Table 1. Statistical evaluation of distribution of rubella and human herpesvirus 6 (HHV-6) antibodies according to retinal disease group or controls.

Group	No. of pairs	Rubella IgG (IU/mL) Geometric mean (quartiles) Cases	Rubella IgG (IU/mL) Geometric mean (quartiles) Controls	Ratio (95% CL)	P	HHV-6 IgG grade (mean [SD]) Cases	HHV-6 IgG grade (mean [SD]) Controls	P
All Pairs	91	56.8 (28, 121)	64.8 (34, 137)	0.88 (0.63, 1.22)	.43	1.57 (0.99)	1.45 (0.95)	.42
Age-related macular degeneration	37	48.6 (25, 107)	66.9 (33, 179)	0.73 (0.45, 1.18)	.19	1.61 (0.99)	1.39 (0.90)	.36
Diabetic background retinopathy	25	60.8 (34, 155)	55.6 (25, 81)	1.09 (0.58, 2.06)	.77	1.68 (0.99)	1.28 (0.93)	.17
Diabetic proliferative retinopathy	13	44.6 (11, 205)	95.9 (46, 351)	0.47 (0.21, 1.74)	.23	1.30 (0.75)	1.62 (0.87)	.30
Rhegmatogenous detachment	16	89.0 (44, 192)	55.8 (37, 104)	1.59 (0.81, 3.14)	.16	1.50 (1.10)	1.81 (1.05)	.43

NOTE. CL, confidence limits.

Conall Mc Caughey, Paula Gormley, John H. Connolly, Desmond B. Archer, and Peter V. Coyle

Regional Virus Laboratory, Ophthalmology Department, Royal Victoria Hospital, Belfast, United Kingdom.

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Quaternary Amine (Protamine Sulfate) Is Bactericidal to *Staphylococcus epidermidis*

Colleagues—*Staphylococcus epidermidis* genitourinary prosthesis infections are a cause of serious morbidity. The usual manner of treating a prosthesis infection is prolonged antibiotic treatment with either prosthesis removal or exchange, both requiring a subsequent operation [1]. The natural history of a prosthesis infection is little altered once *S. epidermidis* is inoculated onto the prosthetic device at the time of implantation. Methods to disrupt this process could reduce this clinical problem. We hypothesize that the quaternary amine protamine sulfate interacts with bacterial biofilm ionically and disrupts the permeability protective barrier biofilm confers. In an attempt to impair the protective effect of the glycocalyx, we examined the ability of protamine sulfate to inhibit viability of *S. epidermidis*.

S. epidermidis was isolated from 6 patients whose prostheses required removal because of infection. The isolates were cultured aerobically at 38°C on Columbia agar (Sigma, St. Louis) containing defibrinated sheep's blood (Hardy Media, Santa Barbara, CA). The organism was confirmed by morphology on Gram's stain of the viable colonies and a negative coagulase test. The isolates were serially inoculated and incubated aerobically in brain-heart infusion (BHI) broth (Becton Dickinson, Cockeysville, MD) at 38°C to maintain the isolates in a logarithmic growth pattern. The bacteria were periodically reverified as *S. epidermidis*.

Organisms were incubated on two media groups: BHI as a control and BHI and protamine sulfate (Sigma) (250 μg/mL–10 mg/mL). Aliquots of each group (100 μL) were plated on Columbia agar with defibrinated sheep's blood and incubated aerobically at 38°C. Viable colony counts per milliliter were determined at 0, 5, and 240 min. Student's *t* test was used for statistical analysis.

All 6 isolates were coagulase-negative staphylococci. There were no contaminant colonies.

The colony count results were averaged. Figure 1 demonstrates a growth curve for media containing protamine sulfate alone in concentrations of 0 or control, 250 μg/mL, 500 μg/mL, 1 mg/mL, and 10 mg/mL. The viable colony counts per milliliter at 5 min and 4 h were, respectively, 7.3×10^{-6} and 6.2×10^{-8}, 1.0×10^{-6} and 1.2×10^{-5}, 7.8×10^{-4} and 3.4×10^{-4} ($P = .08$), 1.3×10^{-3} and 9.1×10^{-2} ($P = .0001$), and 2.9×10^{-3} and 1.4×10^{-5} ($P = .03$). The trend suggests a dose-dependent response.

Recently, Farber and Wolff [2] reported that nonsteroidal antiinflammatory drugs decrease *S. epidermidis* slime production on catheter segments in a dose-dependent fashion. This novel approach suggests that viability of the organism is dependent upon biofilm integrity.

Protamine sulfate is a quaternary amine. It is an anticoagulant when administered intravenously by itself. In the presence of

Reprints or correspondence: Dr. Joel M. H. Teichman, UCSD Medical Center, Division of Urology (8897), 200 W. Arbor Dr., San Diego, CA 92103-3397.

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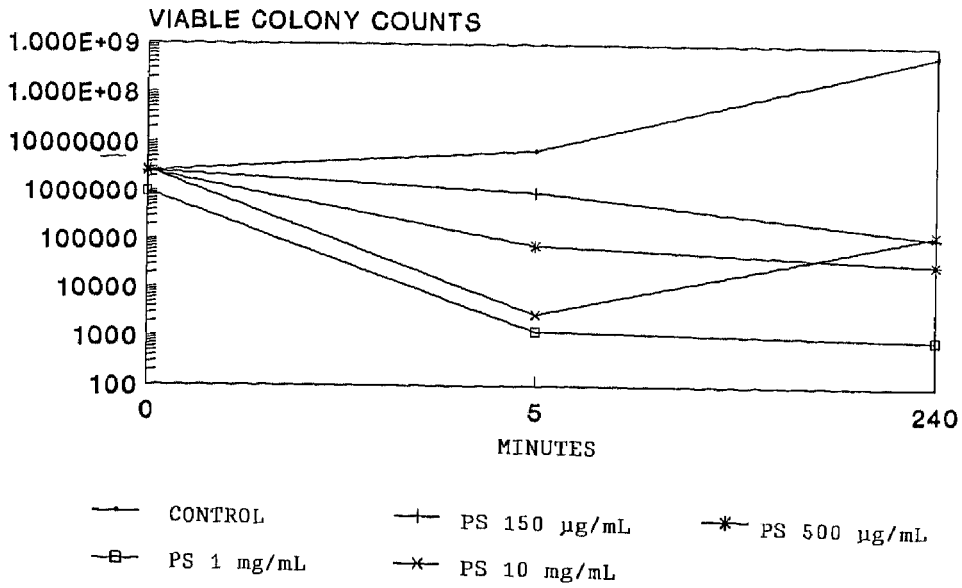

Figure 1. Dose-dependent growth curve for isolates of *S. epidermidis* incubated with protamine sulfate (PS).

heparin, a stable salt is formed that results in loss of coagulant activity for both compounds [3]. Protamine has been shown to alter bladder surface proteoglycans (mucin), an effect that is reversed by the administration of heparin [4–6]. Protamine displaces water molecules from surface proteoglycans by ionically binding to polysaccharides and thereby disrupts the epithelial surface [7]. Parsons et al. [4] have reviewed the heparin-reversible permeability changes exerted by protamine sulfate on epithelial surfaces.

These results demonstrate that protamine sulfate has an immediate biocidal effect when given in sufficient concentration (figure 1). Although this study did not define the mechanisms of action of protamine sulfate, the results support the proposed hypothesis that protamine sulfate exerts its antibacterial action by direct deleterious effects on the surface proteoglycans of the bacterial slime (biofilm) of *S. epidermidis* resulting in an immediate decrease in bacterial viability.

Joel M. H. Teichman, Paul C. Stein, and C. Lowell Parsons
Division of Urology, University of California, San Diego, Medical Center

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Salicylic Acid Decreases Extracellular Biofilm Production by *Staphylococcus epidermidis*: Electron Microscopic Analysis

Colleagues—*Staphylococcus epidermidis* has emerged as a major cause of prosthetic device–related infection. Certain strains produce an extracellular slime-like substance that appears to be an important virulence factor [1–3]. Extracellular slime produced by *S. epidermidis* is made primarily of polysaccharides rich in glucose and galactose [4, 5]. We recently demonstrated that salicylic acid and certain other nonsteroidal antiinflammatory drugs prevent adherence of *S. epidermidis* to medical polymers [6]. Spectrophotometric studies also revealed a dose-related decrease in slime production when organisms were grown in polypropylene wells in increasing concentrations of salicylic acid. Here we report that *S. epidermidis* grown in the presence of salicylic acid results in decreased biofilm production when visualized by electron microscopy.

Trypticase soy broth (10 mL) was prepared alone and containing 5 m*M* and 10 m*M* salicylic acid. The control broth was

Reprints or correspondence: Dr. Bruce F. Farber, Division of Infectious Disease, North Shore University Hospital–Cornell University Medical College, 300 Community Dr., Manhasset, NY 11030.

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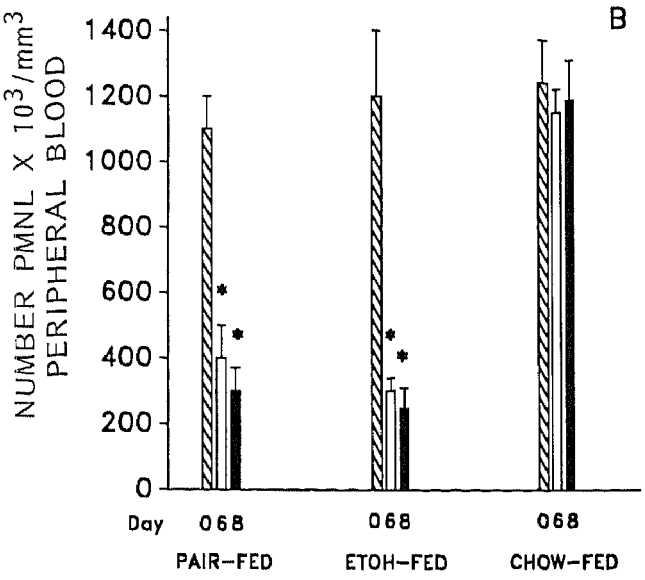
Reference Correction

In the article by Eble et al. (Eble BE, Busch MP, Guiltinan AM, Khayam-Bashi H, Murphy EL. Determination of human T lymphotropic virus type by polymerase chain reaction and correlation with risk factors in Northern California blood donors. J Infect Dis 1993;167:954–7), the year for reference 10 was listed incorrectly. The correct citation is MMWR **1990**;39:915–24.

Figure Corrections

In the article by Lister et al. (Lister PD, Gentry MJ, Preheim LC. Ethanol impairs neutrophil chemotaxis in vitro but not adherence or recruitment to lungs of rats with experimental pneumococcal pneumonia. J Infect Dis 1993;167:1131–7), the *y* axis of figure 1B was labeled incorrectly. The corrected figure is shown below.



In the correspondence by Teichman et al. (Teichman JMH, Stein PC, Parsons CL. Quaternary amine (protamine sulfate) is bactericidal to *Staphylococcus epidermidis*. J Infect Dis 1993;167:1500–1), there is an error in the labeling of figure 1. The amount given as 150 μg/mL should have been 250 μg/mL; the corrected figure is shown below.