

## Hypervirulent Strains of *Clostridium difficile*

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The anaerobic, gram-positive, spore-forming bacterium *Clostridium difficile* was first isolated in 1935. The designated name related to how difficult the original investigators found it to culture. It has been isolated widely in the soil and the gut of many animals and, although a known cause of colitis in animals such as cats, dogs, birds, rodents and neonatal pigs, it was not until 1978 that it was found to also cause human disease (pseudomembranous colitis).

**CAUSES OF CDAD**

Risk factors for *Clostridium difficile* associated diarrhoea (CDAD) comprise those that affect the gut microbial flora, the most common being exposure to antibiotics. Almost all antibiotics have been associated with CDAD, although it is less often associated with some—for example, metronidazole, aminoglycosides, trimethoprim and the quinolones. Clindamycin historically had a particularly infamous relationship to CDAD; animal work showed that following its use there was a particularly long period of gut susceptibility to the disease when challenged with *C difficile* spores. CDAD is a disease predominantly of the aged, but other factors include recent gastrointestinal surgery and immunosuppressive therapy, including cytotoxics. Other independent risk factors described more recently comprise proton pump inhibitors, which increase the risk threefold. It is presumed that increased gastric pH leads to decreased destruction of spores, but colonic receptors do exist for some proton pump inhibitors.

several investigations were performed: rates of CDAD were, 28/1000 admissions (five times the national average of 1997) with an extra 10.7 days in hospital and 30-day attributed mortality rates of 6.9%, these being 0.8–2% in 1997. Perforations, toxic megacolon and colectomy rates had also increased. Between 2004 and 2005 it was estimated that over 14,000 patients had been affected in the province of Quebec, with high mortality and relapse rates. By June 2006 the problem had spread to seven provinces with estimates of 13 cases per 1000 admissions.

Risk factors compared with matched controls comprised, as in many previous studies, cephalosporins (odds ratio (OR) 3.8%, 95% confidence interval (CI) 2.2% to 6.6%) and for the first time fluoroquinolones (OR 3.9%, 95% CI 2.3% to 6.6%). Interestingly it may be that the association is only with certain quinolones; methoxyquinolones (gatifloxacin and moxifloxacin) had been introduced recently

in several of the affected centres, these agents having greater anaerobic activity. However, the situation with antibiotics was not straightforward, as patients received more antibiotics per case (46%) than controls.

Typing was performed and a new strain (ribotype O27) was isolated from 82% of patients. It was assumed that this was related to the increased virulence and relapse rate. There were other relevant factors, however; hospitals agreed that their case mix had changed over the last few years with greater num-



**HYPERVIRULENT CDAD IN NORTH AMERICA**

Increased numbers of patients requiring colectomy alerted a hospital in Montreal in 2002 to the possibility of CDAD with a higher severity, mortality and relapse rate. Over the next two years

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*“The secret of success is constancy of purpose”*

Benjamin Disraeli

## A Safer Future?

Prof. Peter Curson Professor of Population & Security, The University of Sydney, Australia

The recently released WHO World Health Report 2007 A Safer Future holds some chilling messages for all of us facing life in the 21st century. According to the WHO the world faces a new era of infectious disease and as usual the culprit is us. Human behaviour and agency lies at the heart of all the disease threats we face – whether it be how we interact with and transform our natural environment, the growing world trade in wildlife, factory farming of poultry in South Asia, poor food preparation, poor hygiene in our hospitals, or the fact that roughly 2 billion of us now travel by air all over the globe, often passively transporting new infections around the world.

The WHO Report argues that new infections are emerging and spreading faster than at any other time in human history, while older infections, once thought under control and destined for the global scrapheap, are reappearing, redistributing and continuing to wreck havoc. Over the last three decades so called 'new' infections have appeared at the rate of at least one per year and we now face more than 40 infectious diseases, which were unknown or thought controlled a generation ago. In addition, epidemic outbreaks are becoming more common. Since 2002 the WHO has identified at least 1100 such epidemic events worldwide. SARS and Bird Flu remain in the collective memory not only because they caused substantial human suffering and resulted in considerable economic damage, but also because as psycho-social events they captured the public imagination, triggered international concern, and produced a field day for the media ... subsequently producing considerable panic and hysteria worldwide. But they were not alone. Outbreaks of other viral diseases have become common. Ebola, Marburg Virus, Nipah Virus, West Nile Virus all pose threats to world security and raise critical issues about global cooperation, surveillance and response.

But it is not simply new emerging infections which should concern us. Older infections, once thought under control have come back to haunt us. Fifty

years ago we thought that DDT spraying would remove the threat of a wide range of mosquito-borne diseases such as malaria, and dengue. As it turns out nothing could have been further from the truth. These and other mosquito-borne diseases have re-emerged, often in more virulent forms. Dengue in particular has surged in recent years with millions affected, and globally the number of cases reported to the WHO has doubled in each of the last four decades.

Finally, the threat of another pandemic of influenza has preoccupied most governments over the last few years. Based on past experience, some experts predict that in the advent of a new pandemic, 1.5 billion people around the world would be affected. In the words of the WHO, it is naïve and complacent to assume that the world will not see another disease like AIDS or SARS over the next few years.

The global health tally sheet does not stop there. Food borne diseases are having a heyday as globalisation affects production, storage, distribution and preparation. The trade of contaminated foodstuffs between countries is on the rise, as is the incidence of contamination from sloppy institutional and home food preparation.

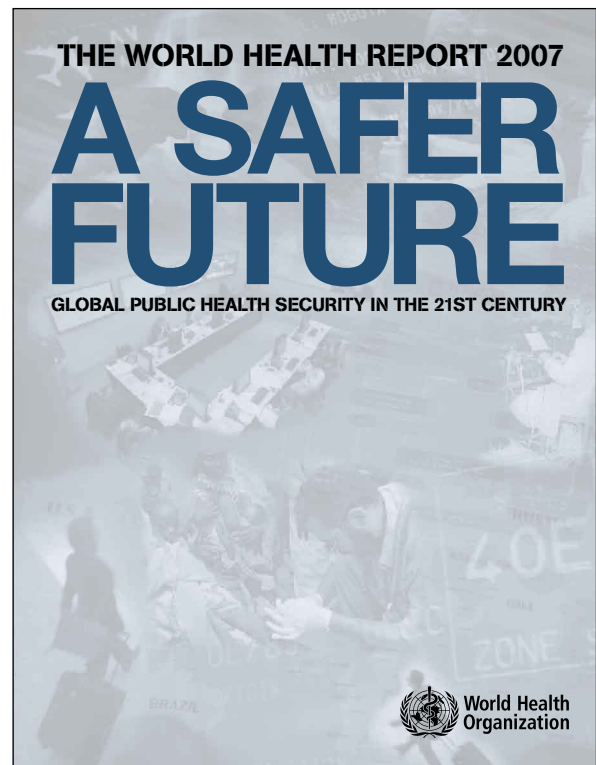
New threats have also appeared in the 21st century. Among these the threat of bioterrorism looms large. The anthrax episode in the USA, when potentially lethal anthrax spores were sent through the postal system, placed bioterrorism firmly on the 21st century security agenda. The use of smallpox as a bioterror weapon continues to worry authorities here and abroad and it is not without note that the US Government has been re-

placing its old smallpox vaccine stocks with a new generation vaccine.

The problem of growing antibiotic resistance and the use and misuse of antibiotics particularly in animals raises other questions. Like food borne disease, antibiotic resistant infections are a growth industry, particularly in our hospitals.

So what needs to be done to secure a safer world? The WHO places emphasis on international cooperation and collaboration, effective systems of surveillance, alert and response, of strengthening local health systems and encouraging cross-sector collaborations within government. More reactive than proactive perhaps, but in an uncertain, insecure world, certainly essential.

[www.who.int/whr/2007/en/index.html](http://www.who.int/whr/2007/en/index.html)



## Virox Update

### Virox Introduces RESCUE Sporocidal Gel

Virox Technologies Inc. of Oakville, Ontario has received a Drug Identification Number (D.I.N) registration from Health Canada for Accel RESCUE Sporocidal Gel, a 4.5% Accelerated Hydrogen Peroxide formulation that achieves sporocidal disinfection in 10 minutes. The intended use is for toilet bowls and commodes as well as inside sinks and basins in the washrooms of *C. difficile* patients where the spore count has been shown to be the highest. The introduction of RESCUE Sporocidal Gel along with Accelerated Hydrogen Peroxide 0.5% TB disinfecting and cleaning solutions allows facilities to have an alternative protocol to bleach when *C.diff* exists or is suspected. The use of bleach is not without disadvantages such as workplace safety concerns. RESCUE Sporocidal Gel maintains the excellent safety profile of the patented Accelerated Hydrogen Peroxide technology.

For more information on the RESCUE product please visit [www.virox.com/medical/acute\\_care.asp](http://www.virox.com/medical/acute_care.asp) or call 800-387-7578.

### Virox receives Canada's first registered EcoLogo disinfectant-cleaner

From its inception in 1998, Virox Technologies has been a firm believer in developing and manufacturing disinfectants that not only provide superior cleaning and efficacy claims, but that are also environmentally sustainable. The use of disinfectant-cleaners is a marketplace reality and these products are commonly used in the institutional and healthcare sectors. However, until February 2007 the Environmental Choice Program did not have a certification criterion that allowed for the registration of disinfectant-cleaners.



Recognizing the changing needs of the healthcare system and the reliance on disinfectant-cleaners by both Canadian and American infection control guidelines, TerraChoice felt there was a need to review the existing Certification Criteria Document CCD 146 for Hard Surface cleaners and subsection H for Disinfectants. As a result, in February 2007

a new Certification Criteria Document CCD 166 for Disinfectants and Disinfectant Cleaners was finalized.

Accelerated Hydrogen Peroxide has proven its superiority with respect to cleaning and disinfection properties and can now proudly display the EcoLogo as Canada's first registered disinfectant-cleaner.

### Accel TB Soft Packs Launched!

At Virox, we are very aware of the increasing importance of pandemic planning and the development of effective pandemic kits within health care facilities as well as within industry. Healthcare and industry are trying to take a proactive role in protecting their staff and clients. The Accel TB Soft Pack maintains the current 30-second sanitizing, 5-minute bactericidal, 5-minute general virucidal (non-enveloped viruses such as noroviruses), 5-minute fungicidal and 5-minute tuberculocidal claims. The Accel TB Soft Packs offers the ability for employees, physicians and nurses to carry personal wipes to clean and disinfect those non-critical devices and surfaces, such as stethoscopes, countertops, light switches, door knobs, elevator buttons etc., that may not be included in regular cleaning and disinfection practices.

Further information on the Accel TB Soft Packs product can be found on the Virox website ([www.virox.com](http://www.virox.com)) including the efficacy study, MSDS, and product brochure.

### New Claims for Accel Hydrotherapy Tub Product!

We are very excited to announce that we have received the DIN approvals for new claims for the Accel Hydrotherapy Tub Product. The new claims include the addition of a 5-minute Fungicidal Claim, a 5-minute General Virucide Claim and a 30-second Broad-Spectrum Sanitizing claim. The product will maintain its current 5-minute Bactericidal Claim. The additional claims allow the Accel Hydrotherapy product to be used in both non-critical and semi-critical hydrotherapy tub, birthing tubs and foot spa baths etc.

**Website Update:** [www.virox.com](http://www.virox.com)

MEMBER SECTION! Do you want to be sure you get all the updates on Virox? Interested in being included on all of the

invitations to all Virox's FREE education seminars? Log on to [www.virox.com](http://www.virox.com) and click the Member's Sign-Up icon to enroll!

Virox prides itself on being a resource tool to the infection control community so please check out our website frequently as new links will be posted regularly.

### What exactly does the Virox Professional & Technical Services Team do?

The Professional & Technical Services (PTS) department's mission is to provide education opportunities to Virox partners, distributors, and end users in all areas pertaining to infection control. The PTS team is a consulting resource that infection control professionals, public health inspectors and nurses, environmental services personnel and distributor sales reps can use for questions pertaining to microbiology, disinfectant chemistries, protocol creation and in-service product training. The PTS group provides services free of charge - conducts training seminars at infection control and public health conferences, sponsors other educational opportunities to the infection control community such as sponsoring Webber Training Teleclasses, and Infection Control Today webinars. Professional and Technical Services has responsibility for the annual CHICA-Canada Virox Patron Member Scholarship Fund, and works with facilities to conduct clinical trials and research studies with the objective of minimizing hospital acquired infections.

If you are interested in learning more about how the Professional and Technical Services team at Virox can provide educational or consulting opportunities at your facility please contact Nicole Kenny at 1-800-387-7578 x118 or via email at [nkenny@virox.com](mailto:nkenny@virox.com).

*Never discourage anyone...who continually makes progress, no matter how slow.*

**- Plato**

## Decreasing *Clostridium difficile* in the Newborn Intensive Care Unit Through Institution of Environmental Cleaning Procedures

Edited from an Article by LM Harper, Intermountain Healthcare, Provo, UT



*Clostridium difficile* is a gram positive spore-forming rod that has been historically associated with antibiotic related diarrheas. This is the most common cause of hospital associated diarrhea – 3 million cases per year in the United States, adding up to \$10,000 per case with an expected two week hospitalization stay.

Our hospital had been tracking the *C. difficile* cases since October of 2003, averaging from 6-8 cases per month for our entire hospital, and the Newborn Intensive Care Unit (NICU) averaging one case every other month. Between July and August of 2005 our NICU reported 8 confirmed cases of *C. diff.* All infants were symptomatic and had positive toxin assays.

An investigation was launched to determine any possible commonalities among the infected infants. We found that all of the 8 infected infants had shared one of three beds in a corner of the NICU. Our objective was to decrease the incidence of *C. difficile* in the NICU through implementation of cleaning measures with an oxidizing disinfectant.

A literature search was launched to find any related studies. The CDC website

was referred to and a call was placed to the CDC to confirm the efficacy of our proposed cleaning. Our environmental services cleaned the affected corner from top to bottom with a disinfectant solution. All moveable items, rockers, screens, scales, etc., were also cleaned. We launched extensive staff education related to *C. difficile* and its ability to be found on environmental surfaces, in tandem with educating to the importance of washing hands with soap and water when you are caring for a patient with *C. difficile*.

The occurrences of *C. difficile* in our NICU have been drastically reduced. The cleaning was done in August of 2005, since that time there has not been one positive toxin assay for *C. difficile* in the NICU.

An incidence of *C. difficile* can cost \$10,000 for the extended hospital stay; therefore by cleaning of environmental surfaces of known *C. difficile* patients, you can prevent transference of this organism to other patients, thus saving money, freeing up hospital space and decreasing cross-contamination.

## MRSA - More Common Than Thought

If the estimates are correct, the number of deaths associated with methicillin-resistant *Staphylococcus aureus* (MRSA) - nearly 19,000 in the United States in 2005 - would exceed those attributed to HIV-AIDS, Parkinson's disease, emphysema, or homicide.

A recent study, published in the October, 2007 issue of the Journal of the American Medical Association, suggests that such infections may be twice as common as previously thought. By extrapolating data collected in nine places, the researchers estimated that 94,360 patients developed an invasive infection from the pathogen in 2005, and that nearly one of every five, or 18,650 of them, died. The study points out that it is not always possible to determine whether a death is caused by MRSA or merely accelerated by it.

A major difference between the new study and its predecessors is that it compiled confirmed cases of MRSA infection, rather than relying on coded patient records that sometimes lack precision. The study found higher prevalence rates and death rates for the elderly, African-Americans and men. The figures also varied by geography, with Baltimore's incidence rates far exceeding those of the eight other locations.

MRSA, which was first isolated in the United States in 1968, causes 10% to 20% of all infections acquired in health care settings, according to the CDC. The prevalence of invasive MRSA — when the bacteria has not merely colonized on the skin, but has attacked a normally sterile part of the body — is greater than the combined rates for other conditions caused by invasive bacteria, including bloodstream infections, meningitis and flesh-eating disease.

The JAMA study also concluded that 85% of invasive MRSA infections are associated with health care treatment. Previous research had indicated that many hospitals and long-term care centers

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## Bacteria Can Hide Out in Cells for Weeks

Nicole Kenny, Virox Technologies Inc.

Another interesting study was released recently that revealed a fascinating survival strategy used by *Staphylococcus aureus*. The paper, "A global view of *Staphylococcus aureus* whole genome expression upon internalization in human epithelial cells", was published earlier this year in BMC Genomics and profiled in ScienceDaily. It explained that Staph. bacteria may evade the immune system's defenses and dodge antibiotics by climbing into our cells and then lying low to avoid detection. The research shows how *S. aureus* makes itself at home in human lung cells for up to two weeks.

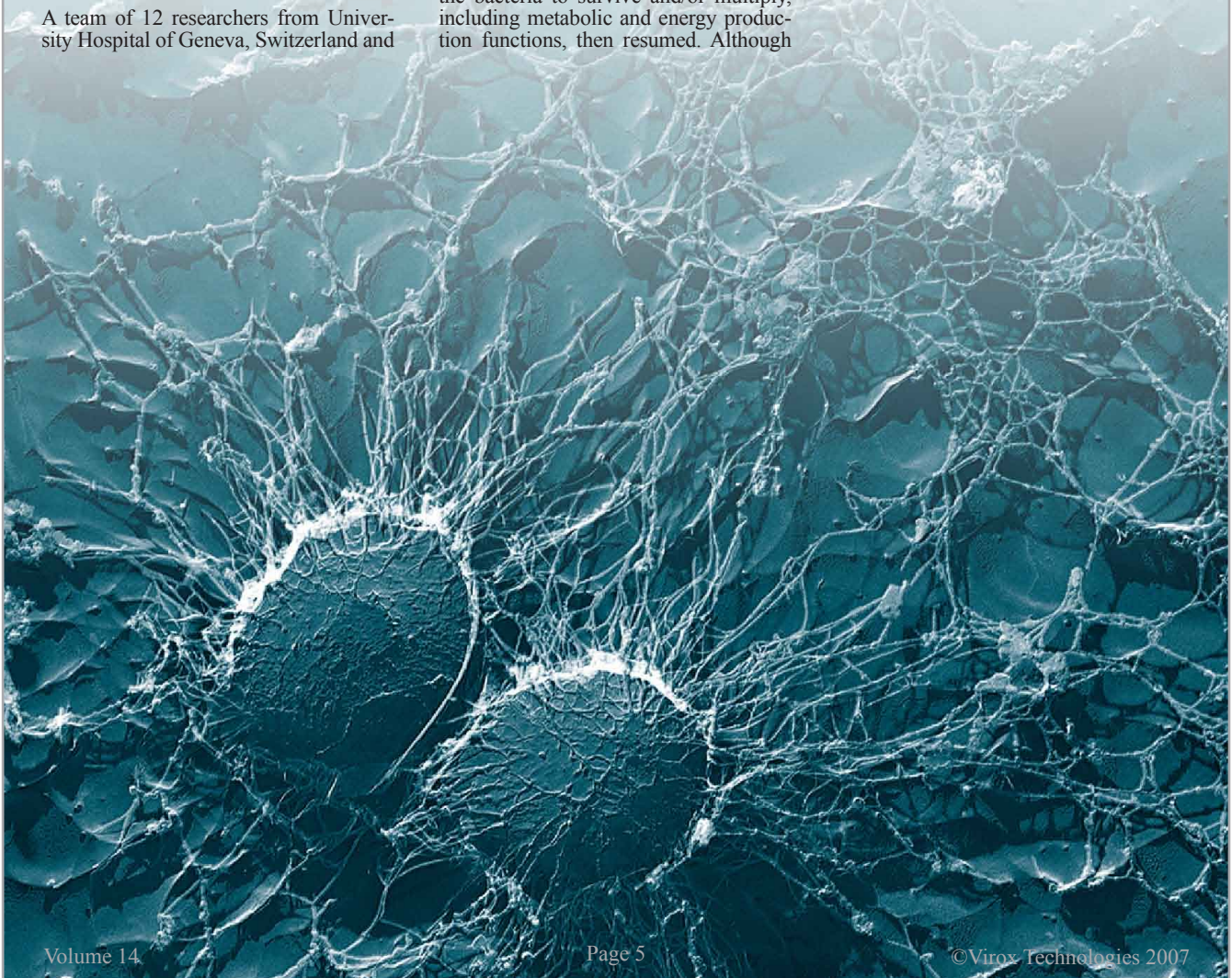
A team of 12 researchers from University Hospital of Geneva, Switzerland and

the Institute of Food Research, Norwich, UK set out to uncover what *S. aureus* did inside human lung epithelial cells using an in vitro model. They found that shortly after *S. aureus* entered the lung cells, the bacteria's gene expression profile dramatically changed: gene expression for bacterial metabolic functions and transport shut down, putting the bacteria in a dormant state.

Simultaneously, production of toxins potentially lethal for the epithelial cells becomes strictly controlled to limit cellular damage. Mechanisms that helped the bacteria to survive and/or multiply, including metabolic and energy production functions, then resumed. Although

most of the bacteria had died by about four days as a result of antibiotic treatment, the team still found viable bacteria in their model system two weeks after infection.

The findings may help in understanding relapsing infections (even years after the first episode was apparently cured), and in designing new antibacterial drugs. *S. aureus* has not traditionally been considered an intracellular pathogen, but the molecular details that govern its extended persistence remain largely unknown.



## Hypervirulent Strains of *Clostridium difficile*

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bers of debilitated, immunocompromised and elderly patients. Another interesting point is that the study of Pepin and colleagues did not show that proton pump inhibitors were an independent risk factor for CDAD, unlike the study quoted above. There are several possible explanations for this—for example, the patients may have been sicker or have some other missed risk factor. Such a risk factor might include patients admitted from the community.

A similar situation to that in Canada had emerged in the USA, with the Centers for Disease Control and Prevention (CDC) showing rates had doubled between 1996 and 2003 from of 31 to 61 cases per 100,000. Isolates from six recent outbreaks in the USA revealed emergence of the same epidemic O27 strain. Higher morbidity and mortality were described in at least 17 states. A nursing home outbreak of CDAD could be related to the switching from levofloxacin to gatifloxacin.

### PATHOGENESIS OF CDAD

When considering the pathogenesis of CDAD it is important to consider the interactions of the organism (the seed), the affected patients (soil) and the environment (climate). We have already mentioned various aspects of the patient case mix for the Canadian outbreaks and similarly alluded to the some of the climatic factors—for example, antibiotic and other drug usage. Although CDAD is under long and continuing study, much is still not known. The inoculum, for example, may be very low.

Several pathogenicity factors are described: there are two large exotoxins (TcdA&B). However, TcdA2/B+ strains are recognized with increasing frequency and truncated A/B strains can cause disease. In 10% of selected strains there is a cdtA-B binary toxin encoding an actin-specific ADP-ribosyltransferase;

this may just produce secretion of fluid by colonic cells but does not result in cell death. Many other factors may also be implicated, including fimbriae and subgroups of adhesions. O27 and O1 may produce higher sporulation levels than other strains and these were even higher when non-chlorinated (ie, non-oxidating) disinfectants were used.

It should be noted that there has been no consistent relationship between severity of disease and toxin concentration in stool. It is clear that, despite years of research, the organism has many hidden secrets and poses many interesting questions. Interestingly, several of the infection control teams in Quebec comment that they no longer see as many cases of serious CDAD and think this may be related to their aggressive early treatment of infection as soon as the diarrhoea.

### PREVENTION AND CONTROL OF CDAD

The number of CDAD cases is increasing throughout the world. This may be related to new factors including the emergence of certain strains, their increasing antimicrobial resistance, the changing case mix, and aspects of healthcare delivery. Prevention and control measures are being reviewed in many countries.

Control will be informed by improved surveillance and typing information. The guidelines point to reinforcement of all of the following: the use of hand washing for soiled hands or close contact with CDAD cases, isolation of patients with diarrhoea, effective stewardship of antibiotics, and proper decontamination of the environment.

A new factor in the rubric of prevention and control are various aspects of clinical governance. These are apparent in reports from the Quebec and other outbreaks. Staffing shortages, high bed occupancy, poorly cleaned and maintained premises, old buildings that need to be replaced, and low priority of infection control resonated. There are other interesting aspects about healthcare delivery. Patient transfers have resulted in the spread of the O27 strain between Belgian

and France, and between hospitals in the Netherlands. The O27 strain is now found in many parts of the UK, and it is interesting to speculate whether this may be caused by increased inter-city patient transfers due to patient choice? We described inter-city spread of epidemic methicillin resistant *Staphylococcus aureus* (MRSA) in the 1990s, perhaps encouraged by this process.

Clearly a holistic approach to prevention and control will be required if we are to make any impact on the increasing numbers of CDAD cases described in many parts of the world.

## Reversing Natural Selection

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had become breeding grounds for MRSA because bacteria could be transported from patient to patient by doctors, nurses and unsanitized equipment.

Among other things, the findings in the JAMA study are likely to stimulate further an already active debate about whether hospitals and other medical centers should test all patients for MRSA upon admission.

*“Many of life’s failures are people who did not realize how close they were to success when they gave up.”*

- Thomas Edison

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