antiplatelet therapy may be the first step in providing a panacea for this dilemma, with the ultimate step being a well-designed clinical trial.

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Commentary: Prescribe two antiplatelet drugs and receive fewer calls for *Staphylococcus aureus*-induced prosthetic endocarditis

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Prosthetic conduit endocarditis, particularly with *Staphylococcus aureus*, is a lethal and increasingly frequent complication of implanted valves/conduits.^{1,2} Ditkowski and colleagues have presented intriguing laboratory work suggesting that daily aspirin and a second antiplatelet drug (ticagrelor) will eliminate a significant incidence of *S aureus* prosthetic endocarditis in their article, "Antiplatelet therapy abrogates platelet-assisted *Staphylococcus aureus* infectivity of biological heart valve conduits,"³ in this issue of the *Journal*.

In an elaborate series using bovine pericardial patch, cryopreserved pulmonary homograft, and bovine jugular vein, the adhesion of *S aureus* to these tissues in flow chambers with various perfusates, including plasma, serum, phosphate-buffered saline, and anticoagulated blood, was assessed. The authors studied the effect of fibrinogen (Fg), platelets, and antiplatelet agents on *S aureus* tissue adhesion. Initially, Fg was shown to bind to graft tissue and *S aureus* adhesion was directly related to the Fg levels.

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CENTRAL MESSAGE

Authors suggest taking two antiplatelet drugs (aspirin and ticagrelor) may be a remedy for *S aureus* prosthetic valve/conduit infections. Is a clinical trial indicated?

Labeled *S aureus* and Fg were colocalized on the graft when microscopically examined.

The next step demonstrated platelet affinity for the graft material (bovine jugular wall and bovine patch had the greatest retention) both at the endothelial cell surface and the subendothelial tissue matrix. This was confirmed with scanning electron microscopy. Platelet adhesion was also directly related to *S aureus* proclivity for graft tissue. Both the platelet and *S aureus* adhesion were blocked by administering eptifibatide, an $\alpha_{IIb}\beta_3$ platelet-binding site antagonist.

The experimental sequence of flow studies demonstrated *S aureus* adhesion to Fg decreased without the presence of platelets and that Fg was necessary for platelet-induced *S aureus* attachment to graft tissue. Making sense of the washing and coating of the grafts before perfusion, adding Fg to serum and other perfusates, the sequence of perfusion,

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washing with eptifibatide, and the perfusate solution carrying the suspended *S aureus* was challenging. However, with a well-marked scorecard, one could eventually discern the delivered components and the effect on *S aureus* adhesion.

Finally, the authors showed that acetylsalicylic acid (ASA), which has a similar mechanism of action to eptifibatide, decreased *S aureus* attachment to graft by approximately 50%. Ticagrelor, another antiplatelet medication, also decreased *S aureus* adhesion by more than 50% as a single agent, and when ASA and ticagrelor were combined, *S aureus* adhesion was reduced by 70%. Thus, graft infection with *S aureus* would potentially be decreased by adopting this protocol.

After perusing this manuscript, one must remember that this is a laboratory model. As the authors mention, other cofactors such as von Willebrand factor in inflammatory states could induce platelet adhesion and trigger this cascade. In addition, the genetic makeup of all real-world *S aureus* may not include clumping factor A and therefore may not behave as predicted in the study.

The study offers intriguing possibilities for decreasing the virulence of *S aureus* infection on prosthetic material. The manuscript details work on bovine material and human cryopreserved homograft but presumably the same mechanisms would affect porcine prostheses and transcatheter aortic valve implants.^{4,5} Does the crimping of the valve in the pulmonary and aortic replacements predispose to endothelial injury and subsequent infection? Does this predilection for infection in percutaneous Melody pulmonary valve implants occur because of the low-pressure right heart conditions as compared with

left-sided transcatheter aortic valve implantation implants? Does the relatively younger age of the patients receiving the right-side implants expose them to greater risk of prosthetic infections?

The recommended ASA and ticagrelor combination have increased the major bleeding complications in some cardiac series (Platelet Inhibition and Patient Outcomes [PLATO] study). Could the more common prescription of this combination invite more clinical complications? Will recent additions to the antiplatelet armamentarium and an old standby (Plavix) have similar anti-*S aureus* effects?

The dual antiplatelet therapy approach to prosthetic implants appears a strategy that deserves a clinical trial. For now, prescribing 2 antiplatelet medications for prosthetic implants may result in fewer calls for *S aureus*-mediated prosthetic endocarditis.

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