Resistance issues for Influenza and *Clostridium difficile*

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Influenza:
A significant public health issue

- Approximately 114,000 hospitalizations annually due to influenza and its complications[1]
- 20,000 to 40,000 influenza-related deaths each year[2]
- Annual direct and indirect costs over $12 billion[3]
- 75 million lost workdays per year[4]

1. Simonsen et al. *Infect Dis*. 2000
2. Thompson et al. *JAMA*. 2003
3. Nichol KL. *N Engl J Med*. 1994
4. Centers for Disease Control and Prevention. At: http://www.cdc.gov/nchswww/fastats/flu.htm

Influenza Background

- Caused by the influenza virus – the illness starts abruptly 1-4 days following an exposure

- Spread by aerosolized virus particles disseminated by infected individuals through coughing, sneezing and speech (close contact – 3 feet)

The percentage of persons exposed that develop influenza, range from **10 to 20%** (up to 50% in closed populations)

Influenza Background

- Associated with a high proportion of secondary complications
- Complications account for much of the morbidity and mortality attributed to influenza
- Superimposed bacterial pneumonia (most common)

Influenza Background

- Abrupt onset of fevers, chills, muscle aches, sore throat, weakness and headaches
- The severity of its symptoms separates influenza from other common respiratory viral illnesses
- On average, influenza is associated with **5-6 days of restricted activity**, including 3-4 days of bed rest

Signs and Symptoms

- Abrupt onset of symptoms
- Fever, usually over 100°F
- Nonproductive cough
- Chills and/or sweats
- Headache
- Myalgia
- Sore throat
- Potentially severe, persistent malaise
- Substernal soreness, photophobia, and ocular problems

Cox and Fukuda. *Infect Dis Clin North Am*. 1998;12:20.

Clinical Description/Diagnosis

Incubation period -- 1 to 4 days

– Adults: infectious from day before to +5 days after illness onset

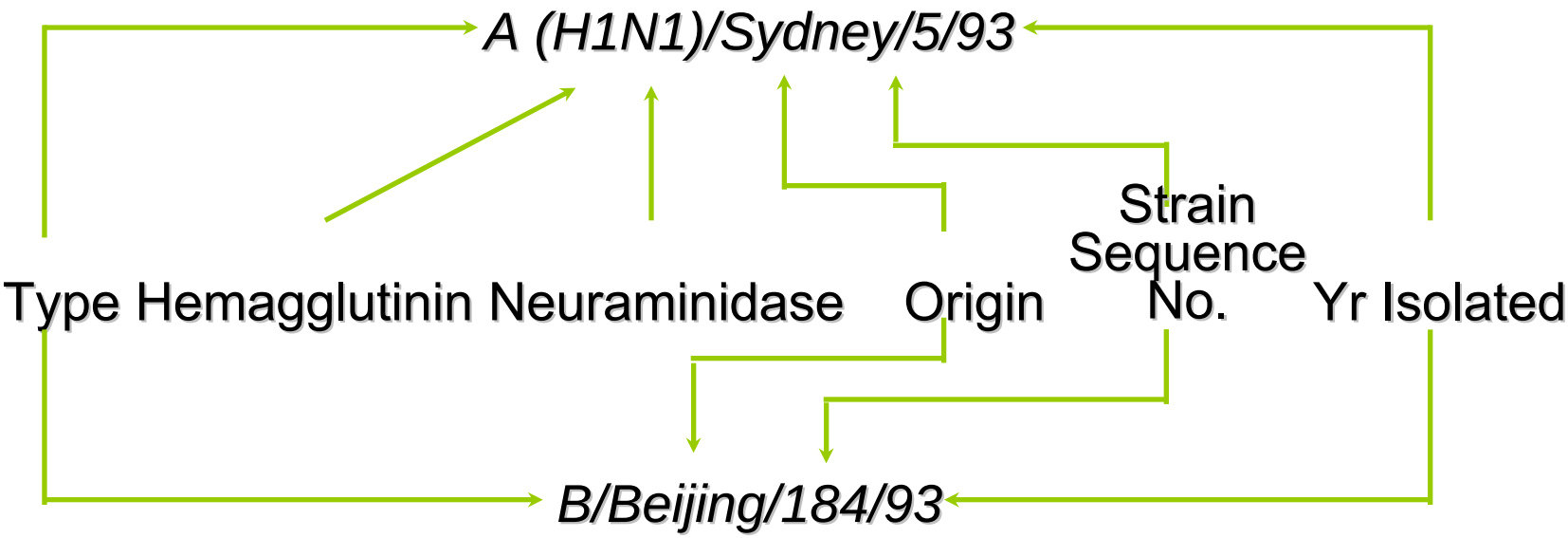
– Children: infectious ≥ 10 days (can shed virus several days before onset)

– Severely immunocompromised: Can shed virus for months

Signs and Symptoms in the Elderly Are Atypical

- Low grade fever (>99.0°F)
- Lassitude
- Confusion
- Nasal obstruction

Naming Influenza Viruses



Influenza Epidemiology

- Influenza is an illness occurring almost exclusively during the winter months

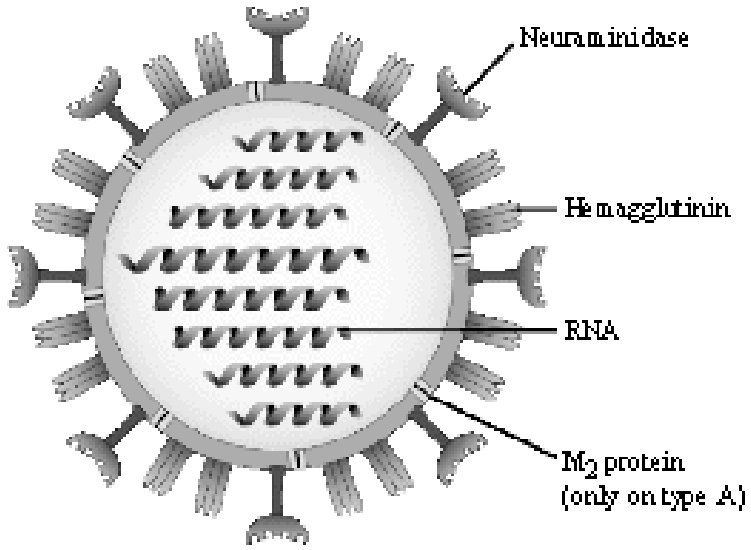
- In the Northern Hemisphere, outbreaks occur between October and April and in the Southern Hemisphere between May and September

In the tropics, influenza can occur year-round

Influenza Virus

- Both hemagglutinin and neuraminidase undergo minor changes as the influenza virus spreads across susceptible populations

- Minor changes result from accumulated point mutations in the RNA molecules, which encode these proteins



Influenza Virus

- **Antigenic drift** is responsible for the distinct **seasonal outbreaks** of influenza

- Antibodies to circulating strains of influenza apply selective evolutionary pressure, promoting the emergence and survival of newer strains of influenza

- Outbreak severity depends upon the susceptibility of a population (proportional to the degree of antigenic drift)

Efficacy of the Influenza Vaccine

- Most effective (70%-90%) in preventing illness in persons aged <65 yrs
- 30%-70% in preventing P/I hospitalization in elderly not in chronic care facility
- 30%-40% in preventing illness in frail elderly
- 50%-60% in preventing P/I hospitalization in nursing home elderly
- 80% in preventing death in nursing home elderly

MMWR. 2003;50:4.

Management Options

- Vaccinate at start of flu season
  - CDC: Primary influenza prevention strategy = annual vaccination
- Treat with antiviral agents
- Give antiviral agents prophylactically

Prophylaxis

- Use in high-risk persons
  - When vaccination occurred after outbreak
  - When antibody response to vaccine may be poor
  - When vaccine contraindicated
- Use in contacts of high-risk persons
  - Unvaccinated persons in frequent contact
  - Unvaccinated employees of health care facilities
  - During outbreak of strain not in vaccine

MMWR. 2001;50:4.

Antiviral Drugs for Influenza A

Agent	Amantadine	Rimantadine
Mechanism	Interferes with replication of type A	Interferes with replication of type A
Efficacy	No activity against type B	No activity against type B
Indications	Administer within 48 hrs to reduce severity and shorten duration of illness	Administer within 48 hrs to reduce severity and shorten duration of illness
	Children and adults	Adults

Shortcomings of Amantadine and Rimantadine

- Effective only against influenza A
- Penetrate CNS; risk for CNS side effects
- Rapid emergence of resistance

How Rapidly Does Amantadine Resistance Develop?

Recommendations for Influenza Outbreak Control in LTCF

- Antiviral prophylaxis x 14 days or 7 days beyond the last new culture-proven case within the facility
- Withhold antivirals from those ill more than 48 hours to reduce development of resistance
- For those who become ill during prophylaxis, presume antiviral resistance; order *strict* isolation; consider treatment and prophylaxis with different antiviral classes

Drinka PJ, et al. *Arch Intern Med* 1998.
Gravenstein S, et al. *Infect Control Hosp Epidemiol* 1992.

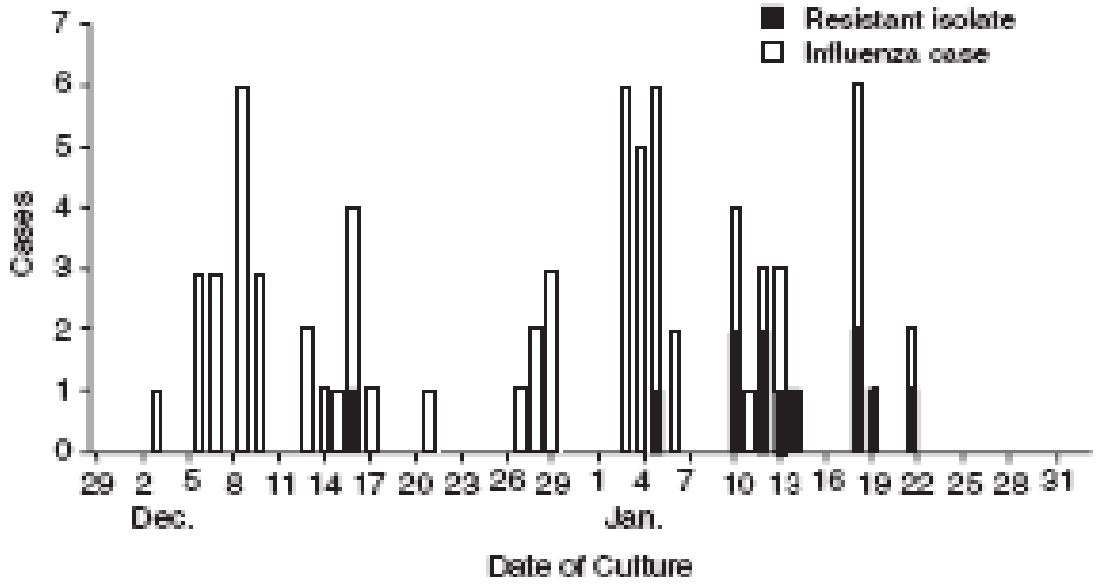


Figure 1. Outbreak curve: Influenza A in a four-building nursing home. Sixty-eight residents (72 total positive cases including cottages) had influenza A isolated from nasopharyngeal/throat swabs during a facility-wide influenza A outbreak, 1993–94. Total of 392 nasopharyngeal/throat cultures were obtained from ill residents (some residents cultured more than once). Amantadine-resistant influenza A was isolated from 12 residents.

Schilling M, Emergence and transmission of amantadine-resistant influenza A in a nursing home. J Am Geriatr Soc. 2004 Dec;52(12):2069-73.

Table. State of Origin and Median Age of Patients From Whom Influenza A(H3N2) Isolates Were Tested for Adamantane Resistance

	No. Resistant/ Tested	Patient Age, Median (Range), y*
Alaska	2/2	16.5 (5-28)
Arizona	14/14	24 (<1-87)
California	6/7	6 (<1-28)
Colorado	6/6	25.5 (7-78)
Florida	3/3	21 (11-50)
Georgia	4/4	20 (12-35)
Hawaii	6/14	18 (3-92)
Idaho	5/5	44.5 (11-93)
Illinois	12/12	7 (5-93)
Iowa	8/8	16.5 (8-85)
Kentucky	2/2	68.5 (64-73)
Maryland	1/1	19
Massachusetts	2/4	49.5 (22-80)
Minnesota	1/1	65
Mississippi	2/2	48.5 (14-83)
Missouri	3/3	11 (<1-22)
Nevada	2/2	14
New Mexico	0/1	8
New York	5/5	57 (43-88)
Oklahoma	1/1	37
Oregon	16/17	58 (13-91)
Pennsylvania	3/3	26 (8-88)
Texas	25/25	19.5 (<1-76)
Utah	7/7	22 (<1-55)
Washington	2/2	56.5 (21-92)
Wisconsin	55/58	27 (<1-92)
Total	193/209 (92.3%)	23 (<1-93)

*Patient age was not reported for 10 isolates tested.

Bright RA. Adamantane resistance among influenza A viruses isolated early during the 2005-2006 influenza season in the United States. JAMA. 2006 Feb 22;295(8):891-4.

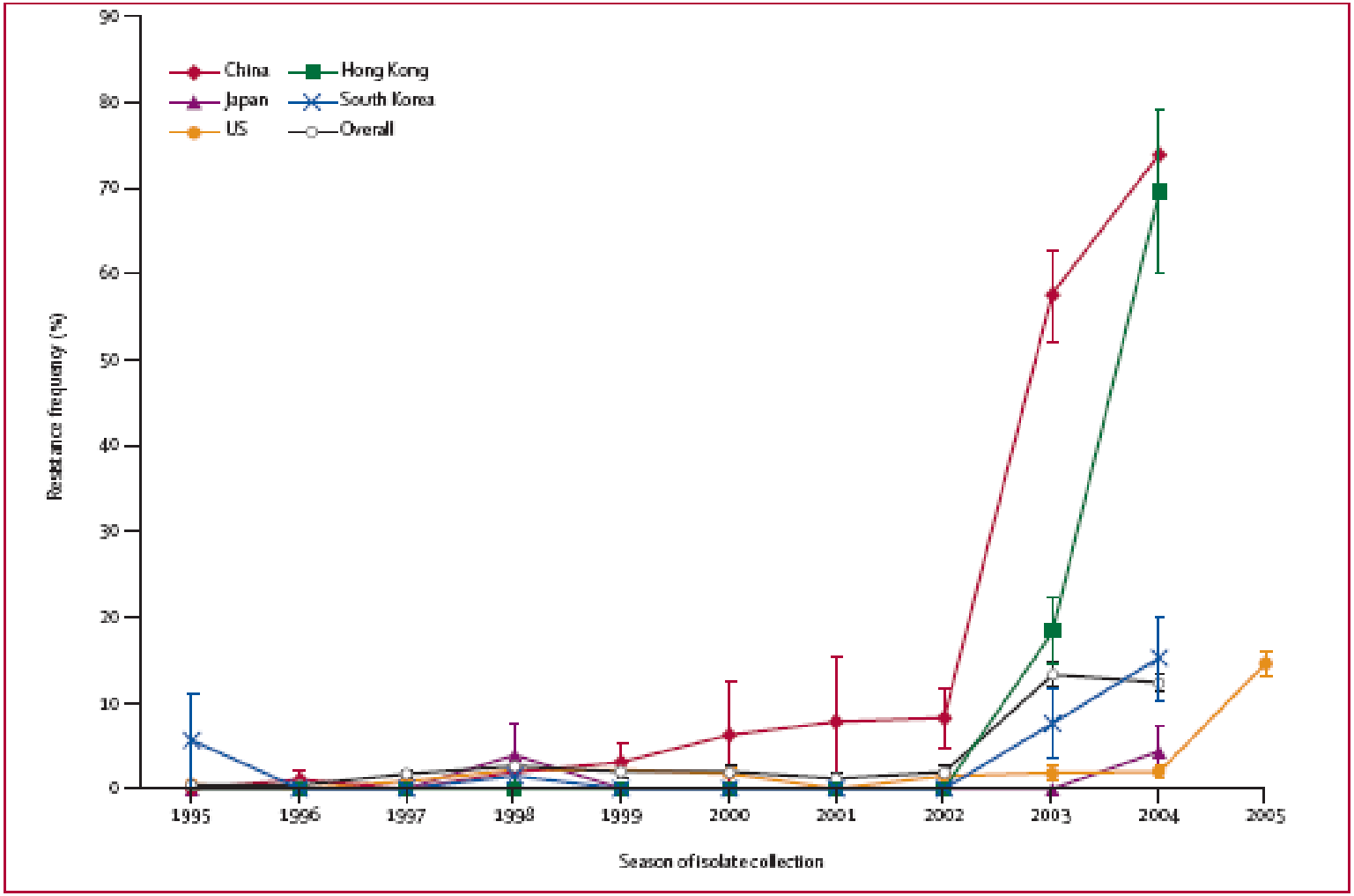


Figure: Trend of adamantane-resistant H3N2 viruses, 1994–2005
Each point represents the percentage of resistant viruses of the total tested. Error bars represent the 95% CI for the proportion of resistant viruses out of the total tested.

Bright RA, Incidence of adamantane resistance among influenza A (H3N2) viruses isolated worldwide from 1994 to 2005: a cause for concern. Lancet. 2005 Oct 1;366(9492):1175-81

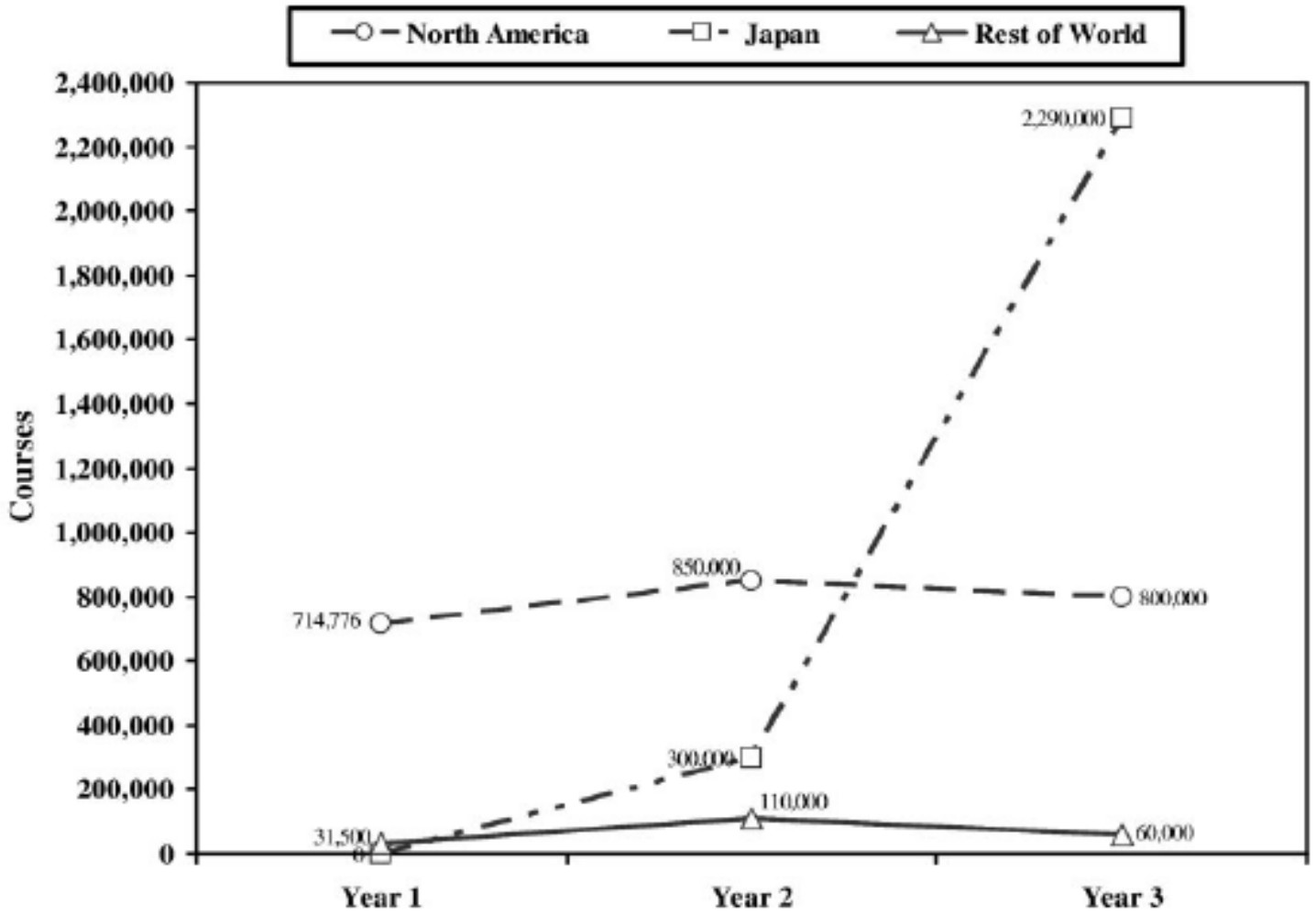


FIG. 1. Estimated numbers of 5-day treatment courses of oseltamivir administered in 1999 to 2000, 2000 to 2001, and 2001 to 2002 (October to September) in various regions of the world.

Monto AS, Detection of influenza viruses resistant to neuraminidase inhibitors in global surveillance during the first 3 years of their use. Antimicrob Agents Chemother. 2006 Jul;50(7):2395-402.

Antiviral Drugs for Influenza A or B

Agent	Zanamivir	Oseltamivir
Mechanism	Interferes with replication of type A and B	Interferes with replication of type A and B
Efficacy	Administer within 48 hrs to reduce severity and shorten duration of illness by 1 day	Administer within 48 hrs to reduce severity and shorten duration of illness by 1 day
Indications	Children and adults	Children and adults

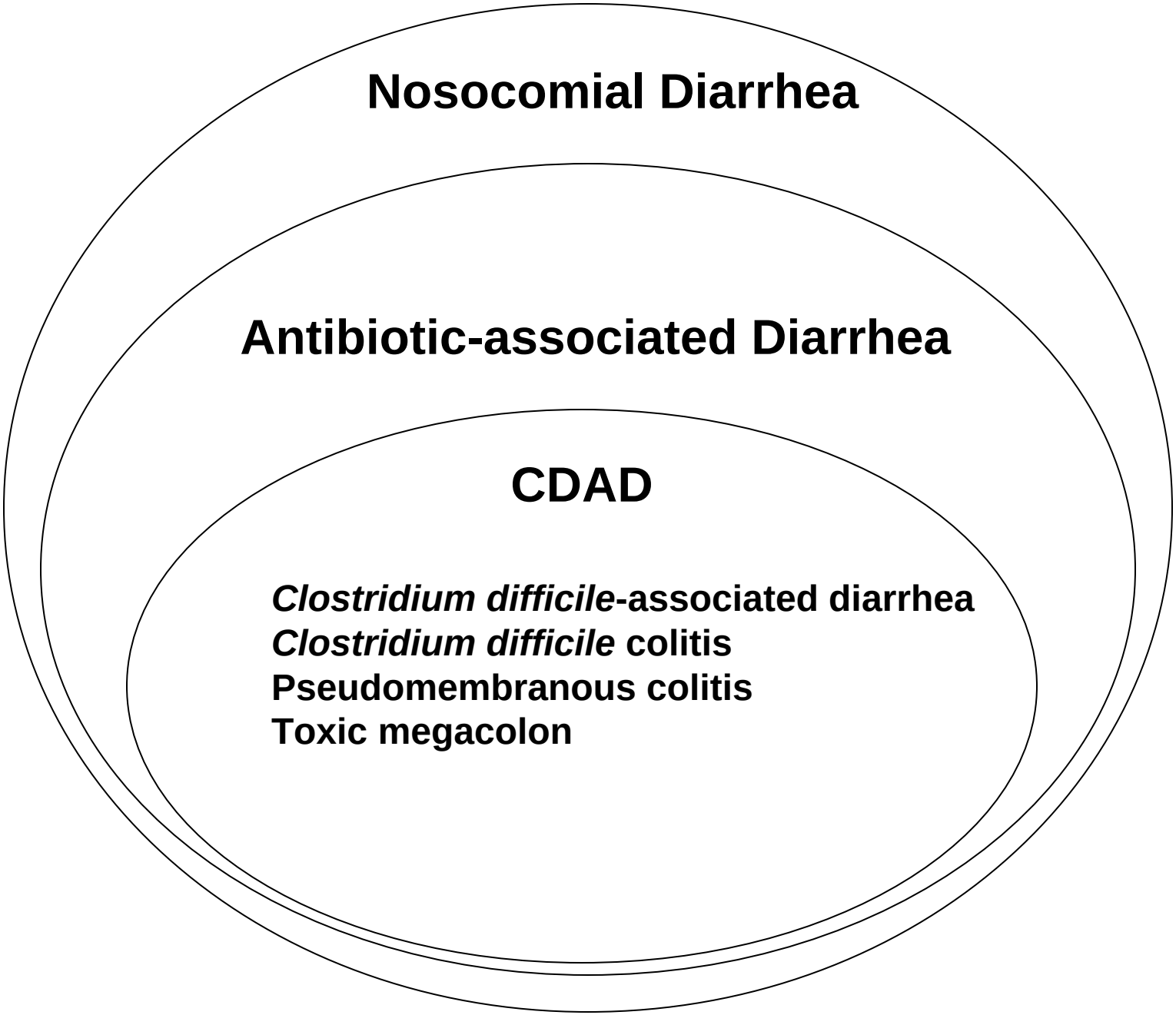
Neuraminidase inhibitors Resistance?

What is the relationship between Influenza and *Clostridium difficile*

Use of antibiotics:

- ↑ by 10% to 30% during influenza season

- The major risk factor for *C. difficile* is antibiotic use


Nosocomial Diarrhea
Antibiotic-associated Diarrhea
CDAD
Clostridium difficile-associated diarrhea
Clostridium difficile colitis
Pseudomembranous colitis
Toxic megacolon

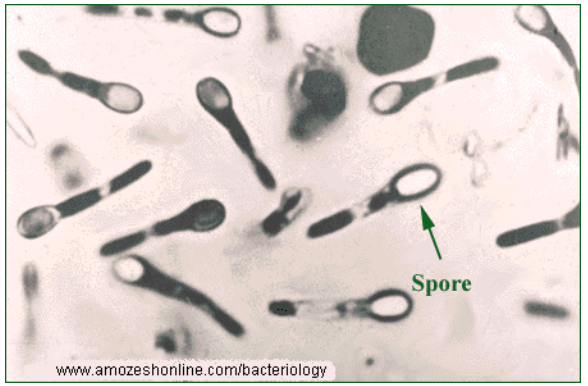
Spectrum of Syndromes

- Asymptomatic colonization
- Diarrhea (mild to severe)
- Colitis +/- pseudomembranes
- Toxic megacolon
- Colonic perforation/peritonitis
- Sepsis and acute abdomen without diarrhea

Disruption of protective colonic flora (loss of competitive exclusion)

↓

Colonization with toxigenic *C. difficile*



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Uncontrolled proliferation of *C. difficile*

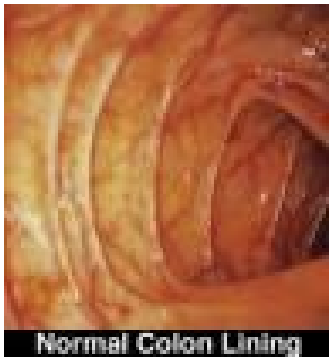
C. difficile grows rapidly in unoccupied niches

↓

Toxin production

↓

Cytoskeletal damage, mucosal injury, inflammation, fluid secretion



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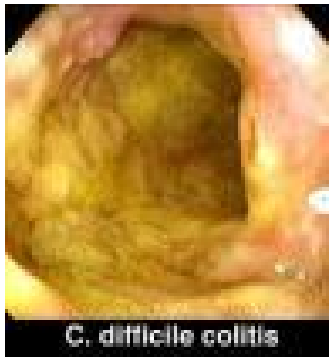
Colitis and Diarrhea



Antibiotics

- High risk for CDAD
  - 2nd generation cephalosporins
  - 3rd generation cephalosporins
  - Clindamycin
  - Quinolones

Risk factors for CDAD (other than antibiotic use)

- Age is consistently a risk factor for CDAD, in all retrospective and prospective studies
- CDAD is also associated with use of proton pump inhibitors

The Epidemiology of *C. difficile*

- World-wide rates increasing

- More Severe Disease
  - More treatment failures (harder to treat)
  - Colectomy rates are increasing
  - More CDAD-related deaths

Superbug overtakes hospitals

Superbug death toll still rising

C. DIFFICILE

Infections have increased by four

Infections microbiennes préoccupantes

Une bactérie a causé plus de morts l'an dernier à Montréal que le SRAS à Toronto

PASCALE BRETON

Plus de patients sont morts à Montréal l'an dernier d'une infection contractée à l'hôpital que dans l'épidémie de SRAS qui a frappé Toronto.

Publiée dans le *Journal de l'Association médicale canadienne* (JAMC), une nouvelle étude recense le nombre de patients qui, lors d'un séjour à l'hôpital, ont contracté une infection à la bactérie *Clostridium difficile* (*C. difficile*), qui s'attaque principalement au côlon.

En 2003 et au début de 2004, la bactérie a été détectée chez 1400 patients hospitalisés dans six établissements montréalais. De ce nombre, 79 personnes sont mortes. Comparativement, 44 personnes sont décédées en Ontario à la suite du syndrome respiratoire sévère aigu (SRAS).

›Voir INFECTIONS en A4

Story, Page A18

Sherbrooke hospital superbug killed 100

DILAPIDATED FACILITIES PARTLY TO BLAME

Expert links epidemic of C. difficile to strain on health-care resources. 'We didn't invest. We didn't modernize. We are paying the price'

BRENDA BRANSWELL
THE GAZETTE

The C. difficile cases also struck with greater severity, the study said. The number of patients who died within 30 days

secret,
l report

Jumpy Montrealers avoiding hospitals

FEAR CONTRACTING BACTERIAL INFECTION

Patients seeking advice, simple reassurance in wake of 79 deaths linked to potent bug

AARON DERFEL
GAZETTE HEALTH REPORTER

Hospitals across Montreal are fielding calls from anxious patients who are concerned about catching an aggressive strain of intestinal bacteria blamed for the deaths of at least 79 people since last year.

Some Montrealers have decided to stay away from hospitals, cancelling blood tests or appointments.

A 75-year-old heart patient called The Gazette yesterday to share his fears about the highly contagious bacterium, Clostridium difficile, which can cause repeated bouts of diarrhea and resist common antibiotics.

"If I go in as an in-patient, I'm worried that I could end up like the 79 that died," said the Côte des Neiges pensioner, who didn't want his name published.

At the Jewish General Hospital, where 16 patients have died, the blood-test centre was eerily quiet at 9:15 a.m. A few patients sat in the waiting area. A woman who went there to have her blood drawn said the centre is usually packed at that hour.

Please see STRAIN, Page A3

LA PRESSE MONTRÉAL SAM

ACTUALITÉS

Bactérie C. *difficile*: Québec crée un comité d'expert

PASCALE BRETON

Après une opération au genou et un traitement aux antibiotiques, Susan McDougall a soudainement eu des poussées de fièvre et de la diarrhée. Deux symptômes de la bactérie *Clostridium difficile* qui auraient dû mettre la puce à l'oreille du personnel de l'hôpital.

Après six jours d'hospitalisation à l'Hôpital général juif de Montréal, Mme McDougall a été envoyée dans un centre de réadaptation. J'avais de la fièvre, de la diarrhée, mais jamais on ne m'a demandé si j'allais bien. Au début, je pensais que c'était normal, que c'était simplement une conséquence de l'opération et des antibiotiques », raconte Mme McDougall.

Afin d'éviter la répétition d'un tel incident, le ministère de la Santé et des Services sociaux a mandaté un comité d'experts pour tenter de comprendre les

« Les moyens ne sont pas très compliqués, mais ils sont compliqués à mettre en place parce qu'ils touchent tout le monde. C'est d'abord l'hygiène. Les gens doivent apprendre à se laver les mains en passant d'un patient à l'autre », indique le Dr Michel A. Bureau, directeur général à la Direction des services de santé et de la médecine universitaire au ministère, en précisant que le personnel médical a encore du progrès à faire en cette matière.

tion des médecins microbiologistes infectiologues du Québec.

Les patients eux-mêmes doivent être vigilants, principalement lorsqu'ils prennent des antibiotiques. « Le patient devrait toujours aviser son médecin lors d'apparition de diarrhée, de douleurs abdominales ou de hausses de température inexpliquées. Ces symptômes peuvent survenir quelques semaines après l'arrêt des antibiotiques », précise le Dr Poirier.

La population ne doit pa
dre pour autant de pren
médicaments, mais « l
d'antibiotiques devrait
être justifiée. Il ne faut ja
sister auprès de son
celui-ci ne le recommand
affirme le Dr Poirier.

Depuis environ un an, le
taux de Montréal font fac
recrudescence des cas d'in
Avant l'éclosion des cas,
decins en voyaient de 2

Superbug most lethal in 10 years — experts

APPEARS TO HAVE MUTATED 18 MONTHS AGO

Microbiologists and physicians have been studying bug for six months to confirm it's a new strain originating in Montreal

AARON DERFEL
GAZETTE HEALTH REPORTER

The virulent strain of bacteria that has killed at least 79 people in Montreal since last year is

A similar outbreak of C. difficile has struck hospitals in Calgary, where 10 people have died. In the U.S. midwest, doctors are reporting a surge in C. difficile infections and recurring cases. Microbiology Internet cha

What about the US?

What About Iowa?

Results

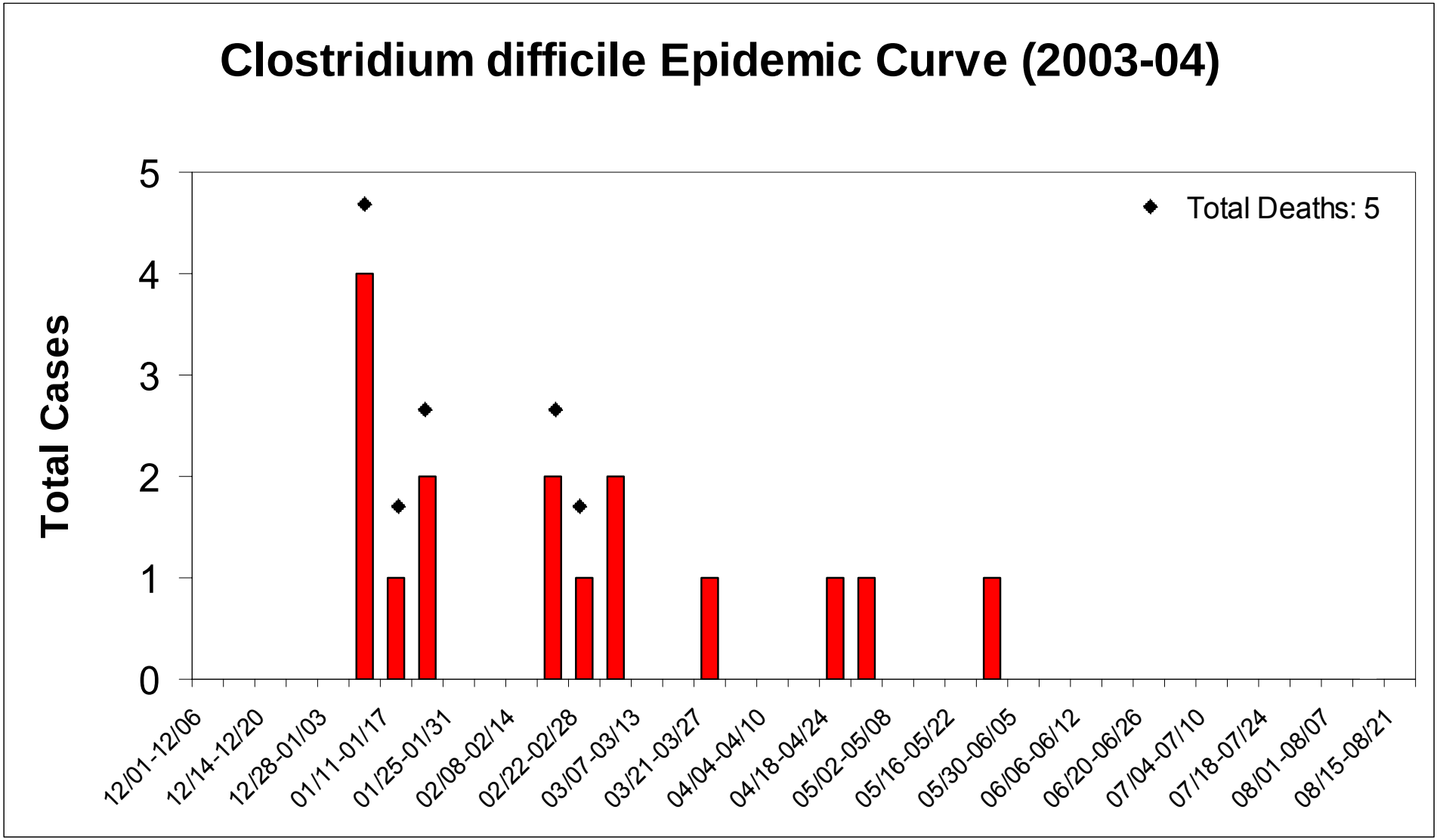

Clostridium difficile Epidemic Curve (2003-04)
Total Cases
0
1
2
3
4
5
Total Deaths: 5
12/01-12/06
12/14-12/20
12/28-01/03
01/11-01/17
01/25-01/31
02/08-02/14
02/22-02/28
03/07-03/13
03/21-03/27
04/04-04/10
04/18-04/24
05/02-05/08
05/16-05/22
05/30-06/05
06/06-06/12
06/20-06/26
07/04-07/10
07/18-07/24
08/01-08/07
08/15-08/21

Table 2

Univariate Results

Variable	**p-value**
Admissions	< 0.0001 (multiple)**
Moxifloxacin	0.0744*
Cephalosporin	< 0.0001**
Other antibiotics	0.0049**
Steroid Use	0.8644
Pneumonia	0.0603*
Admitted From Nursing Home	0.0096**

Multivariate Results

Admissions	< 0.0001 (multiple)**
Cephalosporins	0.0041
Admitted From Nursing Home	0.0875

Comparison of Admitting Diagnosis with Assessments by Pulmonary and Infectious Diseases Consultants

Study ID	Admitting Diagnosis	Pulmonary	Infectious Disease
1	Pneumonia	No	No
2	Pneumonia	Yes/Maybe	Yes
3	Shortness of Breath (treated with abx)	No	No
4	Pneumonia	No	No
5	Pneumonia	Yes/Maybe	Yes
6	Pneumonia	No	No
7	Pneumonia	*No	Yes
8	Bronchitis (treated with abx)	No	No
9	Acute Respiratory Failure (treated with abx)	No	No
10	Acute Cholecystitis		
11	Pneumonia	*Yes/Maybe	No
12	Foot ulcer		
13	Pneumonia	Yes	Yes
14	Pneumonia	Yes	Yes
15	Ruptured Appendix		

What Changed?

- Hand Hygiene?
- Antibiotic Prescribing Patterns?
  - Antibiotic-resistant *C. difficile* strains
- New strains (producing more toxin)?

Hand Hygiene?

Spores only killed by hypochlorite, glutaraldehyde, and acidified nitrite, **not** by 70% alcohol or detergents

Alcohol based hand hygiene agents are not effective at eliminating *Bacillus* spores

Weber, 2003

The Quinolones and *C. difficile*?

Multiple studies have now implicated fluroquinolones in the spread of *C. difficile*

- Levofloxacin (Muto, 2005)
- Gatifloxacin (Gaynes 2004)

C. difficile factors -- BI strains

- The BI group contains a new third toxin called binary toxin and has a deletion in a gene that regulates production of toxins A and B, the usual toxins produced by *C. difficile*

- The BI strains have acquired high-level resistance to newer fluoroquinolone antibiotics widely used in hospitals, namely gatifloxacin, moxifloxacin, and levofloxacin

CDAD - therapy

Removal of offending antibiotic alone may relieve symptoms in 10-20% of mild cases

- metronidazole has been preferred over oral vancomycin because

  - Metronidazole is much less expensive

  - Less risk of VRE

Table 1. Isolates of *Clostridium difficile* According to Health Care Facility and the Proportion of Isolates Belonging to the BI/NAP1 Strain.

Health Care Facility	Date of Onset of Outbreak	No. of Isolates Tested	BI/NAP1 Strain
			no. (%)
Georgia	Oct. 2001	46	29 (63)
Illinois	July 2003	14	6 (43)
Maine, Facility A	March 2002	13	9 (69)
Maine, Facility B	July 2003	48	30 (62)
New Jersey	June 2003	12	9 (75)
Oregon*	April 2002	30	3 (10)
Pennsylvania, Facility A	2000–2001	18	7 (39)
Pennsylvania, Facility B	Oct. 2003	6	3 (50)
Total		187	96 (51)

McDonald LC, An epidemic, toxin gene-variant strain of Clostridium difficile. N Engl J Med. 2005 Dec 8;353(23):2433-41.

Table 2. Resistance of Current BI/NAP1 *Clostridium difficile* Isolates, Current Non-BI/NAP1 Isolates, and Historic BI/NAP1 Isolates to Clindamycin and Fluoroquinolones.*

Antimicrobial Agent	Current BI/NAP1 Isolates (N=24)	Current Non-BI/NAP1 Isolates (N=24)	P Value†	Historic BI/NAP1 Isolates (N=14)	P Value‡
	no. with intermediate resistance or resistant (%)§			*no. with intermediate resistance or resistant (%)*	
Clindamycin	19 (79)	19 (79)	1.0	10 (71)	0.7
Levofloxacin	24 (100)	23 (96)	1.0	14 (100)	1.0
Gatifloxacin	24 (100)	10 (42)	<0.001	0	<0.001
Moxifloxacin	24 (100)	10 (42)	<0.001	0	<0.001

* The fluoroquinolones are levofloxacin, moxifloxacin, and gatifloxacin. Current BI/NAP1 isolates are those obtained since 2001, and historic BI/NAP1 isolates are those obtained before 2001.
† The P value is for the comparison between BI/NAP1 and non-BI/NAP1 isolates.
‡ The P value is for the comparison between current and historic BI/NAP1 isolates.
§ A minimal inhibitory concentration breakpoint of not more than 2 μg per milliliter was used for the definition of susceptibility, on the basis of the recommendations of the Clinical Laboratory Standards Institute for trovafloxacin.

Table 4. Multivariate Model of the Risk of *Clostridium difficile*–Associated Diarrhea According to the Use of Antibiotics among Case Patients, as Compared with Matched Controls, January 11 through June 26, 2004.*

Antibiotic	Odds Ratio	95% Confidence Interval
Any cephalosporin	3.8	2.2–6.6
First-generation	2.4	1.2–4.6
Second-generation	6.0	2.1–17.5
Third-generation	3.0	1.4–6.8
Any fluoroquinolones	3.9	2.3–6.6
Ciprofloxacin	3.1	1.8–5.4
Gatifloxacin or moxifloxacin	3.4	1.5–7.7
Levofloxacin	0.6	0.2–1.9
Clindamycin	1.6	0.5–4.8
Aminoglycosides	0.7	0.3–1.9
Macrolides	1.3	0.6–2.9
Intravenous vancomycin	1.3	0.5–3.1
Penicillins combined with β-lactamase inhibitor	1.2	0.7–2.3
Penicillins	0.7	0.3–2.9
Carbapenems	1.4	0.3–6.3

* Values were adjusted for the use of all other antibiotics, age, sex, number of days at risk for *C. difficile*–associated diarrhea, the Charlson index, and the use of chemotherapy, proton-pump inhibitors, histamine H_2–blockers, and enteral feeding.

Loo VG, A predominantly clonal multi-institutional outbreak of Clostridium difficile-associated diarrhea with high morbidity and mortality. N Engl J Med. 2005 Dec 8;353(23):2442-9.

Increasing Risk of Relapse after Treatment of *Clostridium difficile* Colitis in Quebec, Canada

Jacques Pépin, Marie-Eve Alary, Louis Valiquette, Evelyne Raiche, Joannie Ruel, Katalin Fulop, Dominique Godin, and Claude Bourassa

Department of Microbiology and Infectious Diseases, University of Sherbrooke, Sherbrooke, Quebec, Canada

Results. Among patients who had initially been treated with metronidazole, the proportion whose regimens were switched to vancomycin or for whom vancomycin was added because of a disappointing response did not vary between 1991 and 2002 (66 [9.6%] of 688 patients overall) but more than doubled in 2003 2004 (112 [25.7%] of 435; $P < .001$).

Conclusion. In 2003 2004, there was an increase in the proportion of patients with CDAD believed, by their attending physicians, to have experienced metronidazole treatment failure, as well as an increase in the frequency of post metronidazole therapy recurrences, especially among elderly persons.

Relatively Poor Outcome after Treatment of *Clostridium difficile* Colitis with Metronidazole

Daniel M. Musher,[1,2,3] Saima Aslam,[2] Nancy Logan,[1] Srikanth Nallacheru,[1] Imran Bhaila,[4] Franziska Borchert,[1] and Richard J. Hamill[1,2]

[1]Medical Service, Infectious Diseases Section, Michael E. DeBakey Veterans Affairs Medical Center, and Departments of [2]Medicine and [3]Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas; and [4]Aga Khan University, Karachi, Pakistan

Results. A total of 103 patients (50%) were cured by the initial course of therapy and had no recurrence of disease. Forty-six patients (22%) continued to have symptoms of colitis for 10 days despite treatment.

Conclusions. Because of the relatively poor response to therapy, additional approaches to prevention and/or treatment of *C. difficile* colitis appear to be warranted.

Metronidazole for *Clostridium difficile*–Associated Disease: Is It Okay for Mom?

Dale N. Gerding

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"Do these new observational studies relegate CDAD treatment with metronidazole to secondary status for Mom? Not for the majority of CDAD cases…..but they are a wake-up call for more discrimination in the selection of patients for treatment with metronidazole and for greater vigilance during treatment."

"The mean time for diarrhea resolution has been shown to be **3-4 days** in prospective trials, but improvement should precede diarrhea resolution, and unless her condition is deteriorating, one should not conclude that treatment failure has occurred before days 6-7 of therapy."

But what is failure and what are clearly defined indicators of severe disease that requires alternative therapy?

> "**WBC count >20,000** cells/mm3 and an **elevated creatinine** as indicators of complications in patients receiving metronidazole and recommended vancomycin treatment on the basis of limited observational data but no prospective randomized data."

Also, **if the WBC count increases during therapy**. These patients must be watched carefully for development of an ileus or fulminant CDAD.

Gerding recommends "multiple treatments, including oral vancomycin or vancomycin administered via nasogastric tube and enema, coupled with intravenous metronidazole and **early surgical consultation for possible colectomy**."

Summary

- Changing epidemiology (incidence and severity of CDAD are increasing)
- Fluoroquinolone use is increasingly associated with CDAD
- New BI strains of *C. difficile* are thought to be behind the changing epidemiology

Treatment Tips

Do not treat asymptomatic *C. difficile* colonization

Re-treat first-time recurrences with the same regimen used to treat the initial episode

Avoid antiperistaltic agents: may worsen diarrhea or precipitate toxic megacolon