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Wanted: Plastics with Antimicrobial Properties

Microbial growth on synthetic material can cause a variety of undesirable consequences from the fouling of ships by marine bacteria to the degrading of industrial polymers by yeasts. In this issue of the Journal, Anderson, *et al,* discuss the colonization of pseudomonads, bacteria commonly found in water and soil, in plastic tubing used in the manufacture of iodine-containing antiseptic solutions.[1] Closely related to this phenomenon is the colonization of plastic medical devices by members of the *Staphylococcus epidermidis* group, the so-called coagulase-negative staphylococcus.[2] While these two groups of organisms differ from each other in most characteristics, their activities and colonization on plastic surfaces are remarkably similar and the focus of this editorial.

During the past decade, intrinsic microbial contamination of idophor antiseptic solutions has been well documented.[3] Several investigators have reported pseudobacteremia resulting from the use of povidone-iodine solution contaminated with *Pseudomonas cepacia.*[4–6] Parrott, *et al,* attributed peritoneal infections to use of *Pseudomonas aeruginosa* contaminated poloxamer-iodine.[7] In an attempt to determine the cause of these contaminations, Anderson, *et al,* demonstrated that *P. aeruginosa* could survive in idophor solutions for a prolonged time and suggested that the contaminant had its origin on the inside surfaces of "naturally contaminated polyvinylchloride (PVC) distribution pipes."[8,9]

Costerton and his associates suggested that the survival of microorganisms in iodine-containing solutions may be due to an glycocalyx-like extracellular slime substance that microbes deposit on various surfaces. They suggested that colonization of these microbes on the interior surfaces of PVC pipes and the formation of slime matrixes protect the contaminating organisms from the biocidal activity of antiseptic solutions.[10–12]

The present paper by Anderson, *et al,* discusses the colonization of *Pseudomonas pickettii* and *P. aeruginosa* on the interior surfaces of PVC and other pipes exposed to various classes of disinfectants.[1] Colonization of PVC surfaces, as in previous studies, were examined by scanning electron-microscopy; *P. aeruginosa* was recovered from PVC pipes previously exposed to chlorine, phenolic, quartenary-ammonium, and iodophor disinfectants, while *P. pickettii* was recovered from water in pipes treated with iodophor disinfectant, chlorine and 70 percent ethanol. They concluded, as did Costerton, *et al,*[10–12] that "The existence of glycocalyx-like cellular masses on the interior wall of PVC pipes most likely protected embedded organisms from the microbial action of some of the disinfectants tested and served as the reservoir for continuous contaminations." They outline effective maintenance strategies that routinely sanitize the water or product distribution lines in manufacturing plants and health care facilities for the control of Pseudomonas and other gram-negative water bacteria.[1]

The colonization of staphylococci, especially the coagulase-negative strains reported by Peters,[2] is a fascinating comparison to the colonization of pseudomonads. For many years, it was believed that these strains lacked the pathogenic potential of S. aureus. In the early 1950s it was reported by Sugarman and Young that some coagulase-negative strains were not killed by human white blood cells;[13] however, it was not until the early 1970s that potential pathogenic mechanisms, production of slime and presence of toxins, were described.[14]

In medicine, bacterial adhesions on plastics play an important role in the

development of implants or catheter-related infections. Synthetic polymers such as polyvinylchloride, polyethylene, polyurethane, and silicone make up the majority of plastic materials used in medicine. Besides thrombosis, infection is the most severe complication associated with the use of these materials. The number of patients involved has been increasing due to the progress of modern medicine and, at the present time, the so-called "plastic surface infections" is accepted as an opportunistic nosocomial infection.[2]

Currently, the coagulase-negative staphylococci are implicated in a great proportion of the infections associated with synthetic intravenous, urinary tract, and intraperitoneal catheters and such foreign bodies as cerebrospinal fluid and heart valves, prosthetic hips and atrioventricular shunts.[15]

The first real understanding of the plastic surface infections was obtained by scanning electromicroscopy investigations of infected intravenous catheters.[16,17] They showed a thick matrix composed of multiple stapylococcal cell layers and copious amounts of extracellular slime. Similar observations have been reported with other polymer devices such as transvenous endocardial pacemaker leads.[18]

The pathogenesis of the coagulase-negative staphylococcus infection associated with the presence of foreign devices is characterized by the ability of these organisms to adhere to polymer surfaces. Adherence is followed by colonization and the production of the slime that has been implicated as a major virulence factor in such infections. Unlike the Pseudomonas matrix, the slime produced by coagulase-negative staphylococcus is water soluble and can be largely removed from the cells by washing. It is a complex glycoconjugate and distinguishable from the true bacterial capsule.[19,20]

In vitro and animal experiments suggest that the slime produced by *S. epidermidis* is of high biological potency and interferes with several host defense mechanisms such as inhibition of T-cell and B-cell blastogenesis, immunogloblin production, and bacterial opsonization. It also enhances the virulence of the organism in mice and interferes with the action of anti-staphylococcal antibiotics.[2]

The similarities between the aforementioned two dissimilar groups—the pseudomonads commonly found in water and the *S. epidemidis* group commonly found on the skin—are remarkably close. Both adhere to the surfaces of synthetic polymers, both do not produce a true capsule, both colonize polymers by secreting an extracellular slime of complex glycoconjugate nature, both form a thick matrix composed of many layers of cells within the slime substance, both are protected from antiseptic/antibiotic/host defenses by the extracellular slime, and both demonstrate increased virulence following colonization.

It is obvious that in order to control industrial product degradation and the "plastic surface infections" of medical implants, methods must be found to retard the adherence and colonization of microbes on plastics. Little is known regarding the pseudomonads, while much has been reported on the conditions regulating the colonization of staphylococci. Unfortunately, many of these studies have employed in vitro models; although the mechanisms are not completely understood it has been concluded that hydrophobic and electrostatic interactions play an important role. The few in vivo studies reported suggest that serum and bacterial proteins, and sugars or lectins might be important factors.[2]

In order to prevent colonization, adhering bacteria must first be eliminated. This could be done by incorporating intrinsic anti-adhesive properties into the polymers during the manufacturing process or by coating the polymers with chemicals that will hinder adhesion or kill the microbes upon contact. Jansen *et al,* reported that adhesion of a member of the coagulase-negative staphylococcus to a 2-hydroxyethyl methacrylate-grafted polyetherurethanes with high affinity for albumine is low compared with that to unmodified polyetherurethanes. Antistaphylococcal antibiotics have been incorporated into the matrix of polymers by swelling agents and by solvent casting procedures with little success; the inhibition effects were dissipated after two or three days.[21]

At a time when polymer science is becoming more adept in its ability to control both the polymerization process and the structure of the final product, research should be focused on the manufacture of polymers with antimicrobial properties. There are two levels of approach. The first, an evaluation of fast-acting, wide spectrum antimicrobial chemicals that, when added to the polymer, will leach onto its surface for a prolonged period of time; this process should eliminate the adhering contaminant before the secretion of the protective slime. In other words, the polymer will act as its own "drug delivery system."[21] A second approach should include a study of the adhesion sites on the surfaces of both the organism and polymer together with the mechanisms that control the attraction and interaction between the two; once these are understood, it may be possible to mediate adhering activity of the organism by modifying the polymer surface.[2] It is time for the government, and the chemical, pharmaceutical, and medical device manufacturers to launch a major effort for the prevention of the colonization of polymers used in industry and medicine by pooling the professional expertise of the microbiologist, the clinician and, above all, the polymer engineer.

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Promoting the Art of the Possible in Long-term Care

Lewis and her colleagues at UCLA have helped further our understanding of the dynamics of nursing home care by pointing out that it is not necessarily a final sentence. In their newest report from Southern California, published in this issue of the Journal, the authors indicate that a person who survives admission to a nursing home has a good chance of going home and pretty much staying there.[1] From their series of new admissions, about 29 percent died in the nursing home and another 7 percent died in hospital after transfer there. Among the remaining 64 percent discharged alive, the median survival time approached two years, half of which was spent at home.

This is encouraging news about a group of patients generally written off as hopeless and incapable of recovery. However, there is some basis for concern: findings are generalizable given the previous history of effects reported from these areas (San Bernardino, Riverside, Ontario) running counter to the other reported trends[2,3] and the variation in nursing home performance across the country.[4] The authors' optimism is bolstered by the observation from community studies that the long-term care population may not be as doomed to decline as was formerly thought. Indeed, many disabled persons showed improvement in function over a two-year period.[5]

It is important to bear in mind that this report is not a description of particularly good (or innovative) care, but of what happens under conditions of routine care. With this sense of potential improvability in mind, might we not expect more from long-term care than custodial care? The persistent lack of association between the processes of long-term care and its end-results has prompted some to argue that nothing can be done. In effect, we have begun to rigidify the situation with regulations and payment policies just when we need a burst of innovation that reflects a higher level of expectation from the system and a willingness to pay for it.

The 1986 Institute of Medicine report on nursing homes hinted at the need for more emphasis on the outcomes of care but stopped short of demanding real reform.[6] The current interest in case-mix reimbursement schemes for nursing homes tends to re-enforce the present practices because the cost calculations are based on time and motion studies of contemporary care. The model concretizes the current approach by looking at what *is* done, not what should be. Attention is paid to what is needed to do a more rehabilitative job or the fact that, over the short run, it takes more time and effort to help people do things for themselves than to do the tasks for them. The result is an incentive system that may not discourage homes from taking clients that require much tending but provides little impetus for them to invest the effort needed to help clients to improve.

One answer lies in changing the basis on which long-term care is paid, moving from a process-driven approach to one based on outcomes.[7,8] From the outset, it is crucial to bear in mind that "outcomes" here refers to an appropriately adjusted measure, which reflects the probability of a client improving or worsening. In essence, outcomes are expressed as the ratio of observed to expected. This is, then, the ultimate case correction. Under such an approach, nursing homes would be paid more if their patients' summative ratio of observed/expected was greater than one and less if the opposite were true. How much more or less would depend on whether the funding agency was willing to provide additional funds to encourage better care or insisted on only redistributing existing resources more equitably.

Such an outcome-driven payment approach provides the incentives to make the necessary investments in better, more rehabilitative care. It also provides a means for encouraging experimentation in new care forms, because it frees the providers from many of the current regulatory impedimenta which encourage conformity with approaches that have never been empirically established. Moreover, it provides a means by which one can compare the effectiveness of care across sites, because nothing in the approach defines how or where the care is given.

It is high time we at least put such a system to the test. In the only experiment to test an incentive approach, nursing homes did not respond to monetary incentives to take more complex cases or to improve the status of their clients; but the intervention was short, cheap, complex and poorly understood by the participants.[9,10] At a time when society is demanding better care for the growing numbers of dependent elderly, can we not be more creative than simply calling for