

Guidelines for optimal surveillance of *Clostridium difficile* infection in hospitals

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Summary: *The availability of surveillance data on C. difficile infection in hospitals in England and Wales is being jeopardised by the trend not to culture the organism for diagnostic purposes. NHS trust laboratories that no longer have the ability to isolate C. difficile cannot investigate putative outbreaks or monitor antimicrobial susceptibilities. These laboratories may now need to rely on their local public health laboratory for such investigations. Recent recommendations from the Department of Health(DH)/PHLS have highlighted the need for culture in outbreak investigations, for surveillance purposes, and for monitoring antimicrobial susceptibilities. It is important, therefore, that NHS diagnostic laboratories and public health laboratories, in particular, retain the ability to isolate C. difficile. A cost-effective approach is described that will facilitate surveillance by typing of strains and also enable their antimicrobial susceptibilities to be monitored.*

Key words:

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Hospital acquired gastrointestinal infection with *Clostridium difficile* causes considerable morbidity and mortality among elderly people and costs the United Kingdom (UK) health services millions of pounds each year. Although the exact number of cases is not recorded, this burden appears to be increasing, as annual figures for the detection of faecal toxins A or B, which form the basis of the laboratory diagnosis of *C. difficile* infection, rose by 32% in 1997¹. In a survey of the incidence and impact of *C. difficile* infection in the UK only 31% of the 104 laboratories that responded reported using culture as part of routine investigations². From communications received, the PHLS Anaerobe Reference Unit concurs that a majority of laboratories have abandoned routine culture for *C. difficile* and are therefore now unable to obtain isolates for typing when the need arises. Microbiology laboratories in NHS trusts may seek, and expect, help from their local public health laboratory in culturing *C. difficile* to investigate an outbreak in their own institution. In our experience this help may not be generally available, which flouts Department of Health (DH)/PHLS recommendations. A report on the prevention and management of *C. difficile* infection, compiled by a joint working group of the DH/PHLS³ states that, 'Toxin detection alone is an adequate laboratory investigation for sporadic cases. In outbreaks, when epidemiological studies are required, the dual approach of toxin detection and isolation of *C. difficile* is optimal. The workload may be such, however, that a laboratory might find it difficult to cope with performing both examinations. In such situations the laboratory should perform toxin tests, but also store the stool specimens at 4°C or -20°C for later culture. In this way, the diagnosis of *C. difficile* infection can be confirmed and any immediate action to control the outbreak taken.

Essential epidemiological data can then be obtained by culturing the stored sample and typing the isolates.'³

This was reinforced by the report of the PHLS *C. difficile* working group⁴, which recommended that, 'All laboratories should be able to isolate *C. difficile* from faecal samples for typing when an outbreak is suspected and typing of isolates is necessary'⁴.

Many diagnostic laboratories, including PHLS laboratories, appear not to be following these recommendations, for several reasons. Resource saving exercises, exacerbated to some extent by the centralisation of media production, have led to reduced production of complex and expensive selective media that are seldom used - e.g., cefoxitin-cycloserine egg yolk (CCEY) agar. CCEY is required for *C. difficile* isolation, but is now given a low priority in busy media departments that pour thousands of blood agar plates each day. In addition, PHLS laboratories, in particular, have not fully appreciated their key role in the nationwide surveillance of *C. difficile* infection. As many diagnostic laboratories have abandoned routine culture for *C. difficile*, unnecessary for individual diagnostic purposes³, it is incumbent on PHLS laboratories to support the surveillance of this important nosocomial pathogen.

As for other gastrointestinal pathogens, isolates from cases of infection need to be typed by reference laboratories to provide data on the epidemiology and antimicrobial susceptibility of circulating strains. In this respect, *C. difficile* is unique in that isolation is not a cornerstone of laboratory diagnosis, as it is for most other enteric bacterial pathogens. In 1994, a molecular typing scheme for *C. difficile* surveillance was recommended for England and Wales⁴ and this is currently provided by the polymerised chain reaction (PCR) ribotyping service

Protocol for submission of strains of *C. difficile* for PCR ribotyping to the PHLS Anaerobe Reference Unit

To obtain the maximum benefit from *C. difficile* typing investigations we recommend the following guidelines, which are addressed to primary diagnostic laboratories:

1. Consider your reason for submitting strains for typing. How do you intend using the typing information?
2. Submit only one isolate per patient. In our experience, multiple subcultures from the same plate are unlikely to yield useful information.
3. If you suspect an outbreak, send strains from the index cases and symptomatic cohorts and / or environmental isolates up to a maximum of 20 at one time.
4. Include patient and ward details, also relevant dates of onset of illness if available.
5. Do not submit single isolates. Little useful information can be obtained from examining isolated sporadic cases except as part of planned surveillance studies. Clusters of potentially related cases are appropriate.
6. Subculture strains for typing from a non-selective medium such as blood agar into cooked meat broth and incubate for 48 hours. Send specimens by post in packages labelled in compliance with the relevant postal regulations.
7. Contact the ARU if you wish to discuss a particular problem or to arrange a typing investigation for a special reason.

offered by the PHLS Anaerobe Reference Unit in Cardiff⁵. Since this service began in 1995, it has provided interesting and unexpected evidence that one particular PCR ribotype (type 1) predominates among isolates from hospitals throughout England and Wales⁶. Typing of further isolates is essential to establish the true extent of the spread of this putative clone and the reason for its proliferation. Isolates are also essential for surveillance of the antimicrobial susceptibility of *C. difficile*. Currently, if a strain developed resistance to either of the drugs of choice for treatment – metronidazole or vancomycin – it would go unnoticed by laboratories not equipped to culture *C. difficile*. Metronidazole resistance in *C. difficile* has already been reported from horses in the United States⁷ and we need to be alert to the possibility of this resistance crossing the species barrier as well as the Atlantic.

The optimal approach, therefore, is for diagnostic laboratories, and all public health laboratories in particular, to retain the ability to isolate *C. difficile* in case of:

- a suspected outbreak that becomes apparent by a sudden increase in toxin-positive results from a particular ward or an overall increase in requests for *C. difficile* investigations within the hospital, or
- relapses after treatment or repeated infections in an individual patient.

The second scenario could be due to reinfection with the same or a different strain, failure of treatment, or resistance to the antibiotic used for treatment. The cost of treating a single case of *C. difficile* infection has been estimated at £4000⁸. Surveillance, which is vital for prevention, can be achieved cost-effectively by laboratories following DH/PHLS guidelines - testing for toxins A or B initially, and storing only the toxin-positive stools in the refrigerator or frozen for an agreed period of, say, one month. If either of the scenarios described above occurs, culture can be performed⁹, and the isolates sent to the PHLS Anaerobe Reference Unit for typing and susceptibility testing. It is important to note, however, that even this approach leads to loss of expertise in isolating and recognising *C. difficile*. It may not be necessary, or even appropriate, for all laboratories to be able to culture stored stool specimens on site, provided that arrangements exist for this to be done when needed by a large neighbouring centre, perhaps through PHLS

Group collaboration. Whatever the arrangements are, isolation and identification methods must be quality controlled. The PHLS Anaerobe Reference Unit can provide details of recommended methods⁹. The unit has also produced guidelines for the selection of strains to be submitted for typing (box). The typing service is a core-funded activity provided to PHLS and NHS trust laboratories in England and Wales in support of outbreak investigation and local and national surveillance.

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