diarrhoea, other diagnostic procedures such as colonoscopy, white cell count (WCC), serum creatinine and abdominal computerised tomography (CT) scanning may be required, potentially with referral to a gastroenterologist or gastrointestinal surgeon.

16. Does the combined 'quikchek test' (GDH & Toxin) count as a 1 or 2 stage test; i.e., is the sensitivity of the toxin component of the combined test as good as the sensitivity of the stand alone EIA Toxin test?

This test was not evaluated in the recent large DH study, and it cannot therefore be assured that it is equivalent to the GDH and/or toxin EIAs that were examined.

Laboratories will have to satisfy themselves that any specific assay chosen as part of the algorithm is of an acceptable quality and performance standard.

17. Will a comparison of all commercially available kits be available?

The researchers in the recent DH study did not assess *all* commercially available kits. However, a larger number of kits were assessed previously and published as a CEP evaluation and in a peer-reviewed journal (Planche et al., Lancet Infect Dis. 2008;8: 777-84). At that time, this was the largest study of its kind. The present study recruited more than 20 times more patients (in order to be able to accurately distinguish between tests and combinations), and so had to reduce the number of tests examined.