

# *Clostridium difficile*-associated diarrhoea: challenge for the clinician and for the microbiologist

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ESCMID Summer School 2009, Porto, Portugal

**Will *Clostridium difficile* take  
over the role of MRSA in  
hospitals?**

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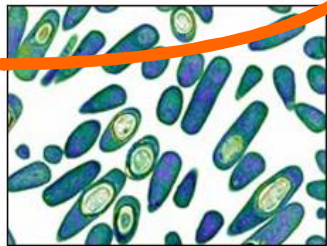
## Hospital superbug deaths reviewed

An inquiry into a fatal outbreak of the superbug *Clostridium difficile* at Prince Charles Hospital, Merthyr Tydfil, has reported its findings.

Three people died and a total of 37 were infected in the outbreak in March and April 2008.

Healthcare Inspectorate Wales (HIW) commended the former North Glamorgan NHS Trust's response to the outbreak but said there were lessons to learn.

Cwm Taf NHS Trust, the successor body, said it welcomed the review's findings.



Three patients died due to *Clostridium difficile* and 39 were infected

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## Cases of hospital superbug *C. difficile* fall by one third

Cases of a potentially deadly hospital superbug have fallen by more than a third in the last year, but still number almost 3,000 a month, official figures show.

By Kate Devlin Medical Correspondent  
Published: 3:42PM BST 23 Oct 2008



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## Deaths from hospital superbug *Clostridium difficile* quadruple

The number of deaths in Britain linked to the potentially deadly superbug *Clostridium difficile* has quadrupled in just five years, a report will warn next week.

Health Correspondent Laura Donnelly  
Published: 12:46AM BST 18 May 2008

More than 6,000 people died in 2006 after becoming infected with the gut infection in hospitals across England and Wales - a more than four-fold rise compared with 2001 figures, the Office of National Statistics will say.

Meanwhile, the number of deaths linked to MRSA rose by more than one third, with the infection mentioned on almost 1,700 death certificates in 2006.

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## Deaths from hospital superbug *C. diff* soar by a THIRD in just one year

By JENNY HOPE  
Last updated at 12:14 AM on 29th August 2008

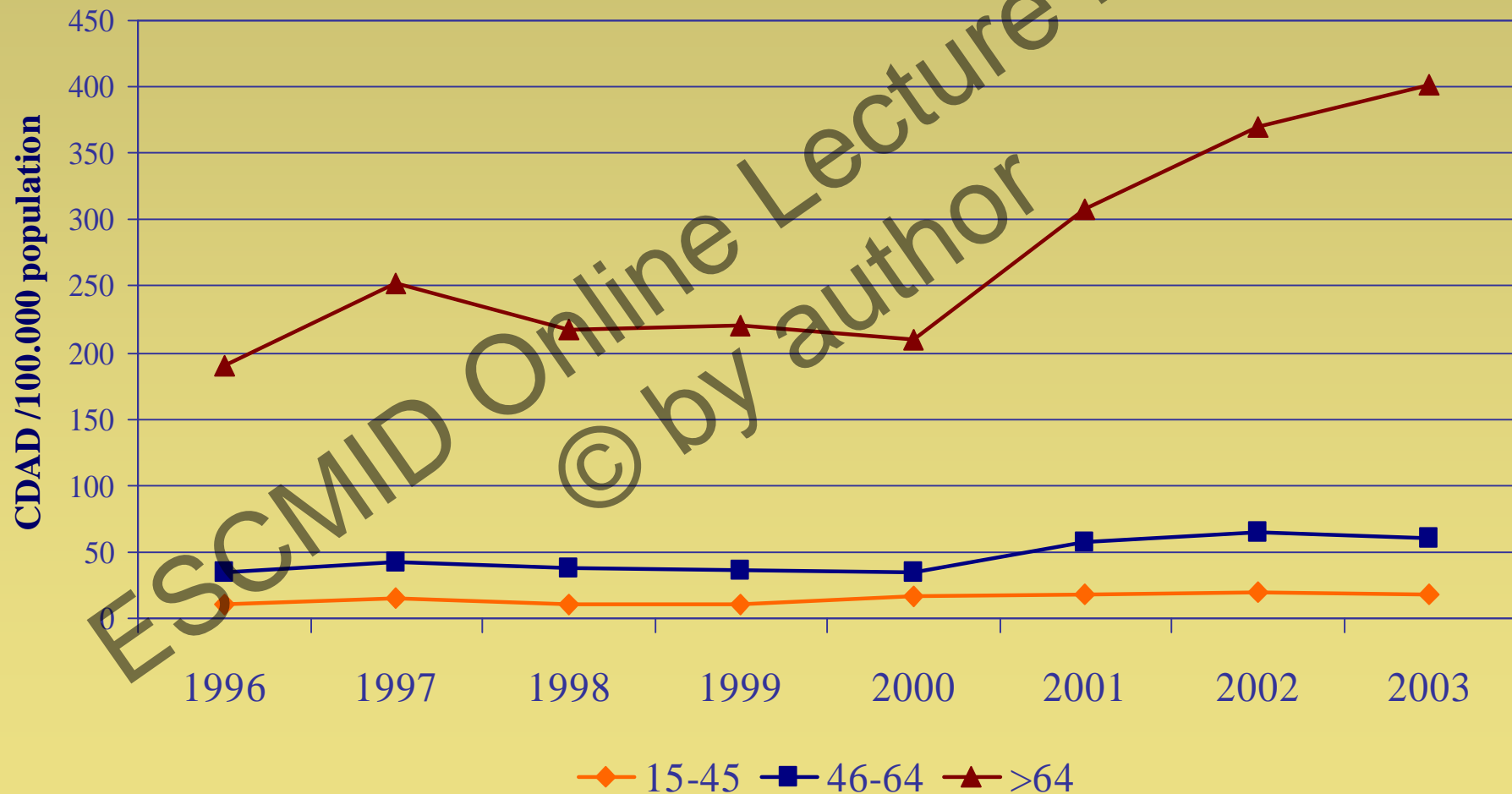
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The number of infections of the superbug *C. diff* included on death certificates has risen 28 per cent.



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# Incidence of *C. difficile* infections in the US between 1996 and 2003



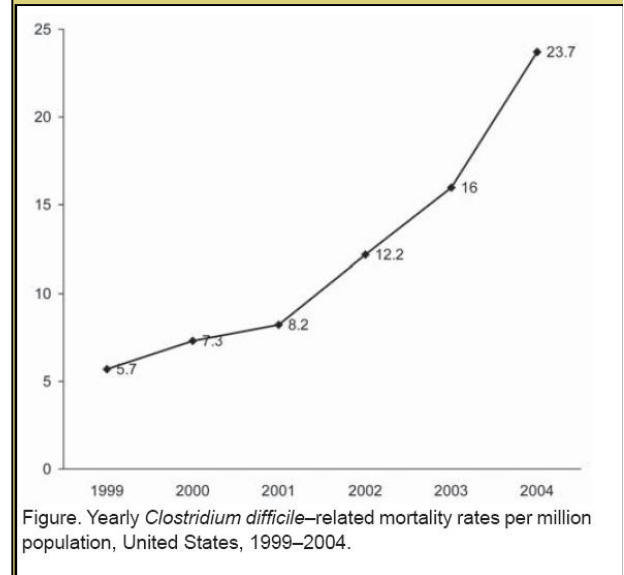
## Increase in *Clostridium difficile*-related Mortality Rates, United States, 1999–2004

Matthew D. Redelings,\* Frank Sorvillo,\*†  
and Laurene Mascola\*

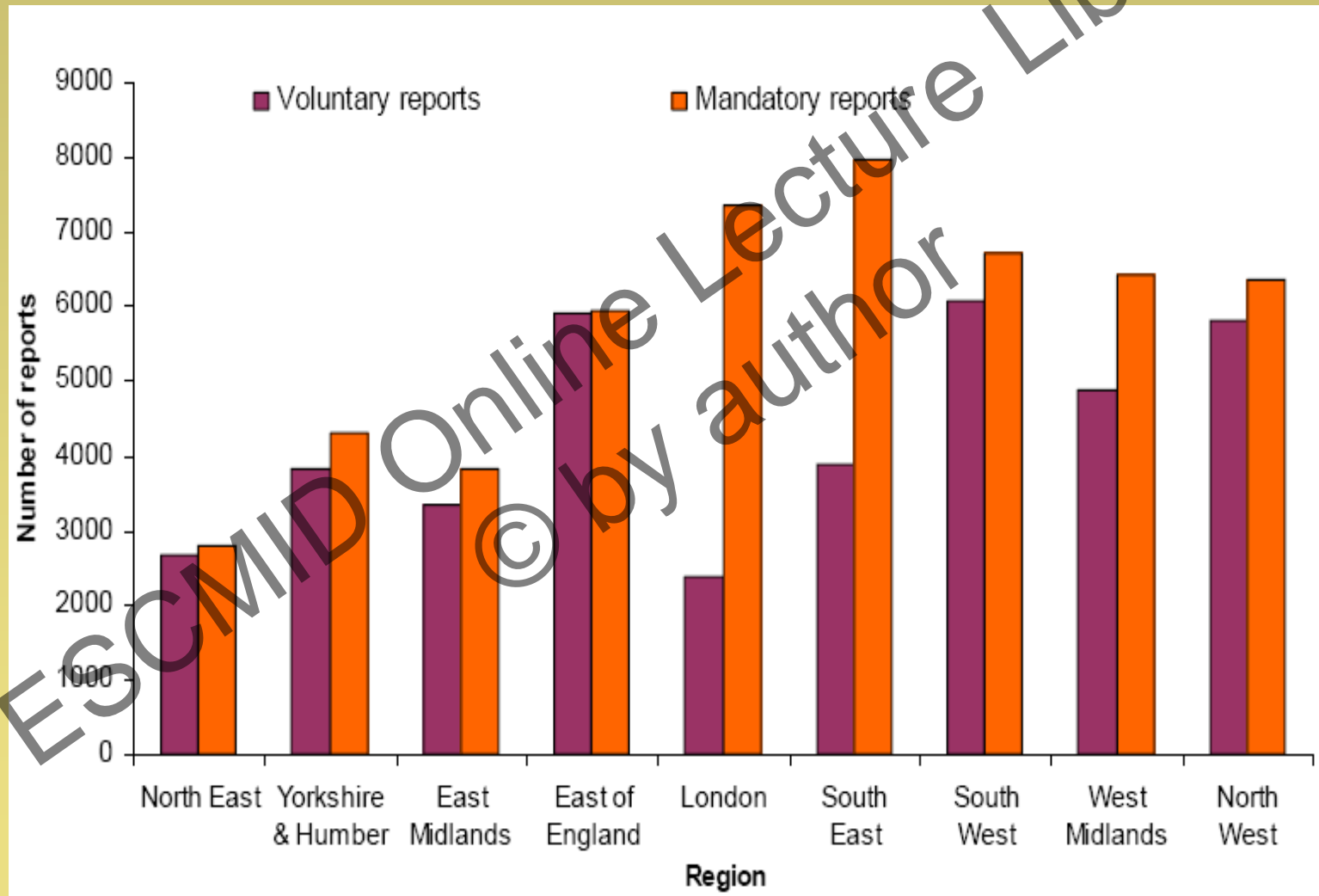
Table. Demographic characteristics of patients with *Clostridium difficile*-related deaths, United States, 1999–2004

Demographic group	<i>C. difficile</i> -related deaths, no. (%)	Age-adjusted mortality rate/million population
<b>Sex</b>		
Female	12,468 (60)	11.8
Male	8,174 (40)	12.7
<b>Race/ethnicity</b>		
White	18,534 (90)	12.9
Hispanic	602 (3)	7.2
Black	1,304 (6)	9.3
Asian/Pacific Islander	139 (1)	3.5
American Indian/Alaska Native	63 (<1)	7.9
<b>Age group, y</b>		
<1	17 (<1)	0.7*
1–4	11 (<1)	0.1*
5–14	12 (<1)	0.1*
15–24	24 (<1)	0.1*
25–34	62 (<1)	0.3*
35–44	171 (1)	0.6*
45–54	464 (2)	2.0*
55–64	1,159 (6)	7.6*
65–74	3,238 (16)	29.3*
75–84	7,859 (38)	104.0*
≥85	7,623 (37)	287.1*
<b>Total</b>	<b>20,642</b>	<b>12.2</b>

\*This statistic is not age-adjusted because it only pertains to 1 age group.



# Reported *C. difficile* associated diarrhoea cases in the UK

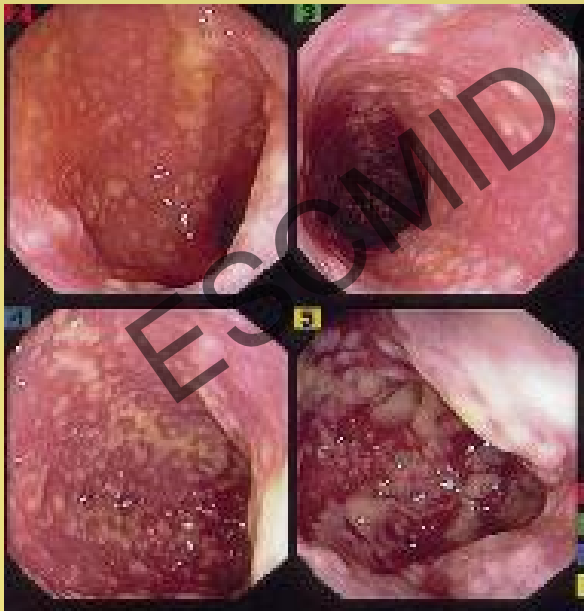


Mandatory reporting started only in 2007

[www.hpa.org.uk](http://www.hpa.org.uk)

## Clinical syndromes caused by *C. difficile*

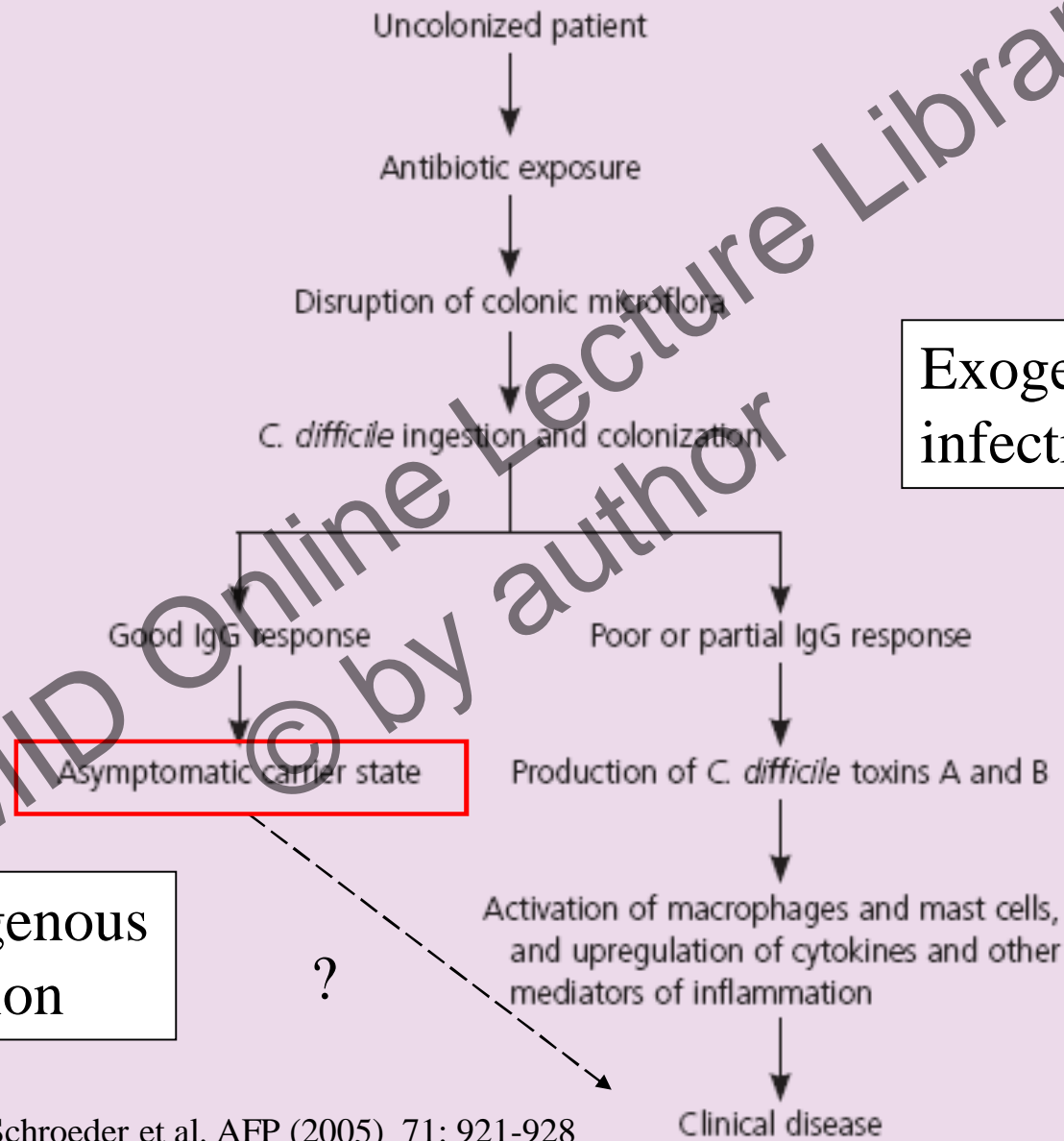
- Pseudomembranous colitis (PMC) 90-95%
- Antibiotic-associated colitis (AAC) 60-75%
- Antibiotic-associated diarrhoea (AAD) 11-33%
- Asymptomatic carriage
- Since 1980 accepted as nosocomial, enteric pathogen



Colonoscopic picture of different forms of *C. difficile*-associated disease (CDAD)

***C. difficile* infection (CDI)**

# Pathogenesis of *Clostridium difficile* Infection



Exogenous infection

Endogenous infection

## *C. difficile* – asymptomatic carriage

- Asymptomatic carriage in humans (Spencer (1998) JAC **41**, Suppl. C, 5):
  - Healthy adults: 3-8% (0.3% - Europe, 15% - Japan)
  - Infants: 15-63% (colonization starts during the 1st-2nd week)
  - During hospital stay: ~20% ( $\geq 30\%$ ), about 2-5x higher than the number of patients with symptoms
  - After antibiotic usage: 46%
  - Transient colonization or component of the stable flora? (Kato et al, (2001) JMM)
- Extraintestinal carriage: rear, in pregnant women the vaginal carriage rate was  $< 18\%$  (McFarland *et al.*, (1999) AJIC **27**: 301)
- Asymptomatic carriage in domestic animals: 20-40% (zoonosis???) (Arroyo et al., (2005) JMM **54**: 163)

## *C. difficile* – asymptomatic carriage

### □ Test or not to test?

- Active screening of non-diarrhoeal patients for *C.difficile* carriage will not decrease the endemic baseline rate of CDI in a hospital  
(Blot et al.: J. Hosp. Infect. 2003)
- Asymptomatic carriers may be a potential source for transmission of epidemic and non epidemic strains among long-term care facility residents  
(Riggs et al.: CID 2007)

## *C. difficile* – asymptomatic carriage

- **Do we need to screen to identify carriers who are at risk of developing endogenous nosocomial CDI?**
  - Symptom-free excretors of *C. difficile* had decreased risk of subsequent CDI (0 versus 3.1% compared to those who were culture negative earlier)  
(Johnson et al.: Lancet 1990, Shim et al.: Lancet 1998)
  - Treatment of asymptomatic carriers is ineffective in eradicating *C. difficile* colonization  
(Johnson et al: Ann Intern med 1992)

# Predisposing factors for *C. difficile* associated disease

- Antibiotic treatment
- Advanced age
- Prolonged hospital stay
- Immunosuppression, severe underlying diseases
- Anti-cancer treatment
- Intra-abdominal surgery
- Others:
  - Health-care workers
  - Cross-transmission between neonates and mothers

# Antibiotics and anti-cancer substances associated with *C. difficile* infection

## Frequently

Cephalosporins (2.3. gen)  
Ampicillin, amoxicillin  
Other beta-lactams (amoxi/clav)  
**Clindamycin**  
Erythromycin, other macrolides  
Tetracycline  
Trimethoprim-sulfamethoxazole

## Less frequently

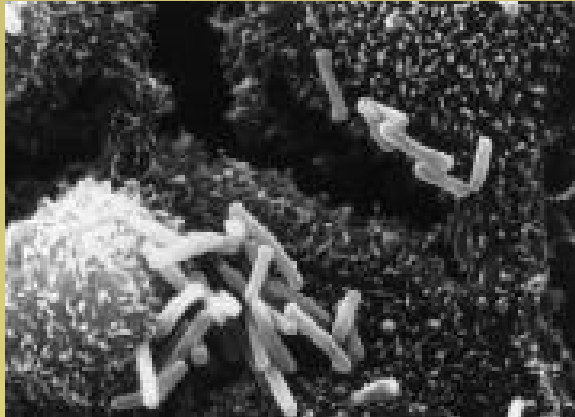
Tricarcillin-clavulanic acid  
Chloramphenicol  
Amphotericin B

Metronidazole  
Rifampicin

Fluoroquinolons!!!  
Aminoglycosides

5-Fluorouracil  
Methotrexate  
Adriamycin  
Cyclophosphamid

# Pathogenic factors of *C. difficile* I.

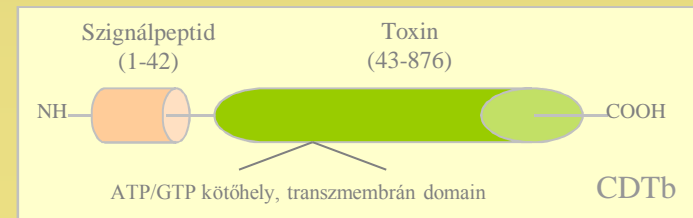
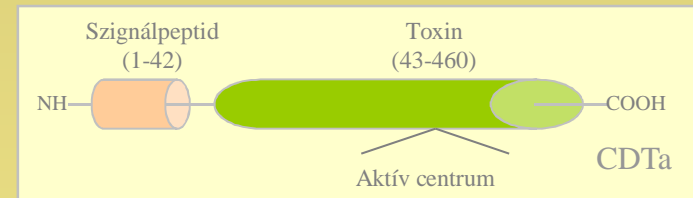
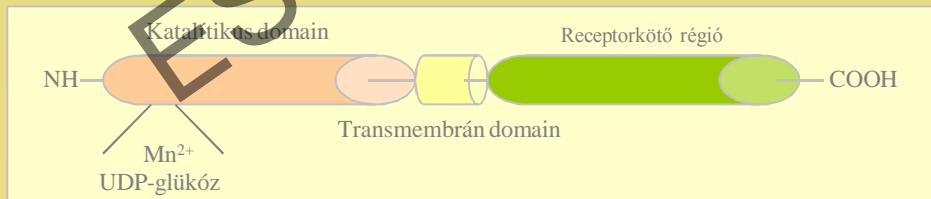
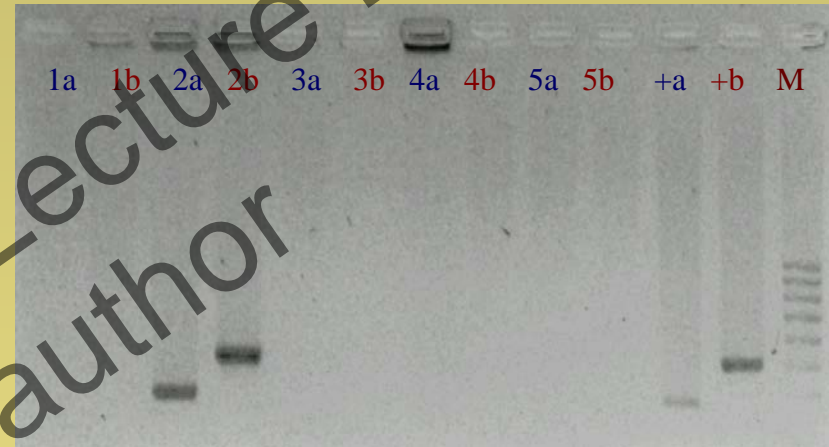
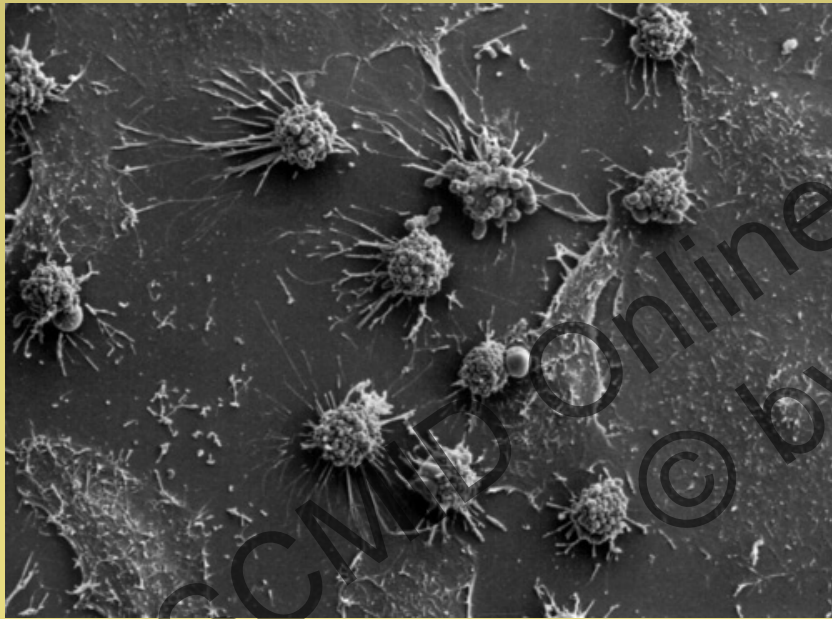


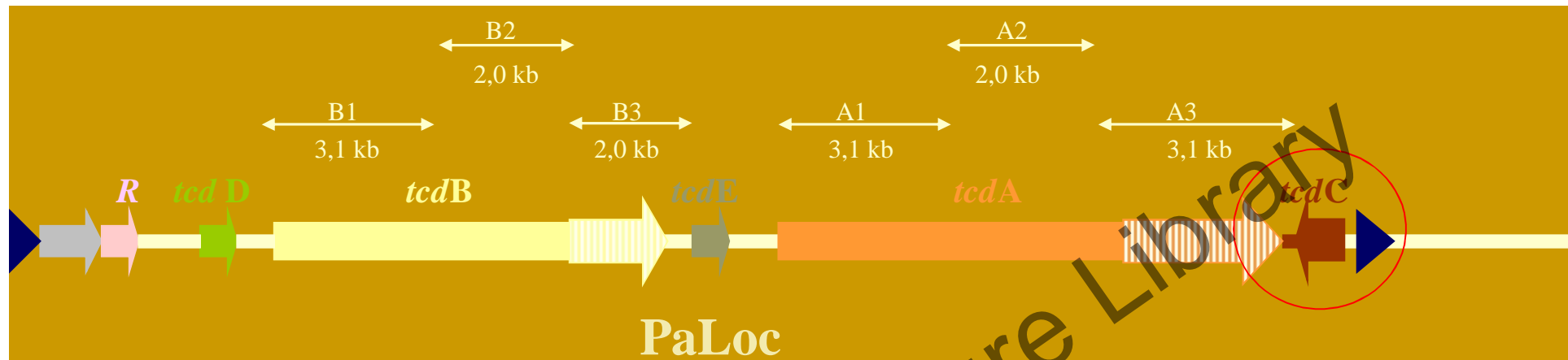
- Adhesion
- Chemotaxis
- S-layer
- Enzymes: hyaluronidase, collagenase, etc.
- **Toxins:**
  - **Toxin A** (enterotoxic activity)
  - **Toxin B** (cytotoxic activity)
  - **Binary toxin** (actin-specific ADP-ribosyl-transferase)

M. Cerquetti *et al.*, (2002) *FEMS Immun Med Microbiol*

# Pathogenic factors of *C. difficile* II.

## Toxin A and B

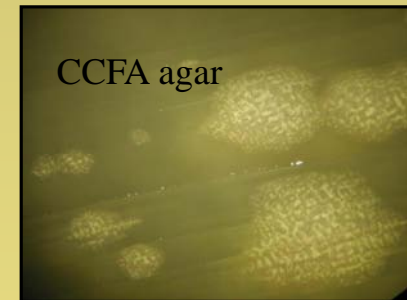




Toxinotype	B1	B2	B3	A1	A2	A3	Toxin A/B	Binary toxin
0	0	0	0	0	0	0	A+/B+	-
I, II, XIII	0	0	0	0	0	V	A+/B+	-
XII	V	0	0	0	0	0	A+/B+	-
XI a/b	na	na	na	na	V	D	A-/B-	+
III - VII, IX, XIV, XV	V	V	V	V	V	V	A+/B+	+
VIII, X	V	V	V	V	V	D	A-/B+	-
XVI, XVII	V	V	V	V	V	D	A-/B+	+
XVIII-XX	0	0	0	0	0	V	A+/B+	-

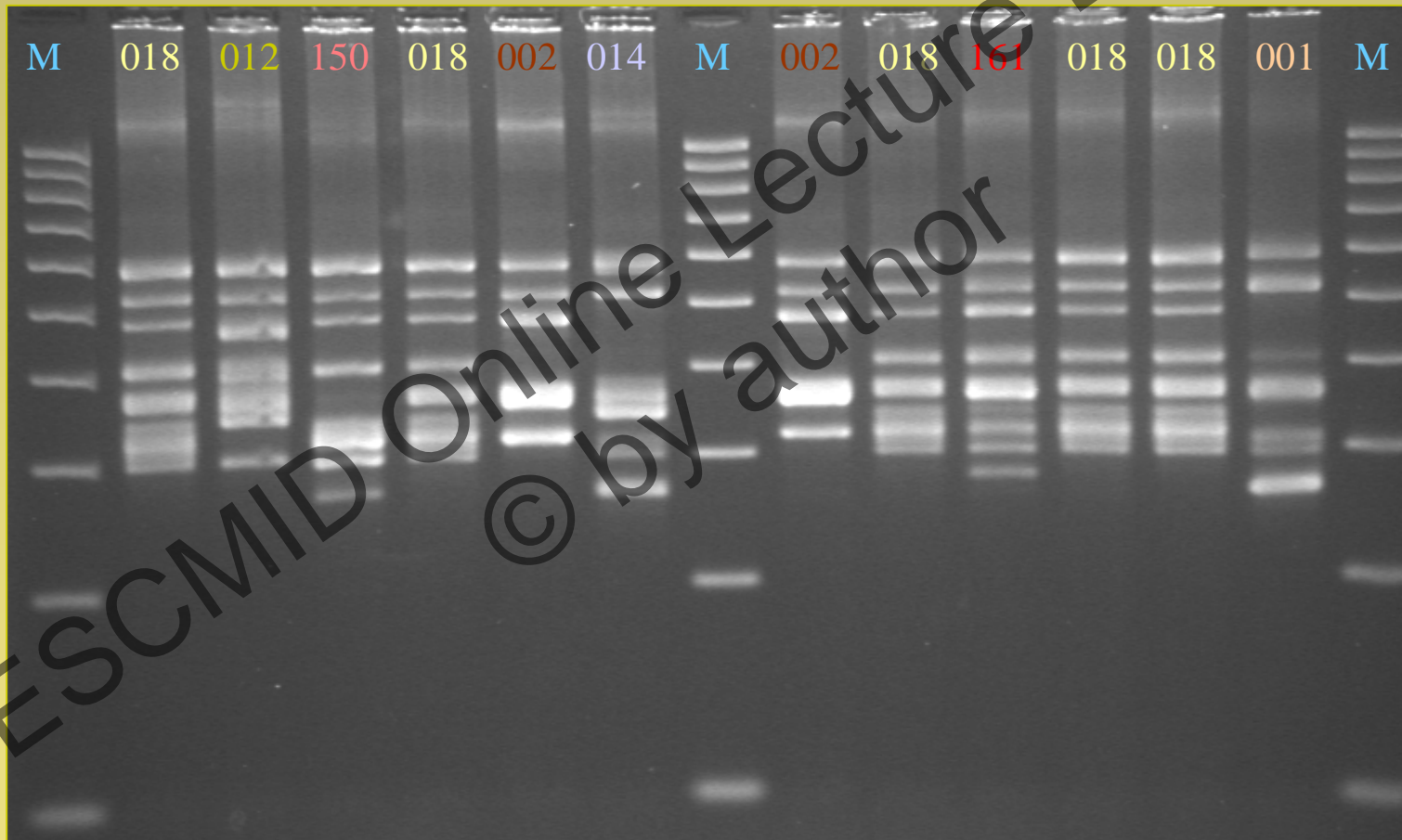
# Advised diagnostic methods at present time

- Direct detection of toxin (A+B) from the faeces (cell culture, ELISA, IC, PCR methods)
- Isolation of the strain + toxin (A+B) detection
- Typing of the strains if needed (PCR ribotyping, PFGE, toxin typing, etc.)



Tests	Distributor	Method	Antigen
Culturette brand toxin CD <sup>®</sup>	Becton Dickinson	ELISA	Toxin A
Premier toxin A <sup>®</sup>	Meridian	ELISA	Toxin A
Prima A	Bartels	ELISA	Toxin A
Tox A test	Techlab	ELISA	Toxin A
VIDAS CD ToxA/B <sup>®</sup>	bioMérieux	ELFA (automated)	Toxin A/B
Cytoclone A+B	Meridian	ELISA	Toxin A/B
Premier Toxins A&B <sup>®</sup>	Meridian	ELISA	Toxin A/B
Ridascreen CD Toxin A/B	R-biopharm	ELISA	Toxin A/B
Tox A/B test	Techlab	ELISA	Toxin A/B
Culturette brand CDT <sup>®</sup>	Becton Dickinson	Latex	GDH
ImmunoCard CD <sup>®</sup>	Meridian	EIA	GDH
Clearview C DIFF A	Unipath	IC	Toxin A
ColorPac Toxin A	Becton Dickinson	IC	Toxin A
ImmunoCard STATITOX A <sup>®</sup>	Meridian	IC	Toxin A
Test CD Toxin A <sup>®</sup>	Oxoid	IC	Toxin A
Toxin A Sign <sup>®</sup>	Servibio	IC	Toxin A
ImmunoCard Tox A	Meridian	IC	Toxin A
Trage CD panel <sup>®</sup>	Biosite	EIA	Toxin A+GDH
ImmunoCard ToxA/B <sup>®</sup>	Meridian	IC	Toxin A/B

## Distribution of *C. difficile* ribotypes among isolates from our hospital (Szeged, Hungary)



(Gabriella Terhes: PhD thesis 2005)

# Commercially available *C. difficile* toxin detecting methods

## BD GeneOhm™ Cdiff Assay

- real-time, multiplex PCR assay with a turn-around time < 2 hours
- look for the toxin B gene (*tcdB*) and an internal control is used
- fluorogenic target-specific hybridization probes
- direct testing from the stool specimen
- cost effective samples size 6 samples

## Cepheid Xpert™ *C. difficile* Assay

- real-time PCR-based method with a turn-around time <1 hours
- multiplex detection of *tcdB* (toxin B), *tcdCΔ117* (deletion in the negative regulator gene), *cdtB* (binary toxin gene)
- sample preparation, amplification, detection in one cartridge

# Direct detection of *C. difficile* toxin B from 586 stool samples by different methods

Methods		BD GeneOhm™ Cdiff Assay	
		Positive	Negative
Cytotoxicity assay	Positive	53	2
	Negative	5	536
VIDAS Toxin A/B assay	Positive	29	8
	Negative	29	500
	Equivocal	0	30

Compared to cytotoxicity: sensitivity: 96.4%; specificity: 99.1%;

PPV: 92%; NPV: 100%

## New facts concerning CDI

- More **community acquired** *C. difficile* diarrhoea (*de novo* or HA)
  - Symptoms: 1–  $\geq$ 8 weeks after antibiotic treatment
  - In the age group of 18-30 years the prevalence of CDI  $\uparrow$
  - In the UK in 1994 – 1 case /100.000, in 2004 – 22 cases/100.000
- **Risk factors other than antibiotic usage**: chemotherapy, proton pump inhibitors, NSAIDs, etc.
- **Toxin A-negative and toxin B-positive strains** can cause severe CDI and hospital epidemics
- **Binary toxin** may play a role in the pathogenesis
- More and more data about the presence of ***C. difficile* in animals**
- Since 2002 the spread of “**new**” **hyper virulent strain(s)** (ribotype 027, toxinotype III, PFGE NAP1) (some other ribotypes as well)

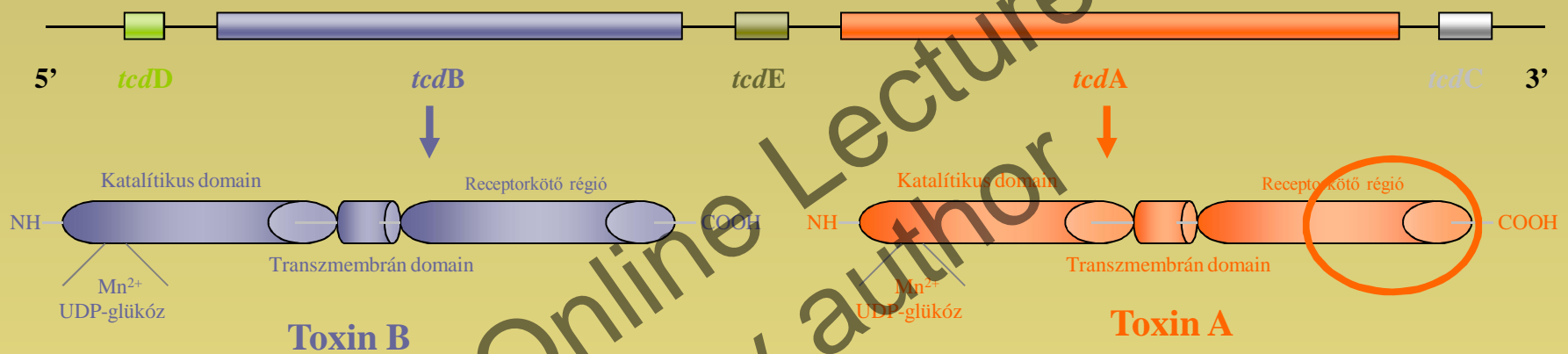
## Nosocomial epidemics caused by toxin A<sup>-</sup>/toxin B<sup>+</sup> *C. difficile* strains

- ❑ Canada (1998 between July and September): 16 cases, 4 wards, relapse rate: 18.75%.
- ❑ Japan (2001 between February and June): 15 cases, oncology ward.
- ❑ Argentina (2000-2003) During a 4-year period A<sup>-</sup>/B<sup>+</sup> strains completely replaced A<sup>+</sup>/B<sup>+</sup> strains in CDAD nosocomial cases
- ❑ The Netherlands (11 months): 24 cases (19 mild, 7 severe, 1 lethal), surgery, relapse rate: 13%
- ❑ Poland (1999-2000) 6 children with haematology disorders had recurrent diarrhoea

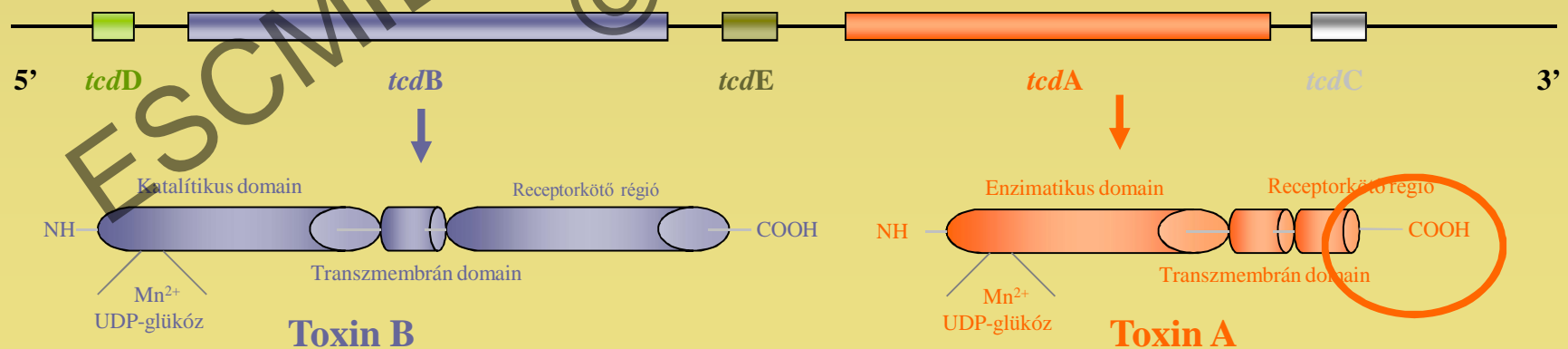
Toxin A<sup>-</sup>/B<sup>+</sup> strains cause diagnostic problems in laboratories which use ELISA, detecting only toxin A

# Why toxin A negative strains can not be detected in most commercial kits?

VPI 10463 toxin A and B positive



Toxin A negative toxin B positive



# New emerging *Clostridium difficile* (027)

## Clinical data

- Mortality within 30 days increased from 4.7% to 13.8%
- Complication rate increased from 7.1% to 18.2%
- Relapse rate increased from 20.8% to 47.2%

## Characteristics of the strain

- *tcdA* and *tcdB* positive
- binary toxin positive
- *tcdC* 18 bp deletion at 117 – toxin hyper production

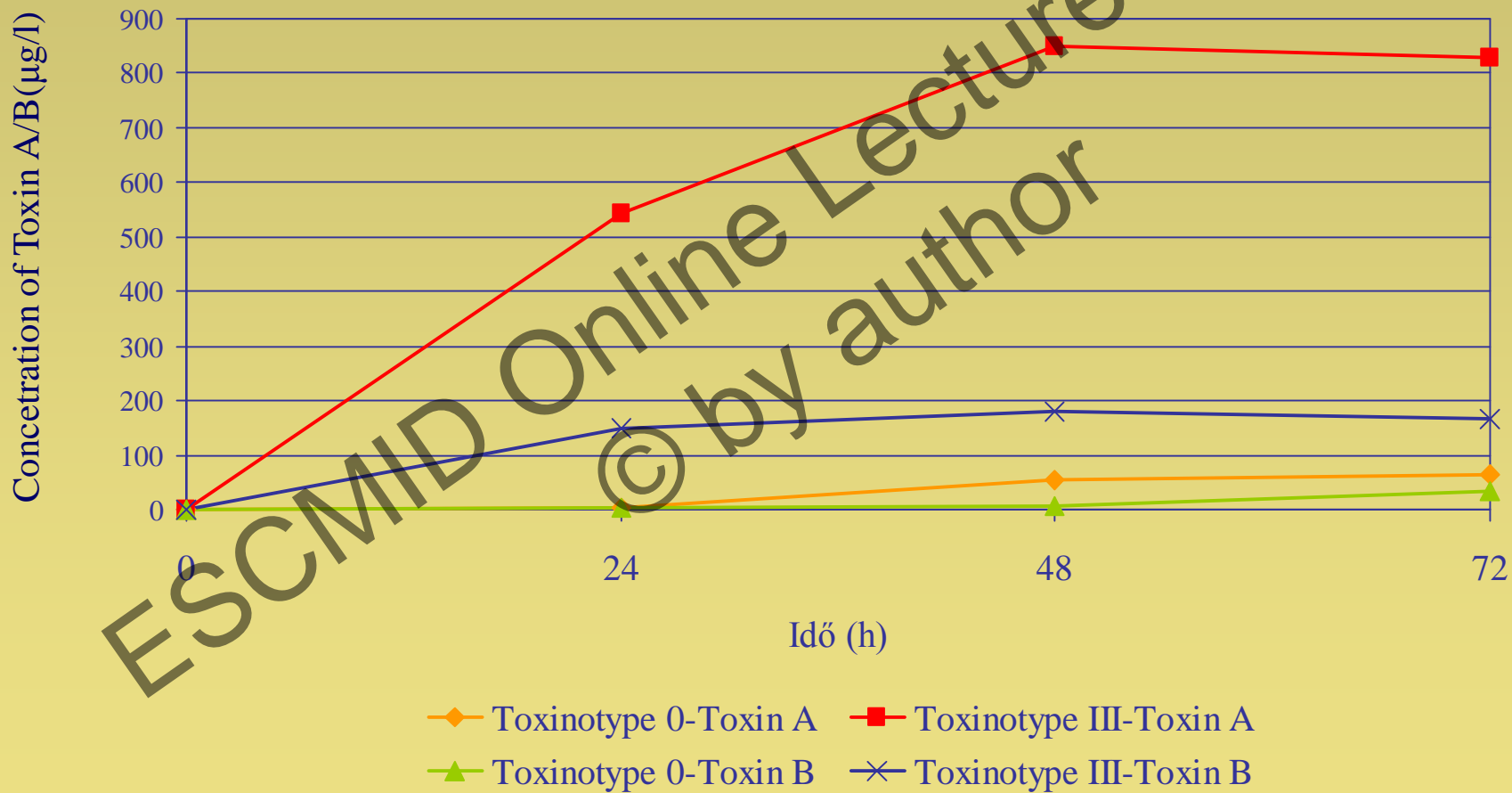
- more intensive sporulation

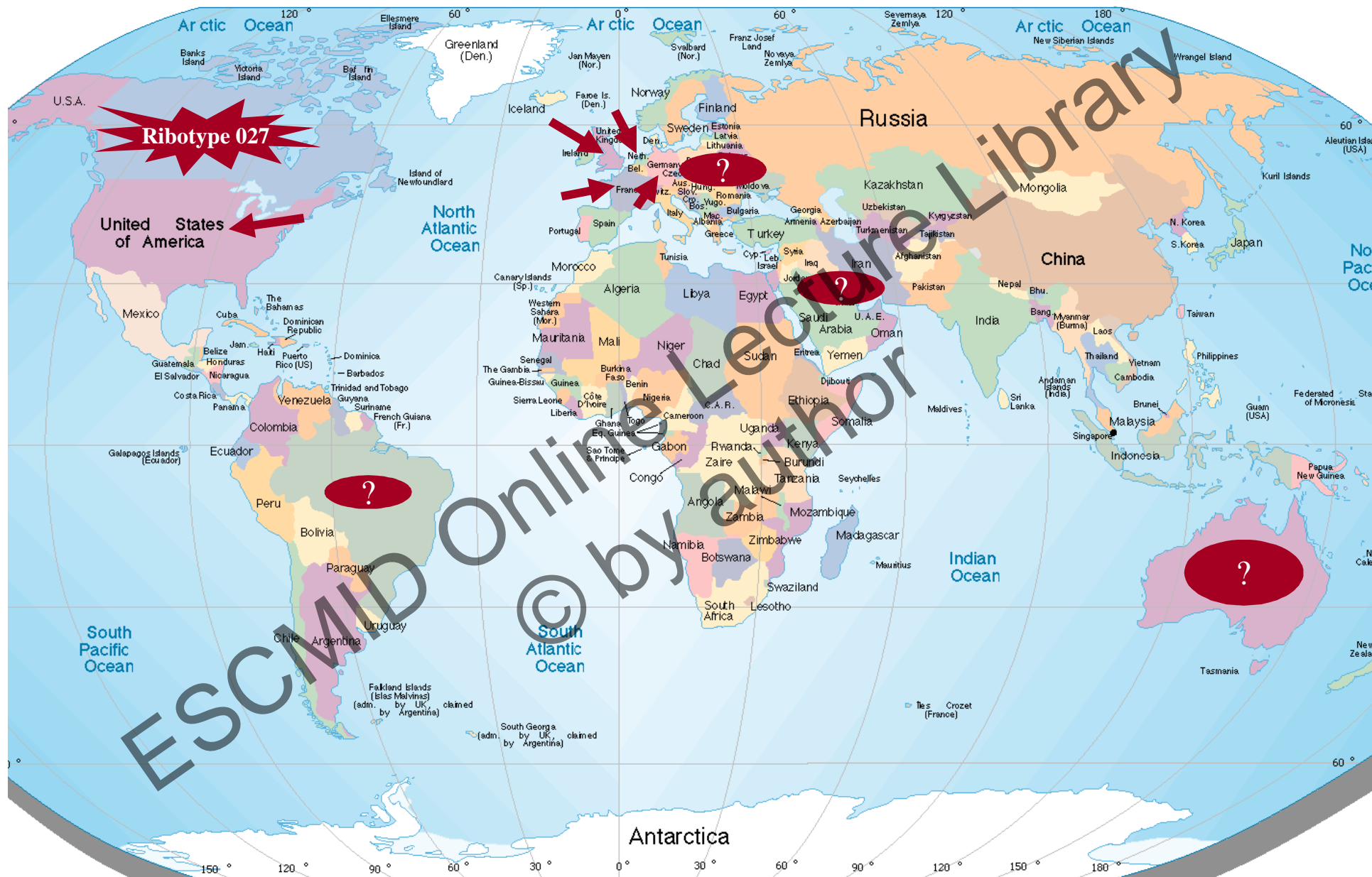
Often resistance to fluoroquinolones!!!

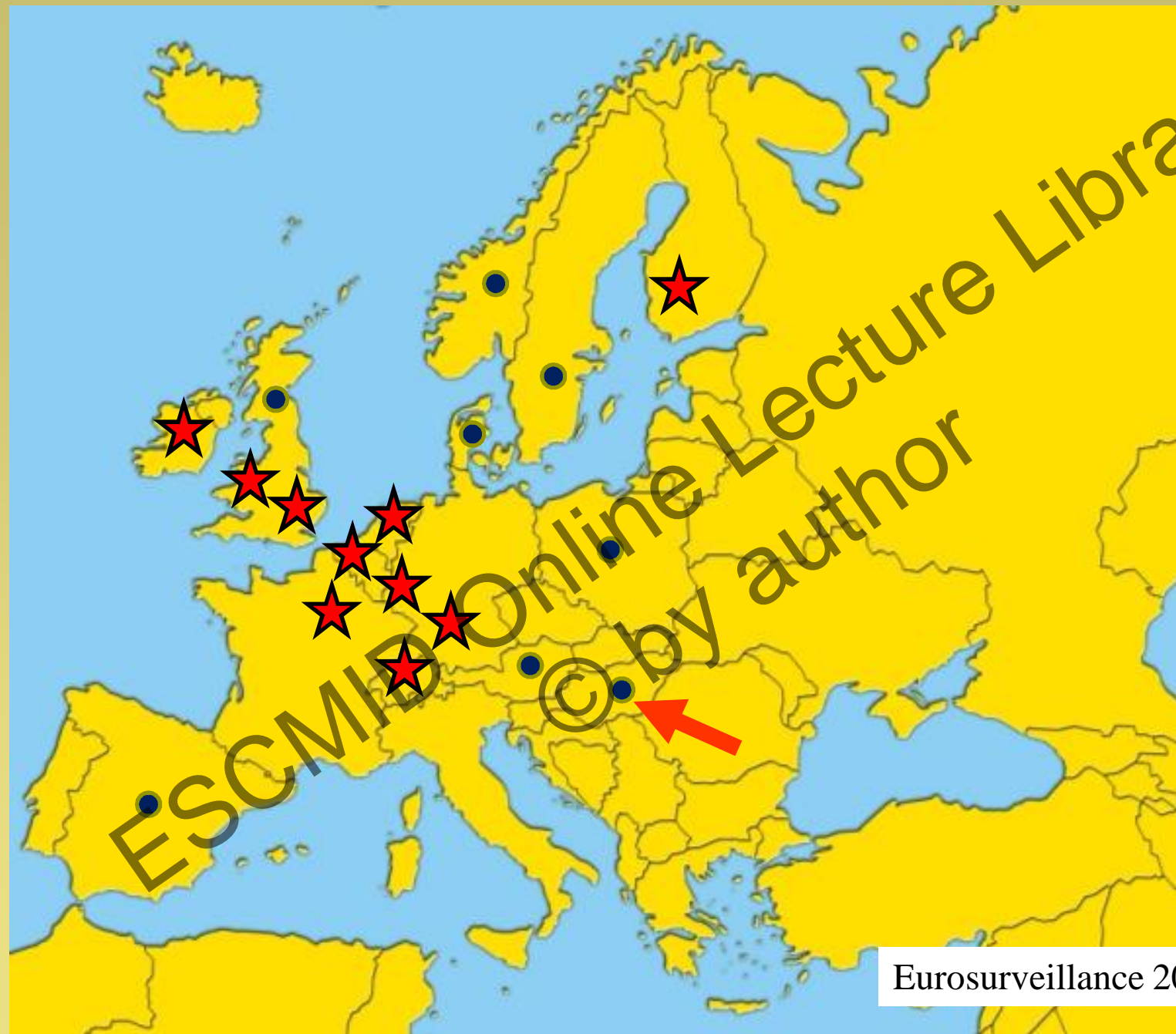
## Genotyping of the strain:

- PCR-ribotyping 027
- REA group BI
- PFGE NAP1
- toxinotyping III
- further subtyping REA and MLVA

# Toxin production of the hyper virulent *C. difficile* strain (ribotype 027)







**Outbreaks due to ribotype 027**



**Sporadic cases due to ribotype 027**

Eurosurveillance 2007-2008

## First Hungarian ribotype 027

53-year-old male patient

Past medical history: hospitalisation two weeks ago

SLE, FUO, mild diarrhoea

Antibiotic therapy: ceftriaxone, clarithromycin, imipenem

On admission: diarrhoea, fever, nausea

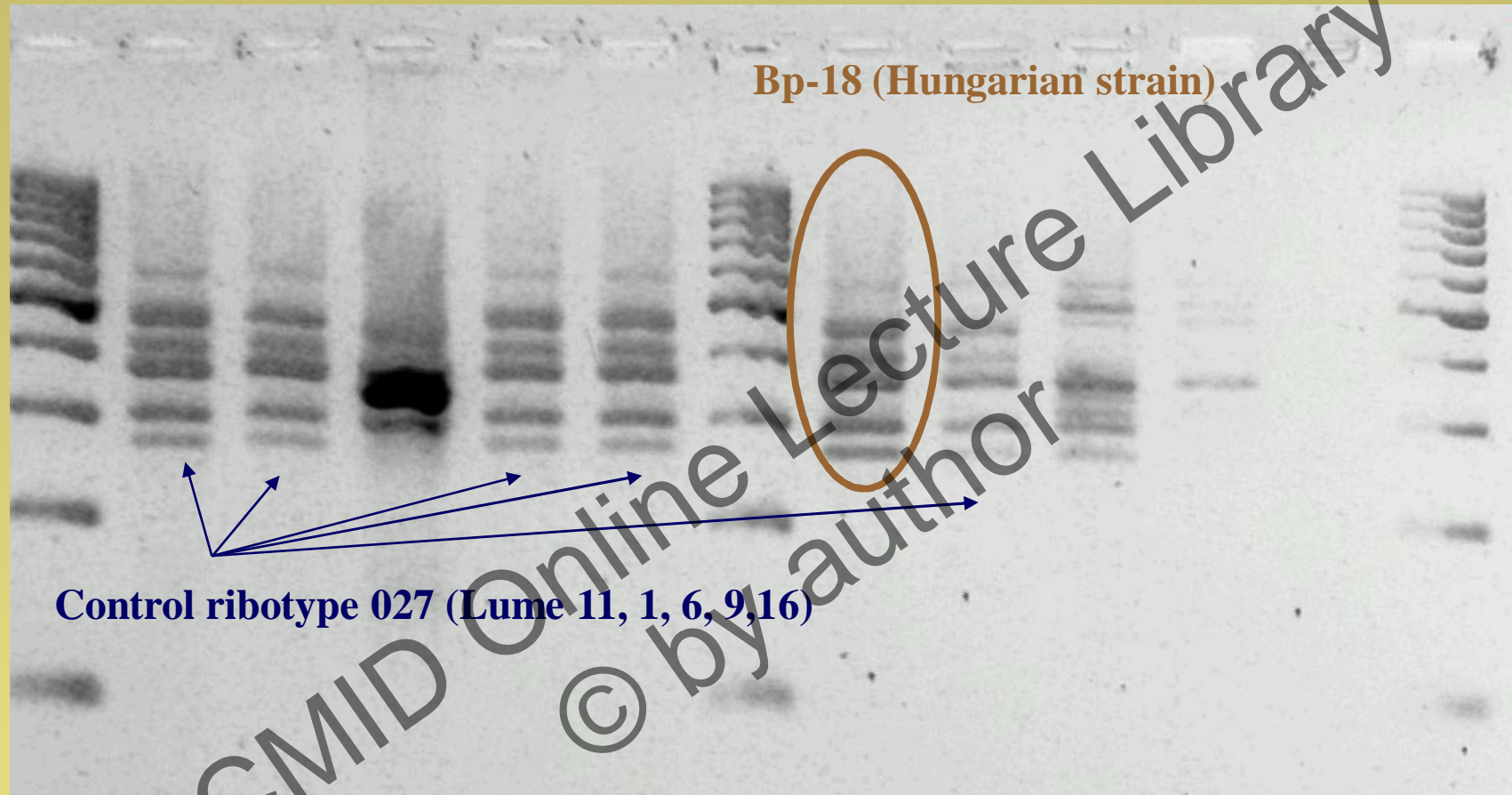
No abdominal tenderness, normal bowel sounds, liver and spleen – normal

Chest X-ray: pneumonia

Due to persistent diarrhoea colonoscopy was carried out: ulcers throughout the colon (size: 3-4 mm) – dg.: ischemic colitis or intestinal manifestation of SLE?

## First Hungarian ribotype 027

- ❑ Culture of faecal specimen for usual pathogens – negative, metronidazole was started empirically
- ❑ Loss of weight, sever diarrhoea, fever
- ❑ Direct toxin detection for toxin A and toxin B by ELISA was positive – vancomycin was started
- ❑ Worsening of the SLE, high fever, pneumonia, sepsis
- ❑ 24 hours after transferring to the ICU the patient died (*E. coli* was isolated from the blood cultures taken just before death)
- ❑ No other cases in the ward and in the ICU
- ❑ *Confirmation of the ribotype in the reference laboratory as a part of a national surveillance half a year later.*



Terhes et al. CMI (in press)

- Background document
- European surveillance studies
- Infection control guideline
- Treatment guideline
- Diagnostic guideline



**ESGCD**  
ESCMID STUDY GROUP  
FOR CLOSTRIDIUM DIFFICILE

## Emergence of *Clostridium difficile*-associated disease in North America and Europe

E. J. Kuijper<sup>1</sup>, B. Coignard<sup>2</sup> and P. Tüll<sup>3</sup> on behalf of the ESCMID Study Group for *Clostridium difficile* (ESGCD)<sup>†</sup>, EU Member States and the European Centre for Disease Prevention and Control (ECDC)<sup>†</sup>

<sup>1</sup>Leiden University, Leiden, The Netherlands, <sup>2</sup>Institut de Veille Sanitaire, Saint-Maurice Cedex, France and <sup>3</sup>ECDC, Stockholm, Sweden

**CLINICAL MICROBIOLOGY AND INFECTION**

VOLUME 12, SUPPLEMENT 6, OCTOBER 2006

## Why now?

- ❑ Historical data
  - ❑ First isolate of 027 in 1988 (France, patient with severe CDAD)
  - ❑ Historical database (>6 000 strains) of Dale Gerding (US): 1984-1993, 14 patients with FQ susceptible isolates of 027
- ❑ Historical isolates and new isolates shared 18bp deletion in *tcdC* and binary toxin genes
- ❑ No gradual increase: new epidemic strain since 2002, outbreaks in Canada, USA and Europe
- ❑ No replacement of existing types
- ❑ Correlation with the (over)use of fluoroquinolones and cephalosporins in the hospitals

## Antimicrobial susceptibility of 405 *C. difficile* strains isolated in Europe in 2005 (Barbut et al. for the ESGCD, CMI 2007)

Data were obtained from 14 countries and 38 hospitals

ATB	MIC50 (mg/l)	MIC90 (mg/l)	Range (min-max)	% R
VA	0.5	0.75	0.25-2	0
MZ	0.06	0.125	0.012-0.75	0
EM	1	>256	0.047->256	45.8
CM	4	>256	0.016->256	50.6
TC	0.032	0.38	0.023->32	9.1
MX	0.5	>32	0.032->32	33.7

# In vitro susceptibility of 258 isolates of *C. difficile*

	MIC <sub>50</sub>	MIC <sub>90</sub>	Range	Breakpoint	% Resistance
Metronidazole	0.25	0.5	≤0.06-1	32	0
Vancomycin	1	1	≤0.5-4	32	0
Rifampicin	≤0.06	≤0.06	≤0.06	4	0
Fusidic acid	1	2	≤0.06-64	2	1.2
Cefotaxime	>128	>128	64->128	64	100
Ceftriaxone	64	128	64->128	64	82.6
Meropenem	2	4	0.5-8	16	0
Pip/Taz	8	8	4->128	128/4	0.4
Clarithromycin	>128	>128	0.125->128	8	85.3
Clindamycin	2	>128	0.125->128	8	14.7
Ciprofloxacin	>128	>128	16->128	8	100
Levofloxacin	>32	>32	>32	8	100
Gatifloxacin	64	128	2->128	8	82.2
Moxifloxacin	64	64	2->128	8	82.2

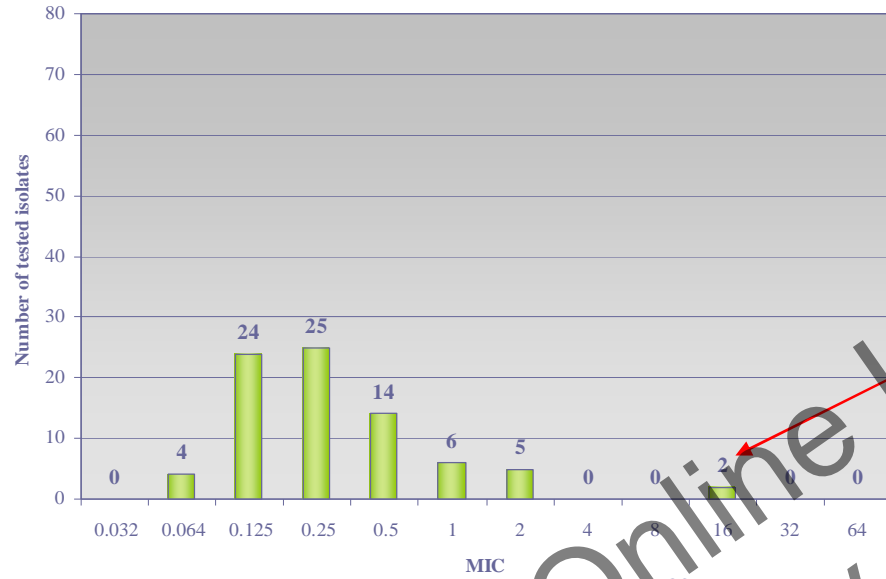
Adapted from: A.M.Bourgault, F.Lamothe et al. 2006 *Antimicrob. Agents Chemother* 50:3473-75

## Data from a recent Hungarian study

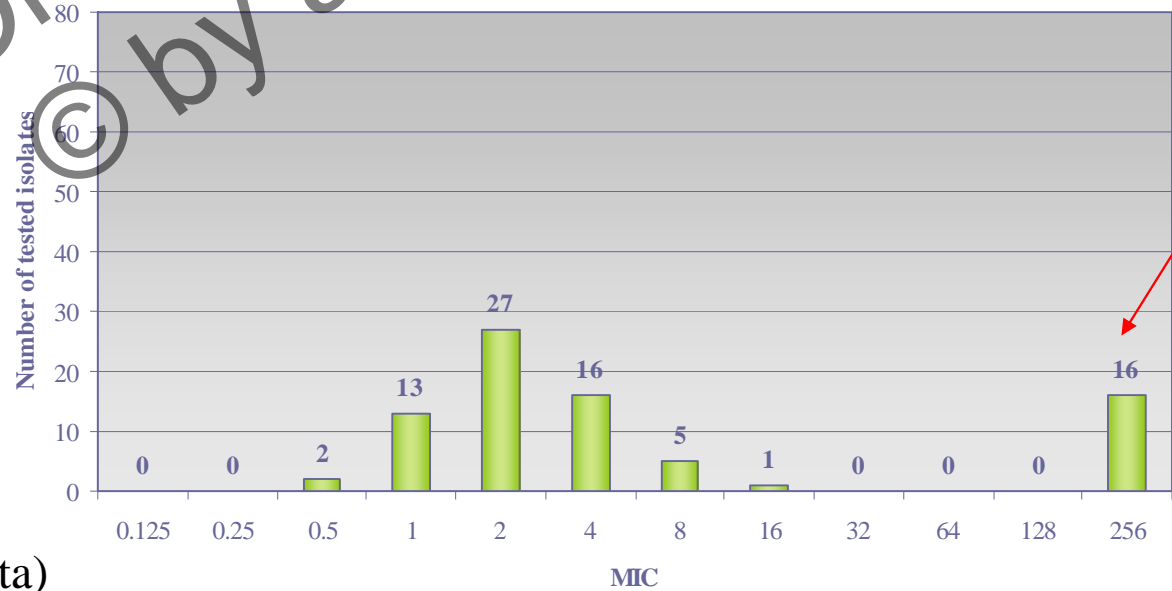
- 80 recent toxin positive *C. difficile* isolates and 20 isolates from our collection (10 years old) were tested by E-test for
  - clindamycin,
  - erythromycin,
  - metronidazole,
  - rifampicin
  - moxifloxacin
  - vancomycin
- Among the 20 “historical” strains no resistant was found for the tested antibiotics

# Metronidazole

Data for 80 recent isolates

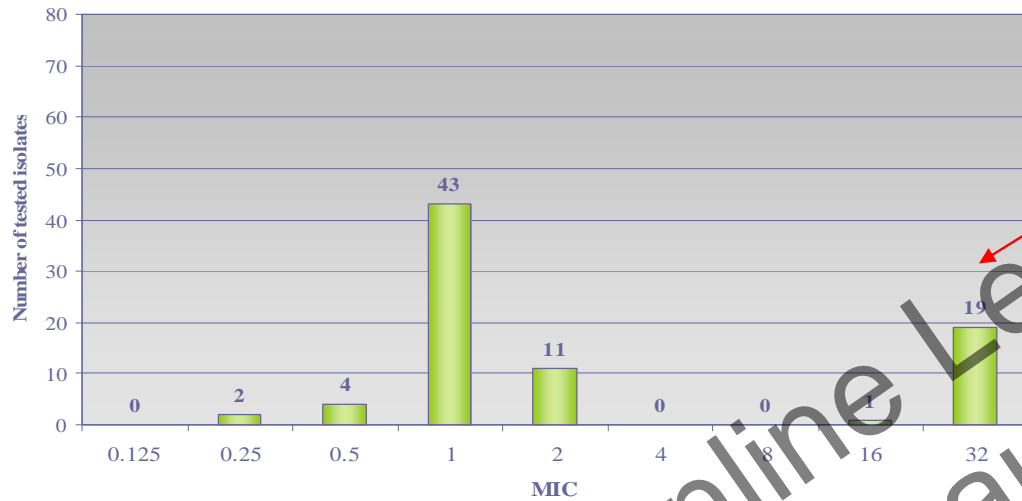


# Clindamycin

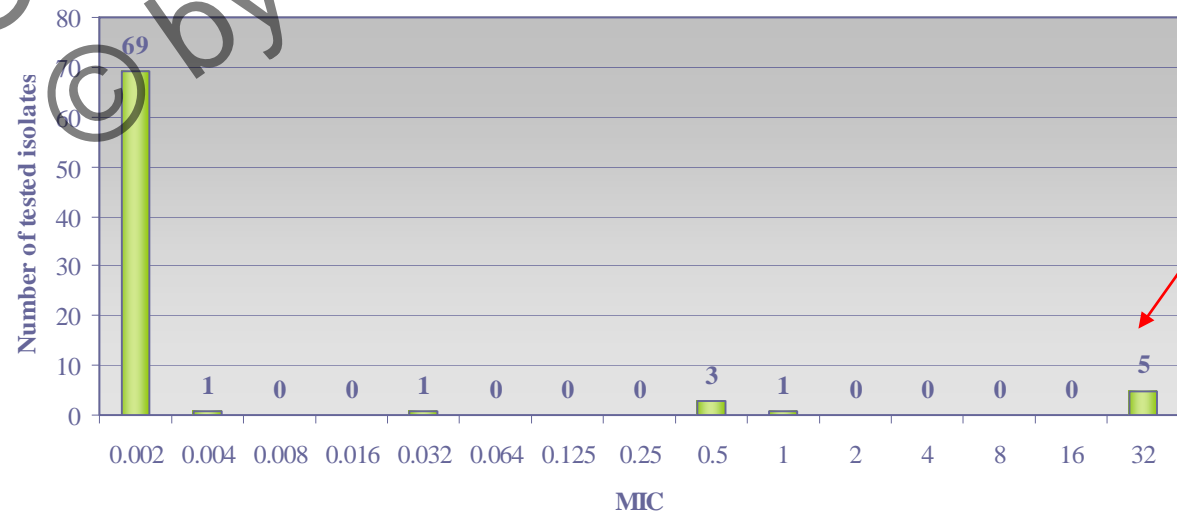


Terhes & Nagy (unpublished data)

## Moxifloxacin



## Rifampicin



All five rifampicin resistant strains were cross resistant to clindamycin, erythromycin and moxifloxacin

Terhes & Nagy (unpublished data)

## Metronidazole resistance in *C. difficile*

- Wong et al.: *Diag. Microbiol. Infect. Dis.* (1999):
  - Out of 100 *C. difficile* isolates 1 had an MIC: 64 µg/ml
- Pelaez et al.: ICCAC abstract C28 (1997) :
  - 9% of 469 *C. difficile* isolates were resistant (MIC:  $\geq 32$  µg/ml)
  - Resistance to metronidazole was more common if the strain was isolated from recurrences (14.5% vs 7.5%)
- Jang et al.: *CID* (1997)
  - Metronidazole resistant strains were found among equine *C. difficile* isolates (MIC: 32 µg/ml)

(Out of 80 recent Hungarian isolates 2 had an MIC 16 µg/ml)

# Therapeutical options to day

Agent	MIC mg/l	Pharmacology	Infection
Metronidazole	0.03-0.1	excreted	moderate
Vancomycin	0.02-1.0	not absorbed	sever
Teicoplanin	0.02-1.0	not absorbed	sever
Fusidic acid*	0.06-64	poorly absorbed	mild/mod.
Rifampin	0.002-0.2	enterohepatic	mild/mod.
Rifaximin*	0.007-0.02	not absorbed	mild/mod.
Rifalazil*	0.007-0.02	enterohepatic poor absorption	mild/mod.

\*resistant mutans s already discribed

# New therapeutic options under investigation

## Antibiotics

	MIC $\mu\text{g/ml}$
❑ Ramoplanin (not absorbed)	0.1-1.0
❑ Daptomycin (cyclic lipopeptide)	0.5
❑ Tigecycline (analog of minocycline)	0.06
❑ Fidaxomicin (not absorbed, severe infection)	0.1-0.25

## Toxin binder

- ❑ TOLEVAMER

Vaccine or antibodies (monoclonals, IgG, IgM)

Probiotics (*Saccharomyce boulardii*, *Lactobacillus rhamnosus*)

# Fidaxomicin versus Vancomycin for Treatment of *Clostridium difficile* Infections

## Clinical Cure Rates

<b>Patients</b>	<b>Fidaxomicin</b>	<b>Vancomycin</b>
<b>Clinically evaluable</b>	<b>244/265 (92.1%)</b>	<b>254/283 (89.8%)</b>
<b>Intent to treat</b>	<b>253/287 (88.2%)</b>	<b>265/309 (85.8%)</b>

**Louie et al. 2009**

# Fidaxomicin versus Vancomycin for Treatment of *Clostridium difficile* Infections

## Recurrence Rates

<b>Patients</b>	<b>Fidaxomicin</b>	<b>Vancomycin</b>
<b>Clinically evaluable</b>	<b>28/211 (13.3%)</b>	<b>53/221 (24.0%)</b>
<b>Intent to treat</b>	<b>39/253 (15.4%)</b>	<b>67/265 (25.3%)</b>

**Louie et al. 2009**

# Fidaxomicin versus Vancomycin for Treatment of *Clostridium difficile* Infections

## Global Cure Rates

<b>Patients</b>	<b>Fidaxomicin</b>	<b>Vancomycin</b>
<b>Clinically evaluable</b>	<b>206/265 (77.7%)*</b>	<b>190/283 (67.1%)</b>
<b>Intent to treat</b>	<b>214/287 (74.6%)*</b>	<b>198/309 (64.1%)</b>

**Louie et al. 2009**

# Ecological Differences between Fidaxomicin and Vancomycin (I)

Antimicrobial Susceptibilities  
*Clostridium difficile* (n=208)

Antimicrobial agent	Range	MIC (mg/l)	
		MIC <sub>50</sub>	MIC <sub>90</sub>
Fidaxomicin	0.06-1.0	0.25	0.5
Vancomycin	0.5-4.0	0.5	1.0

Karlowsky et al. 2008

# Ecological Differences between Fidaxomicin and Vancomycin (II)

Antimicrobial Susceptibilities  
*Bacteroides fragilis* (n=50)

Antimicrobial agent	MIC (mg/l)		
	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
Fidaxomicin	256->1024	256	>1024
Vancomycin	16-256	64	128

Finegold et al. 2004

## Summary

- **When should we look for the presence of *C. difficile* and/or its toxins?**
  - Nosocomial diarrhoea (3-day testing rule) or diarrhea at admission
  - Accept only unformed stool samples
  - Do not perform "test of cure"
  - Repeated testing of stool (if negative) is not cost-effective
  - In cases of relapse (exclude first other pathogens)

# Suggested procedure for laboratory diagnosis of CDAD (CDI)

## □ In sporadic cases

- Direct detection of toxin A and B from the faeces by a suitable ELISA, IC or PCR method is adequate

## □ In outbreaks epidemiological studies are needed

- Besides direct detection of toxin A and B
- Isolation of the strain is needed or store the stool specimen at 4 °C or -20 °C for later culture in the reference lab if isolation was not carried out
- Use ribotyping (or other molecular typing) to confirm the spread of an epidemic strain

## Infection control measures to limit the spread of *C. difficile*; conclusions from the literature (Vanberg et al. CMI 2008 Supplement 5)

- ❑ Early diagnosis of carriers with symptoms
- ❑ Active surveillance of CDI in hospital settings
- ❑ Surveillance of the antibiotic usage in the hospital wards. (Limit the use of fluoroquinolons and cephalosporines)
- ❑ Hand washing: 4% polyvidone soap > chlorhexidine > non-medical soap > alcohol-based products
- ❑ Isolate the patients with CDI in single room, in cohorts or in isolation ward
- ❑ Isolation can be terminated if normal bowel motion has returned for 48 h.

## Infection control measures to limit the spread of *C. difficile* (cont.)

- If there is a proven CDI case, prevent the spread of stool
- Wear gloves, gowns or aprons when in contact with patients who have CDI
- Disinfect objects contaminated with *C. difficile* with
  - sodium hypochlorite,
  - hypochlorite in combination with detergent,
  - alkaline glutaraldehyde
  - or peracetic acid
- Educate medical (and cleaning!!) staff about the disease and its epidemiology

