

Wrestling with Microbes

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Combating Staph

Daptomycin is a cyclic lipopeptide antibiotic that is rapidly bactericidal in vitro against most clinically relevant gram-positive bacteria, including *Staphylococcus aureus*. In patients with *S. aureus* bacteraemia or right-sided endocarditis, daptomycin was shown to be equally efficacious to standard antimicrobial therapy (vancomycin or an anti-staphylococcal penicillin with low-dose gentamicin).^{1,2} Two-hundred and thirty-six patients with *S. aureus* bacteraemia with or without endocarditis were randomized to receive 6 mg of daptomycin intravenously per kilogram of body weight daily or to receive standard therapy. Success was assessed 42 days after the end of therapy. The two groups were found to be equally responsive (daptomycin: 44.2% vs. standard: 41.7%) for complicated bacteraemia, right-sided endocarditis, and methicillin-resistant *S. aureus*. There was slightly increased drug resistance in the daptomycin group, whereas treatment failure caused by an adverse drug reaction occurred more often in the standard-

therapy group. e.g. renal dysfunction was twice as common in the standard therapy group compared to daptomycin. Thus daptomycin is a suitable alternative in *S. aureus* sepsis and endocarditis especially in a complicated patient with renal failure.

1. Grayson ML. The treatment triangle for staphylococcal infections. *N Engl J Med*. 2006;17;355:724-7.
2. Fowler VG Jr, Boucher HW, Corey GR, Abrutyn E, Karchmer AW, Rupp ME, et al. *S. aureus* Endocarditis and Bacteremia Study Group. Daptomycin versus standard therapy for bacteremia and endocarditis caused by *Staphylococcus aureus*. *N Engl J Med* 2006;17;355:653-65.

Community acquired MRSA

Shortly after the introduction of methicillin in 1959, outbreaks of methicillin-resistant *Staphylococcus aureus* (MRSA) infections started. Methicillin resistance in *S. aureus* is in fact defined as an oxacillin resistance in vitro. Isolates resistant to oxacillin or methicillin are also resistant to all beta-lactam agents including cephalosporins. Methicillin resistance is mediated by the *mecA* gene, which

encodes an abnormal low-affinity binding protein, PBP-2a, that permits the organism to grow and divide in the presence of methicillin and other beta-lactam antibiotics, thus rendering the antibiotics ineffective. To date there have been five major MRSA clones identified worldwide which are responsible for a variety of toxins. MRSA is increasingly recognized in infections in the community without established risk factors for MRSA.

In a large multicenter study of MRSA in adults presenting to a university-affiliated emergency departments, *S. aureus* was isolated from 320 of 422 patients with skin and soft-tissue infections (76 percent).¹ The prevalence of MRSA was 59 percent overall and ranged from 15 to 74 percent in individual institutions. Among the MRSA isolates, 100 percent were susceptible to rifampin and trimethoprim-sulfamethoxazole (TMP-SMZ), 95 percent to clindamycin, 92 percent to tetracycline and 60 percent to fluoroquinolones. The study concluded that MRSA was the most common identifiable cause of skin and soft-tissue infections in USA hospital ER. When antimicrobial therapy is indicated for the treatment of skin and soft-tissue infections, cultures should be obtained and empirical therapy modified to provide appropriate coverage.

Community acquired MRSA infections are susceptible to TMP-SMZ (Bactrim), clindamycin, tetracycline / doxycycline, and ciprofloxacin / levofloxacin. These should be considered first-line agents in Community acquired MRSA infections and vancomycin, daptomycin, ticoplanin, tigecycline and linezolid used only in case of resistance to treatment.

1. Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, et al. EMERGency ID Net Study Group. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med* 2006; 17;355:666-74.

Antibiotics and Ear infection

Acute otitis media (AOM) is the most common reason for which an antibiotic is prescribed to children in the USA (15 million antibiotic prescriptions per year). Untreated AOM has a high rate of spontaneous resolution, with similar rates of complications whether antibiotics are prescribed or withheld.¹ Resistance to antibiotics is a major public health concern worldwide and is associated with the widespread use of antibiotics. A randomized controlled trial was conducted at Yale to evaluate a "wait-and-see prescription" (WASP) for antibiotics, where parents were asked not to fill the prescription unless the child either was not better or was worse in 48 hours.

All participants received complimentary bottles of ibuprofen suspension (100 mg/5 mL) and otic analgesic drops (each milliliter contains antipyrone, 54 mg/benzo-

caine, 14 mg). Treating pain associated with AOM has been recommended by current guidelines.²

Overall, 283 patients were randomized either to the WASP group (n = 138) or the standard prescription (SP) group (n = 145). AOM was unilateral in ~85% both groups and were mostly given a prescription for a 10-day course of amoxicillin. Substantially more parents in the WASP group did not fill the antibiotic prescription (62% vs 13%; $P < .001$). There was no statistically significant difference between the groups in the frequency of subsequent fever, otalgia, or unscheduled visits for medical care. Within the WASP group, both fever ($P < .001$) and otalgia (RR, 1.62; 95% CI, 1.26 - 2.03; $P < .001$) were associated with filling the prescription.

The WASP reduced the use of antibiotics by 56% in children between 6 months and 12 years of age diagnosed as having AOM.³

1. Le Saux N, Gaboury I, Baird M, et al. A randomized, double-blind, placebo-controlled noninferiority trial of amoxicillin for clinically diagnosed acute otitis media in children 6 months to 5 years of age. *CMAJ* 2005;172:335-41.
2. Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics* 2004;113:1451-65.
3. Spiro DM, Tay KY, Arnold DH, Dziura JD, Baker MD, Shapiro ED. Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial. *JAMA* 2006;296:1235-41.

Physician Burnout and Medical Errors

Physicians who believe they have committed a major medical error in the previous three months are more likely to report symptoms of burnout and depression, which may also increase the risk of a future error.¹ Since the Institute of Medicine's 1999 report that as many as 100,000 patients die each year because of preventable medical errors, several studies of physicians in medical and surgical residency programs have found that a significant proportion of medical trainees make medical errors.

Previous studies asking residents about errors either had taken a single snapshot in time or asked residents to look back on their entire residency and recollect whether they had made a serious error. This is the first study which followed a group of residents prospectively, enabling researchers to examine the relationship between physician distress and the future likelihood of an error.

The researchers followed 184 medical residents from 108 U.S. and international medical schools who were continuing their training in the Mayo Clinic Rochester Internal Medicine Residency Program. Residents completed quarterly surveys asking, "Are you concerned you have made any major medical errors in the last three months?" They also completed validated survey instruments to measure quality of life and burnout, and to screen for depression.

On average, 14.7 percent of the participants reported making an error in the previous three months on each quarterly survey. Those who reported an error experienced substantially higher levels of burnout and were more than three times more likely to have a screening test indicate possible depression.

The connection between errors and various measures of distress also operated in reverse; those who scored high on burnout measures were twice as likely to report an error in the next three months as those with low burnout. The study also found a trend toward increased future errors for physicians with symptoms of depression. Sleep deprivation has been previously found to be comparable to alcohol intoxication.² It is noteworthy that hospitals and governing bodies will bar alcohol intoxicated doctors from treating patients but not sleep-deprived Residents capable of incurring major medical errors, risking lives of patients.

1. Association of Perceived Medical Errors With Resident Distress and Empathy: A Prospective Longitudinal Study. Colin P. West; Mashele M. Huschka; Paul J. Novotny; Jeff A. Sloan; Joseph C. Kolars; Thomas M. Habermann; Tait D. Shanafelt JAMA 2006; 296:1071-78.
2. Fairclough SH, Graham R. Impairment of driving performance caused by sleep deprivation or alcohol: a comparative study. Hum Factors 1999;41:118-28.

Green tea and heart disease

Tea is the most consumed beverage in the world aside from water. Three billion kilograms of tea are produced each year worldwide. Because of the high rates of tea consumption in the global population, even small effects in humans could have large implications for public health. Tea

is generally consumed in the forms of green, oolong, and black tea, all of which originate from the leaves of the plant *Camellia sinensis*. Among teas, green tea polyphenols have been extensively studied as cardiovascular disease (CVD) and cancer chemopreventive agents.¹

A population-based, prospective cohort study was conducted in Japan on >40 thousand adults aged 40 to 79 years without history of stroke, coronary heart disease, or cancer at baseline. Over 11 years of follow-up (follow-up rate, 86.1%), 4209 participants died, and over 7 years of follow-up (follow-up rate, 89.6%), 892 participants died of CVD and 1134 participants died of cancer. Green tea consumption was inversely associated with mortality to CVD. Among the types of CVD mortality, the strongest inverse association was observed for stroke mortality. In contrast, green tea consumption was not preventive for mortality from cancer.

Chinese tea (Oolong) or Black tea was not associated with mortality from CVD or cancer. However risk ratios for black tea consumption >1 cup ranged from 0.8 to 1.5, indicating that drinking more than 1 cup of black tea per day may in fact be detrimental to health.

1. Zaveri NT. Green tea and its polyphenolic catechins: medicinal uses in cancer and noncancer applications. Life Sci 2006;78:2073-80.
 2. Kuriyama S, Shimazu T, Ohmori K, Kikuchi N, Nakaya N, Nishino Y, et al. Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: the Ohsaki study. JAMA 2006;296:1255-65.
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