**SUMMARY**

*Clostridium difficile* is a hospital acquired infection which causes diarrhoea and colitis, and can lead to pseudomembranous colitis or toxic megacolon which can be life threatening. It has become a common pathogen in hospital acquired diarrhoea, often as a complication of antibiotic therapy. The correct and timely detection of *C. difficile* infection (CDI) is the cause of much debate due to both the financial penalties imposed on hospitals which exceed their allotted target for CDI by the Department of Health, and the infection control issues that arise from a confirmed case of CDI.

These issues have led to a Department of Health commissioned study to improve the accuracy of testing algorithms for *C. difficile* infection for use in diagnostic laboratories. It has previously been reported that a two stage algorithm should be used but no definite recommendations were published, the authors of this latest report have recommended two possible algorithms. The first testing algorithm involves a two test protocol comprising a test for *C. difficile* antigen (GDH) followed by a toxin detection test. The second recommends a first line molecular test followed by a toxin detection test. The combination of these tests results will aid clinical categorisation. See Fig.1

In view of the reported variability in the sensitivity and specificity of enzyme immunoassay methods, it was decided to evaluate a novel molecular test for *tcdB* and to compare it with the more traditional methods of detecting CDI with the aim of developing a sensitive, specific and cost effective algorithm for use in a routine diagnostic laboratory.

**METHODS**

Faecal samples (*n*=100) were tested retrospectively using six commercial techniques between December 2012 and April 2013 at Barnsley Hospital NHS Foundation Trust. Samples were divided into positive (*n*=50) and negative (*n*=50) groups based on the detection of *C. difficile* antigen by the Meridian ImmunoCard™ method (Meridian Biosciences, Europe), the current in house method. The samples were tested following the manufacturers instructions in line with the recommendations of the PHE. All faecal samples were categorised as either a 6 or 7 on the Bristol Stool chart, were from patients >65 years of age and/or stated colitis or recent antibiotic therapy in the clinical details.

**RESULTS**

GDH detection

ProFlu™ GDH was detected in 49 of the 100 samples tested. Prolisa™ GDH was detected in 50 of the 100 samples tested. ImmunoCard™ GDH was detected in 50 of the 100 samples tested.

The ProFlu™ gave a sensitivity of 96% and specificity of 98%; the other two GDH assays performed the same giving a sensitivity and specificity of 98% and 98% respectively.

Toxin Detection

Toxin was detected by the VIDAS in 31 of 50 samples (62%) and NOT detected in 18 of the 50 patient samples (36%). These 18 samples were further tested by the gold standard CCTA and were found to be toxin positive. The VIDAS gave a sensitivity and specificity of 63% and 100% respectively.

**NAAT tcdB gene detection**

The Portrait Analyser detected the tcdB gene in 46 of the 50 toxin positive samples (note: insufficient sample volumes for two samples), and detected the tcdB gene in 2 of the toxin negative samples. Overall sensitivity and specificity was 94% and 96% respectively.

**DISCUSSION**

Using GDH and VIDAS toxin detection in a two step algorithm is more cost effective, but does reduce the Negative Predictive Value (NPV).

Using GDH and NAAT in a two-step algorithm produces the fastest and most reliable results and requires the least hands on time; however it is the more costly option.

A three-step algorithm of GDH to screen out the true negative samples, followed by toxin test, would mean only GDH+/Toxin- samples would require further NAAT testing. This algorithm would give a PPV of 100% and a NPV of 98.5%.

**CONCLUSION**

Our results suggest a three-step algorithm whereby screening is performed with a GDH test, followed by a toxin test, and a NAAT test is performed on GDH positive/toxin negative samples.

Given the equal performance of the GDH kits in this limited study, we have adopted the ProFlu™ GDH test as our front line screen as it confers much improved turn-around time and ease of use.

This three-step algorithm would be as sensitive and specific as using an NAAT test as a screening method, but would be much more cost effective.

The simplicity and robustness of the Great Basin system would allow the introduction of this molecular technique into any laboratory.

**REFERENCES**

2. Planche et al., Lancet Infect Dis 2008; 8:777-84