What Is Platelet Gel?

"Autologous Platelet Rich Plasma" *(Platelet Gel)* was developed in the early 1970's as a by-product of multicomponent pheresis. Techniques and equipment have dramatically improved through the 1990's. This is a new procedure which utilizes the patient's own (autologous) platelets. Briefly, here's how the procedure works:

One unit of whole blood (approximately 450 milliliters) is drawn, either pre-operatively or in the Operating Room, into a standard blood collection bag containing a citrate-phosphate-dextrose anticoagulant. There are also new machines that are able to utilize as little as 50 milliliters of blood to produce ***Platelet Gel***. The blood is then centrifuged by using a variable-speed centrifuge autotransfusion machine or portable machine, to separate the buffy coat suspended in plasma from the red blood cell pack and platelet-poor plasma fraction. This is the platelet concentrate used for ***Platelet Gel***. Depending on the initial platelet counts, it is common to achieve platelet counts in excess of over three to five (3-5) times baseline counts. Other important factors in quality of ***Platelet Gel*** are platelet viability and percent retained on the procedure. While white cell content increases 125% with selection for lymphocytes and monocytes, the inclusion of platelets and white cells appears have several beneficial aspects. White cells confer additional healing cytokines while providing antibacterial activity.

On activation with thrombin/calcium to form a coagulum, the platelets interdigitate with the forming fibrin web, developing a gel with adhesiveness and strength materially greater than the plasma alone. Thrombin/calcium also causes platelets to immediately release highly active vasoconstrictors, including beta thromboxane, serotonin and PDGF.

Related Reference Articles to Thrombin:

- Rapaport, S.I., Zivelin, A., Minow, R.A., et al. Clinical Significance of Antibodies to Bovine and Human Thrombin and Factor V After Surgical Use of Bovine Thrombin, *Am J. Clin Pathol*, 1992; 97:84-96.
- Zehnder, J.L., Leung, LLK., Development of Antibodies to Thrombin and Factor V with Recurrent Bleeding in a Patient Exposed to Topical Bovine Thrombin, *Blood*, 1990; 76:2011-2016.
- Nichols, W.L., Daniels, T.M., Fisher, P.K., et al, Antibodies to Bovine Thrombin and Coagulation Factor V Associated with the Surgical Use of Topical Bovine Thrombin or "Glue": A Frequent Finding, *Blood*, 1993; 82:59 (abstract).
- Christie, R.J., Carrington, L., Alving, B., Postoperative Bleeding Induced by Topical Bovine Thrombin: Report of Two Cases, *Surgery*, 1997; 121(6):708-710.

In addition, platelets contain many tissue growth factors. These predominant growth factors are:

- PDGF **(Platelet Derived Growth Factor)** - PDGF is a very powerful regulatory growth factor and a sentinel growth factor that begins nearly all wound healing. PDGF's main function is to stimulate cell replication (mitogenesis) of healing capable stems and premitotic partially differentiated osteoprogenitor cells which are part of the connective tissue-bone healing cellular make-up. PDGF also causes replication of endothelial cells, causing budding of new capillaries (angiogenesis). PDGF exists in three forms: PDGFaa, PDGFbb, PDGFab.

differentiation of multiple cell types. TGF found in platelets is subdivided into TGFB1 and TGFB2, which are the more generic connective tissue growing factors involved with matrix formation influencing osteoblasts to lay down bone matrix through the process of osteogenesis. Also cells activated by TGFB1 and TGFB2 include fibroblasts, endothelial and osteoprogenitor cells, chondroprogenitor cells and messenchymal stem cells. A condoroprogenitor cell will further differentiate and produce the matrix for cartilage. A messenchymal stem cell stimulated to mitose provides wound healing cells.

Other important growth factors in platelets are:

- EGF **(Epidermal Growth Factor)** - EGF is responsible for cell differentiation and stimulates re-epitheliation, angiogenesis and collangenase activity.
- IGF **(Insulin Growth Factors)** - IGF is also important in wound healing, and stimulates
  both proliferation and differentiated function in osteoblasts.

There are over 30 known growth factors to date. These **Platelet Growth Factors**:

- Increase tissue vascularity through increased angiogenesis
- Are chemotactic for monocytes, macrophages, and fibroblasts
- Enhance collagen synthesis
- Increase the rate of epitheal and granulation tissue production
- Enhance osteogenesis
- The high concentration of leukocytes in the buffy coat add an antimicrobial effect, while wound hemostasis and lymphatic sealing provide an opportunity to eliminate post-operative drains and reduce pain
- Provides watertight seal for dural closures
- When mixed auto/allograft bone fragments, it forms a putty-like form ideal for packing of structural reconstructions
- Provides for an immediate surgical hemostatic agent that is biocompatible, effective and safe.

Related Reference Articles:

- Scott, John D., Pawson, Tony, Cell Communication: The Inside Story, *Scientific American*, 2000; 282:72-79.
- Martin, P., et al, Growth Factors and Cutaneous Wound Repair, *Progress in Growth Factor Research*, 1992; 4:25-44.
- Hom, David B., Maisel, Robert H., Angiogenic Growth Factors: Their Effects and Potential in Soft Tissue Wound Healing, *Ann Otol Rhinol Laryngol*, 1992; 101:349-354.
- Herndon, D., et al, Growth Factors Local and Systemic, *Archives of Surgery*, 1993; 128:1227-1233.
- Lind, et al, Growth Factors: Possible New Clinical Tools, *Acta Orthop Scand*, 1996; 67(4): 407-417.
- Roberts, et al, Physiological Actions and Clinical Applications of Transforming Growth Factor-beta (TGF-beta), Growth Factors, 1993; 8:1-9.
- Slater, Micheal, et al, Involvement of Platelets in Stimulating Osteogenic Activity, *Journal of Orthapaedic Research*, 1995; 13:655-663.
- Hannon, Timothy J., Autologous Platelet Gel, 1999; 1-13.
- Harrison, P., Cramer, E.M., Platelet a-Granules, *Blood Reviews*, 1993; 7:52-62.
- Lozano, Teresa, Broumand, Vistaub, Marx, Robert E., Evaluation of Risk with the use of Bovine Thrombin in the Clot Initiation of Platelet Rich Plasma, 1998; 1-2.

Reesink, H.W., Platelet activation during preparation of platelet concentrates: a comparison of the platelet-rich plasma and the buffy coat methods, *Transfusion*, 1990; 634-638.
- Ernesto, C., Clinical Review 35: Growth Factors and their Potential Clinical Value, J. Clin Endocrinology Metabol., 1992; 75:1-4.
- Lynch, S.E., Colvin, R.B., Antoniades, H.N., Growth Factors in Wound Healing: Single and Synergistic Effect on Partial Thickness Porcine Skin Wounds, J. Clin Invest, 1989; 84:640-646.
- Zimmermann, R., Jakubietz, R., Jakubietz, M., Strasser, E., Schlegel, A., Wiltfang, J., Eckstein, R., Different Preparation Methods to Obtain Platelet Components as a Source of Growth Factors for Local Application, *Transfusion AABB*, Volume 41, October 2001, 1217-1223.
- Editorial: Topical Platelet Growth Factor Therapy: Of Lotions and Potions, *Transfusion AABB*, Volume 41, October 2001, 1186-1189.

Autologous ***Platelet Gel***:

- is safe
- is non-toxic to tissue
- is autologous
- is easily prepared
- is readily available
- is cost effective
- promotes a firm seal in minutes
- is reabsorbed by the body in days to a few short weeks
- promotes local tissue growth and repair

Autologous Platelet Gel is the Perfect Operating Sealant!

Autologous Platelet Rich Plasma (Platelet Gel), on activation with thrombin/calcium, is a fibrin tissue adhesive, having hemostatic and tissue sealing properties, but differs from fibrin tissue adhesives (Fibrin Glue) in its ability to improve wound healing and enhance osteogenesis.

Current Wound Sealants

Cyanoacrylates have been used in the closure of tension-free wounds, but are limited in clinical applications. The acrylic plastic cyanoacrylates are biodegradable and bacteriostatic, and use of these short chain methyl- and ethylcyanoacrylates can result to severe histotoxic responses (neural toxicity). When longer chain butyl- and isobutylcyanoacrylates are utilized, there is an increase in inflammatory responses and foreign body giant cell reactions. When neovascularization is compromised through mechanical blockage, normal wound healing is affected. Recently, topical applications of octylcyanoacrylates have been used and reported in clinical studies. They have limited usage, and are for external use only.

Fibrin Glue - Some of the first applications of Fibrin Glue are reported by Matras in Vienna. Fibrin tissue adhesives (Fibrin Glue) involve thrombin activation of concentrated fibrinogen with the presence of Factor XIII, the plasma proteins Fibronectin and cold-insoluble Globulin, Aprotinin and

Calcium Chloride.

The commercial preparation of Fibrin Glue involves cryoprecipitation of Fibrinogen from single donor or pooled homologous human blood by adding calcium and thrombin at the time of usage. A fibrin clot is produced.

Commercial preparations currently under the brand name Tissel™ (Baxter AG, Deerfield, IL) use purified clotting factors derived from pooled homologous human blood products. They have been virally inactivated by heat vaporization or solvent detergent methods. These preparations contain high concentrations of fibrinogen (70-140 mg/ml). Also Fibronectin, Factor XIII and antifibrinolytics may be included.

Also a fibrin sealant, Hemaseal© has been licensed for use in the United States. In addition, autologous cryoprecipitated fibrinogen preparations have been employed in the United States.

Related Reference Articles:

- Touriumi, D.M., Raslan, W.F., Friedman, M., Tardy, M.E., Variable Histotoxicity of Histoacryl When Used In A Subcutaneous Site, *Arch Oto. He N Surgery*, 1990; 277:1527-1530.
- Bruck, H.G., Fibrin Tissue Adhesion And It's Use In Rhtidectomy, *Aesth Plast Surg*, 1982; 6:197.
- Matras, H., Zur Nahtlosen Interfaszikularen Nervetransplantation in Tierexpieriment, *Wien Medical Wochenschreibe*, 1992; 122:517.
- Quinn, J., Wells, G., Sutcliffe, T., et al, A Randomized Trial Comparing Octylcyanoacrylate Tissue Adhesive and Sutures in the Management of Lacerations, *JAMA*, 1997; 277:1527-1530.
- Revocation of Fibrinogen License, *FDA Drug Bulletin*, 1978; 8:15.
- Wilson, S.M., Dell, P., Donegan, E.A., HIV Transmission Following The Use Of Cryoprecipitated Fibrinogen and Gel/Adhesive, *Transfusion*, 1991; 31s:51s.
- Oz, M.C. Jeevanandam, V., Smith, C.R., Autologous Fibrin Glue From Intraoperatively Collected Platelet-Rich Plasma, *Ann Thor Surgery*, 1992; 53:530-531.
- Man, Daniel, Posker, Harvey, Winland-Brown, Jill E., The Use of Autologous Platelet-Rich Plasma (Platelet Gel) and Autologous Platelet-Poor Plasma (Fibrin Glue) in Cosmetic Surgery, *Plastic and Reconstructive Surgery*, 2001; 229-239.
- Sierra, D.H., Fibrin Sealant Adhesive Systems: A Review Of Their Chemistry, Material Properties and Clinical Applications, *J Biomat Applicat*, 1993; 7:309-352.
- Tawes, R.L., Sydorak, G.R., DuVall, T.B., et al, Autologous Fibrin Glue: The Last Step In Operative Hemostasis, *Am J Surg*, 1994; 168:120-122.
- Brittberg, M., Sjogien-Jansson, E., Lindahl, A., Peterson, L., Influence Of Fibrin Sealant (Tissel™) On Osteochondral Defect Repair In The Rabbit Knee, *Biomaterials*, 1997; 18(3):235-242.
- Siriex, D., Chemla, E., Catier, Y., et al, Comparative Study Of Different Biological Glues In An Experimental Model Of Surgical Bleeding In Anesthetized Rats: Platelet-Rich and -Poor Plasma-Based Glue With and Without Aprotinin Versus Commercial Fibrinogen-Based Glue, *Ann Vasc Surg*, 1998; 12(4):311-316.
- Oz, M.C., et al, Autologous Fibrin Flue From Intraoperatively Collected Platelet-Rich Plasma, *Annals of Thoracic Surgery*, 1992; 53:530-531.
- Gibble, J.W., et al, Fibrin Glue: The Perfect Operative Sealant?, *Transfusion*, 1990; 30:741-747.
- Hartman, A.R., et al, Autologous Whole Plasma Fibrin Gel - Intraoperative Procurement, *Arch Surgery*, 1992; 127:357-359.

- Radosevich, M., et al, Fibrin Sealant: Scientific Rationale, Production Methods, Properties, and Current Clinical Use, *Vox Sang*, 1997; 72:133-134.
- Dhall, T.Z., et al, Fibrin Network Structure: Modification by Platelets, *Thromb Haemostas*, 1983; 49:42-46.
- Dulchavsky, Scott A., et al, Autologous Fibrin Gel: Bactericidal Properties in Contaminated Hepatic Injury, The Journal of Trauma, 1991; 31:991-994.
- McGill, Victoria, et al, Use of Fibrin Sealant in Thermal Injury, *Journal of Burn Care & Rehabilitation*, 1997, 18:429-434.
- Byrne, D.J., et al, Effect of Fibrin Glues on the Mechanical Properties of Healing Wounds, *British Journal of Surgery*, 1991; 78:841-843.
- Blackstone, Michael O., Fibrin Glue for Bleeding Peptic Ulcers, *The Lancet*, 1997, 350:679.
- Kram, Harry B., Fibrin Glue Achieves Hemostasis in Patients with Coagulation Disorders, *Arch Surgery*, 1989; 124:385-387.
- Holcomb, John. B., et al, Implications of New Dry Fibrin Sealant Technology for Trauma Surgery, *Surgical Clinics of North America*, 1997; 77:943-952.
- NewsEdge, Repair of Chronic Anorectal Fistulae Using Commercial Fibrin Sealant, *Arch Surg*, 2000; 135:166-169.
- Cintron, Jose R., Commercial Fibrin Sealant Safe and Effective Treatment for Anorectal Fistulae, *Arch Surg*, 2000; 135:166-169.
- Marx, Robert E. D.D.S., Kevy, Sherwin V., M.D., Jacobson, May S., PhD, *Platelet Concentrate Preparation in the Office Setting: A Comparison of Manual and Automated Devices*, July-September 2001.
- Marx, Robert E. D.D.S., Kevy, Sherwin V., M.D., Jacobson, May S., PhD, *Platelet Concentrate Preparation in the Office Setting: A Comparison of Manual and Automated Devices*, Update March 2002.
- Marx, Robert E., D.D.S., Platelet-Rich Plasma (PRP): What Is PRP and What Is Not PRP?; *Implant Dentistry*, Vol. 10 No. 4 2001.