

MOSAR PRESS REVIEW

June 2008

Upcoming Events 2008

Events organized by MOSAR Partners

14-25th July 2008

"INTRODUCTION TO INFECTIOUS DISEASE MODELLING AND ITS APPLICATIONS"

Organized jointly between the London School of Hygiene & Tropical Medicine and the Health Protection Agency Centre for Infections, UK

Venue: London School of Hygiene & Tropical Medicine

Further details are available at: <http://www.lshtm.ac.uk/prospectus/short/siidma.html>

1 - 12 Sept 2008

EPIDEMIOLOGY & CONTROL OF INFECTIOUS DISEASES: Introduction to mathematical models of global and emerging infections

Venue: Imperial College London

For full programme details, please contact Ulrika Wernmark on: Telephone: +44 (0)20 7594 6886

Email: cpd@imperial.ac.uk

For more information please visit: www.imperial.ac.uk/cpd/epidemiology

25-28 October, 2008

48TH ANNUAL ICAAC/IDSA 46TH ANNUAL MEETING : JOINT MEETING OF ICAAC AND IDSA
Washington, DC, USA

Abstract preparation and electronic submission process will be available beginning January 8, 2008 at:

<http://www.icaacidsa2008.org/>

19-21 November 2008

2ND EUROPEAN SCIENTIFIC CONFERENCE ON APPLIED INFECTIOUS DISEASE
EPIDEMIOLOGY (ESCAIDE)

Berlin, Germany.

A wide range of topics related to applied infectious disease epidemiology will be covered. Abstracts are invited in the areas of applied public health research, outbreak investigations and evaluation of public health surveillance, but also other areas in applied epidemiology or public health.

For registration, the conference programme and other information, visit: <http://www.escaide.eu/>

27-28 November 2008

THE POLITICS OF KNOWING: RESEARCH, INSTITUTIONS AND GENDER IN THE MAKING
Prague, République Tchèque

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> California Releases 3rd Report On Community-Acquired Pneumonia

Medical News Today, 30 June 2008

Californians hospitalized with community-acquired pneumonia (CAP) could more than double their chances of survival if they are treated at one of the top-rated hospitals, according to a newly released report from the Office of Statewide Health Planning and Development (OSHPD), "Community Acquired Pneumonia: Hospital Outcomes in California, 2003-2005." In this third report on CAP quality of care, the report provides statistical analysis on the outcomes of 208,000 adult pneumonia patients admitted to 354 California hospitals over the study's three-year period. While statewide about 12% of these patients died within 30 days of admission, patients at the "best" hospitals had an 8% death rate and patients at the "worst" hospitals had a 17% death rate. "This report reinforces Governor Schwarzenegger's commitment towards making our healthcare system more transparent and improving consumer access to information on quality and performance," stated OSHPD Director Dr. David Carlisle. "The community-acquired pneumonia report will give healthcare consumers and purchasers the tools to assess the relative value of healthcare delivered to patients and promote quality improvement by hospitals." Of the 354 hospitals that reported community acquired pneumonia cases, the majority, 259, were rated "as expected." Forty-eight (48) hospitals had death rates "better than expected," and 47 hospitals ranked "worse than expected." The quality of hospital performance was assessed by comparing each hospital's risk-adjusted death rate for CAP patients with the statewide rate. Taking into account patients' severity of illness prior to admission allows fair comparison of each hospital's death rate with the statewide rate and with other hospitals. All hospitals caring for CAP patients should implement "best practices" guidelines supported by the medical community. Hospitals with poor outcomes should review their clinical practices to identify and correct shortcomings. Pneumonia is an inflammation of the lungs caused by bacteria, viruses, fungi, particles, or other objects and organisms. The report provides information on cases of pneumonia acquired in the community -- such as at home or work -- which resulted in hospital admission. The report does not assess the treatment of pneumonia acquired by patients in the hospital after surgery or other treatments. As one of thirteen departments within California's Health and Human Services Agency, the Office of Statewide Health Planning and Development (OSHPD) is committed to "Equitable Healthcare Accessibility for California." OSHPD analyzes and supports the state's healthcare infrastructure, promoting medical care transparency for Californians. OSHPD also supports a diverse and culturally competent workforce, ensures safety of buildings used to provide healthcare, insures loans to develop healthcare facilities, and facilitates development of a sustained capacity for communities to address their healthcare concerns.

The community acquired pneumonia report is available online at <http://www.oshpd.ca.gov>.

> MARKHAM, ON, June 3 /PRNewswire-FirstCall/ - **AlphaRx** (OTC BB:ALRX) is pleased to announce pre-clinical data on **Zysolin(TM)**, a Tobramycin compound encapsulated in the company's Nano Drug Delivery Platform intended for the treatment of Cystic Fibrosis and an adjunctive treatment of Gram-negative pneumonia in intubated and mechanically-ventilated patients.

In the recent animal study, the therapeutic efficacy of Zysolin was investigated in a mouse model of *Pseudomonas aeruginosa* pneumonia. In this acute model, pneumonia developed rapidly, resulting in a high mortality rate, no mice survived after 24 hours of infection without treatment. Mice treated with Zysolin(TM) showed significantly better efficacy than Tobramycin, achieving 60% survival rate vs. 40% in the Tobramycin treatment group. An increase of survival by 50% or more, relative to vehicle control, indicates significant anti-microbial effect. The Tobramycin treatment group did not meet the study's end point.

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> **Funding For Superbug Spin-Out**

Medical News Today, 9 June 2008

Procarta Biosystems, the company spun-out of the John Innes Centre in 2007 to develop a technology designed to defeat antibiotic-resistant superbugs, has received significant seed funding. The Rainbow Seed Fund and the IcenI Seedcorn Fund will enable Procarta to further develop its DNA decoy technique, which aims to restore antibiotic efficacy against resistant superbugs, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). Procarta's pioneering approach to combating the threat of superbugs is based on injectable DNA therapies, called Transcription Factor Decoys (TFDs). TFDs are short pieces of DNA which inactivate the resistance genes the bacteria need to counter antibiotics. This new funding will initially allow Procarta to develop TFDs that prevent resistance to vancomycin, the so-called antibiotic of last resort. "We plan to be able to use this latest and valuable support to further validate the outstanding potential of our proprietary approach to combating resistant superbugs," said Procarta's Research Director, Dr Michael McArthur. Mark White of the Rainbow Seed Fund said: "We have worked alongside the John Innes Centre and its commercialisation arm PBL for some time and have a high regard for their ability to spot promising commercial opportunities. In Procarta's case we were particularly impressed by the skills of the key people involved as well as the scale of the opportunity. In addition, we were attracted to the possibility of achieving a significant breakthrough in an important but somewhat neglected area of healthcare. There remains a lot of work to be done, but the venture holds a great deal of promise." Procarta's unique technology can breathe new life into existing drugs and prolong the commercial usefulness of antibiotics and in doing so counter growing concern over the rise of drug-resistance in bacterial infections. The scientific founders, Dr. Michael McArthur and Professor Mervyn Bibb, hope to move to pre-clinical trials in 2009 with their first product, after which Procarta will work with pharmaceutical companies to bring it to market. Having established the proof of concept with vancomycin, Procarta plans to build a strong product pipeline by applying its proprietary technology to reinvigorate the use of a broad range of valuable antibiotics. "We are extremely excited about the promise of Procarta's technology, targeting as it does one of the most significant issues to hit the public healthcare system in the 21st Century," said a spokesman for IcenI.

Procarta Biosystems will be moving its operations to the Norwich Bioincubator on 1st July 2008 and has also recently appointed Dr Nigel Crockett as Commercial Director. Dr Crockett has over 15 years of experience in the Pharma-biotech sector, especially in early stage R&D collaborations and licensing.

> **AVMA Testifies On Antimicrobial Resistance Before Senate Committee**

Medical News Today, 26 June 2008

The American Veterinary Medical Association (AVMA) testified before the U.S. Senate Committee on Health, Education, Labor and Pensions, addressing the preventative use of antimicrobials in food animals and reiterating the necessity of antibiotic use in livestock for ensuring food safety. Dr. Lyle P. Vogel, AVMA's assistant executive vice president, testified at the hearing, which focused on the emergence of antimicrobial-resistant "superbugs" in humans. Mollifying concerns that use of antimicrobials - such as penicillin and tetracycline - in food animals leads to human resistance of the drugs, Vogel made clear that protecting human health is paramount to America's veterinarians. "Because veterinarians are ethically charged with promoting public health in addition to protecting animal health and welfare, we participate in the prevention of both human and animal disease," Vogel told the committee. Vogel stated that scientific data does not support a ban on the preventative use of antibiotics in food animals. Evidence suggests, he noted, that when livestock are not given antimicrobials as prevention for disease - as has happened in Denmark since the 1990s - an increase in illnesses is likely to occur. "Risk assessments demonstrate a very low risk to human health from the use of antimicrobials in food animals, and some models predict an increased human health burden if the use is withdrawn," Vogel testified. "Non-risk based bans of approved uses of antimicrobials will negatively impact animal health and welfare without predictably improving public health." Antibiotic

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resistance in some instances, he added, is ten times greater in Denmark than in the United States despite the Danish ban. Vogel told the committee that the Food & Drug Administration's evaluations of antibiotics used in livestock are more stringent than for human antibiotics. The FDA evaluates each food animal antibiotic for human, environmental and animal safety, and additionally, public and private surveillance systems monitor the use of the drugs for the emergence of antibiotic resistance.

The AVMA's written testimony and information about the issue will be posted on the AVMA's food safety advocacy web site, <http://www.keepourfoodsafesite.org>.



Immediate Action Taken On Healthcare Commission Improvement Notice - Hospital Acquired Infections Continue To Fall At Ashford & St. Peter's Hospitals

Medical News Today, 25 June 2008

"The Healthcare Commission have an important role to play in ensuring high standards and we welcomed and cooperated fully with their inspection of both Ashford and St. Peter's Hospitals on 5th and 6th June," says Ashford and St. Peter's Chief Executive, Paul Bentley. "Whilst the initial feedback we received from the visit was positive we were concerned to learn on the afternoon of 13th June that an improvement notice was to be issued in respect of a special pressure relieving 'air' mattress decontamination room and a risk assessment on a bench top steriliser, at Ashford Hospital. Acknowledging these observations we have already taken action to start to resolve these issues including the immediate closure on the evening of 13th June of the small decontamination room." Ashford and St. Peter's is a 534 bed hospital service with 66 beds on the Ashford Hospital site. Ordinary mattresses used for the majority of patients are cleaned on the wards and are not affected by the improvement notice. The small mattress decontamination room at Ashford Hospital, mentioned in the improvement notice, was used to hand clean two or three special pressure relieving 'air' mattresses per week. Due to the nature of services at Ashford Hospital the turnover on these special pressure relieving 'air' mattresses is small and does not impact on the delivery of clinical services. Mattress decontamination at St. Peter's Hospital is entirely separate and is not identified in the improvement notice. Patient services at both Ashford and St. Peter's have not been affected by the closure of the small decontamination facility at Ashford. Mr Bentley continued: "I have asked our Deputy Chief Executive and Medical Director, Dr Mike Baxter, to urgently review the issues raised by the Healthcare Commission. I know that this news may be of concern to our patients. However Dr Baxter and I can reassure patients and the public that both Ashford and St. Peter's are hospitals where we strive to ensure safety and reduce risks. We are not aware that any of our patients who used the special pressure relieving air mattresses or the bench top steriliser have been adversely affected by the issues raised by the Healthcare Commission. Indeed our falling rates of hospital acquired infections are a good indicator of this." The rate of MRSA bacteraemia at Ashford and St. Peter's has fallen to such an extent that the Trust now has the lowest rate in Surrey and levels of *C. difficile* have fallen significantly since July 2007 but can be driven down further. In 2007/08 there were a total of 15 cases of MRSA bacteraemia - less than half the number of cases in 2006/07. Of these 15 cases 7 (47%) were admitted from the community with MRSA including one from a hospital abroad. In January to March 2008 there were 68 cases of *C. difficile*. This compares to 94 cases in October to December 2007 and 123 cases July to September 2007. These include inpatients and community cases and *C. difficile* remains a national problem with rates increasingly significantly when areas are affected by Norovirus. Initiatives introduced by the Infection Control Team at both Ashford and St. Peter's Hospitals to combat Healthcare Acquired Infections (HCAs) include:

- 'Clean Your Hands' campaign with gel dispensing machines and signage placed at entrances throughout both hospital sites
- 'talking frames' near ward and clinical areas which are activated by movement and remind people to cleanse their hands;
- introduction of the Microfibre cleaning system at Ashford Hospital;
- a review of Antibiotic prescribing guidelines and employment of a dedicated antibiotics pharmacist;

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- a review of the widely used Infection Control Manual and the introduction of Infection Control 'outbreak packs' to wards and clinical areas enabling them to quickly implement additional infection control measures when they are needed.

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> **MRSA Incidence Reduced By Better Hand Hygiene**

Medical News Today, 2 June 2008

New hand hygiene programs in Victorian hospitals have led to marked reductions in infections with methicillin-resistant *Staphylococcus aureus* (MRSA), according to a research article published in the latest issue of the *Medical Journal of Australia*. Professor Lindsay Grayson, from the Department of Medicine at Austin Hospital and University of Melbourne, and his co-authors carried out a two-year pilot program using alcohol-based hand rub solutions (ABHRs) in six Victorian health care institutions. After the pilot program, the hand hygiene culture-change program was implemented throughout Victorian public hospitals over a 12-month period. Mean hand hygiene compliance improved significantly at all pilot program sites - from 21 per cent to 48 per cent at the end of the two-year trial. A similar change in hand hygiene compliance occurred over the 12 months of the statewide program. In both the pilot program and in the statewide rollout, the number of patients with MRSA in the blood more than halved. "This appears to be possibly the single most effective initiative to addressing the current problems with MRSA in our hospitals", state the authors. The study dispels previous doubts about whether hand hygiene programs could be effectively introduced as a statewide policy initiative. The authors believe their data clearly demonstrate that generic multi-site hand hygiene culture-change programs can be highly effective if they are carefully planned and implemented. "Long-term sustainability of improved hand hygiene compliance is likely to require that such programs become a permanent feature of how each hospital does business," say the authors. "Infection Control needs to become everyone's business, not just hospitals".

> **A Milestone In The Fight Against MRSA Is Reached With Antibiotic Impregnated Catheters**

Medical News Today, 2 June 2008

Data presented at a conference in America shows that catheters impregnated with the antibiotics minocycline and rifampin not only reduce the risk of bacteraemia (the presence of bacteria in the blood), but also the likelihood of bacteria developing antibiotic resistance. This research has very positive implications for those fighting the spread of healthcare associated infections (HAIs) - which affect at least 100,000 people a year in the UK and cost the NHS in the region of £1,000 million.[1] Dr Duncan Wyncoll, a Consultant Intensivist in London believes that the findings will be of significant interest to doctors in the UK. He said: "It is very reassuring that resistance doesn't increase with long term use of the antibiotic impregnated catheters. It is also great to see such a long term and sustained decrease in catheter related bloodstream infection (CRBSI) rates with use of these catheters. "Bloodstream infections are the fourth most common healthcare associated infection in the UK, and over 60 percent of these infections occur as a result of the use of catheters, intravenous feeding lines or similar devices. This is a significant step forward in the fight against healthcare associated infections." Previously, some medical researchers had expressed concern that the use of these devices could promote antimicrobial resistance. However, Issam I. Raad, M.D., an infectious disease expert at the University of Texas M.D. Anderson Cancer Centre, presented this data that disputes this perception at the Society of Healthcare Epidemiology of America's annual conference. The research demonstrates that after seven years of extensive use of central venous catheters impregnated with minocycline and rifampin, the rate of microbial resistance to minocycline and rifampin actually decreased after use of these catheters. Charles McIntosh, M.D., chief medical science and technology officer for Cook Group, which manufactures the minocycline/rifampin catheter, explains how this decrease in resistance has come about: "This study is proof of the well known concept that to reduce the amount of resistant bacterial strains one must decrease antibiotic use throughout the treatment pathway and beyond. It is through overuse of antibiotics that bacteria have had the opportunity to develop resistance. "In this study Cook's minocycline and rifampin impregnated catheter reduced blood stream infection rates by a factor of 12 over a seven year period compared with catheters simply coated with antiseptic or invasive agents. By reducing the incidence of CRBSIs, the need for systemic

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antibiotics like vancomycin is reduced. Thus in this study the levels of resistant MRSA strains decreased after to a long term reduction in antibiotic use. "

Data Explained: In his presentation, Dr. Raad noted that after more than 500,000 catheter-days using the antibiotic-impregnated catheter, the rate of resistance to tetracyclines (the 'family' of antibiotics, which minocycline belongs to) and rifampin dramatically decreased. The data demonstrated that the percentage of MRSA resistance to tetracycline decreased from 12 to 7 percent and MRSA resistance to rifampin decreased from 12 to 4 percent ($P < 0.01$). Dr. Raad is the co-inventor of the synergistic pairing of the antibiotics minocycline and rifampin that are impregnated within the catheter material of the Cook Spectrum® catheter. His institution receives a royalty payment based upon Cook's licence to use this patented technology.

Notes: The Society of Healthcare Epidemiology of America held its 18th annual conference from April 5th - 8th in Florida, US. For further information, please visit <http://www.shea-online.org>.

> **Prevention of the spread of infection – the need for a family-centred approach to hygiene promotion**

S. Bloomfield et al, Eurosurveillance, Volume 13, Issue 22, 29 May 2008

Infectious diseases circulating in the home and community are a continuing and significant burden on the health and prosperity of the European community. They could, however, be significantly reduced by better standards of hygiene. Across Europe, public health is currently structured such that the separate aspects of hygiene in different settings (food hygiene, personal hygiene, handwashing, pandemic flu preparedness, patient empowerment etc.) are dealt with by separate agencies. If efforts to promote hygiene at community level are to be successful in changing behaviour, we need a concerted family-centred approach to ensure that a basic understanding of infectious disease agents and their mechanisms of spread, together with an understanding of a risk-based approach to hygiene, are promoted as part of the school curriculum and as part of public health campaigns. Alongside this, we also need unambiguous communication with the public on issues such as the hygiene hypothesis and environmental issues.

> **First cases of Clostridium difficile PCR ribotype 027 acquired in Austria**

A. Indra et al, Eurosurveillance, Volume 13, Issue 20, 15 May 2008

In Austria, *Clostridium difficile* is the leading cause of community-acquired bacterial diarrheal illness and the most frequently identified cause of hospital-acquired diarrhea [1]. It is the causative agent of pseudomembranous colitis. A new emerging hypervirulent strain of *C. difficile* – PCR ribotype 027 – causes more severe disease and is associated with a higher case-fatality-ratio than other types [2]. This increased virulence is associated with two deletions in a toxin regulator gene resulting in hyperproduction of toxins A and B. The incidence of *C. difficile*-associated disease (CDAD) due to type 027 is increasing in the United States, Canada, Asia and Europe [2,3,4,5,6]. In Austria, *C. difficile* type 027 has so far only been discovered once, in a British tourist with pseudomembranous colitis in 2006 [7]. In April 2008, *C. difficile* PCR ribotype 027 was found in two cases of *C. difficile*-associated disease affecting Austrian citizens treated in hospitals in Vienna and Graz, Austria.

> **Molecular typing for public health purposes**

A Ammon, Eurosurveillance, Volume 13, Issue 19, 08 May 2008

In this issue, seven networks/projects are presented that are dedicated to the molecular typing of bacteria (SeqNet: *Staphylococcus aureus*; MLVA-Net: *Salmonella Typhimurium*, *Enterobacter sakazakii*, *Listeria monocytogenes*; HARMONY: *Staphylococcus aureus*; DIPNET: *Corynebacterium diphtheriae*) or viruses (HepSEQ: hepatitis B virus; FBVE: noroviruses and other gastrointestinal viruses; MeaNS: measles). They represent only a few of an increasing number of typing networks.

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However, they illustrate a couple of relevant issues that need to be considered before implementing these methods for different public health purposes.

Other articles of interest:

- HARMONY – the International Union of Microbiology Societies' European Staphylococcal Typing Network B Cookson et al.
- A European laboratory network for sequence-based typing of methicillin-resistant Staphylococcus aureus (MRSA) as a communication platform between human and veterinary medicine – an update on SeqNet.org AW Friedrich et al.
- MLVA-NET – a standardised web database for bacterial genotyping and surveillance G Guigon et al.
- Development of an online database for diphtheria molecular epidemiology under the remit of the DIPNET project T Dallman et al.
- On-line Global/WHO-European Regional Measles Nucleotide Surveillance S Gnaneshan et al.
- HepSEQ – an Integrated Hepatitis B Epidemiology and Sequence Analysis Platform R Myers et al.
- Typing database for noroviruses E Duizer et al.
- EFSA launches public consultation on food-borne antimicrobial resistance as a biological hazard Eurosurveillance editorial team

> C. Difficile: Advances In Research

Medical News Today, 3 June 2008

New research into the toxins, virulence, spread and prevention of the superbug *Clostridium difficile* is reported in the June special issue of the Journal of Medical Microbiology. These findings will play a crucial role in providing us with ammunition in the fight against a sometimes deadly pathogen. *Clostridium difficile* is found in the environment but is most common in hospitals. It can cause a serious hospital-acquired infection when antibiotics are used as they upset the balance of the normal gut flora, allowing *C. difficile* to grow and produce toxins. It is carried in the guts of 3% of healthy humans but carriage rates in hospital patients tend to be much higher and elderly people in hospitals, being treated with antibiotics are most at risk of developing infection. The bacteria produce spores when they encounter unfavourable conditions. Transmission of infection is through the ingestion of these spores which can survive on surfaces and floors for years and are resistant to many disinfectants and antiseptics, including alcohol hand gel. Symptoms include diarrhoea, nausea, abdominal pain, loss of appetite, fever, bowel inflammation and possible perforation, which can be fatal. Only two antibiotics are regularly used to treat *C. difficile* infection: metronidazole and vancomycin, but relapse is a common problem following treatment. In 2004, a hypervirulent strain (*C. difficile* 027/NAP1/BI) was reported, which appears to make toxins more rapidly and at higher levels than other strains, as well as being resistant to many antibiotics, including fluoroquinolones. Several studies in the Journal of Medical Microbiology look at the spread of *C. difficile* in different countries, including Austria and Korea. Research shows that the use of antibiotic increased the risk of outbreaks of the hypervirulent strain of *C. difficile* in the Netherlands. The issue also contains evidence to suggest that *C. difficile* could be spread between animals and humans - researchers have isolated the bacterium from food animals in Slovenia. Scientists investigated the effects of antibiotics, antigens and other agents on the virulence and pathogenicity of *C. difficile*. Toxins were also studied; research reveals some important information about the synthesis, processing and effects of different toxins. A new gene sequence has been discovered in the hypervirulent *C. difficile* 027 strain, which could be related to its increased virulence by affecting toxin binding. The potential for a 'designer' probiotic for *C. difficile* is discussed. Professor Ian Poxton, former Editor-in-Chief of the Journal of Medical Microbiology said "this is an important approach that is hopefully much better than previously reported studies using commercially available yoghurt-like drinks, and certainly more palatable than 'faecal transplants'."

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> **MRSA Survives On Antibacterial Wipes Used In Hospitals, And Can Be Spread By Them**

Medical News Today, 4 June 2008

Antibacterial wipes are supposed to kill bacteria. However, the Welsh School of Pharmacy has found that MRSA (superbug) survive in many antibacterial wipes - the wipes themselves can then contaminate anything that comes into contact with them. It is crucial, say the researchers, that the wipes are thrown away after one clean. Dr. Gareth Williams, a microbiologist at the Welsh School of Pharmacy, says it is more important to focus on the dirt and debris bacteria thrive on, than to kill them instantly wherever they might be. Dr. Williams presented the research findings at the American Society of Microbiology's Annual Meeting, Boston, USA. The team found that it is not uncommon for hospital staff to clean more than one surface with the same wipe. Dr. Williams explained that staff would wipe one thing, perhaps a bed rail, and then move on to several other surfaces (with the same wipe). The researchers went back to the laboratory to see how different wipes performed under these conditions. They found that the wipes were good at taking bacteria away from the first surface - but the bacteria did not die quickly. Subsequent cleaning with the same wipe resulted in contamination. "What is remarkable is that some of these wipes actually have the words 'kills MRSA' written on the box. We found that, under the conditions we observed in actual hospitals, this wasn't the case," said Dr. Williams. Even if a wipe is advertised as antibacterial, Dr. Williams stresses that a wipe should only be used for one surface clean, and then discarded - it should never be used for further cleaning.

> **FDA Lowers Vancomycin Breakpoints for Staph Infections**

IDSA News, Volume 18, Number 5, May 2008

The Food and Drug Administration (FDA) has lowered the breakpoints for vancomycin in the treatment of *Staphylococcus aureus* to reflect growing rates of resistance, and in response to urging from IDSA and others.

According to a recently updated package insert for Baxter Healthcare Corporation's vancomycin injection in GALAXY plastic containers, the susceptibility test interpretive criteria for *S. aureus* have been changed as follows:

	Minimum Inhibitory Concentration (MIC) (µg/mL)		
	Susceptible (S)	Intermediate (I)	Resistant (R)
Updated	≤2	4-8	≥16
Previous	≤4	8-16	≥32

The breakpoints for other infections remain unchanged.

Clinicians are encouraged to make sure that clinical microbiology laboratories with which they are associated are using the revised vancomycin susceptibility breakpoints for *S. aureus*.

The change follows mounting evidence that patients infected with *S. aureus* strains with MIC of 4 µg/mL were failing therapy. Robert C. Moellering, Jr., MD, FIDSA, past president of IDSA, and Fred C. Tenover, PhD, FIDSA, published a "Viewpoints" article in the May 1, 2007 issue of *Clinical Infectious Diseases* detailing the rationale for lowering the breakpoints. The article was based on data Dr. Tenover had collected and presented to the Clinical and Laboratory Standards Institute (CLSI), which updated its breakpoints last year and submitted a "Citizens' Petition" to FDA advising the agency to do the same.

For years, IDSA has been urging FDA to update breakpoints for key antimicrobials and backed legislation passed last fall requiring the agency to do so. This is the second time in recent months that FDA has updated breakpoints for a major antibiotic and suggests a new willingness on the part of the agency to modify these important benchmarks.

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> **Antibiotics May Prevent Catheter-related Bloodstream Infections—But Use Caution**

Sara E. Cosgrove, MD, MS - IDSA News, Volume 18, Number 5, May 2008

Both topical and intraluminal antibiotics helped prevent catheter-related bloodstream infection (CR-BSI) among hemodialysis patients in a meta-analysis published in the April 15 issue of *Annals of Internal Medicine*, but it may be too soon to consider changing practice. Mupirocin or polysporin triple-antibiotic ointment at the catheter insertion site decreased CR-BSI, *Staphylococcus aureus* bacteremia, and exit site infections compared to no ointment in three pooled studies. Use of intraluminal antibiotics (or “antibiotic lock therapy”), in which antibiotic solutions are placed in the lumen of the catheter between dialysis sessions, decreased CR-BSI but not *S. aureus* bacteremia or exit site infections compared to no antibiotics in 11 pooled studies; gentamicin was the most commonly studied agent. However, some additional factors should be considered before changing practice in this area. First, several of the studies included in the meta-analysis were small and unblinded, and use of meta-analysis cannot compensate for flaws in individual studies. Second, rates of emergence of resistance—always a serious concern—were not evaluated. Non-antimicrobial alternatives are available, such as povidone-iodine antiseptic at exit sites, which is recommended in the current IDSA guidelines for prevention of catheter-related infections. At this point, use of topical and intraluminal antibiotics should likely be reserved for patients with recurrent CR-BSIs who have limited options for vascular access. (James et al., *Ann Intern Med.* 2008;148:596-605.)

> **IDSA Urges FDA to Dedicate Resources to Antimicrobial Resistance**

IDSA News, Volume 18, Number 5, May 2008

IDSA presented testimony* to a US Food and Drug Administration (FDA) panel on April 28 to address the increasingly troublesome issue of antimicrobial resistance. FDA’s hearing is a promising sign that the agency is moving forward to address antimicrobial policy issues after years of delays.

In their testimony, John G. Bartlett, MD, FIDSA, chair of IDSA’s Antimicrobial Availability Task Force, Neil Fishman, MD, chair of the Society’s Antimicrobial Resistance Work Group, and Robert Guidos, IDSA’s director of public policy and government relations, warned of a potential impending health crisis due to decreases in research and development, impediments and uncertainty in FDA’s antibacterial drug review process, and the lack of federal funding and attention paid to this important medical/public health problem. They set forth numerous recommendations aimed at reducing the impact of antimicrobial resistance on the public and galvanizing the development of new products to address the increase in antibacterial resistant infections.

The Society called for reestablishing consistency, predictability, and timeliness in FDA’s antibacterial drug review process while providing economic and other incentives to spur the development of new antibacterial products. IDSA called upon FDA to commission a study to determine which incentives might work best.

IDSA also supports the creation of a strategic research plan for antimicrobial resistance to establish priorities and strengthen collaborations between FDA, the National Institutes of Health, the Centers for Disease Control and Prevention, the Departments of Agriculture, Veteran Affairs, and Defense, and the Environmental Protection Administration. IDSA also proposes improving data collection on clinical, veterinary, and human antibacterial use.

Improving surveillance efforts to detect and monitor the emergence of resistance is especially crucial given the diminishing numbers of antibacterial drugs, IDSA leaders said.

Other solutions proposed by the Society include educating physicians and patients about the appropriate use of antibacterial drugs and preventing antibiotics of critical consequence to human health from being used in agriculture, as well as developing better options for antibacterial drug use in animals and agriculture.

In December 2000, FDA’s Task Force on Antimicrobial Resistance issued a report** containing priority recommendations the agency was to implement to address the antimicrobial resistance and pipeline problems. Few of these recommendations have been implemented to date. Such past inaction on

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FDA's part has raised questions about the agency's commitment to address the brewing antimicrobial resistance crisis—a problem that infectious diseases physicians believe should be a significant priority of the U.S. government.

"IDSA leaders hope that the hearing signals a turning point in FDA's level of commitment and a demonstration of agency leaders' desire to tackle these critical patient safety and public health problems," Guidos said. "To confirm this, FDA should act immediately to dedicate the resources and staff time necessary to implement the recommendations of its own task force as well as the recommendations that IDSA has proposed."

*Available at: <http://www.idsociety.org/WorkArea/showcontent.aspx?id=11150&LangType=1033>

** FDA Task Force on Antimicrobial Resistance: Key Recommendations and Report (December 2000) can be downloaded at: <http://www.fda.gov/oc/antimicrobial/taskforce2000.html>

> **Zysolin Shows Promising Results in Animal Study**

PR Newswire, June 3, 2008

AlphaRx's specially-formulated Tobramycin nanoparticles increase survival rate in mice infected with Gram negative *Pseudomonas Aeruginosa*, suggesting Zysolin has potential in the treatment of Cystic Fibrosis and Gram-negative pneumonia. ARKHAM, ON, June 3 /PRNewswire-FirstCall/ -- AlphaRx (OTC BB:ALRX) is pleased to announce pre-clinical data on Zysolin(TM), a Tobramycin compound encapsulated in the company's Nano Drug Delivery Platform intended for the treatment of Cystic Fibrosis and an adjunctive treatment of Gram-negative pneumonia in intubated and mechanically-ventilated patients. In the recent animal study, the therapeutic efficacy of Zysolin was investigated in a mouse model of *Pseudomonas aeruginosa* pneumonia. In this acute model, pneumonia developed rapidly, resulting in a high mortality rate, no mice survived after 24 hours of infection without treatment. Mice treated with Zysolin(TM) showed significantly better efficacy than Tobramycin, achieving 60% survival rate vs. 40% in the Tobramycin treatment group. An increase of survival by 50% or more, relative to vehicle control, indicates significant anti-microbial effect. The Tobramycin treatment group did not meet the study's end point.

> **Community-Acquired Pneumonia In The Elderly: Every Tenth Patient Dies In Western Countries**

Medical News Today, 29 June 2008

Community-acquired pneumonia (CAP) represents a public health problem of substantial magnitude, and remains the leading cause of death due to infectious diseases, with an incidence ranging from 1.6 to 10.6 per 1,000 adults per year in Europe. Owing to demographic changes, elderly patients now represent about 50% of CAP patients in western countries. Considering that there is much discrepancy in the literature regarding factors influencing the outcome in this subgroup, a prospective study undertaken by Henning Kothe (University of Lübeck, Germany) and his colleagues was conducted to assess the prognostic factors of CAP with a special emphasis on age, residence status, comorbidities and antimicrobial treatment. The data were derived from a multicentre cohort study initiated by the German Competence network for CAP (CAPNETZ; <http://www.capnetz.de>), which includes 10 clinical centres (hospitals and outpatient facilities from all levels of healthcare). The authors evaluated 2,647 patients (1,298 < 65 years, 1,349 > 65 years) with CAP. A total of 72.3% were hospitalised, and 27.7% were treated in the community. Clinical history, residence status, course of disease, microbiological findings and antimicrobial treatment were prospectively documented. Factors related to mortality were included in multivariate analysis. The study shows that 30-day mortality is 6.3% and that elderly patients have a significantly higher mortality rate (10.3% in patients >65 years old). The following factors are independently associated with death: age, living in a nursing home, the CURB severity score, comorbidities and failure of antibiotic therapy. Nursing home

residents have a four-fold increase in mortality rate, a higher CURB score and an increased rate of Gram-negative infections, when compared to community dwellers from the same age group. The authors conclude that age and residence status are independent risk factors for mortality after controlling for comorbidities and disease severity. Failure of initial therapy was the only prognostic factor that can be modified by an optimised management of disease. The risk factors described in this study may help to better define CAP patients with increased mortality risk who require special attention during the course of disease. This seems to be of particular importance because of the demographic changes in western countries with an increasing proportion of elderly patients and nursing home residents.

Title Of The Original Article *Outcome of community-acquired pneumonia: influence of age, residence status and antimicrobial treatment*

> Hidden Areas Of Infection In U.S. Hospitals

Medical News Today, 28 June 2008

Health care facilities in the U.S. are entering a new era of "zero tolerance" for healthcare-associated infections (HAI). Could there be hidden areas of infection that are being overlooked? A new public health education program from the production company Mission Critical attempts to answer that question. The program, entitled "Hidden Areas of Infection," (<http://www.missioncriticaltv.com/index-8-1.html>) documents how an acute care facility in Virginia is solving this enormous infection control problem through planning, education, and the right equipment -- including the widespread use of disposable products. Prime targets for disposable technologies are reusable products that see use on thousands of different patients, which can dramatically increase the risk of cross-contamination. Examples include blood pressure cuffs, pulse oximetry sensors, and electrocardiogram (ECG) wires. Public awareness of the HAI epidemic is growing, helped by advocacy groups such as the non-profit Committee to Reduce Infection Deaths (RID). Dr. Betsy McCaughy, the former Lt. Governor of New York, founded this group in response to a stunning statistic: Annual deaths from hospital infections in the U.S. -- some 103,000 deaths per year -- exceed the death toll from AIDS, breast cancer, and auto accidents combined (<http://www.hospitalinfection.org>). In addition to the moral imperative, hospitals will soon have another compelling incentive to reduce infection rates -- one that affects their bottom lines and reputations. In October 2008, the Centers for Medicare and Medicaid Services (CMS) will begin limiting reimbursements for certain infections as part of the HAI zero tolerance mandate. Through these and other actions, Congress hopes to create greater transparency around HAI events, including making hospital infection data available to the public. It is hoped that the end result will be a reduction in the number of HAIs as hospitals commit larger resources to combat the problem, which could also save taxpayers millions of dollars. This documentary program from Mission Critical sheds light on long-overlooked practices that have been taken for granted by many in the health care community, until now. One of these practices is the implementation of strict cleaning protocols meant to reduce infection risks from reusable devices. However, as the program points out, cleaning procedures alone do not ensure the elimination of harmful pathogens. There is evidence, for example, that reusable ECG lead wires could be a significant hidden reservoir for the microorganisms that are now running rampant in U.S. health care facilities, despite the presence of cleaning procedures. In fact, one study conducted at the University of Wisconsin found that over 77% of reusable ECG lead wires tested harbored some strain of potentially deadly antibiotic-resistant pathogen after they had been cleaned.(1) Inevitably, the cost of disposable devices needs to be weighed against the benefits. Fortunately, the experience of Bon Secours St. Francis Hospital in Richmond, Virginia offers proof that the strategic use of disposable monitoring accessories, along with a comprehensive infection reduction program, can dramatically reduce not only cross-contamination risks, but also costs.(2) It is hoped that educational programs such as "Hidden Areas of Infection" can continue to raise public awareness of this important issue and help hospitals prepare for potentially reduced CMS reimbursements related to hospital-acquired infections. As many health care providers are beginning to realize, reaching for "zero" infections is not only attainable, it is also cost-effective. The Hidden Areas of Infection program will be broadcast into 89,000 hospitals in 88 countries within the next month. The Medical Broadcasting Channel reaches an estimated 14 million nurses, 9 million physicians, and an additional 5 million healthcare workers such as administrators and pharmacy.

References: (1) Jancin, B. (2004, March). Antibiotic-resistant pathogens found on 77% of ECG lead wires. *Cardiology News*. vol 2. (2) Holden, D. (Project Manager). (2008, March). Hidden Areas of Infection [DVD]. Mission Critical: Capital Media Group; LS-954 - Bon Secours mentioned in DVD video.

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> **MRSA Worsened By Hospital Overcrowding And Understaffing**

Medical News Today, 24 June 2008

A review published in *The Lancet Infectious Diseases* finds that the inability to control the meticillin-resistant *Staphylococcus aureus* (MRSA, or "super-bug") is partly due to hospital overcrowding and understaffing. Dr. Archie Clements (School of Population Health, University of Queensland, Australia) and colleagues argue that a vicious cycle continues with increased inpatient hospital stays, bed-blocking, and further failure to control the infection. In high income countries, efficiency and cost-cutting measures have changed the structure of health-care systems. Australia has seen a decrease of 40% in public hospital beds per head, but a 20% increase in patient throughput (from 1982 to 2000) and a 14% increase the total number of patients treated (from 1995 to 2000). Most of these changes are the product of same-day admissions and discharges. The outpatient movement has also affected the UK, USA, and Canada, countries which have reported a decline in inpatients relative to outpatients. A higher rate of patient admissions in the UK coupled with bed reductions has resulted in 71% of health trusts surpassing the 82% target set by the government. "The drive towards greater efficiency by reducing the number of hospital beds and increasing patient throughput has led to highly stressed health-care systems with unwelcome side-effects," write the authors. Clements and colleagues also predict a worsening of conditions in high-income countries due to population growth and aging. In addition, the health-care workforce is reducing in these countries as fewer people select nursing as a career. The nursing supply is also getting older: the average age of nurses in the USA in 1983 was 37.4 and in 2004 was 46.8. The researchers add that, "Understaffing is both an ongoing and long-term future problem with severe consequences for hospital patients." The relationship between infection rates and health-care worker to patient ratios is quite clear. According to one analysis, over 25% of health-care-acquired infection (HAI) in intensive care units could have been prevented if hospitals had at or below 2.2 patients per health-care worker. Additional papers have revealed that increases in HAIs have moderated any cost-benefits gained from re-designing the workforce using agency staff or having fewer full-time staff. In order to reduce the spreading of MRSA, it is necessary for hospital staff to frequently wash their hands. Handwashing compliance, according to several studies, is low among nurses and even worse among doctors. When staff is short and workloads are high, compliance is further reduced. Hospitals try other methods of controlling MRSA, such as isolating infected patients or grouping them by cohorts who are treated by specific health-care workers; however, these strategies fail because of the same reasons: overcrowding and understaffing. The presence of MRSA infected patients, who usually have extended hospital stays, results in fewer beds available for new admissions and puts additional stress on both the affected wards and the wards to which new patients are sent. Sometimes the number of MRSA patients exceeds isolation capacities and "bed-blocking" occurs - when multi-bed rooms are used for isolation prohibiting the use of both occupied and unoccupied beds. "MRSA also contributes directly to staffing deficits when health-care workers are excluded as a result of colonisation, detected via routine or outbreak screening," indicate the authors. Problems can become nearly unmanageable as outbreaks overload hospital staff. Patients staying longer and becoming severely ill substantially increase the workloads of nurses involved in HAI management. In order to control, prevent, and reduce MRSA outbreaks, cost-effective infection control strategies at the national level must be implemented. Successful programs have resulted in low rates in The Netherlands and Scandinavia and a decline or at least stabilization in Australia and the UK. "Although the burden of HIA is enormous," write Clements and colleagues, "it has been estimated that 15-32% of cases can be prevented and economic losses reduced." "Overcrowding and understaffing have had a negative effect on patient safety and quality of care, evidenced by the flourishing of health-care-acquired MRSA infections in many countries, despite efforts to control and prevent these infections occurring... There is an urgent need for detailed study of the relative effects of acute short-term and chronic long-term resource constraints on the dynamics of MRSA infection and a concurrent requirement for developing resource allocation strategies that minimise MRSA transmission without compromising the quality and level of patient care," conclude the authors.

Ref: **Overcrowding and understaffing in modern health-care systems: key determinants in**

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meticillin-resistant Staphylococcus aureus transmission Archie Clements, Kate Halton, Nicholas Graves, Anthony Pettitt, Anthony Morton, David Looke, Michael Whitby - *The Lancet Infectious Diseases* (2008); 8: 427-34

> **Relationship between Vancomycin MIC and Failure among Patients with MRSA Bacteremia Treated with Vancomycin.**

Lodise TP et al, Antimicrob Agents Chemother. 2008 Jun 30

There is a growing concern that vancomycin has diminished activity for MRSA with vancomycin MIC values at the high end of the CLSI susceptibility range. Despite this growing concern, there are limited clinical data to support this notion. To better elucidate this, a retrospective cohort study was conducted among patients with MRSA bloodstream infection who were treated with vancomycin between 01/2005 and 5/2007. The inclusion criteria were: age ≥ 18 years old, non-neutropenic, MRSA culture met CDC criteria for bloodstream infection, received vancomycin therapy within 48 hours of index blood culture, and survived > 24 hours after vancomycin administration. Failure was defined as 30-day mortality, bacteremia ≥ 10 days on vancomycin therapy, or recurrence of MRSA bacteremia within 60 days of vancomycin discontinuation. Classification and regression tree (CART) analysis identified the vancomycin MIC breakpoint associated with an increased probability of failure. During the study period, 92 patients met the inclusion criteria. The vancomycin MIC value breakpoint derived by CART analysis was ≥ 1.5 mg/L. The 66 patients with a vancomycin MIC value ≥ 1.5 mg/L had a 2.4-fold increase in failure compared to patients with an MIC value ≤ 1.0 mg/L (36.4% and 15.4%, respectively, $p=0.049$). In the poisson regression, vancomycin MIC value ≥ 1.5 mg/L was the independently associated with failure (Adjusted risk ratio 2.7, 95% CI: 1.3- 5.7, $p=0.008$). These data strongly suggest that patients with MRSA bloodstream infections with vancomycin MIC values ≥ 1.5 mg/L respond poorly to vancomycin. Alternative anti-MRSA therapies should be considered for these patients.

> **Screening for Carriage of Methicillin-Resistant Staphylococcus aureus Shortly After Exposure May Lead to False-Negative Results.**

Evison J and Mühlemann K., Infect Control Hosp Epidemiol. 2008 Jun 30

We evaluated a double screening strategy for carriage of methicillin-resistant Staphylococcus aureus (MRSA) in patients exposed to a newly detected MRSA carrier. If the first screening of the exposed patient yielded negative results, screening was repeated 4 days later. This strategy detected 12 (28%) of the 43 new MRSA carriers identified during the study period. The results suggest that there is an incubation period before MRSA carriage is detectable.

> **[Trends in Staphylococcus aureus antimicrobials susceptibilities: Is methicillin still a relevant multiresistance marker?]**

Grohs P., Pathol Biol (Paris). 2008 Jun 27 - [Article in French]

OBJECTIVE: Recent change was noted in S. aureus epidemiology, especially for none multiresistant methicillin-resistant S. aureus (MRSA) and for multiresistant methicillin-susceptible S. aureus (MSSA). So, a six-year retrospective study was conducted to follow trends in antimicrobials resistance and to determine if methicillin remained a relevant multiresistant marker. METHODS: All S. aureus isolates (duplicates excluded) isolated between 2001 and 2006 in a French 800-beds-teaching-hospital were included in the study. RESULTS: Four thousand four hundred and fifty-five isolates providing from 3602 patients were identified between 2001 and 2006. MRSA rate and incidence for 1000 hospitalization-days significantly decreased from 34.7 to 22.6% and 1.3 to 0.6% respectively ($p<0.001$). Significant decrease was observed for multiresistant MRSA (72.9 to 46.3%, $p<0.001$), while no change was observed for multiresistant MSSA (2.9 to 3.4%). Among the 186 different antibiotic patterns isolated, four MRSA-phenotypes significantly decreased whereas two MSSA-phenotypes

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significantly increased. The main MRSA phenotype, resistant to kanamycin, tobramycin, macrolides-lincosamides-streptograminsB, and fluoroquinolones, significantly decreased from 11.9 to 5.9% ($p < 0.001$). Glycopeptide Intermediate *S. aureus* (GISA) phenotypes disappeared. CONCLUSION: At this date, methicillin remains in our institution a relevant marker of multiresistance but trend is changing.

> **The role of virulence determinants in community-associated MRSA pathogenesis.**

Diep BA and Otto M., Trends Microbiol. 2008 Jun 26

The recent emergence of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) marked a quantum change in the biology and epidemiology of a major human pathogen. Various virulence determinants unique to CA-MRSA have been uncovered recently, which shed light on how these strains spread easily and sustainably among humans and frequently cause severe disease. The role of the Pantone Valentine leukocidin (PVL) in CA-MRSA pathogenesis is a matter of much debate. Although epidemiological data have indicated a role for PVL in the CA-MRSA disease process, recent data from relevant animal models indicate that PVL does not impact virulence of prevalent CA-MRSA strains. Identifying specialized pathogenic traits of CA-MRSA remains a challenge that will yield new diagnostic tools and therapeutic targets for drug and vaccine development. Here, we discuss the roles of PVL, the arginine catabolic mobile element and phenol-soluble modulins in the pathogenesis of prevalent CA-MRSA strains.

> **[Prevention of transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) infection: standard precautions instead of isolation : A 6-year surveillance in a University hospital.]**

Kappstein I, et al, Chirurg. 2008 Jun 20 - [Article in German]

BACKGROUND: This study was carried out to evaluate whether the risk of acquiring methicillin-resistant *Staphylococcus aureus* (MRSA) is increased compared to reference data when standard precautions are practiced instead of strict or contact isolation. METHODS: From 2000 through 2005, all patients with MRSA at a university hospital were prospectively surveyed. The isolates were investigated using molecular microbiology methods (PFGE, PCR) and compliance with hand hygiene was indirectly monitored using the consumption of disinfection solutions and glove use as surrogate markers. RESULTS: The MRSA rates of the 797 patients were lower than for the reference data (PEG, KISS), the incidence of MRSA infections was reduced continuously, MRSA transmissions to contact patients could be demonstrated in about 30%, and the consumption of hand disinfection solutions as well as gloves was significantly higher in 2005 compared to 2000. CONCLUSIONS: There is no evidence from our results that practicing standard precautions would increase the risk for the acquisition of MRSA compared to strict or contact isolation.

> ***Staphylococcus aureus* Nasal Colonization in Preoperative Orthopaedic Outpatients.**

Price CS et al, Clin Orthop Relat Res. 2008 Jun 19.

Nasal colonization with *Staphylococcus aureus* (SA) increases the risk of surgical site infection (SSI). We first (1) determined the prevalence of asymptomatic nasal colonization with SA, (2) assessed trends in methicillin resistance with time, (3) ascertained risk factors for nasal colonization; and (4) correlated SSI to nasal colonization status and procedure. We performed a cross-sectional analysis of SA nasal colonization among healthy preoperative orthopaedic outpatients between 2003-2005 who were within 2 weeks of surgery. Of 284 patients, 86 (30%) carried SA; of these, 81 (94%) were colonized with methicillin-sensitive and five (6%) with methicillin-resistant SA (MRSA). Total SA colonization increased from 25/78 (32%) in 2003 to 37/97 (38%) in 2005, and colonization with MRSA increased from 0/78 (0%) to four of 97 (4%), respectively. We found no associations between nasal carriage and demographics or procedures. Surgical site infection occurred in nine of 282 (3%), four of

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which were attributable to SA; these included 0/43 (0%) carriers who received decolonization with 2% mupirocin, two of 43 (4.7%) who declined decolonization, and two of 196 (1.0%) who were noncarriers. Nasal colonization with SA, including MRSA, among preoperative orthopaedic outpatients is increasing and their rates reflect community rates. Knowledge of colonization status may be important in decolonization, choosing perioperative or any subsequent empiric antibiotics.

> **Multidrug-Resistant Gram-Negative Bacteria in a Long-Term Care Facility: Prevalence and Risk Factors.**

Pop-Vicas A et al, J Am Geriatr Soc. 2008 Jun 16

OBJECTIVES: To quantify the prevalence, risk factors, and mode of transmission associated with colonization by multidrug-resistant gram-negative bacteria (MDRGN) in the long-term care (LTC) setting. **DESIGN:** Cross-sectional. **SETTING:** Four nursing units in a 648-bed LTC facility in Boston, Massachusetts. **PARTICIPANTS:** Eighty-four long-term care residents. **MEASUREMENTS:** Nasal and rectal swabs were obtained to determine colonization with MDRGN; if present, molecular typing was performed. The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) was also determined. Demographic and clinical characteristics were obtained from the medical record. Multivariable analysis was used to identify factors independently associated with MDRGN colonization. **RESULTS:** A total of 51%, 28%, and 4% subjects were colonized with MDRGN, MRSA, and VRE, respectively. After multivariable adjustment, advanced dementia (adjusted odds ratio (AOR)=2.9, 95% confidence interval (CI)=1.2-7.35, P=.02) and nonambulatory status (AOR=5.7, 95% CI=1.1-28.9, P=.04) were the only independent risk factors for harboring MDRGN. Molecular typing indicated person-to-person transmission. **CONCLUSION:** Colonization with MDRGN is common in the LTC setting. A diagnosis of advanced dementia is a major risk factor for harboring MDRGN.

> **Vancomycin MICs did not creep in *Staphylococcus aureus* isolates from 2002 to 2006 in a setting with low vancomycin usage.**

Alós JI et al, J Antimicrob Chemother. 2008 Jun 13

Objectives The aim of this study was to evaluate MIC trends for clinical isolates of *Staphylococcus aureus* to vancomycin over a 5 year period (2002-06) in a hospital in Spain. **Methods** All clinical isolates of *S. aureus* (one per patient) from clinical samples of patients at Hospital Universitario de Getafe from January 2002 to December 2006 were used. MICs of vancomycin were determined by the CLSI broth microdilution procedure. For analysis of MIC trends over the 5 years, we grouped the isolates into those with MIC ≤ 1 mg/L [2428 methicillin-susceptible *S. aureus* (MSSA) and 518 methicillin-resistant *S. aureus* (MRSA)] and those with MIC ≥ 2 mg/L (MIC = 2 mg/L: 141 MSSA and 47 MRSA; MIC = 4 mg/L: 5 MSSA and 1 MRSA). MICs for the different groups in the different years were compared with the linear-trend chi(2) test. **Results** A total of 3141 strains of *S. aureus* collected over the 5 year period was included in this analysis. Of these, 2574 (82%) strains were MSSA and 566 (18%) strains were MRSA. One of the 566 MRSA strains (0.18%) and 5 of the 2574 MSSA strains (0.19%) were vancomycin-intermediate (not significant). The rest were susceptible. The overall percentage of MRSA isolates with a vancomycin MIC of ≥ 2 mg/L was much higher than that of MSSA during the 5 year period [8.5% (48/566) versus 5.7% (146/2574); P = 0.012]. No statistically significant change in the percentage of isolates with a vancomycin MIC of ≥ 2 mg/L was observed over the years for MRSA (chi(2) = 0.01; P = 0.91) or MSSA (chi(2) = 0.08; P = 0.78). Annual consumption of parenteral vancomycin in our hospital in daily defined doses/100 stays was: 2002 (1.91), 2003 (1.63), 2004 (1.74), 2005 (2.06) and 2006 (1.64). **Conclusions** In a setting of low consumption of vancomycin and with a large collection of *S. aureus* clinical isolates, we have demonstrated the stability of vancomycin MICs over time.

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> **Validation Study of Artificial Neural Network Models for Prediction of Methicillin-Resistant Staphylococcus aureus Carriage.**

Hsu CC et al, Infect Control Hosp Epidemiol. 2008 Jun 12

Objective. Use of active surveillance cultures for methicillin-resistant *Staphylococcus aureus* (MRSA) for all patients admitted to the intensive care unit has been shown to reduce nosocomial transmission. However, the cost-effectiveness and the utility of implementing use of active surveillance cultures nationwide remain controversial. We sought to develop an artificial neural network (ANN) model that would predict the likelihood of MRSA colonization. **Setting.** Two acute care hospitals, one in Pittsburgh (hospital A) and one in Kaohsiung, Taiwan (hospital B). **Methods.** Nasal cultures were performed for all patients admitted to the hospitals. A total of 46 potential risk factors in hospital A and 86 potential risk factors in hospital B associated with MRSA colonization were assessed. Culture results were obtained; 75% of the data were used for training our ANN model, and the remaining 25% were used for validating our ANN model. The culture results were the "gold standard" for determining the accuracy of the model predictions. **Results.** The ANN model predictions were accurate 95.2% of the time for hospital A (sensitivity, 94.3%; specificity, 96.0%) and 94.2% of the time for hospital B (sensitivity, 96.6%; specificity, 91.8%), integrating all potential risk factors into the model. Only 17 potential risk factors were needed for the hospital A ANN model (accuracy, 90.9%; sensitivity, 98.5%; specificity, 83.4%), and only 20 potential risk factors were needed for the hospital B ANN model (accuracy, 90.5%; sensitivity, 96.6%; specificity, 84.3%), if the minimal risk factor method was used. Cross-validation analysis showed an average accuracy of 85.6% (sensitivity, 91.3%; specificity, 80.0%). **Conclusion.** Our ANN model can be used to predict with an accuracy of more than 90% which patients carry MRSA. The false-negative rates were significantly lower than the false-positive rates in the ANN predictions, which can serve as a safety buffer in case of patient misclassification.

> **Detection of Methicillin-Resistant Staphylococcus aureus and Vancomycin-Resistant Enterococci on the Gowns and Gloves of Healthcare Workers.**

Snyder GM et al, Infect Control Hosp Epidemiol. 2008 Jun 12.

Objective. To assess the rate of and the risk factors for the detection of methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococci (VRE) on the protective gowns and gloves of healthcare workers (HCWs). **Methods.** We observed the interactions between HCWs and patients during routine clinical activities in a 29-bed medical intensive care unit at the University of Maryland Medical Center, an urban tertiary care academic hospital. Samples for culture were obtained from HCWs' hands prior to their entering a patient's room, from HCWs' disposable gowns and gloves after they completed patient care activities, and from HCWs' hands immediately after they removed their protective gowns and gloves. **Results.** Of 137 HCWs caring for patients colonized or infected with MRSA and/or VRE, 24 (17.5%; 95% confidence interval, 11.6%-24.4%) acquired the organism on their gloves, gown, or both. HCW contact with the endotracheal tube or tracheostomy site of a patient ($P < .05$), HCW contact with the head and/or neck of a patient ($P < .05$), and HCW presence in the room of a patient with a percutaneous endoscopic gastrostomy and/or jejunostomy tube ($P < .05$) were associated with an increased risk of acquiring these organisms. **Conclusions.** The gloves and gowns of HCWs frequently become contaminated with MRSA and VRE during the routine care of patients, and particularly during care of the patient's respiratory tract and any associated indwelling devices. As part of a larger infection control strategy, including high-compliance hand disinfection, they likely provide a useful barrier to transmitting antibiotic-resistant organisms among patients in an inpatient setting.

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- > **Interventions to control MRSA: high time for time-series analysis?**
Harbarth S and Samore MH., J Antimicrob Chemother. 2008 Jun 12
Time-series methods are useful in quasi-experimental study designs in which rates of antibiotic-resistant infections are ascertained before and after an intervention. However, uncertainties remain regarding the use of time-series analysis as an appropriate research methodology for analysing the effect of infection control interventions and antibiotic policies on the epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA). In particular, there is still a substantial gap in our understanding of what actually happens to MRSA incidence when a planned intervention is made on use of one or more antibiotic drug classes.
- > **Which patients are most at risk of methicillin resistant *Staphylococcus aureus*: a review of admissions to a regional maxillofacial ward between 2001 and 2005.**
Rogers SN et al, Br J Oral Maxillofac Surg. 2008 Jun 11
This study aimed to identify all *Staphylococcus aureus* (MRSA) cases on a Regional Maxillofacial ward, to estimate incidence and to ascertain who were most at risk. The study also explored clinical and demographic factors associated with MRSA in a subset of consecutive patients managed by primary surgery for previously untreated oral and oropharyngeal squamous cell carcinoma (OOSCC) over the same time period. Patients admitted from 1st April 2001 to 31st March 2006 to the Regional Maxillofacial Unit ward, Liverpool were identified by a retrospective review of the hospital MRSA database and there were 10109 patient admissions. MRSA (1.1%) occurred in 115 patient episodes involving 97 patients. There were 84 patients having a single episode and 13 more than one. There were no cases of mortality due to MRSA. Of the MFU patients 73 were oncology and 7 trauma. In the oncology group the commonest primary sites were wound (41) and sputum (11). Of new patients admitted for definitive treatment for OOSCC, 14% had MRSA and the two main risk factors were stage of cancer ($P < 0.001$) and free flap ($P < 0.001$). The risk of MRSA infection on our maxillofacial ward is low though MRSA infection is more prevalent among oncology patients particularly those requiring free tissue transfer. Careful adherence to infection prevention and control precautions is essential and practical methods to reduce MRSA need further evaluation.
- > **Are there better methods of monitoring MRSA control than bacteraemia surveillance? An observational database study.**
Walker S et al, PLoS ONE. 2008 Jun 11;3(6):e2378.
BACKGROUND: Despite a substantial burden of non-bacteraemic methicillin resistant *Staphylococcus aureus* (MRSA) disease, most MRSA surveillance schemes are based on bacteraemias. Using bacteraemia as an outcome, trends at hospital level are difficult to discern, due to random variation. We investigated rates of nosocomial bacteraemic and non-bacteraemic MRSA infection as surveillance outcomes. METHODS AND FINDINGS: We used microbiology and patient administration system data from an Oxford hospital to estimate monthly rates of first nosocomial MRSA bacteraemia, and nosocomial MRSA isolation from blood/respiratory/sterile site specimens ("sterile sites") or all clinical samples (screens excluded) in all patients admitted from the community for at least 2 days between April 1998 and June 2006. During this period there were 441 nosocomial MRSA bacteraemias, 1464 MRSA isolations from sterile sites, and 3450 isolations from clinical specimens (8% blood, 15% sterile site, 10% respiratory, 59% surface swabs, 8% urine) in over 2.6 million patient-days. The ratio of bacteraemias to sterile site and all clinical isolations was similar over this period (around 3 and 8-fold lower respectively), during which rates of nosocomial MRSA bacteraemia increased by 27% per year to July 2003 before decreasing by 18% per year thereafter (heterogeneity $p < 0.001$). Trends in sterile site and all clinical isolations were similar. Notably, a change in rate of all clinical MRSA isolations in December 2002 could first be detected with conventional statistical significance by August 2003 ($p = 0.03$). In contrast, when monitoring MRSA bacteraemia, identification of probable changes in trend took longer, first achieving $p < 0.05$ in July 2004. CONCLUSIONS: MRSA

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isolation from all sites of suspected infection, including bacteraemic and non-bacteraemic isolation, is a potential new surveillance method for MRSA control. It occurs about 8 times more frequently than bacteraemia, allowing robust statistical determination of changing rates over substantially shorter times or smaller areas than using bacteraemia as an outcome.

> **Susceptibility of 170 isolates of the USA300 clone of MRSA to macrolides, clindamycin and the novel ketolide cethromycin.**

Luna VA et al, J Antimicrob Chemother. 2008 Jun 10.

No Abstract available

> **Four Country Healthcare Associated Infection Prevalence Survey 2006: overview of the results.**

Smyth ET, McIlvenny G, Enstone JE, Emmerson AM, Humphreys H, Fitzpatrick F, Davies E, Newcombe RG, Spencer RC; on behalf of the Hospital Infection Society Prevalence Survey Steering Group. J Hosp Infect. 2008 Jun 10

A survey of adult patients was conducted in February 2006 to May 2006 in acute hospitals across England, Wales, Northern Ireland and the Republic of Ireland to estimate the prevalence of healthcare-associated infections (HCAIs). A total of 75 694 patients were surveyed; 5743 of these had HCAIs, giving a prevalence of 7.59% (95% confidence interval: 7.40-7.78). HCAI prevalence in England was 8.19%, in Wales 6.35%, in Northern Ireland 5.43% and in the Republic of Ireland 4.89%. The most common HCAI system infections were gastrointestinal (20.6% of all HCAI), urinary tract (19.9%), surgical site (14.5%), pneumonia (14.1%), skin and soft tissue (10.4%) and primary bloodstream (7.0%). Prevalence of MRSA was 1.15% with MRSA being the causative organism in 15.8% of all system infections. Prevalence of *Clostridium difficile* was 1.21%. This was the largest HCAI prevalence survey ever performed in the four countries. The methodology and organisation used is a template for future HCAI surveillance initiatives, nationally, locally or at unit level. Information obtained from this survey will contribute to the prioritisation of resources and help to inform Departments of Health, hospitals and other relevant bodies in the continuing effort to reduce HCAI.

> **Clinical and molecular epidemiology of community-acquired, methicillin-resistant *Staphylococcus aureus* infections in children in central Greece.**

Niniou I et al, Eur J Clin Microbiol Infect Dis. 2008 Jun 7

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections in children have increased considerably in our area. In this study, we prospectively examined the epidemiological, clinical and molecular profile of CA-MRSA infections in children in central Greece. A total of 198 staphylococcal strains were isolated from patients with community-acquired infections over a 28-month period and 88 (44%) were found to be methicillin-resistant. Most patients with CA-MRSA had skin and soft-tissue infections (73%). Hospitalisation and surgery were more commonly required for patients with MRSA strains ($p = 0.001$ and $p < 0.001$, respectively). The presence of Panton-Valentine leukocidin (PVL) genes was identified in 28/41 (68%) CA-MRSA strains. All PVL(+) strains were found to carry a staphylococcal chromosomal cassette (SCC) mec element type IV and belonged to a single electrophoretic type similar to the European multi-locus sequence type 80 (ST80). The recent increase in CA-MRSA infections in children in our area is largely associated with the spread of the ST80 clone and their clinical characteristics are similar to those described in other parts of the world where different MRSA clones predominate.

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> **Invasive Infections with Community-Associated Methicillin-Resistant Staphylococcus aureus After Kidney Transplantation.**

Adeyemi OA et al, J Clin Microbiol. 2008 Jun 4.

We report two cases of invasive infections caused by Panton-Valentine leukocidin (PVL)-positive community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) after kidney transplantation. This report emphasizes the clinical importance of considering CA-MRSA as a causative agent in the differential diagnosis of infections of skin and soft tissues in organ transplant recipients.

> **A computational model of antibiotic-resistance mechanisms in Methicillin-Resistant Staphylococcus aureus (MRSA).**

Murphy JT et al, J Theor Biol. 2008 Jun 4.

An agent-based model of bacteria-antibiotic interactions has been developed that incorporates the antibiotic-resistance mechanisms of Methicillin-Resistant Staphylococcus aureus (MRSA). The model, called the Micro-Gen Bacterial Simulator, uses information about the cell biology of bacteria to produce global information about population growth in different environmental conditions. It facilitates a detailed systems-level investigation of the dynamics involved in bacteria-antibiotic interactions and a means to relate this information to traditional high-level properties such as the Minimum Inhibitory Concentration (MIC) of an antibiotic. The two main resistance strategies against beta-lactam antibiotics employed by MRSA were incorporated into the model: beta-lactamase enzymes, which hydrolytically cleave antibiotic molecules, and penicillin-binding proteins (PBP2a) with reduced binding affinities for antibiotics. Initial tests with three common antibiotics (penicillin, ampicillin and cephalothin) indicate that the model can be used to generate quantitatively accurate predictions of MICs for antibiotics against different strains of MRSA from basic cellular and biochemical information. Furthermore, by varying key parameters in the model, the relative impact of different kinetic parameters associated with the two resistance mechanisms to beta-lactam antibiotics on cell survival in the presence of antibiotics was investigated.

> **Staphylococcus aureus Community-Acquired Pneumonia During the 2006 to 2007 Influenza Season.**

Kallen AJ et al, Ann Emerg Med. 2008 Jun 3.

STUDY OBJECTIVE: Staphylococcus aureus is a cause of community-acquired pneumonia that can follow influenza infection. In response to a number of cases reported to public health authorities in early 2007, additional case reports were solicited nationwide to better define S aureus community-acquired pneumonia during the 2006 to 2007 influenza season. **METHODS:** Cases were defined as primary community-acquired pneumonia caused by S aureus occurring between November 1, 2006, and April 30, 2007. Case finding was conducted through an Emerging Infections Network survey and through contacts with state and local health departments. **RESULTS:** Overall, 51 cases were reported from 19 states; 37 (79%) of 47 with known susceptibilities involved infection with methicillin-resistant S aureus (MRSA). The median age of case patients was 16 years, and 44% had no known pertinent medical history. Twenty-two (47%) of 47 case patients with information about other illnesses were diagnosed with a concurrent or antecedent viral infection during their illness, and 11 of 33 (33%) who were tested had laboratory-confirmed influenza. Of the 37 patients with MRSA infection, 16 (43%) were empirically treated with antimicrobial agents recommended for MRSA community-acquired pneumonia. Twenty-four (51%) of 47 patients for whom final disposition was known died a median of 4 days after symptom onset. **CONCLUSION:** S aureus continues to cause community-acquired pneumonia, with most reported cases caused by MRSA and many occurring with or after influenza. In this series, patients were often otherwise healthy young people and mortality rates were high. Further

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prospective investigation is warranted to clarify infection incidence, risk factors, and preventive measures.

> **Staphylococcus aureus Bloodstream Infections: Risk Factors, Outcomes, and the Influence of Methicillin Resistance in Calgary, Canada, 2000-2006.**

Laupland KB et al, J Infect Dis. 2008 Jun 3.

Background. Reports have suggested that the epidemiological profile of invasive *Staphylococcus aureus* infections is changing. We sought to describe the epidemiological profile of *S. aureus* bacteremia and to assess whether the incidence and severity of and the antimicrobial resistance rates associated with this bacteremia are increasing. **Methods.** Population-based surveillance for *S. aureus* bacteremias was conducted in the Calgary Health Region (population, 1.2 million) during 2000-2006. **Results.** The annual incidence of *S. aureus* bacteremia was 19.7 cases/100,000 population. Although rates of health care-associated and nosocomial methicillin-susceptible *S. aureus* (MSSA) bacteremia were similar throughout the study, rates of community-acquired MSSA bacteremia gradually decreased, and rates of methicillin-resistant *S. aureus* (MRSA) bacteremia dramatically increased. The clonal type predominantly isolated was CMRSA-2 (i.e., Canadian [C] MRSA-2), but CMRSA-10 (USA300) strains have been increasingly isolated, especially from community-onset infections, since 2004. Dialysis dependence, organ transplantation, HIV infection, cancer, and diabetes were the most important risk factors and were comparable for MSSA and MRSA bacteremias. The overall case-fatality rate was higher among individuals with MRSA (39%) than among those with MSSA (24%; [Formula: see text]). The annual overall population mortality rate associated with *S. aureus* bacteremia did not significantly change during the study. **Conclusions.** Although the overall influence of *S. aureus* bacteremia has not significantly changed, MRSA has emerged as an important etiology in our region.

> **Potent in Vitro Activity of Tomopenem (CS-023) against Methicillin-Resistant Staphylococcus aureus and Pseudomonas aeruginosa.**

Koga T et al, Antimicrob Agents Chemother. 2008 Jun 2.

Tomopenem (formerly CS-023) is a novel 1beta-methylcarbapenem with broad-spectrum coverage of gram-positive and gram-negative pathogens. Its antibacterial activity against European clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* was compared with those of imipenem and meropenem. The MICs at which 90% of the isolates tested were inhibited of tomopenem against MRSA and *P. aeruginosa* were 8 and 4 microg/ml, respectively, and were equal to or more than fourfold lower than those of imipenem and meropenem. The antibacterial activity of tomopenem against MRSA was correlated with the higher affinity for the penicillin-binding protein 2a. Its activity against laboratory mutants of *P. aeruginosa* with (i) overproduction of chromosomally coded AmpC beta-lactamase; (ii) overproduction of the multidrug efflux pumps MexAB-OprM, MexCD-OprJ, and MexEF-OprN; (iii) deficiency in OprD, and (iv) various combinations of AmpC-overproduction, MexAB-OprM-overproduction, and OprD-deficiency were tested. Increase in MIC of tomopenem against each single mutant compared with its parent strain was within fourfold. Tomopenem exhibited antibacterial activity against all mutants with an observed MIC range of 0.5 to 8 microg/ml. These results suggest that the antibacterial activity of tomopenem against the clinical isolates of MRSA and *P. aeruginosa* would be ascribed to its high affinity for PBP 2a and its activity against the mutants of *P. aeruginosa*, respectively.

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> **Evaluation of the activity of ceftobiprole, linezolid, vancomycin, and daptomycin against Community-associated (CA-MRSA) and Hospital-associated (HA-MRSA) methicillin-resistant *Staphylococcus aureus*.**

Leonard SN et al, Antimicrob Agents Chemother. 2008 Jun 2.

We evaluated the activity of ceftobiprole against 100 community-associated MRSA (CA-MRSA) and 100 hospital-associated MRSA (HA-MRSA). Eight isolates were evaluated by time-kill for kill rate and potential for synergy with tobramycin. Ceftobiprole MIC₅₀/MIC₉₀ were 1/2 microg/mL against CA-MRSA and HA-MRSA. In time kill analysis, ceftobiprole was bactericidal at all concentrations tested.

> **Clinical failures of appropriately-treated methicillin-resistant *Staphylococcus aureus* infections.**

Dombrowski JC and Winston LG, J Infect. 2008 Jun 2.

OBJECTIVES: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections can be difficult to treat. We evaluated the rate of clinical failure in appropriately-treated patients and determined risk factors for failure. **METHODS:** We retrospectively studied a cohort of patients with invasive MRSA infections who completed recommended therapy at one hospital over a 7year period. **RESULTS:** Two-hundred and fifteen cases were included. Vancomycin monotherapy was given in 73%. Failure rates by infection site were as follows: osteomyelitis 37/81 (46%), epidural abscess five/18 (28%), surgical wound four/15 (27%), pneumonia eight/45 (18%), endocarditis five/32 (16%), bloodstream five/42 (12%), joint one/23 (4%), and meningitis zero/one (0%). In multivariate analysis, only a diagnosis of osteomyelitis was independently associated with relapse ($p < 0.001$). **CONCLUSIONS:** We found a high rate of treatment failure in an urban population among patients who completed recommended therapy, largely with vancomycin alone. Failure in osteomyelitis was particularly common. High quality comparative studies of antibiotic regimens for MRSA infections, particularly osteomyelitis, are needed.

> **Significant reductions in methicillin-resistant *Staphylococcus aureus* bacteraemia and clinical isolates associated with a multisite, hand hygiene culture-change program and subsequent successful statewide roll-out.**

Grayson ML et al, Med J Aust. 2008 Jun 2;188(11):633-40.

OBJECTIVE: To assess the efficacy of a multimodal, centrally coordinated, multisite hand hygiene culture-change program (HHCCP) for reducing rates of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia and disease in Victorian hospitals. **DESIGN, PARTICIPANTS AND SETTING:** A pilot HHCCP was conducted over a 24-month period (October 2004 to September 2006) in six Victorian health care institutions (4 urban, 2 rural; total beds, 2379). Subsequently, we assessed the efficacy of an identical program implemented throughout Victorian public hospitals over a 12-month period (beginning between March 2006 and July 2006). **MAIN OUTCOME MEASURES:** Rates of hand hygiene (HH) compliance; rates of MRSA disease (patients with bacteraemia and number of clinical isolates per 100 patient discharges [PD]). **RESULTS:** Mean HH compliance improved significantly at all pilot program sites, from 21% (95% CI, 20%-22%) at baseline to 48% (95% CI, 47%-49%) at 12 months and 47% (95% CI, 46%-48%; range, 31%-75%) at 24 months. Mean baseline rates for the number of patients with MRSA bacteraemia and the number of clinical MRSA isolates were 0.05/100 PD per month (range, 0.00-0.13) and 1.39/100 PD per month (range, 0.16-2.39), respectively. These were significantly reduced after 24 months to 0.02/100 PD per month for bacteraemia ($P = 0.035$ for trend; 65 fewer patients with bacteraemia) and 0.73/100 PD per month for MRSA isolates ($P = 0.003$; 716 fewer isolates). Similar findings were noted 12 months after the statewide roll-out, with an increase in mean HH compliance (from 20% to 53%; $P < 0.001$) and reductions in the rates of MRSA isolates ($P = 0.043$) and bacteraemias ($P = 0.09$). **CONCLUSIONS:** Pilot and subsequent statewide implementation of a multimodal HHCCP was effective in significantly improving HH compliance and reducing rates of MRSA infection.

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> **Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates.**

Asbell PA et al, Am J Ophthalmol. 2008 Jun;145(6):951-958. Epub 2008 Mar 28

PURPOSE: Ocular Tracking Resistance in U.S. Today (TRUST) annually evaluates in vitro antimicrobial susceptibility of *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* to ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, penicillin, azithromycin, tobramycin, trimethoprim, and polymyxin B in national samples of ocular isolates. **DESIGN:** Laboratory investigation. **METHODS:** Prospectively collected ocular isolates (197 *S. aureus*, 49 *S. pneumoniae*, and 32 *H. influenzae*) from 35 institutions and archived ocular isolates (760 *S. pneumoniae* and 356 *H. influenzae*) from 34 institutions were tested by an independent, central laboratory. Mean minimum inhibitory concentrations that would inhibit growth of 90% of the tested isolates (MIC₉₀) were interpreted as susceptible, intermediate, or resistant according to standardized breakpoints for systemic treatment. *S. aureus* isolates were classified as methicillin susceptible (MSSA) or methicillin resistant (MRSA). **RESULTS:** MSSA or MRSA susceptibility patterns were virtually identical for the fluoroquinolones, that is, MSSA susceptibility was 79.9% to 81.1% and MRSA susceptibility was 15.2%. Trimethoprim was the only agent tested with high activity against MRSA. All *S. pneumoniae* isolates were susceptible to gatifloxacin, levofloxacin, and moxifloxacin; 89.8% were susceptible to ciprofloxacin. *H. influenzae* isolates were 100% susceptible to all tested agents but trimethoprim. Ocular TRUST 1 data were consistent with the eight-year longitudinal sample of archived ocular isolates. **CONCLUSIONS:** The fluoroquinolones were consistently active in MSSA, *S. pneumoniae*, and *H. influenzae*. After more than a decade of intensive ciprofloxacin and levofloxacin use as systemic therapy, 100% of ocular *S. pneumoniae* isolates were susceptible to gatifloxacin, levofloxacin, and moxifloxacin; nonsusceptibility to ciprofloxacin was less than 15%. High-level in vitro MRSA resistance suggests the need to consider alternative therapy to fluoroquinolones when MRSA is a likely pathogen.

> **Ceftobiprole: an extended-spectrum anti-methicillin-resistant *Staphylococcus aureus* cephalosporin.**

Anderson SD and Gums JG, Ann Pharmacother. 2008 Jun;42(6):806-16. Epub 2008 May 13.

OBJECTIVE: To summarize and evaluate the literature concerning ceftobiprole. **DATA SOURCES:** Literature identification was conducted through MEDLINE (1966-February 2008) and International Pharmaceutical Abstracts (1970-February 2008) using the terms ceftobiprole, medocaril, BAL 5788, RO-5788, BAL 9141, RO 63-9141, pyrrolidinone cephalosporin, MRSA, complicated skin and skin-structure infections (cSSSIs), community-acquired pneumonia, and nosocomial pneumonia. Additional publications were identified through a review of articles and abstracts from infectious disease meetings. **STUDY SELECTION AND DATA EXTRACTION:** All articles in English were evaluated and all pertinent information was included. **DATA SYNTHESIS:** Ceftobiprole medocaril is an extended-spectrum cephalosporin with activity against methicillin-resistant *Staphylococcus* spp., vancomycin-resistant *Staphylococcus aureus*, penicillin-resistant *Streptococcus pneumoniae*, vancomycin-resistant *Enterococcus faecalis*, Enterobacteriaceae, and *Pseudomonas aeruginosa*. Inactivity includes extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and *Enterococcus faecium*. Preliminary data suggest that ceftobiprole may be effective with a 1-hour infusion of 500 mg every 12 hours for gram-positive infections and 500 mg every 8 hours with a 2-hour infusion for polymicrobial infections. Two clinical trials support these dosing regimens for cSSSIs. Ceftobiprole was noninferior to vancomycin in suspected gram-positive cSSSIs, with cure rates of 93.3% and 93.5%, respectively. Furthermore, ceftobiprole was noninferior to vancomycin and ceftazidime in polymicrobial cSSSIs (cure rates 90.5% vs 90.2%, respectively). Although the total number of adverse effects was similar to those of the comparator, more patients in the ceftobiprole group experienced nausea, vomiting, and dysgeusia. **CONCLUSIONS:** The activity of ceftobiprole and limited clinical data suggest that it may be useful as empiric monotherapy for cSSSI and in combination with other antimicrobials in lower respiratory tract infections for which Phase 3 clinical trials are currently exploring. Although not shown

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in vitro, ceftobiprole may induce resistance due to its broad spectrum of activity. Approval is expected for the treatment of cSSSI.

> **Activities of clindamycin, daptomycin, doxycycline, linezolid, trimethoprim-sulfamethoxazole, and vancomycin against community-associated methicillin-resistant *Staphylococcus aureus* with inducible clindamycin resistance in murine thigh infection and in vitro pharmacodynamic models.**

LaPlante KL et al, Antimicrob Agents Chemother. 2008 Jun;52(6):2156-62. Epub 2008 Apr 14

Controversy exists about the most effective treatment options for community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) and about the ability of these strains to develop inducible resistance to clindamycin during therapy. Using both in vitro pharmacodynamic and murine thigh infection models, we evaluated and compared several antimicrobial compounds against CA-MRSA. Strains with inducible macrolide lincosamide-streptogramin type B (iMLS(B)) resistance and strains in which resistance was noninducible were evaluated. Two levels of inocula (10⁵ and 10⁷) were evaluated for clindamycin activity in the in vivo model. In both models, the antimicrobial evaluation was performed in triplicate, and bacterial quantification occurred over 72 h, with drug doses that were designed to simulate the free drug area-under-the-concentration-time curve values (fAUCs) obtained from human samples. When the activity of clindamycin against the iMLS(B) strains was evaluated, constitutive resistance was noted at 24 h (MIC of >256), and failure was noted at an inoculum of > or =10⁶ in the in vivo models. However, at a low inoculum (10⁵) in the murine thigh-infection model, clindamycin demonstrated modest activity, reducing the CFU/thigh count for clindamycin resistance-inducible strains at 72 h (0.45 to 1.3 logs). Overall, administration of daptomycin followed by vancomycin demonstrated the most significant kill against all strains in both models. Against the clindamycin noninducible strain, clindamycin and doxycycline demonstrated significant kill. Doxycycline, linezolid, and trimethoprim-sulfamethoxazole (not run in the murine model) demonstrated bacteriostatic activity against clindamycin resistance-inducible isolates. This study demonstrates that clindamycin's activity against the iMLS(B) strains tested is partially impacted by inoculum size. At present, there are several alternatives that appear promising for treating clindamycin resistance-inducible strains of CA-MRSA.

> **In vitro selection and characterization of ceftobiprole-resistant methicillin-resistant *Staphylococcus aureus*.**

Banerjee R et al, Antimicrob Agents Chemother. 2008 Jun;52(6):2089-96. Epub 2008 Mar 31

Methicillin-resistant *Staphylococcus aureus* (MRSA) is resistant to beta-lactam antibiotics because it expresses penicillin-binding protein 2a (PBP2a), a low-affinity penicillin-binding protein. An investigational broad-spectrum cephalosporin, ceftobiprole (BPR), binds PBP2a with high affinity and is active against MRSA. We hypothesized that BPR resistance could be mediated by mutations in *mecA*, the gene encoding PBP2a. We selected BPR-resistant mutants by passage in high-volume broth cultures containing subinhibitory concentrations of BPR. We used strain COLnex (which lacks chromosomal *mecA*) transformed with pAW8 (a plasmid vector only), pYK20 (a plasmid carrying wild-type *mecA*), or pYK21 (a plasmid carrying a mutant *mecA* gene corresponding to five PBP2a mutations). All strains became resistant to BPR by day 9 of passaging, but MICs continued to increase until day 21. MICs increased 256-fold (from 1 to 256 microg/ml) for pAW8, 32-fold (from 4 to 128 microg/ml) for pYK20, and 8-fold (from 16 to 128 mug/ml) for pYK21. Strains carrying wild-type or mutant *mecA* developed six (pYK20 transformants) or four (pYK21 transformants) new mutations in *mecA*. The transformation of COLnex with a *mecA* mutant plasmid conferred BPR resistance, and the loss of *mecA* converted resistant strains into susceptible ones. Modeling studies predicted that several of the *mecA* mutations altered BPR binding; other mutations may have mediated resistance by influencing interactions with other proteins. Multiple *mecA* mutations were associated with BPR

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resistance in MRSA. BPR resistance also developed in the strain lacking *mecA*, suggesting a role for chromosomal genes.

> **Design and synthesis of benzenesulfonanilides active against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*.**

Namba K et al, Bioorg Med Chem. 2008 Jun 1;16(11):6131-44. Epub 2008 Apr 24

Vancomycin is mainly used as an antibacterial agent of last resort, but recently vancomycin-resistant bacterial strains have been emerging. Although new antimicrobials have been developed in order to overcome drug-resistant bacteria, many are structurally complex beta-lactams or quinolones. In this study, we aimed to create new anti-drug-resistance antibacterials which can be synthesized in a few steps from inexpensive starting materials. Since sulfa drugs function as p-aminobenzoic acid mimics and inhibit dihydropteroate synthase (DHPS) in the folate pathway, we hypothesized that sulfa derivatives would act as folate metabolite-mimics and inhibit bacterial folate metabolism. Screening of our sulfonanilide libraries, including benzenesulfonanilide-type cyclooxygenase-1-selective inhibitors, led us to discover benzenesulfonanilides with potent anti-methicillin-resistant *Staphylococcus aureus* (MRSA)/vancomycin-resistant *Enterococcus* (VRE) activity, that is, N-3,5-bis(trifluoromethyl)phenyl-3,5-dichlorobenzenesulfonanilide (16b) [MIC=0.5microg/mL (MRSA), 1.0microg/mL (VRE)], and 3,5-bis(trifluoromethyl)-N-(3,5-dichlorophenyl)benzenesulfonanilide (16c) [MIC=0.5microg/mL (MRSA), 1.0microg/mL (VRE)]. These compounds are more active than vancomycin [MIC=2.0microg/mL (MRSA), 125microg/mL (VRE)], but do not possess an amino group, which is essential for DHPS inhibition by sulfa drugs. These results suggested that the mechanism of antibacterial action of compounds 16b and 16c is different from that of sulfa drugs. We also confirmed the activity of these compounds against clinical isolates of Gram-positive bacteria.

> **Management of methicillin-resistant *Staphylococcus aureus* bacteremia.**

Cosgrove SE and Fowler VG Jr. Clin Infect Dis. 2008 Jun 1;46 Suppl 5:S386-93.

Staphylococcus aureus bacteremia and endocarditis are serious infections that demand prompt clinical attention to ensure good outcomes. Of foremost importance is identifying and managing the source of infection and any associated complications. Evaluation for the presence of cardiac involvement is essential because inadequately managed *S. aureus* endocarditis is life threatening. Thus, physicians must aggressively negotiate treatment paths, considering whether the *S. aureus* bacteremia is complicated, whether foreign sources of infection should be removed or replaced, and whether surgical intervention is necessary. Selection of an antibiotic treatment is also an essential factor for optimal management. The increasing prevalence of methicillin-resistant *S. aureus* (MRSA) infections has created a tremendous demand for effective and safe antimicrobial agents other than the historic anti-MRSA agent vancomycin.

> **Pneumonia caused by methicillin-resistant *Staphylococcus aureus*.**

Rubinstein E et al, Clin Infect Dis. 2008 Jun 1;46 Suppl 5:S378-85

A recent increase in staphylococcal infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), combined with frequent, prolonged ventilatory support of an aging, often chronically ill population, has resulted in a large increase in cases of MRSA pneumonia in the health care setting. In addition, community-acquired MRSA pneumonia has become more prevalent. This type of pneumonia historically affects younger patients, follows infection with influenza virus, and is often severe, requiring hospitalization and causing the death of a significant proportion of those affected. Ultimately, hospital-acquired MRSA and community-acquired MRSA are important causes of pneumonia and present diagnostic and therapeutic challenges. Rapid institution of appropriate antibiotic therapy, including linezolid as an alternative to vancomycin, is crucial. Respiratory infection-control measures and de-

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escalation of initial broad-spectrum antibiotic regimens to avoid emergence of resistant organisms are also important. This article reviews the clinical features of, diagnosis of, and therapies for MRSA pneumonia.

> **Increasing antibiotic resistance among methicillin-resistant *Staphylococcus aureus* strains.**

Sakoulas G and Moellering RC Jr, Clin Infect Dis. 2008 Jun 1;46 Suppl 5:S360-7.

Vancomycin use has increased dramatically worldwide since the mid-1980s, largely as a result of empirical and directed therapy against burgeoning methicillin-resistant *Staphylococcus aureus* (MRSA) infections. With limited choices, clinicians have traditionally relied on vancomycin alone in the management of serious MRSA infections and have enjoyed a significant period free of vancomycin resistance in *S. aureus*. Even now, 5 decades after its introduction, vancomycin resistance among *S. aureus* strains, as currently defined microbiologically, remains rare. Yet it is becoming clear that vancomycin is losing potency against *S. aureus*, including MRSA. Serious infections due to MRSA defined as susceptible in the laboratory are not responding well to vancomycin. This is demonstrated by increased mortality seen in patients with MRSA infection and markedly attenuated vancomycin efficacy caused by vancomycin heteroresistance in *S. aureus*. Therefore, it appears that our definition of vancomycin susceptibility requires further scrutiny as applied to serious MRSA infections, such as bacteremia and pneumonia.

> **Pathogenesis of methicillin-resistant *Staphylococcus aureus* infection.**

Gordon RJ and Lowy FD, Clin Infect Dis. 2008 Jun 1;46 Suppl 5:S350-9.

Staphylococcus aureus is a versatile pathogen capable of causing a wide range of human diseases. However, the role of different virulence factors in the development of staphylococcal infections remains incompletely understood. Some clonal types are well equipped to cause disease across the globe, whereas others are facile at causing disease among community members. In this review, general aspects of staphylococcal pathogenesis are addressed, with emphasis on methicillin-resistant strains. Although methicillin-resistant *S. aureus* (MRSA) strains are not necessarily more virulent than methicillin-sensitive *S. aureus* strains, some MRSA strains contain factors or genetic backgrounds that may enhance their virulence or may enable them to cause particular clinical syndromes. We examine these pathogenic factors.

> **Epidemiology of methicillin-resistant *Staphylococcus aureus*.**

Boucher HW and Corey GR, Clin Infect Dis. 2008 Jun 1;46 Suppl 5:S344-9

The frequency of methicillin-resistant *Staphylococcus aureus* (MRSA) infections continues to grow in hospital-associated settings and, more recently, in community settings in the United States and globally. The increase in the incidence of infections due to *S. aureus* is partially a consequence of advances in patient care and also of the pathogen's ability to adapt to a changing environment. Infection due to *S. aureus* imposes a high and increasing burden on health care resources. A growing concern is the emergence of MRSA infections in patients with no apparent risk factors. MRSA infection in community settings involves considerable morbidity and mortality, as does nosocomial MRSA infection. For community-associated MRSA, person-to-person transmission has been reported, and several factors have been shown to predict disease. We examine the trends in both nosocomial and community-associated MRSA infections and explore recent studies of the mechanisms that allow *S. aureus* to become resistant to currently available drugs.

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> **The use of active surveillance cultures in adult intensive care units to reduce methicillin-resistant *Staphylococcus aureus*-related morbidity, mortality, and costs: a systematic review.**

McGinigle KL et al, Clin Infect Dis. 2008 Jun 1;46(11):1717-25

Active surveillance cultures (ASCs) are universal or targeted microbiological screening cultures for patients admitted to a hospital. ASCs have been proposed to control the increasing numbers of infections due to multidrug-resistant organisms, but their efficacy and cost-effectiveness are unproven. We conducted a systematic review of the literature pertaining to the use of ASCs and control of methicillin-resistant *Staphylococcus aureus* (MRSA). We searched relevant journals and the PubMed Medline, Web of Science, CINAHL, and Cochrane Library databases. No randomized, controlled trials were identified. Sixteen observational studies and 4 economic analyses were reviewed. Only 2 of the observational studies had a control group. None of the studies were of good quality. Thus, we identified important gaps in the literature, including a need for a clear definition of ASCs, a clear implementation protocol, and rigorous economic evaluations. Existing evidence may favor the use of ASCs, but the evidence is of poor quality, and definitive recommendations cannot be made.

> **A population-based study of the incidence and molecular epidemiology of methicillin-resistant *Staphylococcus aureus* disease in San Francisco, 2004-2005.**

Liu C et al, Clin Infect Dis. 2008 Jun 1;46(11):1637-46

BACKGROUND: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections have become a major public health problem in both the community and hospitals. Few studies have characterized the incidence and clonal composition of disease-causing strains in an entire population. Our objective was to perform a population-based survey of the clinical and molecular epidemiology of MRSA disease in San Francisco, California. **METHODS:** We prospectively collected 3985 MRSA isolates and associated clinical and demographic information over a 12-month period (2004-2005) at 9 San Francisco-area medical centers. A random sample of 801 isolates was selected for molecular analysis. **RESULTS:** The annual incidence of community-onset MRSA disease among San Francisco residents was 316 cases per 100,000 population, compared with 31 cases per 100,000 population for hospital-onset disease. Persons who were aged 35-44 years, were men, and were black had the highest incidence of community-onset disease. The USA300 MRSA clone accounted for 234 cases of community-onset disease and 15 cases of hospital-onset disease per 100,000 population, constituting an estimated 78.5% and 43.4% of all cases of MRSA disease, respectively. Patients with community-onset USA300 MRSA versus non-USA300 MRSA disease were more likely to be male, be of younger age, and have skin and soft-tissue infections. USA300 strains were generally more susceptible to multiple antibiotics, although decreased susceptibility to tetracycline was observed in both community-onset ($P = .008$) and hospital-onset ($P = .03$) USA300 compared to non-USA300 strains. **CONCLUSIONS:** The annual incidence of community-onset MRSA disease in San Francisco is substantial, surpassing that of hospital-onset disease. USA300 is the predominant clone in both the community and hospitals. The dissemination of USA300 from the community into the hospital setting has blurred its distinction as a community-associated pathogen.

> **A comparative in-vitro evaluation of resistance selection after exposure to teicoplanin, vancomycin, linezolid and quinupristin-dalfopristin in *Staphylococcus aureus* and *Enterococcus* spp.**

Drago L et al, Clin Microbiol Infect. 2008 Jun;14(6):608-11. Epub 2008 Apr 5

The ability of breakpoint and serum concentrations of teicoplanin, vancomycin, linezolid and quinupristin-dalfopristin to select resistance was compared for isolates of methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), *Enterococcus faecalis* and *Enterococcus faecium*. Mutation frequencies were always $<10^{-10}$, except for two isolates grown in

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the presence of teicoplanin at the trough serum concentration. After multistep selection, linezolid selected for resistance in staphylococci and enterococci, and serial exposure to certain concentrations of linezolid was more likely to select for stable resistance in MRSA, MSSA and enterococci than was exposure to glycopeptides and quinupristin-dalfopristin.

> **DNA microarray-based genotyping of methicillin-resistant *Staphylococcus aureus* strains from Eastern Saxony.**

Monecke S et al, Clin Microbiol Infect. 2008 Jun;14(6):534-45. Epub 2008 Mar 27

A diagnostic microarray was used to characterize a collection of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from hospitals in the German region of Eastern Saxony. The most abundant epidemic MRSA (EMRSA) strains were ST5-MRSA II (Rhine-Hesse EMRSA, EMRSA-3), CC5/ST228-MRSA I (South German EMRSA), ST22-MRSA IV (Barnim EMRSA, EMRSA-15) and ST45-MRSA IV (Berlin EMRSA). Other strains were found only as sporadic isolates or in minor outbreaks. These strains included ST1-MRSA IV, ST8-MRSA IV (Hannover EMRSA and others), clonal group 5 strains carrying SCCmec type IV elements (Paediatric clone), ST45-MRSA V, CC8/ST239-MRSA III and ST398-MRSA V. Panton-Valentine leukocidin-positive MRSA isolates were still very rare. The predominant strain was ST80-MRSA IV, although increasing numbers of different strains have recently been detected (ST8-MRSA IV, ST30-MRSA IV and ST59-MRSA V). For more common MRSA strains, it was possible to detect variants that differed mainly in the carriage of additional resistance determinants and certain virulence-associated genes. Detection of such variants can sometimes allow epidemic strains to be resolved beyond spa types to a hospital-specific level, which is of significant value for epidemiological purposes.

> **Bloodstream Infections Caused by Extended-Spectrum {beta}-Lactamase-Producing *Escherichia coli*: Risk Factors for Inadequate Initial Antimicrobial Therapy.**

Tumbarello M et al, Antimicrob Agents Chemother. 2008 Jun 30

Extended-spectrum beta-lactamase-producing strains of *Escherichia coli* (ESBL-Ec) are a significant cause of bloodstream infections (BSI) in hospitalized and non-hospitalized patients. We previously showed that delaying effective antimicrobial therapy in BSI caused by ESBL producers significantly increases mortality. The aim of this retrospective 7-year analysis was to identify risk factors for inadequate initial antimicrobial therapy (IIAT) (i.e., empirical treatment based on a drug to which the isolate had displayed *in vitro* resistance) in inpatients with ESBL-Ec BSI. Of the 129 patients considered, 56 (43.4%) received IIAT for 48 to 120 hours (mean, 72 h). Independent risk factors for IIAT include unknown BSI source (odds ratios [OR], 4.86; 95% confidence interval [CI], 1.98 to 11.91; $P = 0.001$); isolate co-resistance to ≥ 3 antimicrobials (OR, 3.73; 95% CI, 1.58 to 8.83; $P = 0.003$); hospitalization during the 12 months preceding BSI onset (OR, 3.33, 95% CI, 1.42 to 7.79; $P = 0.005$); and antimicrobial therapy during the 3 months preceding BSI onset (OR, 2.65; 95% CI, 1.11 to 6.29; $P = 0.02$). IIAT was the strongest risk factor for 21-day mortality, and it significantly increased the length of hospitalization after BSI onset. Our results underscore the need for a systematic approach to the management of patients with serious infections by ESBL-Ec. It should be based on sound, updated knowledge of local infectious-disease epidemiology, detailed analysis of the patient history with emphasis on recent contact with the healthcare system, and aggressive attempts to identify the infectious focus that has given rise to the BSI.

> **A novel SHV-type beta-lactamase variant (SHV-89) in clinical isolates in China.**

Li JB et al, Mol Biol Rep. 2008 Jun 29

Two clinical strains of *Klebsiella pneumoniae* (*K. pneumoniae*) and one isolate of *Escherichia coli* (*E. coli*) were collected from two large general hospitals in China. Conjugation experiment, susceptibility

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testing, isoelectric focusing, PCR, and sequencing techniques as well as clone, expression, purification and kinetics were carried out to describe the characterization of the novel SHV-type enzyme. The analysis of plasmid profiling and pulsed-field gel electrophoresis of the novel enzyme were performed to investigate epidemiology. These isolates had CTX-M-14 and SHV-89 beta-lactamases. SHV-89 beta-lactamase of pl 7.6 is a novel variant with two substitutions compared with the sequence of SHV-1: Leu35Gln and Met129Val. Its gene also had two silent mutations at positions 369 and 774, respectively. The results of substrate profiles and MIC determinations showed the activity of the novel enzyme was insufficient for the enzyme to count as an extended-spectrum beta-lactamase (ESBL). The substrates of the enzyme were also characterized. Furthermore, the three novel SHV enzyme-producing strains were epidemiologically unrelated. The emergence of a novel SHV-type beta-lactamase is rarely described in other areas. This study illustrates the importance of molecular surveillance in tracking SHV-producing strains in large teaching hospitals and emphasizes the need for epidemiological monitoring.

> **Prevalence and characterization of extended-spectrum beta-lactamases in *Klebsiella pneumoniae* in Algiers hospitals (Algeria).**

Messai Y et al, Pathol Biol (Paris). 2008 Jun 26

AIM OF THE STUDY: To determine the prevalence and the diversity of extended-spectrum beta-lactamases (ESBLs) in 196 *Klebsiella pneumoniae* clinical isolates collected from three hospitals in Algiers. **MATERIALS AND METHODS:** Antibigrams were done on Mueller-Hinton agar plates with the disc-diffusion method and MICs were determined by agar-dilution method. Mating experiments were performed in agar medium. Plasmid DNA was extracted by the alkaline-lysis method. Total DNA was extracted with a Qiagen mini kit and screened for bla(TEM) and bla(CTX-M) genes by PCR. Linkage of bla(CTX-M) genes with insertion sequence ISEcp1B and class 1 integrons was investigated by PCR. PCR products were sequenced by the Sanger method. The epidemiological relationships between ESBL-producing *K. pneumoniae* isolates were analyzed by ERIC-PCR. **RESULTS:** Thirty-nine (19.9%) isolates were found to produce ESBLs belonging to CTX-M-1 group and TEM penicillinases (CTX-M-3, CTX-M-15 and TEM-1). ERIC-PCR analysis showed that the isolates are genetically unrelated. The bla(TEM) and bla(CTX-M) genes as well as aminoglycosides and sulfonamides resistance determinants were found located in self-transferable plasmids of approximately 85kb. The class 1 integrons and the insertion sequence ISEcp1B were present in the isolates and in their transconjugants. ISEcp1B was found genetically linked to the bla(CTX-M) genes and located 127bp upstream, with the presence of the V and W sequences. **CONCLUSION:** The study revealed a high rate of ESBL-producing *K. pneumoniae* in Algerian hospitals, resulting from horizontal dissemination of mobile bla(CTX-M) genes.

> **High rate of Intestinal Colonization with Extended Spectrum {beta}-Lactamases Producing Organisms in Household Contacts of Infected Community Patients.**

Valverde A et al, J Clin Microbiol. 2008 Jun 18.

Fecal carriage with extended-spectrum beta-lactamase (ESBL)-organisms was detected in 70% of index cases (n=40) with community-acquired infections due to ESBL-producers and reached 16.7% in household contacts (n=54). Sixty-six percent of ESBL-organisms from index cases were indistinguishable (PFGE) when compared with household isolates. Community-patients and their households represent a reservoir for ESBL-producers, increasing dispersal of resistance in healthy people.

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> **Extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in paediatric wards: A nested case-control study.**

Demir S et al, J Paediatr Child Health. 2008 Jun 12

Aim: A high rate (48.6%) of extended spectrum beta-lactamase production among *Klebsiella pneumoniae* (ESBL-KP) clinical isolates in the paediatric wards of our hospital prompted the introduction of enhanced infection control measures, and after the implementation of these measures, we instituted a prospective surveillance programme, with a nested case-control study to determine the risk factors for rectal colonisation by ESBL-KP. **Methods:** Over a 1-year period, rectal swabs from patients and samples from the environment and the hands of health-care workers were cultured. Strain typing of ESBL-KP isolates was performed using pulsed-field gel electrophoresis. Characteristics of patients who were colonised with ESBL-KP during hospital stay were compared with those of patients who remained negative for ESBL-KP. Multivariate analysis was performed with model-building using stepwise logistic regression to determine independent risk factors for ESBL-KP acquisition. **Results:** Forty (18.5%) of 216 patients became colonised with ESBL-KP. The strongest independent predictors of ESBL-KP colonisation were mechanical ventilation (odds ratio (OR): 4.28) and hospitalisation for longer than 14 days (OR: 6.97). Genotyping of the isolates indicated probable patient-to-patient transmission; however, we could not determine the route of this spread. During the study period, a 1.6% rate of ESBL-KP clinical infection per 500 patient admissions was observed, in contrast to a 7% rate in the previous year. **Conclusions:** Prolonged length of stay and mechanical ventilation were independent predictors of ESBL-KP colonisation. Enhanced infection control measures, antimicrobial stewardship and screening for rectal carriage were associated with a substantial decrease in paediatric units.

> **Antimicrobial susceptibility of multidrug-resistant Gram negative bacteria to fosfomycin.**

Falagas ME et al, Eur J Clin Microbiol Infect Dis. 2008 Jun;27(6):439-43. Epub 2008 Jan 23.

We evaluated the antimicrobial activity of fosfomycin against a randomly selected sample of 30 *Klebsiella pneumoniae*, 30 *Pseudomonas aeruginosa*, and 30 *Acinetobacter baumannii* multidrug-resistant, clinical isolates from patients in a general tertiary care hospital in Athens, Greece. Standard laboratory methods were used for susceptibility testing to commonly used antibiotics and the detection of extended-spectrum-beta-lactamase (ESBL) and metallo-beta-lactamase (MBL) production. The minimum inhibitory concentration (MIC) of fosfomycin for each isolate was determined by the agar dilution method. All *K. pneumoniae* isolates were both ESBL and MBL producers; all *P. aeruginosa* isolates were ESBL producers. The *K. pneumoniae* strains had fosfomycin MICs distributed across a range of 8-64 mug/ml; MIC(50) was 16 mug/ml and MIC(90) 32 mug/ml. The fosfomycin MICs of the *P. aeruginosa* strains had a distribution across a range of 4 to over 512 mug/ml; MIC(50) was 32 mug/ml and MIC(90) 128 mug/ml. The fosfomycin MICs of the *A. baumannii* strains had a distribution across a range of 64 to over 512 mug/ml; MIC(50) was 256 mug/ml and MIC(90) more than 512 mug/ml. Although standardized fosfomycin MIC interpretative breakpoints for the species studied are lacking, the findings of our study support the idea that fosfomycin may be further investigated as one among a decreasing list of therapeutic options for the treatment of infections due to multidrug-resistant strains of, primarily, *K. pneumoniae* and, secondly, *P. aeruginosa*.

> **Intensive care unit outbreak of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* controlled by cohorting patients and reinforcing infection control measures.**

Laurent C et al, Infect Control Hosp Epidemiol. 2008 Jun;29(6):517-24

OBJECTIVE: To describe an outbreak of extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae* in the intensive care units (ICUs) of a hospital and the impact of routine and

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reinforced infection control measures on interrupting nosocomial transmission. DESIGN: Outbreak report. SETTING: A 31-bed intensive care department (composed of 4 ICUs) in a university hospital in Belgium. INTERVENTION: After routine infection control measures (based on biweekly surveillance cultures and contact precautions) failed to interrupt a 2-month outbreak of ESBL-producing *K. pneumoniae*, reinforced infection control measures were implemented. The frequency of surveillance cultures was increased to daily sampling. Colonized patients were moved to a dedicated 6-bed ICU, where they received cohorted care with the support of additional nurses. Two beds were closed to new admissions in the intensive care department. Meetings between the ICU and infection control teams were held every day. Postdischarge disinfection of rooms was enforced. Broad-spectrum antibiotic use was discouraged. RESULTS: Compared with a baseline rate of 0.44 cases per 1,000 patient-days for nosocomial transmission, the incidence peaked at 11.57 cases per 1,000 patient-days (October and November 2005; rate ratio for peak vs baseline, 25.46). The outbreak involved 30 patients, of whom 9 developed an infection. Bacterial genotyping disclosed that the outbreak was polyclonal, with 1 predominant genotype. Reinforced infection control measures lasted for 50 days. After the implementation of these measures, the incidence fell to 0.08 cases per 1,000 patient-days (rate ratio for after the outbreak vs during the outbreak, 0.11). CONCLUSION: These data indicate that, in an intensive care department in which routine screening and contact precautions failed to prevent and interrupt an outbreak of ESBL-producing *K. pneumoniae*, reinforced infection control measures controlled the outbreak without major disruption of medical care.



Dissemination of extended-spectrum beta-lactamase-producing bacteria: the food-borne outbreak lesson.

Lavilla S et al, J Antimicrob Chemother. 2008 Jun;61(6):1244-51. Epub 2008 Mar 12

OBJECTIVES: Commensal and opportunistic bacteria producing extended-spectrum beta-lactamases (ESBL-PB) have undergone a broad and rapid spread within the general population; however, the routes of dissemination have not been totally elucidated. The aim of this study was to determine whether individuals involved in an outbreak of acute gastroenteritis, in addition to the enteropathogenic microorganism, share an ESBL-PB as indirect demonstration of its transmission from a common food source. METHODS: From 2003 to 2004 in Barcelona, Spain, stool samples from 905 people involved in 132 acute gastroenteritis outbreaks and 226 food handlers related to the outbreaks were investigated. RESULTS: In 31 outbreaks, 58 diners carrying one or more ESBL-PB were detected. In 10 outbreaks, two or more diners shared the same ESBL-PB, and in four of them, the strain was shared with the food handlers. CONCLUSIONS: This study provides circumstantial evidence that foods can be a transmission vector for ESBL-PB, probably from two reservoirs, food animals and food handlers.