Clostridium difficile: The most common cause of infectious diarrhoea but where is it coming from and how can we stop it?

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Significance for Western Australia: Our work will reduce the risk and severity of *C. difficile* infection (CDI) for Western Australians by identifying the source of the organism leading to appropriate interventions.

Research Group Objective

To reduce the occurrence of CDI

by determining circulating strains of *C. difficile*, the characteristics of affected patients, and potential sources of the organism so that measures to control and prevent infection can be identified.

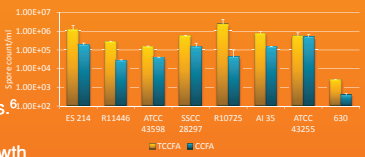
BACKGROUND

- *C. difficile* is a spore-forming bacterium
- It is from the same family that causes tetanus, botulism and gangrene
- *C. difficile* is the leading cause of infectious diarrhoea in hospital patients but also causes more severe disease (pseudomembranous colitis) which can lead to the surgical removal of the colon or death[1]
- The CDC just ranked *C. difficile* as one of the three most threatening antibiotic-resistant microorganisms in the USA, responsible for 250,000 infections and 14,000 deaths per year at an extra US$1 billion per year[2]
- Only a third of hospital cases can be linked to previous hospital cases[3]
- *Clostridium difficile* infections (CDI) are increasingly recognised in the community[4] so other potential sources of the organism must be considered

How can we improve CDI detection?

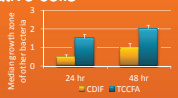
Background: Diagnosing infection by growing *C. difficile* in the laboratory is slow (takes at least 1 day) and can be difficult because spores need to germinate into vegetative cells to grow, *C. difficile* will not grow in the presence of oxygen, and faeces contain many other bacteria that can outgrow *C. difficile*.[5]

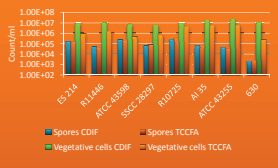
1. Adding the bile salt sodium taurocholate (T) to growth media (CCFA) significantly improved detection of *C. difficile* spores.[6]



2. A commercially available growth medium (ChromID C. difficile agar, Biomerieux [CDIF]) also improved detection of vegetative cells[7]

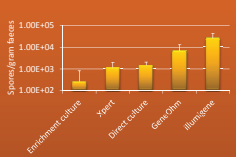
and the inhibition of other bacteria.[8]



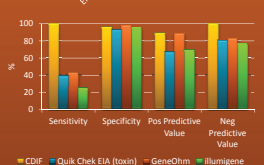


3. CDIF was more likely than TCCFA to detect *C. difficile* in *C. difficile* DNA-positive human faeces: From 50 faeces, 47 (94%) and 41 (82%) grew *C. difficile* on CDIF and TCCFA, respectively.[8]

4. Three examples of rapid alternative tests (the BD GeneOhm Cdiff assay, the Meridian illumigene *C. difficile* and the Cepheid Xpert *C. difficile*), which instead detect *C. difficile* DNA, provided results within 2 hours but were less sensitive than growth methods.[9]



5. DNA-detection and toxin-detection methods, were also inferior to growing *C. difficile* for detecting the bacterium in piglets.[10]

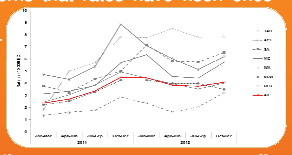


Is *C. difficile* infection becoming more common in WA?

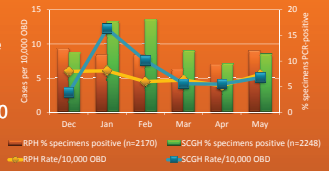
Background: In 1983 there were approximately 3 new cases of CDI per 10,000 occupied bed days (OBDs) at Sir Charles Gairdner Hospital, WA. By 1988 this had increased to 7 new cases and stabilised.[11] In 1998 this fell to <2/10,000 OBDs following restriction of certain antibiotics.[12] There are concerns that rates have risen once again as has been seen globally.[13]

1. State-wide surveillance of hospital-identified (HI) CDI has shown a rising rate of infection in WA.[14]

   Rates of CDI were higher in the summertime.



2. From Jan 2011-Dec 2012 there were 4.6 cases of HI-CDI per 10,000 OBDs in WA.[14] In Jan 2012 it reached 16.3 per 10,000 OBD at SCGH.[15]



3. Almost half (46%) of 80 HI-CDI cases investigated began in the community (occurred <2 days into hospital stay)
   – most (62%) of these patients had recently stayed in hospital while 16% had no recent history of hospitalisation.[15]

Who is being affected?

- Patients with CDI were older (median age, 60.5)
- 26% had three or more other health conditions (most commonly oesophageal reflux [46%], hypertension [43%] or chronic lung disease [36%])
- Most patients (63%) had taken antibiotics in the last 3 months[15]

Could livestock be a source of *C. difficile* in the community?

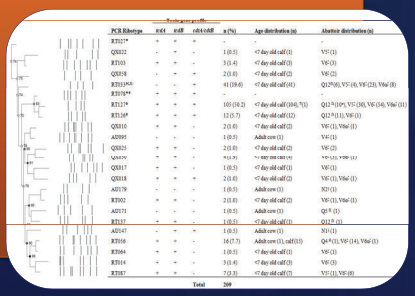
Background: While in the Northern hemisphere there are reports of strains of *C. difficile* (eg. RT 078) previously only found in animals now causing human infections, as yet there is no direct evidence proving transmission between humans and animals or via contaminated food.[16]

1. Strains of *C. difficile* that have caused human CDI in Australia were isolated from local sheep and lambs but the carriage rate was low (0.6% and 6.5%, respectively, of 371 samples) suggesting they are unlikely to be a major source of human infections.[17]

2. In contrast, 56% of samples from <7-day-old calves contained *C. difficile*; the prevalence decreased with increasing age.[18]

Age group	Sample	Prevalence		
Calf, <7 days	Faeces	56%	(203/360)	[no WA samples]
Calf, 2 months	Faeces	20%	(1/5)	[no WA samples]
Calf, 4 months	Faeces	0%	(0/4)	[no WA samples]
Calf, 6 months	Faeces	0%	(0/17)	[no WA samples]
Adult	Faeces	2%	(5/280)	[0/15 from WA]
	Gastrointestinal contents	0%	(0/158)	[only WA samples]
	Carcass washings	0%	(0/151)	[only WA samples]

3. The animal *C. difficile* strains isolated did not include the dominant livestock strain in the Northern hemisphere (RT 078) but did include strain types associated with human infection.[18]



Conclusions

Disease surveillance is important in identifying increases in disease occurrence which might suggest: 1) circulation of particularly harmful bacterial strains, 2) a more susceptible population, or 3) an increase in exposure to the organism. There has been a significant increase in the rate of CDI in Western Australia which is also occurring Australia-wide. Particular strain types have emerged, the susceptible population is increasing as the population ages and sicker people are being hospitalised in place of those who can be treated in the home, and community-acquired CDI appears to be increasing suggesting more exposure to the organism. A potential source of human CDI is livestock since similar strain types are being found but there remains a lack of evidence of direct or indirect transmission between animals and humans.

ACKNOWLEDGEMENTS

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