Staphylococcus aureus (MRSA) or *Pseudomonas aeruginosa*. Mice randomly received a resorbable antibody delivery vehicle at the implant site: a blank carboxymethylcellulose (CMC) aqueous gel or the same CMC gel containing 10 mg of pooled polyclonal human immunoglobulin G locally on the implant after infection, either alone or in combination with systemic doses of cefazolin or vancomycin antibiotics. Human antibodies were rapidly released (first-order kinetics) from the gel carrier to both peritoneal fluids and serum in both infection scenarios. Inocula required for lethal infection were substantially reduced by surgery and the presence of the implant versus a closed lethal peritonitis model. Survival to 10 days with two different *P. aeruginosa* strains was significantly enhanced ($P < .01$) by the direct application of CMC gel containing antibodies alone to the surgical implant site.

Human-equivalent doses of systemic vancomycin provided a significantly improved benefit ($P < .01$) against lethal, implant-centered, gram-positive MRSA infection. However, locally delivered polyclonal human antibodies in combination with a range of systemic vancomycin doses against MRSA failed to improve host survival. Successful antibody therapy against gram-negative, implant-centered infections complements the clinically routine use of systemic antibiotics, providing a mechanism of protection independent of antibiotic resistance.

FROM: Poelstra KA, Barekzi NA, Rediske AM, Felts AG, Slunt JB, Grainger DW. Prophylactic treatment of gram-positive and gram-negative abdominal implant infections using locally delivered polyclonal antibodies. *J Biomed Mater Res* 2002;60:206-215.

Fibrin Sheath Enhances Central Venous Catheter Infection

Mehall and colleagues from the University of Arkansas for Medical Sciences, Little Rock, Arkansas, conducted a study to determine whether fibrin-coated central venous catheters have a higher infection rate, and spawn more septic emboli, than uncoated catheters after exposure to bacteremia. The study compared catheter infection and blood cultures of fibrin-coated and uncoated catheters exposed to bacteremia using adult male Sprague–Dawley rats.

A total of 210 rats had catheters placed with the proximal end buried subcutaneously. Rats were divided into three groups: tail vein bacterial injection on day 0 (no fibrin group) or on day 10 (fibrin group), or no injection/saline injection (control, n = 40). Bacterial injections were 1×10^8 colony-forming units of either *Staphylococcus epidermidis* (n = 100) or *Enterobacter cloacae* (n = 60). Animals were killed 3 days after injection. Blood cultures were obtained via cardiac puncture, and catheters were removed via the chest. Half of the catheter was rolled onto agar and the other half was placed in trypticase soy broth. Plates and broth were incubated at 37°C for 48 hours. The presence of more than 15 colonies on roll plates, or growth in broth, was accepted as a positive sign of infection. Thirty animals without catheters had bacterial injections and had blood cultures 3 days after injection.

Catheter infection with *S. epidermidis* occurred in 32% of roll plates and 80% of broth from the fibrin group versus 4% of roll plates and 20% of broth from the no fibrin group ($P < .01$ for each). Catheter infection with *E. cloacae* occurred in 50% of roll plates and 80% of broth from the fibrin group versus 0% of roll plates and 12% of broth from the no fibrin group ($P < .01$ for each). Positive blood cultures occurred in 47 of 68 animals from the fibrin group versus 8 of 68 from the no fibrin group ($P < .01$). Microscopy showed a fibrin sheath on 20 of 20 catheters. Without catheters, 30 of 30 blood cultures were negative.

The authors concluded that the fibrin sheath significantly enhanced catheter-related infection and persistent bacteremia.

FROM: Mehall JR, Saltzman DA, Jackson RJ, Smith SD. Fibrin sheath enhances central venous catheter infection. *Crit Care Med* 2002;30:908-912.

P. aeruginosa Cells Adapted to Benzalkonium Chloride Are Not Antibiotic Resistant

Loughlin and colleagues from the United Kingdom conducted studies to determine whether strains of *Pseudomonas aeruginosa* can adapt to growth in increasing concentrations of the disinfectant benzalkonium chloride, and whether co-resistance to clinically relevant antimicrobial agents occurs. Attempts were made to determine what phenotypic alterations accompanied resistance and whether these explained the mechanism of resistance. Strains were serially passaged in increasing concentrations of benzalkonium chloride in static nutrient broth cultures. Serotyping and genotyping were used to determine the purity of the cultures. Two strains were examined for cross-resistance to other disinfectants and antibiotics by broth dilution minimum inhibitory concentration determination. Alterations in outer membrane proteins and lipopolysaccharide expressed were determined, as well as cell surface hydrophobicity and charge, uptake of disinfectant, and proportion of specific fatty acid content of outer and cytoplasmic membranes.

Two *P. aeruginosa* strains showed a stable increase in resistance to benzalkonium chloride. Co-resistance to other quaternary ammonium compounds was observed in both strains; chloramphenicol and polymyxin B resistance was observed in one and a reduction in resistance to tobramycin was observed in the other. However, no increased resistance to other biocides (chlorhexidine, triclosan, and thymol) or antibiotics (ceftazidime, imipenem, ciprofloxacin, and tobramycin) was detected. Characteristics accompanying resistance included alterations in outer membrane proteins, uptake of benzalkonium chloride, cell surface charge and hydrophobicity, and fatty acid content of the cytoplasmic membrane, although no evidence was found for alterations in lipopolysaccharide. Each of the two strains had different alterations in pheno-

type, indicating that such adaptation is unique to each strain of *P. aeruginosa* and does not result from a single mechanism shared by the whole species.

FROM: Loughlin MF, Jones MV, Lambert PA. *Pseudomonas aeruginosa* cells adapted to benzalkonium chloride show resistance to other membrane-active agents but not to clinically relevant antibiotics. *J Antimicrob Chemother* 2002;49:631-639.

Biofilms: Survival Mechanisms of Clinically Relevant Microorganisms

Donlan and Costerton point out that although biofilms were first described by Antonie van Leeuwenhoek, the theory describing the biofilm process was not developed until 1978. It is now understood that biofilms are universal, occurring in aquatic and industrial water systems and in a large number of environments and medical devices relevant for public health. Using tools such as the scanning electron microscope and, more recently, the confocal laser scanning microscope, biofilm researchers now understand that biofilms are not unstructured, homogeneous deposits of cells and accumulated slime, but rather complex communities of surface-associated cells enclosed in a polymer matrix containing open water channels.

Further studies have shown that the biofilm phenotype can be described in terms of the genes expressed by biofilm-associated cells. Microorganisms growing in a biofilm are highly resistant to antimicrobial agents by one or more mechanisms. Biofilm-associated microorganisms have been shown to be associated with several diseases in humans, such as native valve endocarditis and cystic fibrosis, and to colonize a wide variety of medical devices. Although epidemiologic evidence points to biofilms as a source of several infectious diseases, the exact mechanisms by which biofilm-associated microorganisms elicit disease are poorly understood. Detachment of cells or cell aggregates, production of endotoxin, increased resistance to the host immune system, and provision of a niche for the generation of resistant organisms are all biofilm processes that could initiate the disease process. Effective strategies to prevent or control biofilms on medical devices must take into consideration the unique and tenacious nature of biofilms. Current intervention strategies are designed to prevent initial device colonization, minimize microbial cell attachment to the device, penetrate the biofilm matrix and kill the associated cells, or remove the device from the patient. In the future, treatments may be based on the inhibition of genes involved in cell attachment and biofilm formation.

FROM: Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. *Clin Microbiol Rev* 2002;15:167-193.

The Success of Routine, Voluntary Inpatient HIV Testing

Despite current recommendations for human immunodeficiency virus (HIV) counseling and testing among patients admitted to hospitals with at least a 1% prevalence of HIV infection, an estimated 300,000 individuals in the United States remain unaware of their HIV infection. Walensky and colleagues implemented the Think HIV program, which offered voluntary HIV counseling and testing to patients admitted to the medical service of a Boston, Massachusetts, teaching hospital. The results of this effort were compared with testing results from a 15-month historical control period.

Patients admitted during the program period were 3.4 times more likely to undergo testing for HIV than were those admitted during the control period (95% confidence interval [CI_{95}], 2.8 to 4.1). The testing program detected approximately two new diagnoses of HIV infection per month, compared with one per month during the control period. Patients who underwent testing during the program, and who likely would not have done so without this initiative, had an estimated prevalence of HIV infection of 3.8% (CI_{95}, 1.8% to 5.8%).

The authors concluded that testing efforts for HIV targeted at only symptomatic patients are inadequate to identify the one-third of HIV-seropositive individuals in the United States who are unaware of their infection. They point out that their results show that in a single urban hospital, voluntary, routine inpatient HIV counseling and testing was successful as a screening program by identifying a substantial number of patients with undiagnosed HIV. These patients then can be informed, counseled, and linked to care and treatment. Seventy-two hospitals nationwide have demographics similar to those of the study hospital, suggesting that these results are generalizable to many urban hospitals.

FROM: Walensky RP, Losina E, Steger-Craven KA, Freedberg KA. Identifying undiagnosed human immunodeficiency virus: the yield of routine, voluntary inpatient testing. *Arch Intern Med* 2002;162:887-892.