In the Literature

Antibiotic Use and Resistance in the Pneumococcus


Microbial evolutionary adaptation requires horizontal transfer of genetic material or genetic mutability, each of which result in the requisite genetic plasticity for species survival under environmental pressure. Horizontal transfer of DNA in Streptococcus pneumoniae is accomplished by bacterial transformation, a mechanism that allows uptake of exogenous DNA and its integration into the genome of the recipient bacterial cell. The competence needed for efficient acquisition and integration of exogenous DNA is a transient state that is accompanied by simultaneous ability to kill neighboring cells that are not competent for this process, an ability that has been called “pneumococcal fratricide.” Competence in S. pneumoniae is induced by the competence-stimulating peptide (CSP), a pheromone that is sensed by a histidine kinase receptor that is part of a 2-component regulatory system that transports a signal leading to transcriptional activation of the competence regulon, which comprises >100 genes, including recA. recA catalyzes homologous recombination, thus integrating the DNA that has been internalized into the genome of the recipient bacterium.

The activation of the SOS stress response is an important mechanism by which many organisms increase their mutation rate. The SOS response is activated by, among other things, exposure to one of several antibiotics, and in addition to potentially leading to antibiotic resistance mutations, it increases the horizontal transfer of virulence and antibiotic resistance factors. S. pneumoniae lacks an SOS system, but Prudhomme and colleagues now provide evidence that bacterial transformation plays a similar role in this organism. Thus, aminoglycosides and fluoroquinolones, as well as mitomycin C, each induced transformation in S. pneumoniae, although cell wall–active antibiotics and rifampin did not. Competence for transformation is, therefore, a general stress response in S. pneumoniae, analogous to the SOS response in other bacteria. The result is, among other things, a mechanism by which antibiotic use, both appropriate and inappropriate, drives the emergence of resistance in the pneumococcus.

Cardiac Valve Surgery in Patients with Infective Endocarditis and Stroke: Is It Safe? Must It Be Delayed?


Cerebral embolic events are a common complication of infective endocarditis. The clinician is often faced with a dilemma when a patient who has had such an occurrence requires urgent cardiac valve surgery, because of concern about exacerbating the neurological lesion. These concerns are based on the loss of peri-infarct vascular autoregulation for as long as 4 weeks after stroke and on potentially adverse conditions during cardiopulmonary bypass. The latter include induced hypotension, which has the potential to exacerbate ischemic effects and to increase cerebral edema at the margins of the infarct, as well as the requirement for heparinization, which may lead to hemorrhagic conversion of an ischemic infarction. These concerns have led to recommendations for a delay in cardiac surgery in patients who have had recent strokes. Thus, current Infectious Diseases Society of America–endorsed guidelines state, “To prevent hemorrhagic complications, it has been suggested that valve surgery be delayed for a minimum of 2 weeks after either a central nervous system embolic event or bleed or repair of intracranial mycotic aneurysms” [1].

Ruttmann and colleagues have addressed the actual risk of neurologic complications of cardiac surgery in a large series of patients who had already experienced embolic strokes. Sixty-five (30.4%) of 214 patients who underwent cardiac surgery for management of left-side infective endocarditis had a stroke (n = 61) or transient ischemic attack (n = 4) before undergoing surgery. The median interval from the cerebral event to valve surgery was 4 days (range, 0–38 days). Two of 6 patients with intracranial hemorrhage underwent craniotomy before cardiac surgery. Cardiac surgery was performed with the use of extra-corporeal circulation, with mild hypothermia and full anticoagulation with heparin.

The perioperative mortality rate was 16.9% and did not significantly differ from the mortality rate among patients who had not had a stroke before undergoing surgery (16.9% vs. 12.8%; P = .42). Patients with stroke who had additional preoperative neurological complications, such as meningitis, cerebral hemorrhage, or brain abscess, had a higher risk of perioperative death than did patients without such complications (38.9% vs. 8.5%; P = .007). Four of the 6 patients with cerebral hemorrhage died after cardiac surgery, but only 1 of these deaths was caused by recurrence of intracranial bleeding. Two of 5 patients with intracerebral abscess died of persisting sepsis, without evidence of postoperative neurological complication. The actuarial survival rates at 1, 5, and 10 years among patients who had a stroke did not significantly differ from the rates among patients who did not have a stroke.

Overall, 70% of survivors subsequently achieved full neurological recovery. Compared with surgery delayed for >4 days, cardiac surgery within the first 4 days after stroke was not associated with a signifi-
cantly increased risk of perioperative neurological complication (0% vs. 3.2%; \( P = .32 \)) or with reduced postoperative neurological recovery (70% vs. 75%; \( P = .68 \)).

The overall lessons that may be drawn from this experience include the fact that patients with uncomplicated embolic stroke as the result of infective endocarditis, including those who require cardiac surgery, have a generally favorable prognosis. There was no apparent increased risk of neurologic complications in patients undergoing surgery within 4 days of the cerebral event, compared with those for whom surgery occurred later, suggesting that delaying cardiac surgery in patients with ischemic cerebral events may not be warranted. Little can be said of the safety of early surgery in patients with hemorrhagic infarcts, but only 1 of 6 patients with this problem who underwent surgery had postoperative exacerbation of their cerebral hemorrhage.

Reference


Triple-Antibiotic Ointment (TAO): Still Active after All These Years


TAO contains neomycin, polymyxin B, and bacitracin and has long been an over-the-counter preparation in the United States. Despite its widespread use, Jones and colleagues report no evidence of an increase in resistance among a variety of bacterial species during the period 1997–2002. All 10 strains of Pseudomonas aeruginosa (30% of which were resistant to gentamicin), all 20 strains of Escherichia coli, and all 51 strains of coagulase-negative staphylococci tested were susceptible to a 1:100 dilution of TAO. Five percent of 110 strains of S. aureus were resistant to this concentration. A separate analysis of gentamicin-resistant strains of S. aureus (76% of which were methicillin-resistant S. aureus [MRSA]), only 1% of which were resistant to TAO, found that 11% exhibited high-level resistance to mupirocin. As expected, bacitracin was the individual component of TAO with the most activity against S. aureus.

Among the available topical antimicrobial preparations, the isoleucyl-tRNA synthetase (IleS) inhibitor, mupirocin, is widely used for, among other things, the treatment of cutaneous infections due to S. aureus; it has also been used in attempts to eradicate MRSA from the nares of individuals who are colonized with this organism. Unfortunately, an increasing prevalence of high-level resistance of MRSA to mupirocin has been reported by a number of investigators. A gene encoding high-level resistance to mupirocin, \( \text{ileS} \), carried on a conjugal plasmid, PUSA03, which also carries \( \text{ermC} \), has been detected in 46% of multidrug-resistant strains of USA300, the most prevalent strain of community-acquired MRSA in the United States [1]. Bacitracin, which is actually a mixture of high–molecular weight polypeptides that act by binding to undecaprenol monophosphate in the bacterial cell membrane, is the component of TAO with the greatest activity against S. aureus. Both bacitracin used alone and as part of a triple-antimicrobial combination comprising bacitracin, gramicidin, and polymyxin B have been used as components in successful MRSA decolonization [2, 3]. Given the cost of mupirocin ointment, together with the apparently increasing prevalence of resistance to it among MRSA strains, the potential for TAO (or, perhaps, bacitracin alone) as a substitute treatment is intriguing. In addition, at least 1 other agent (REP8839, an inhibitor of methionyl tRNA synthetase) is in clinical development as a topical agent with activity against MRSA [4].

References


Biofilm: Persistent Infection in Children with Chronic Otitis Media


In this study, although only 6 (22%) of 27 middle ear effusions from children with chronic otitis media yielded pathogens on culture, there was evidence of bacterial infection in all 27 when tested by PCR. Mucosal bacterial biofilm, which was detected by a variety of methods, was present in 92% of biopsy specimens obtained from patients and from none of the biopsy specimens obtained from 8 control subjects. These findings provide a plausible explanation for the frequent lack of efficacy of antibiotic therapy and for the persistence of infection in children with chronic otitis media.