A Cost Effective Approach for the Diagnosis of *Clostridium difficile* Infection

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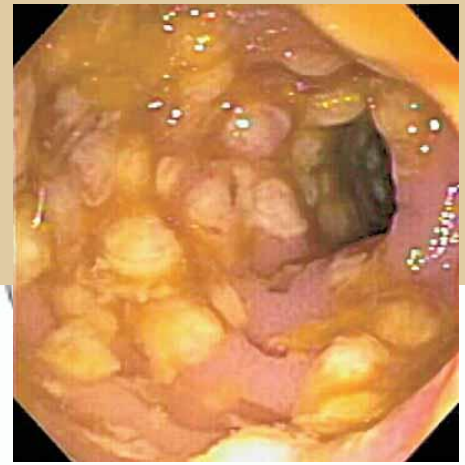
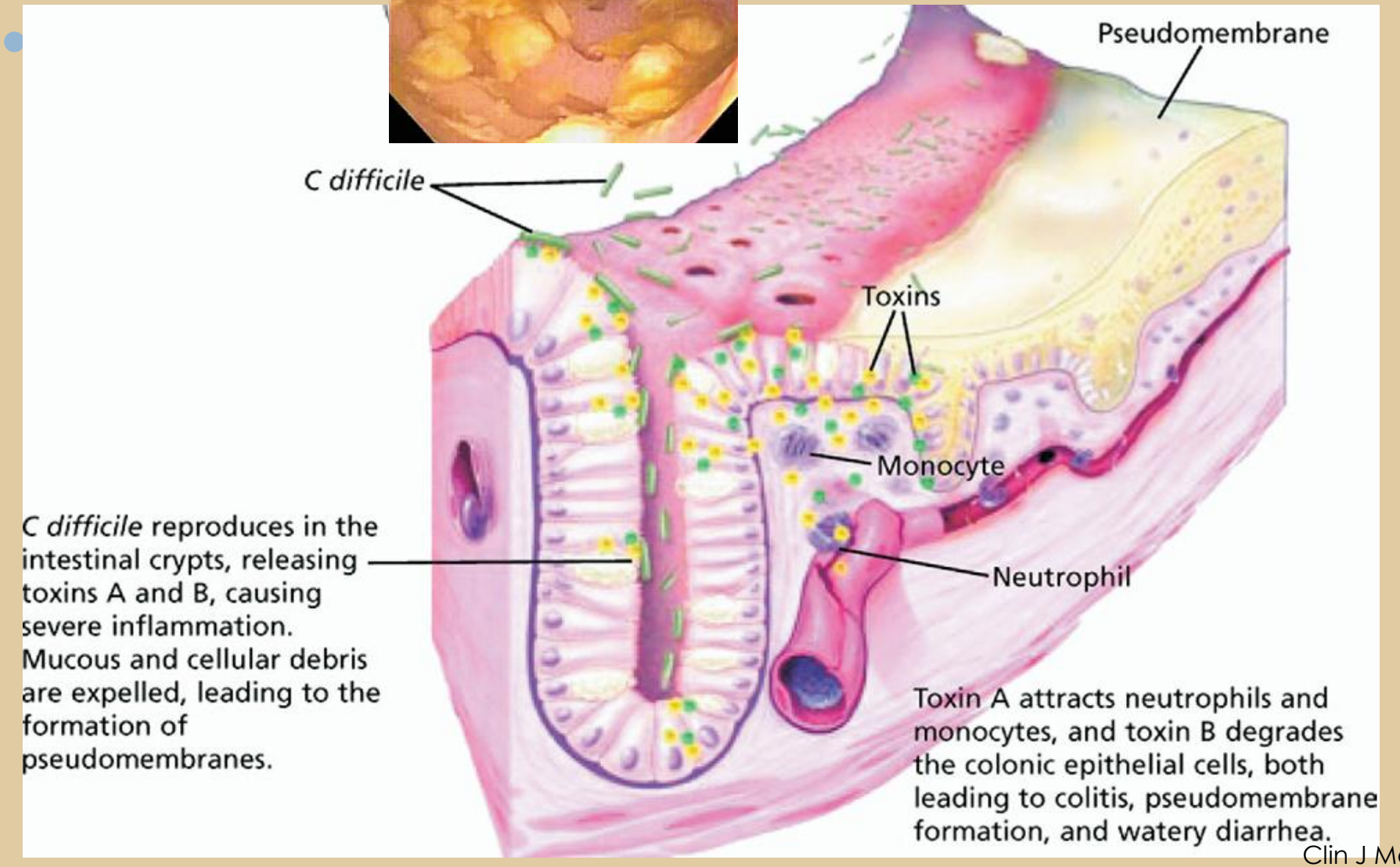
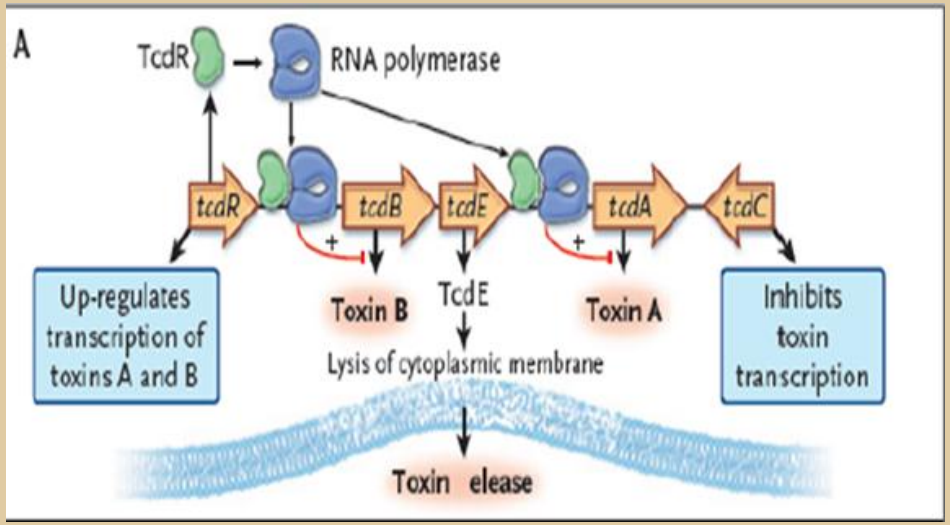


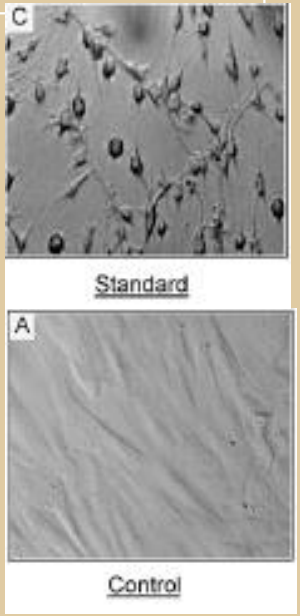
Pathogenesis



Clin J Med 2006; 73:187-197

Detection of toxin

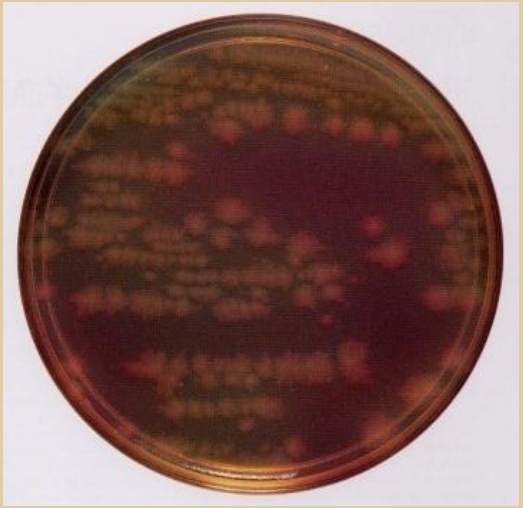




* Cell culture cytotoxicity neutralization assay (24-48h)
- Toxin enzyme linked immunoassay (not sensitive)
- Nuclear Acid amplification tests (expensive)

*Gold Standard

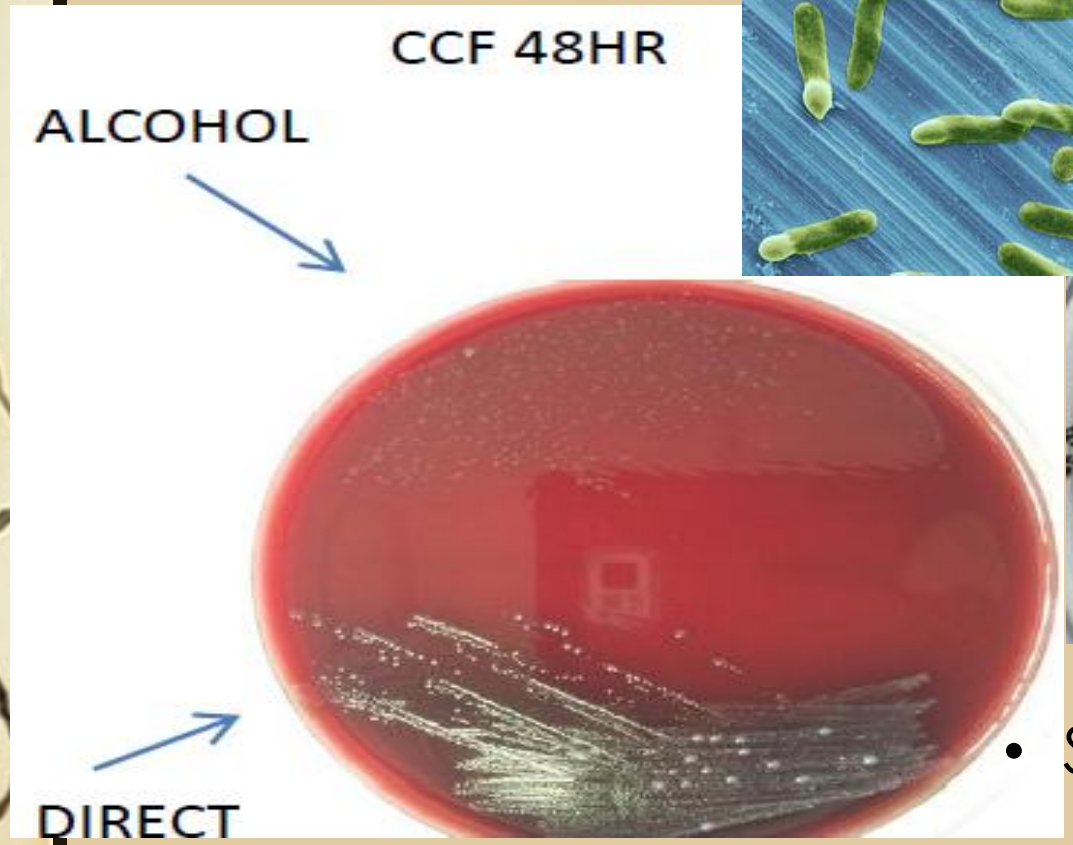
Detection of toxigenic C. *difficile*



* Toxigenic culture (> 48h)
- Glutamate dehydrogenase (need confirmation)

Kelly C & LaMont JT, NEJM 2008, 359: 1932-40

Back to culture – impractical?



- Superior ability to stimulate germination
- β-glucosidate – chromogenic substrate grey to black

A Cost-Effective Approach for Detection of Toxigenic *Clostridium difficile*: Toxigenic Culture Using ChromID *Clostridium difficile* Agar

Shik Luk, Wing Kin To, Tak Keung Ng, Wai Ting Hui, Wing Keung Lee, Florence Lau, Almond Man Wai Ching

Department of Pathology, Princess Margaret Hospital, Hong Kong, China

We evaluated the performance and the cost of toxigenic culture using a commercial chromogenic medium (CDIF) for 538 stool specimens. Compared with real-time PCR, this method was found to detect an additional 9% of positive specimens and result in 61% reduction in material costs, with a trade-off increase in turnaround time of 1 day.

February 2014 Volume 52 Number 2 Journal of Clinical Microbiology p. 671–673

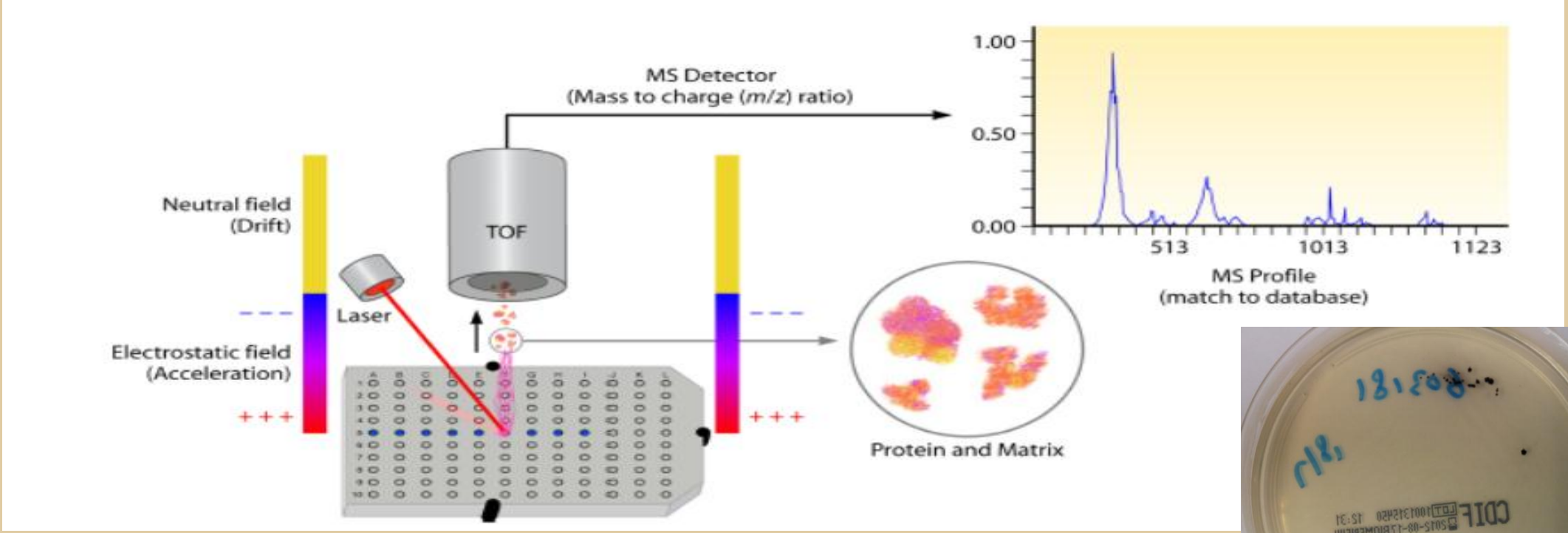
Overnight culture on ChromID C. *difficile* agar

Same date identification by mass spectrometry

Same date confirmation of toxin gene by PCR

TAT 20 - 36h Vs TAT > 48h

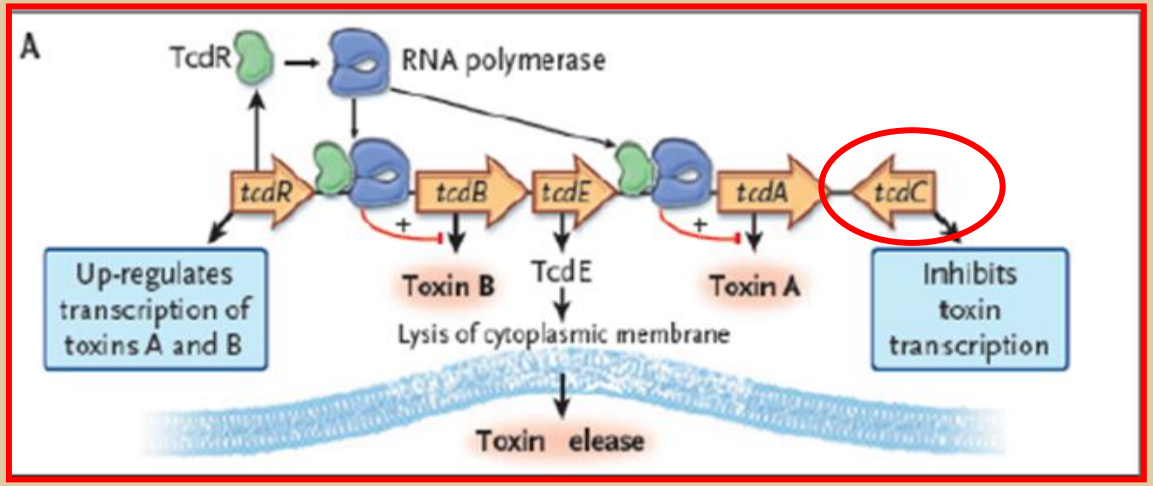
Mass Spectrometry



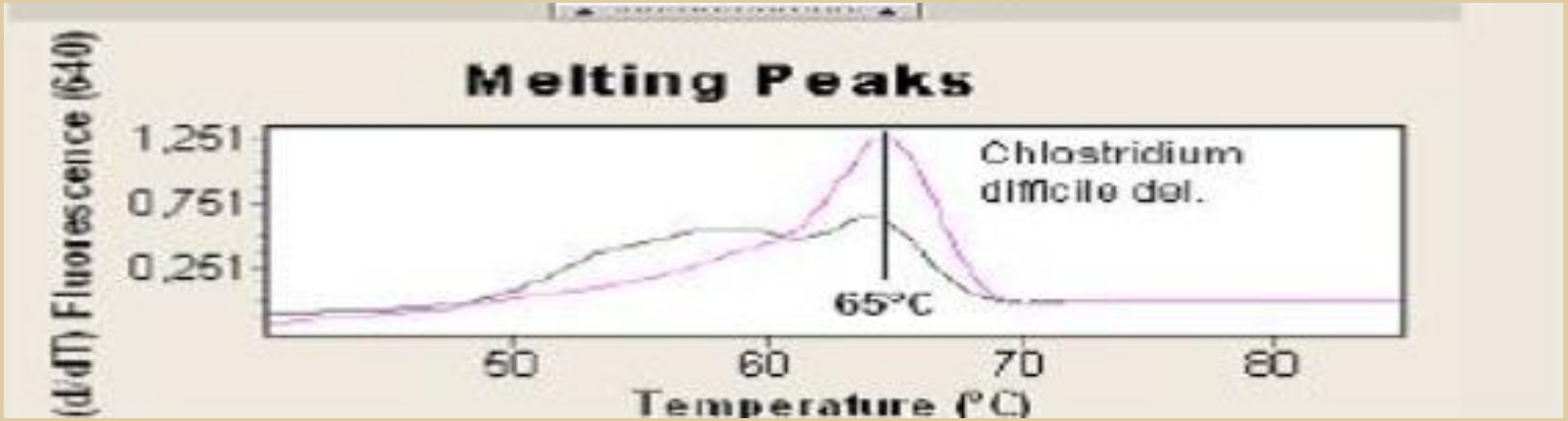
Clin Microbiol Rev 2013; 26:547-603

ONLY a few colonies would be needed with instant result!

Real-time PCR



- Detects the presence of 176 bp fragment of the *tcdC* gene, and deletions found in a 158 bp fragment
- Early identification of hypervirulent ribotype 027 (18 bp del), 078 (39 bp del)



J Clin Microbiol 2008; 46:1996-2001

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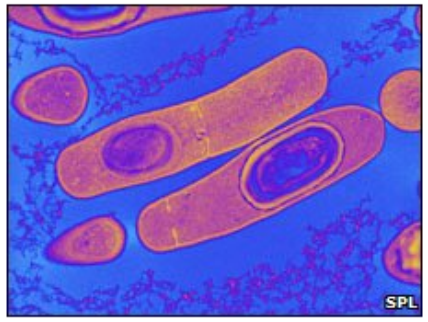
C. diff rise due to 'gene switch'

The rise in Clostridium difficile infections in recent years is due to genetic changes rather than dirty hospitals, say UK researchers.



Most deaths from C. difficile occur in the over 65s

Comparison of an historic strain and a strain from the outbreak at Stoke Mandeville hospital in 2003 found it had evolved to be more virulent.

It can spread more easily and cause more severe symptoms, the team reports in Genome Biology journal.

NHS trusts have a target to cut C. difficile infections by 30% by 2010/11.

The bacteria are present in the gut of as many as 3% of healthy adults and 66% of infants.

It rarely causes problems in healthy people but can lead to illness when the normal balance of bacteria in the gut is disrupted, for example with use of certain antibiotics, and it is the leading cause of hospital-acquired diarrhoea.

In the past five years, a new group of highly virulent C. difficile strains has emerged - PCR-ribotype 027 - which cause more severe diarrhoea and a higher rate of deaths.

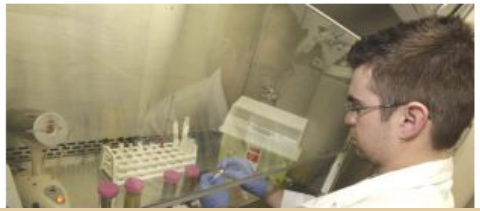
> **"The deep clean programme was never going to work against this organism in the long term"**
>
> Professor Brendan Wren

Sixth death reported during C. difficile outbreak

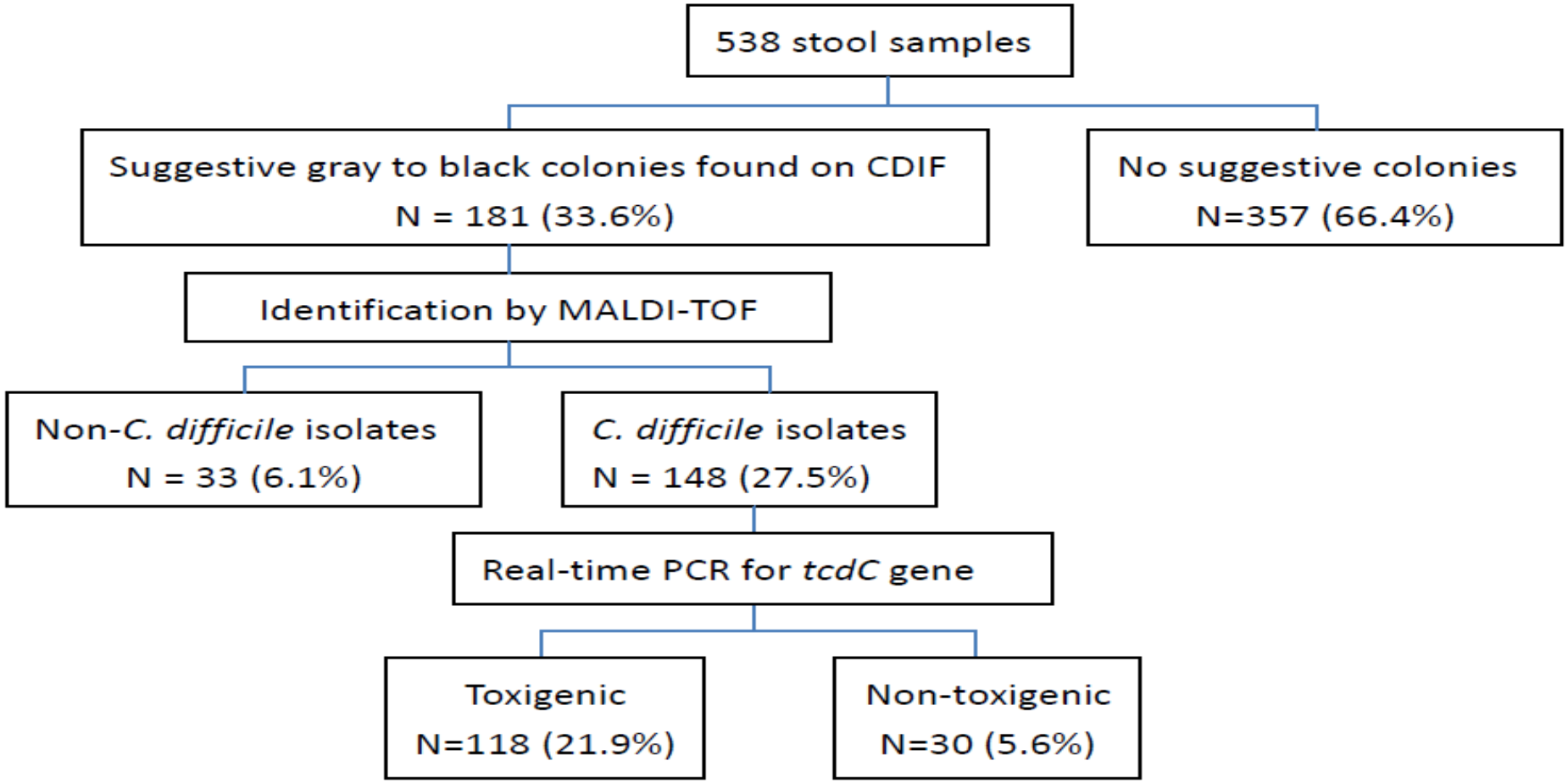
Published on January 27, 2012

By Greg McNeil-Cape Breton Post

SYDNEY — The Cape Breton District Health Authority is reporting a sixth death related to the current outbreak of hospital-acquired Clostridium difficile.



Toxigenic culture using chromogenic agar



Luk S, To WK, Ng TK et al. J Clin Microbiol 2014; 52:671-673.

Toxigenic culture detects an additional 9% of positive specimens

(p= .02 by McNemar's test for paired proportions)

TABLE 1. Comparison of direct stool real-time PCR results with those of toxigenic culture for the diagnosis of CDI

Assay	Result	Comparison to toxigenic culture results[a]					
		No. of specimens		Sensitivity	Specificity	PPV[c]	NPV[c]
		positive	negative				
Real-time PCR[b]	Positive	106	2	90.6%	99.5%	98.1%	97.4%
	Negative	11	416				

[a] Anaerobic culture was performed on the 538 test stools by plating the specimens onto CDIF medium. All *C. difficile* culture isolates were tested for the presence of toxin production (as evidenced by detection of the *tcd*C gene) by real-time PCR.

[b] Direct stool real-time PCR was performed on 535 stool specimens for the presence of *tcd*C. The quantities of three specimens were insufficient for real-time PCR.

[c] PPV, positive predictive value; NPV, negative predictive value

Luk S, To WK, Ng TK et al. J Clin Microbiol 2014; 52:671-673

Cost Saving $$$

PCR performed on every stool sample

$106 (extraction + PCR) x 535 = $56710

1.5h hand on time

61% cost saving!!
Test volume 3000/yr
-> 0.2m

Toxigenic culture

$15 (chromogenic agar) x 538

= $8070 (0.5h)

$1 (MALDI-TOF MS) x 181 (33.6%)

= $181 (0.5h)

$92 (PCR) x 148 (27.5%)

= $13616 (1 h)

Luk S, To WK, Ng TK et al. J Clin Microbiol 2014; 52:671-673.

Increased in turn around time?

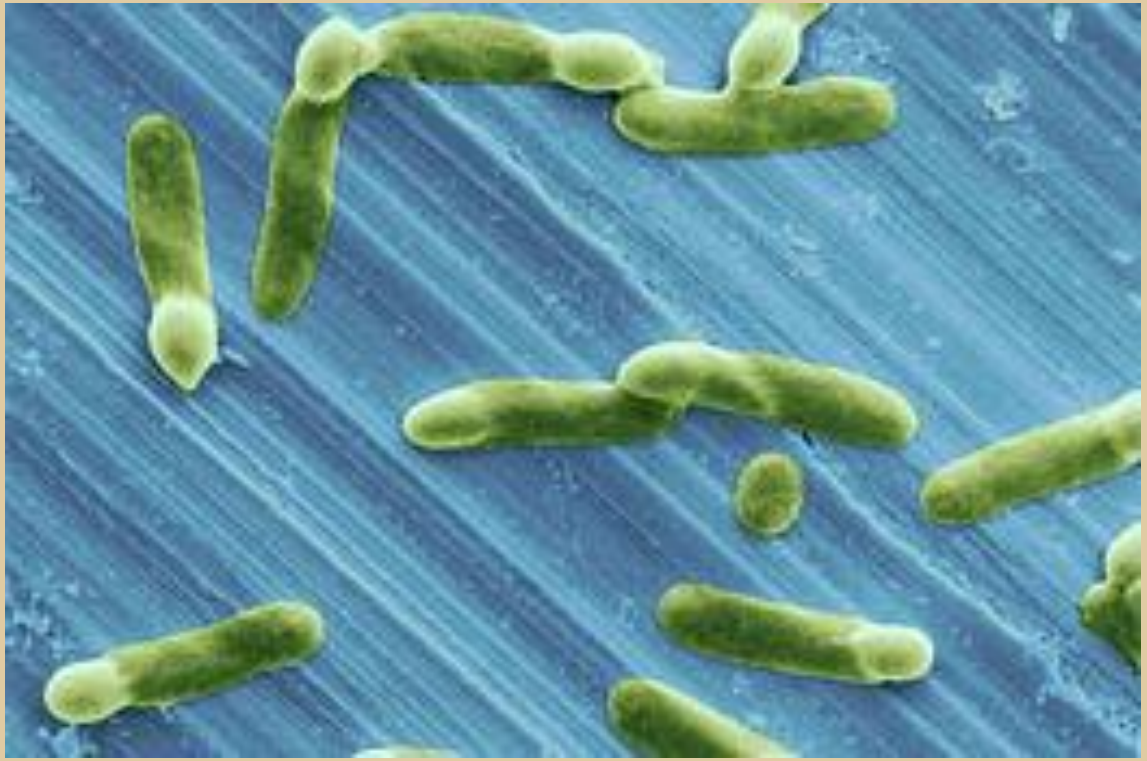
- Direct stool PCR: 3 times / week (cut-off: noon)
  6% specimen same day TAT
- Toxigenic culture: daily put up and follow up
  (cut-off: 5 pm)

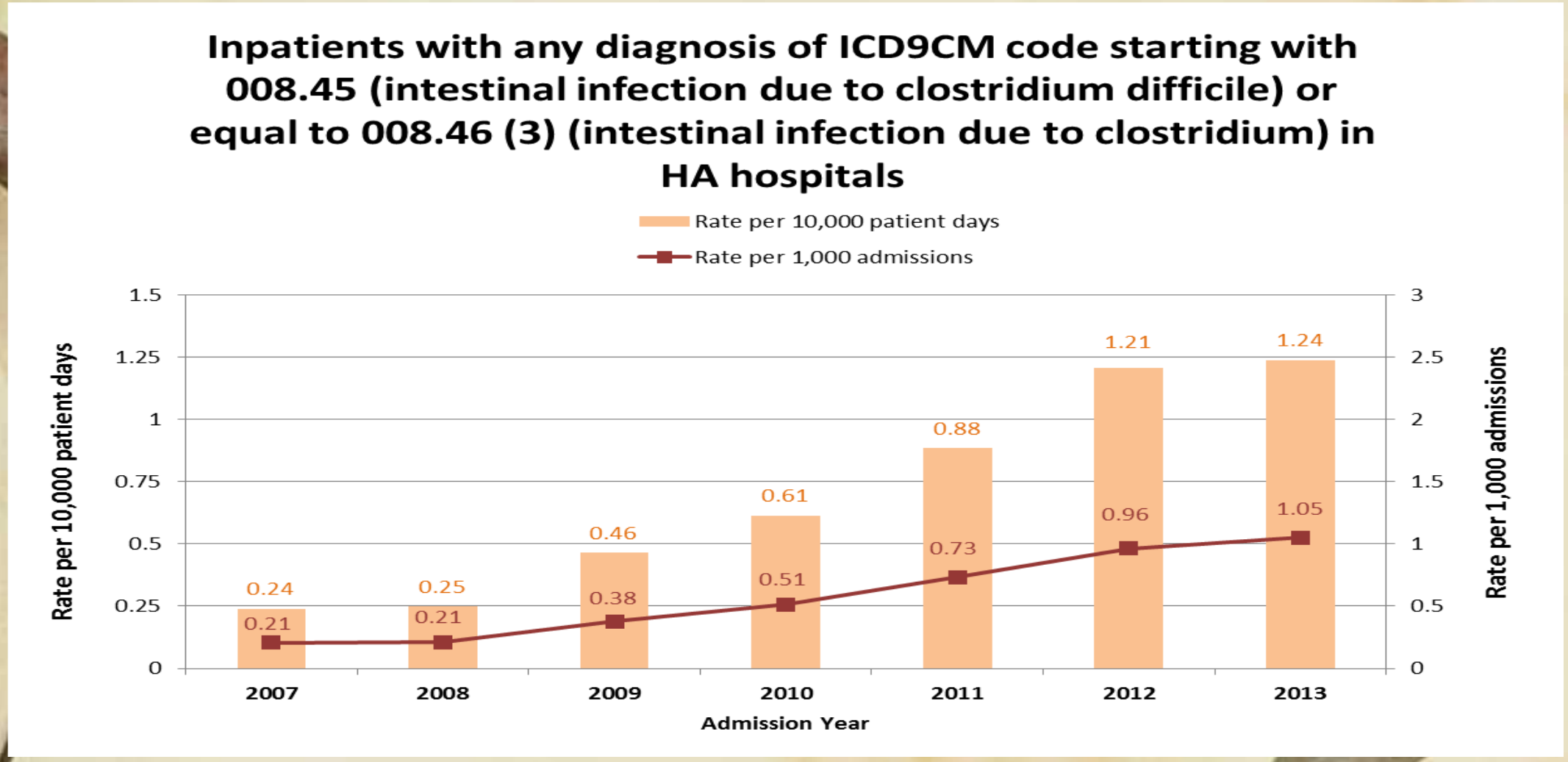
TAT_{80} the same

Conclusions

- For epidemiology study and molecular typing
- Assist management decision for patients with persistence of symptoms after CDI treatment
- The most sensitive diagnostic test
  - isolate and prevent further transmission
- Substantial cost-saving without compromising the quality of service

THE END.





Clinical Data Analysis and Reporting System (CDARS). Hospital Authority

Rates of CDAD for facilities where CDI is endemic range from 5-10 case / 10,000 patient-days

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY FEBRUARY 2007, VOL. 28, NO. 2