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PLATELET GEL AS AN INTRAOPERATIVELY PROCURED PLATELET-BASED ALTERNATIVE TO FIBRIN GLUE

Sir:

We enjoyed reading the article by Kulher et al. about the use of fibrin sealant in the prevention of seromas in a rat model (*Plast. Reconst. Surg.* 99: 842, 1997). We agree that the best management of seromas is prevention. We would like to briefly describe the use of platelet gel as a wound sealant and dural waterproofing agent that has been used successfully in numerous specialties at our institution for the past 18 months. Platelet gel is a platelet-based wound sealant that uses the concentrated platelets harvested by three-component centrifugal separation of autologous whole blood (Medtronic Sequestra 1000 autotransfusion system, Parker, Colo.) to create a platelet concentrate intraoperatively. One unit of whole blood, approximately 450 ml, is drawn, either in the holding area or the operating room, into a standard labeled blood collection bag containing citrate-phosphate-dextrose anticoagulant. The blood is centrifuged in the operating room by using a dual-speed autotransfusion system to separate the buffy coat suspended in 30 ml of plasma from the red blood cell pack and platelet-poor plasma fraction. This is the platelet concentrate used for the platelet gel. Depending on initial platelet counts, it is common to achieve platelet counts of 310,000 to 1 Million per from this three-component separation technique. The standard spin/soft spin technique used is similar to the method that the blood bank uses, to separate platelets from whole blood.

The critical differences in composition between platelet gel and fibrin glue are the presence of a high concentration of platelets and a naive concentration of fibrinogen in platelet gel. We believe that platelet gel offers significant advantages over previously described fibrinogen-based wound sealants. The inclusion of a buffy

coat of platelet- and leukocyte-enriched plasma appears to have several beneficial effects.

With platelet counts of 500,000 to 1 million per ml, the various cytokines and mediators found in the platelet's alpha and dense granules can promote angiogenesis and collagen synthesis, thereby enhancing soft-tissue wound healing. Clever mediators include platelet-derived growth factor (PDGF), platelet-derived epidermal growth factor (PDEGF), fibroblast growth factor (FGF), transforming growth factor-beta (TGF- β), and platelet-derived angiogenesis factor (PDAF).^{2,4} Platelet-derived growth factor and transforming growth factor-beta have been found to increase the collagen content and early rate of gain of strength in wounds.² Platelet-derived growth factor is known to be chemotactic for monocytes, macrophages, and fibroblasts; it is also an activator of collagenase within the later stages of wound healing, allowing for remodeling of collagen to promote wound strength. Transforming growth factor-beta is known to activate fibroblasts to form procollagen that results in collagen deposition

within the wound. In human and animal trials, these mediators have been found to accelerate epidermal regeneration and angiogenesis and to enhance collagen synthesis in various models.³ In addition to the growth factors elaborated by activated platelets, there is the local release of thrombin, thromboxane A₂, and adenosine diphosphate from the platelet granules. These function in attracting additional platelets to the developing clot, thus enhancing the hemostatic response. Although currently speculative, the high concentration of leukocytes in the buffy coat should add an antimicrobial effect to platelet gel as well as elaborate additional regulatory factors that enhance the wound healing process. Finally, the native concentration of fibrinogen in platelet gel increases its working time, and once activated by calcified thrombin it imparts a gelatinous adhesive consistency to the gel, allowing for ease of injection into the surgical site.

The advantages of platelet gel over previously described biologic sealants include safety and convenience for the patient as well as improved support for tissue healing. Because the processing time required for separation of the autologous blood into the components by this technique is less than 30 minutes, the option exists for the anesthesiologist to return the remaining erythrocytes and platelet-poor fractions to the patient before the induction of anesthesia. If an autologous alternative to fibrin glue is desired, the collection of blood in the immediate preoperative period avoids a time-consuming visit to the blood bank for the patient. Furthermore, use of autologous platelet gel eliminates the risk of clerical errors when the blood is predated and moved to a site distant from the patient. More patients are eligible for this procedure which is performed in the perioperative period, because the strict criteria for blood bank donation do not have to be met. Given the monitored setting of the operating room and the presence of an anesthesiologist, we are now able to offer the option of autologous platelet gel to many patients who would not normally be candidates for blood bank pre-donation. This would include children as young as age 6 or weighing 25 kg or more, the elderly patients, patients with anemia, and those with medical conditions that would preclude the blood bank from withdrawing a unit of whole blood. The presence of platelets and leukocytes in the formulation adds hemostatic and antimicrobial support and brings cytokines and growth factors to the site of surgery in a manner that would not be found in fibrin glue. Thus, platelet gel offers an immediately available surgical tool to provide wound hemostasis, lymphatic sealing, and a watertight dural closure, but perhaps more importantly, it further benefits the patient by offering a reconstructive growth factor matrix to promote wound healing. Formal studies are underway to prove scientifically the success we are experiencing clinically.

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**FAILURE OF SILICONE GEL BREAST IMPLANTS:
ANALYSIS OF LITERATURE DATA FOR 1652
EXPLANTED PROSTHESES**

Sir:

In recent correspondence, Goldberg et al. aggregated silicone breast implant rupture data from a select number of clinical studies and produced what they called a failure rate master curve. Based on their analysis and resultant graph, they concluded that breast implants fail at an "extraordinary rate," on the order of 50 percent at 8 years. Unfortunately, in addition to being selective in their use of the literature, they ignored the selection bias inherent to those papers they did reference. As a result, their findings are meaningless.

Others, including some referenced by Goldberg et al., have acknowledged the problem of selection. For example, commenting on most explanation studies, including three used by Goldberg et al., Peters and associates recently emphasized that the majority of women in all of these explanation studies had requested surgery because they were having problems related to their implants. It is possible, therefore, that the implant failure properties of these patients may be higher than that of 'control' or 'asymptomatic' patients who are not having problems related to their implants." Peters et al. also discussed some other limitations of the explant literature: confounding by implant generation, lack of suitable controls, and the paucity of denominator data.

Goldberg et al. appeared to be particularly influenced by the work of Robinson and colleagues, calling it "the most extensive" and using multiple data points from that report in their master curve. However, the Robinson et al. work actually demonstrates how clinical research can go astray if funda-

mental concepts of data collection and analysis are ignored, and how important clinical decisions (i.e., explanation) can be inappropriately influenced by such work. By way of example, Robinson et al. started with 495 women, only 314 of whom were Robinson's original patients (the remainder were implanted by other surgeons). Among the 495, only 300 elected implant removal, and among these, 214 (71.3 percent of the 300) had "disrupted" implants. However, in sworn testimony, Robinson claims to have implanted not 300 patients but more than 4000. Using 4000 as the denominator, the "disruption" rate approximates 5 percent. The rate is far lower still if all the women implanted by the other surgeons were added. Limiting the calculations to those with ruptured implants or to the smaller number of those with clinically significant ruptured implants, as opposed to Robinson's "disrupted" implants, would drive the rate even lower, quite possibly lower than the rates reported by Handel et al. or Gabriel and colleagues. With due consideration for the potential morbidity associated with any surgery, a single-digit rupture rate does not warrant a policy of wholesale explanation, certainly not one encompassing all implanted women as Robinson recommends.

In summary, the failure rate master curve is a masterpiece of failure. Goldberg et al. have taken data, some of which are valid albeit not for calculating true rupture rates, and developed a flawed analysis. Consequently, they have made interpretations that are also flawed and that appear to support policies that could have significant negative public health implications.

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