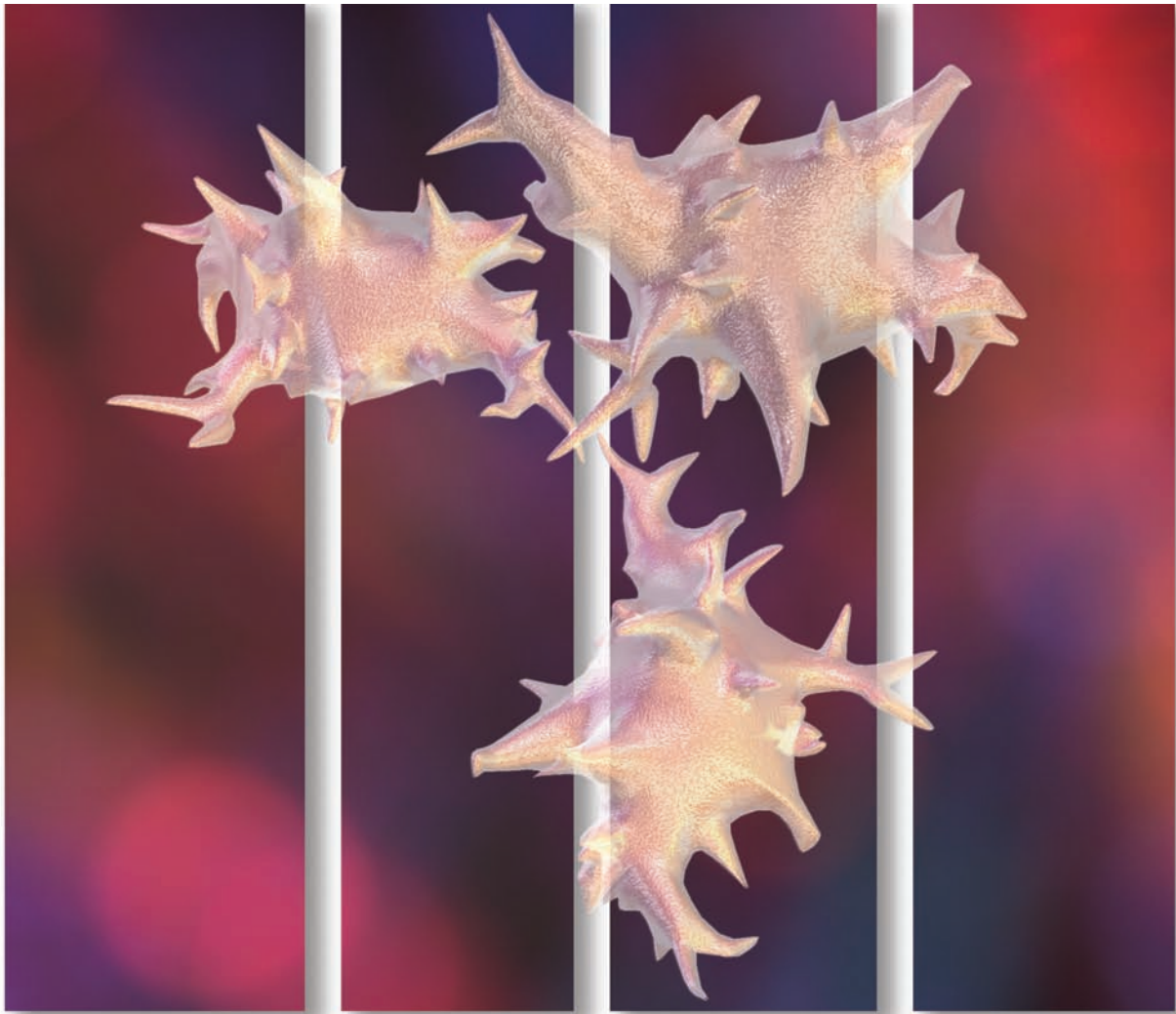


CLINICAL UPDATES IN PLATELET GEL

*Using Autologous Platelet Gel to
Reduce the Incidence of Mediastinitis*



Foreword

Despite the fact that the national incidence of mediastinitis is relatively low, the costs associated with it are high; a 2006 filing from the Centers for Medicaid and Medicare Services (CMS) reports that patients who developed secondary mediastinitis after a CABG operation had average hospital charges of \$304,747.¹

Beginning in October 2008, hospitals will bear the full burden of that cost. As part of the Deficit Reduction Act of 2005 and the CMS Quality Improvement initiative, CMS will no longer reimburse the treatment of mediastinitis,¹ a move that is prompting many U.S. hospitals to take additional measures to reduce its incidence.

The use of autologous platelet gel has emerged as a potential solution. Numerous published studies have demonstrated its effect on accelerating wound healing and reducing infection in general and mediastinitis specifically.

The Clinical & Economic Implications of Mediastinitis

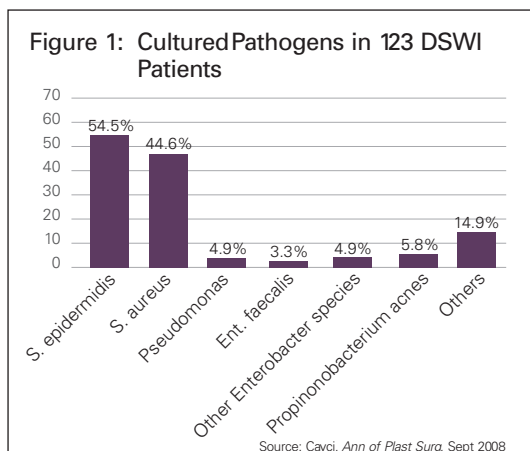
Studies have documented that mediastinitis associated with cardiac surgery contributes to increased morbidity, mortality, total length of hospital stay and additional cost. Although its incidence is fairly low nationally—occurring in only 1% to 5% of surgical cases—surgical site infections associated with bypass surgery have a significant socioeconomic impact and remain one of the challenges associated with cardiac surgery.

While the pathology of mediastinitis is most likely multi-factorial, the most common pathogens include staphylococcus epidermidis and staphylococcus aureus.² (figure 1) In addition, several risk factors may predispose patients to mediastinitis including: obesity, diabetes, smoking, pulmonary disease, history of stroke and the use of bilateral internal mammary artery grafting.³ The majority of patients who develop this complication will undergo a second surgery that includes debridement, sternal refixation and pectoral myoplasty. In a study done by Cayci, the authors found that 93.6% of patients who developed a deep sternal wound infection received immediate debridement followed by bilateral pectoralis major flap.² (figure 2)

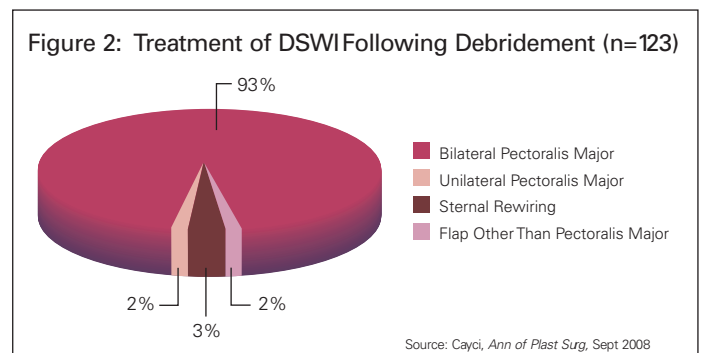
Recent published studies have characterized the impact and costs associated with mediastinitis:

- In Hollenbeak's study, the authors found that patients who developed a deep chest infection had a 21% higher mortality rate, accumulated 20 additional hospital days and incurred an additional \$20,012 in hospital costs compared to patients who had no chest infection.⁴
- In a 1,700-patient study published in 2007, Diez found the incidence of postoperative mediastinitis was 2.65% and reported total hospital length of stay of 45 days versus 19 days for patients without infection; on average, mediastinitis patients were hospitalized 24 days longer than those without the complication.³

Medicare will no longer pay the cost of treating mediastinitis starting in October 2008 as part of the Deficit Reduction Act of 2005 and the CMS Quality Improvement initiative. In the filing issued by CMS, they found that patients who received a CABG operation and developed secondary mediastinitis had average hospital charges of \$304,747 for the year 2006.



Sternal wound culture results in patients with DSWI (deep sternal wound infection).



Treatment methods for patients with DSWI (deep sternal wound infection).

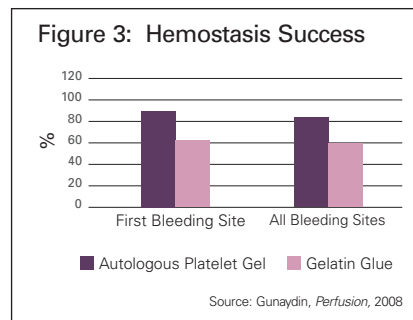
Autologous Platelet Gel

As the following studies indicate, autologous platelet gel is proven to reduce infection and bleeding in cardiac surgery, and improve the healing process. Developed as a by-product of large volume plasmapheresis and produced pre-operatively in approximately 16 minutes in some platelet concentrate systems,⁵ platelet gel provides a high dose of concentrated platelets and growth factors to the wound site and works to accelerate the regenerative process. Several platelet mediators found in platelet gel have proven to enhance angiogenesis and collagen synthesis, including platelet derived growth factor (PDGF), platelet derived epidermal growth factor and transforming growth factor beta.⁶ (table 2) Additionally, PDGF works to recruit monocytes, macrophages and fibroblasts to the wound site.

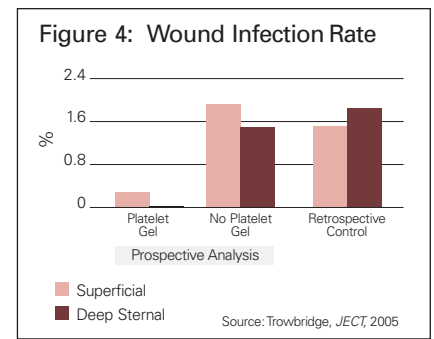
With platelet counts more than 4.5 times native levels, platelet gel delivers a high dose of platelet proteins and works to accelerate wound healing and hemostasis.⁷ Platelet gel is produced from a small sample of the patient’s blood collected prior to surgery. The blood is then centrifuged yielding a platelet rich plasma component. This platelet rich plasma is then combined with a thrombin activator and delivered in a spray or liquid application to the wound site.

Several studies have characterized the bioactivity and anti-microbial properties of platelet gel:

- In 2007, Overdeest demonstrated that “platelet gel provides significant antimicrobial activity against *S. Aureus*” and “appears to be a useful prophylactic strategy against post operative infections.”⁷
- In Gunaydin’s 2008 study, the authors measured the phagocytic and hemostatic capacity of platelet gel compared to gelatine glue and found the platelet gel group “demonstrated increased resistance to infection” and was “significantly better than controls with respect to hemostatic success rate and wound healing.”⁸ (figure 3)



Percent hemostatic success of oozing category in first and all bleeding sites.



Overall rate of superficial and deep sternal wound infections.

A significant body of evidence has been developed on the impact of autologous platelet gel and its use in cardiac surgery. In general, studies have demonstrated that the use of platelet gel significantly reduces the incidence of sternal infection, as well as reduces chest tube and leg wound drainage:

- In a 2,200-patient prospective and retrospective study, Trowbridge found that the use of platelet gel significantly reduced both superficial and deep sternal wound infections.⁹ (figure 4)
- In a 1,128-patient study published in The European Journal of Cardio-Thoracic Surgery in August 2008, Khalafi found that the application of platelet gel significantly reduced the incidence of sternal infection compared to a control group that did not receive platelet gel. Following propensity scoring, the study concluded that platelet gel reduced the odds of chest infection by 93%. In addition, the authors found chest tube drainage was reduced by 96% and leg wound drainage by 88%.¹⁰ (table 1)

Table 1: Analysis of outcome variables prior to adjustment for selection bias

VARIABLE	PLATELET GEL	CONTROL	p-value (Fisher's exact)	p-value (Logistic regression)
Chest infection	1 (0.18%)	11 (1.98%)	<0.001	<0.01
Chest drainage	3 (0.53%)	30 (5.39%)	<0.001	<0.001
Leg infection	0 (0%)	3 (0.66%)	NS	NS
Leg drainage	61 (10.89%)	212 (46.49%)	<0.001	<0.001

Source: Khalafi, Eur J Cardiothorac Surg, August 2008

Table 2: Synopsis of growth factors present in Autologous Platelet Gel

GROWTH FACTOR	FUNCTION
Transforming growth factor-beta, TGF-β	Stimulates undifferentiated mesenchymal cell proliferation; regulates endothelial, fibroblastic and osteoblastic mitogenesis; regulates collagen synthesis and collagenase secretion; regulates mitogenic effects of other growth factors; stimulates endothelial chemotaxis and angiogenesis; inhibits macrophage and lymphocyte proliferation
Basic fibroblast growth factor, bFGF	Promotes growth and differentiation of chondrocytes and osteoblasts; mitogenetic for mesenchymal cells, chondrocytes and osteoblasts
Platelet derived growth factor, PDGFA-b	Mitogenetic for mesenchymal cells and osteoblasts; stimulates chemotaxis and mitogenesis in fibroblast/glia/smooth muscle cells; regulates collagenase secretion and collagen synthesis; stimulates macrophage and neutrophil chemotaxis
Epidermal growth factor, EGF	Stimulates endothelial chemotaxis/angiogenesis; regulates collagenase secretion; stimulates epithelial/mesenchymal mitogenesis
Vascular endothelial mitogenesis for endothelial cells	Increases angiogenesis and vessel permeability; stimulates growth factor, VEGF
Connective tissue growth factor, CTGF	Promotes angiogenesis, cartilage regeneration, fibrosis and platelet adhesion

Source: Everts, *JECT*, 2006

Summary

Mediastinitis remains one of the most devastating complications of cardiac surgery in the U.S. today. Although its incidence remains less than 5% nationally, it represents one of the most significant burdens to the health care system, contributing to increased hospital stays, morbidity and mortality, and a dramatic increase in overall hospital costs. With new CMS policy changes no longer covering mediastinitis events in Medicare patients, mediastinitis will provide a serious challenge to the bottom line of many health care institutions.

The use of autologous platelet gel may provide a potential prophylactic therapy that significantly reduces the chance of a sternal wound complication. Numerous studies have documented the benefits of this technology to significantly reduce the incidence of both superficial and deep sternal infection, as well as provide improved overall healing and hemostatic benefits.

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