Ozone and Autologous Therapies

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MediOzon Clinics

Ozone, PRP and other Autologous Therapies

http://medical-dictionary.thefreedictionary.com/autologous

au·tol·o·gous (aw-tol'ŏ-gŭs),

1. Occurring naturally and normally in a certain type of tissue or in a specific structure of the body.
2. In transplantation, referring *to transfer of an organ or other tissue from one location to another in the same person; or to blood or blood components that the donor has previously donated and receives at a later time*, usually perioperatively.
3. Rarely used to denote a neoplasm derived from cells that occur normally at that sight, for example, a squamous cell carcinoma in the upper esophagus.

Synonym(s): autogenous (1)

[auto- + G. logos, relation]

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Autologous Therapies

- **Defination:**

  The therapy that is done by transferring cells, tissues, body liquids originating of the recipient rather than from donor.

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Research Paper

Mediators of Inflammation, **8**, 205–209 (1999)

Studies on the biological effects of ozone: 10. Release of factors from ozonated human platelets

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In a previous work we have shown that heparin, in the presence of ozone (O_3), promotes a dose-dependent platelet aggregation, while after Ca^{2+} chelation with citrate, platelet aggregation is almost negligible. These results led us to think that aggregation may enhance the release of platelet components. We have here shown that indeed significantly higher amount of platelet-derived growth factor (PDGF), transforming growth factor β1 (TGF-β1) and interleukin-8(IL-8) are released in a dose-dependent manner after ozonation of heparinised platelet-rich plasma samples. These findings may explain the enhanced healing of torpid ulcers in patients with chronic limb ischemia treated with O_3 autohaemoteraphy (O_3-AHT).

Key words: ozone, platelets, aggregation, growth factors, inteleukin-8

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Abstract

In a previous work we have shown that heparin, in the presence of ozone (O3), promotes a dose-dependent platelet aggregation, while after Ca2+ chelation with citrate, platelet aggregation is almost negligible. These results led us to think that aggregation may enhance the release of platelet components. We have here shown that indeed ***significantly higher amount of platelet-derived growth factor (PDGF), transforming growth factor beta1 (TGF-beta1) and interleukin-8 (IL-8) are released in a dose-dependent manner after ozonation*** of heparinised platelet-rich plasma samples. These findings may explain the enhanced healing of torpid ulcers in patients with chronic limb ischemia treated with O3 autohaemoteraphy (O3-AHT).

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Clinical Study

Increased Growth Factors Play a Role in Wound Healing Promoted by Noninvasive Oxygen-Ozone Therapy in Diabetic Patients with Foot Ulcers

Jing Zhang, Meiping Guan, Cuihua Xie, Xiangrong Luo, Qian Zhang, and Yaoming Xue

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Management of diabetic foot ulcers (DFUs) is a great challenge for clinicians. Although the oxygen-ozone treatment improves the diabetic outcome, there are few clinical trials to verify the efficacy and illuminate the underlying mechanisms of oxygen-ozone treatment on DFUs. In the present study, a total of 50 type 2 diabetic patients complicated with DFUs, Wagner stage 2~4, were randomized into control group treated by standard therapy only and ozone group treated by standard therapy plus oxygen-ozone treatment. The therapeutic effects were graded into 4 levels from grade 0 (no change) to grade 3 (wound healing). The wound sizes were measured at baseline and day 20, respectively. Tissue biopsies were performed at baseline and day 11. The expressions of vascular endothelial growth factor (VEGF), transforming growth factor-β (TGF-β), and platelet-derived growth factor (PDGF) proteins in the pathologic specimens were determined by immunohistochemical examinations. The effective rate of ozone group was significantly higher than that of control group (92% versus 64%, $P < 0.05$). The wound size reduction was significantly more in ozone group than in control group ($P < 0.001$). After treatment, the expressions of VEGF, TGF-β, and PDGF proteins at day 11 were significantly higher in ozone group than in control group. Ozone therapy promotes the wound healing of DFUs via potential induction of VEGF, TGF-β, and PDGF at early stage of the treatment. (Clinical trial registry number is ChiCTR-TRC-14004415).

Jing Zhang, Meiping Guan, Cuihua Xie, Xiangrong Luo, Qian Zhang, and Yaoming Xue, "Increased Growth Factors Play a Role in Wound Healing Promoted by Noninvasive Oxygen-Ozone Therapy in Diabetic Patients with Foot Ulcers," Oxidative Medicine and Cellular Longevity, vol. 2014, Article ID 273475, 8 pages, 2014. doi:10.1155/2014/273475

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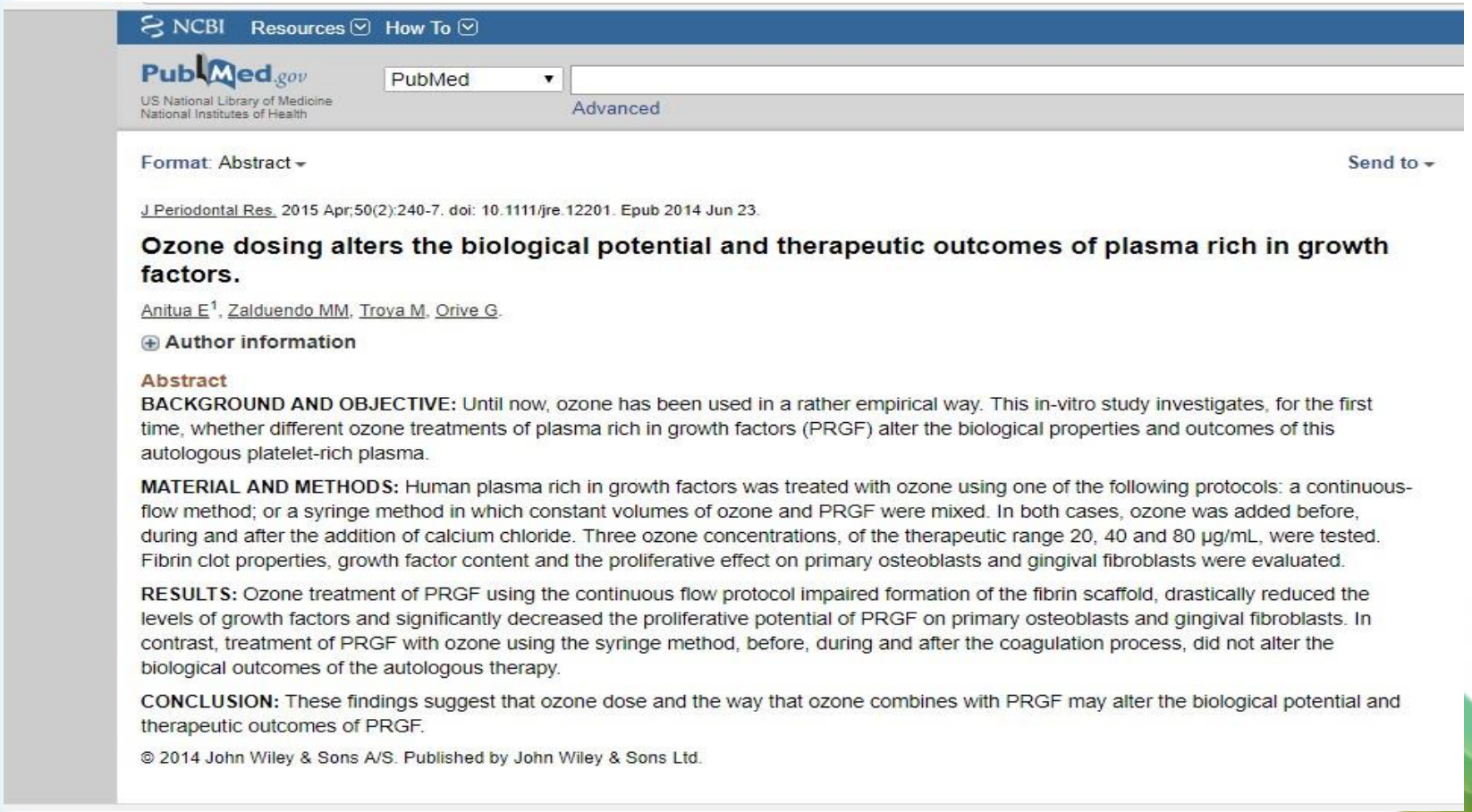

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J Periodontal Res. 2015 Apr;50(2):240-7. doi: 10.1111/jre.12201. Epub 2014 Jun 23.

Ozone dosing alters the biological potential and therapeutic outcomes of plasma rich in growth factors.

Anitua E[1], Zalduendo MM, Troya M, Orive G.

Author information

Abstract

BACKGROUND AND OBJECTIVE: Until now, ozone has been used in a rather empirical way. This in-vitro study investigates, for the first time, whether different ozone treatments of plasma rich in growth factors (PRGF) alter the biological properties and outcomes of this autologous platelet-rich plasma.

MATERIAL AND METHODS: Human plasma rich in growth factors was treated with ozone using one of the following protocols: a continuous-flow method; or a syringe method in which constant volumes of ozone and PRGF were mixed. In both cases, ozone was added before, during and after the addition of calcium chloride. Three ozone concentrations, of the therapeutic range 20, 40 and 80 μg/mL, were tested. Fibrin clot properties, growth factor content and the proliferative effect on primary osteoblasts and gingival fibroblasts were evaluated.

RESULTS: Ozone treatment of PRGF using the continuous flow protocol impaired formation of the fibrin scaffold, drastically reduced the levels of growth factors and significantly decreased the proliferative potential of PRGF on primary osteoblasts and gingival fibroblasts. In contrast, treatment of PRGF with ozone using the syringe method, before, during and after the coagulation process, did not alter the biological outcomes of the autologous therapy.

CONCLUSION: These findings suggest that ozone dose and the way that ozone combines with PRGF may alter the biological potential and therapeutic outcomes of PRGF.

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Role of Ozone/Oxygen in Fibroblast Growth Factor Activation. Discovering the Facts

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[2] *Medinat srl Clinic; Camerano, Italy*
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Key words: ozone, fibroblast growth factor, platelet rich plasma

SUMMARY - *Basic fibroblast growth factor (bFGF) is a pleiotropic mitogen which plays an important role in cell growth, differentiation, migration and survival in different cells and organ systems. Application of bFGF has been shown to promote cellular proliferation and collagen synthesis in vivo. FGF is markedly up-regulated following bone or tendon injury and active at multiple stages of the healing stimulation process, local blood circulation, lipolysis and smooth muscle. Looking at the physical and chemical properties of the ozone molecule, the present work deals with its possible therapeutic action as an FGF activator. Incubation (2 h) of platelet-rich plasma with 80 µg/mL O_2/O_3 increases the basal concentration of FGF by approximately 600%. This fact in combination with previous demonstration of the stimulating action of O_3, releasing other platelet factors may potentially allow autologous treatment in aesthetic and clinical tissues conditions in which FGF has a leading role. The versatility and broad beneficial effect of ozone has become evident in orthopedics, cutaneous and mucosal infections as well as in dentistry. The induction of FGF and other growth factors by ozone can support and potentiate those applications.*

Re, Lamberto & Martínez-Sánchez, G & Perez-Davison, G & Sirito, M. (2010). Role of ozone/oxygen in fibroblast growth factor activation. Discovering the facts. International Journal of Ozone Therapy. 9. 55-58.

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Effect of ozone on vascular endothelial growth factor (VEGF) and related inflammatory cytokines in rats with diabetic retinopathy

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ABSTRACT. The aim of this study was to investigate the effect of ozone on inflammatory cytokines in diabetic retinopathy (DR) rats. Male rats (40) weighing 300-360 g were included in this study. Thirty rats were randomly divided into the model and ozone groups after DR was induced by streptozotocin. Ten rats served as the blank group. After the diabetic models were established for one month, the rats in the ozone group were treated with 50 mg/kg ozone coloclysis for one month (three times a week). After the rats were anesthetized by intraperitoneal injection, blood samples from the abdominal aorta were collected, and the supernatant was obtained by centrifugation. Vascular endothelial growth factor (VEGF) and inflammatory cytokine content in the serum was detected by enzyme linked immunosorbent assay. The values of VEGF, intercellular cell adhesion molecule-1, interleukin-1 beta, tumor necrosis factor-a, and IL-6 were significantly different among the three groups ($P < 0.05$). The cytokine levels in the model group were higher than those in the blank group ($P < 0.05$). The level T.Y. Xie et al. 2 Genetics and Molecular Research 15 (2): 15027558 ©FUNPEC-RP www.funpecrp.com.br of each cytokine in the ozone group was higher than that in the blank group. Compared with the model group, the cytokine levels in the ozone group were significantly reduced ($P < 0.05$). Ozone had no effect on the blood glucose of diabetic rats. Treatment with ozone coloclysis may effectively reduce the secretion of VEGF and inflammatory cytokines in diabetic retinopathy rats. Key words: Diabetic retinopathy; Ozone treatment; VEGF; Inflammatory cytokines

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Therapeutic Effects of Topical Application of Ozone on Acute Cutaneous Wound Healing

This study was undertaken to evaluate the therapeutic effects of topical ozonated olive oil on acute cutaneous wound healing in a guinea pig model and also to elucidate its therapeutic mechanism. After creating full-thickness skin wounds on the backs of guinea pigs by using a 6 mm punch biopsy, we examined the wound healing effect of topically applied ozonated olive oil (ozone group), as compared to the pure olive oil (oil group) and non-treatment (control group). The ozone group of guinea pig had a significantly smaller wound size and a residual wound area than the oil group, on days 5 (P<0.05) and 7 (P<0.01 and P<0.05) after wound surgery, respectively. Both hematoxylin-eosin staining and Masson-trichrome staining revealed an increased intensity of collagen fibers and a greater number of fibroblasts in the ozone group than that in the oil group on day 7. Immunohistochemical staining demonstrated upregulation of platelet derived growth factor (PDGF), transforming growth factor-β (TGF-β) and vascular endothelial growth factor (VEGF) expressions, but not fibroblast growth factor expression in the ozone group on day 7, as compared with the oil group. In conclusion, these results demonstrate that topical application of ozonated olive oil can accelerate acute cutaneous wound repair in a guinea pig in association with the increased expression of PDGF, TGF-β, and VEGF.

Key Words : *Collagen; Ozone; Wound Healing*

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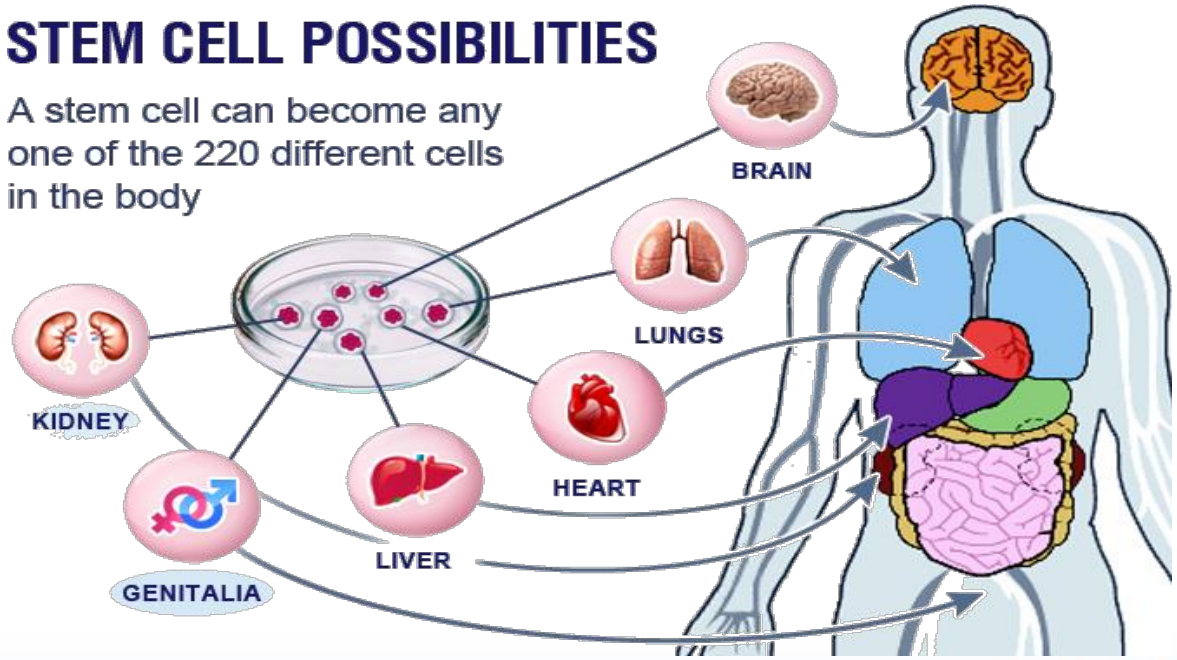
Types of Autologous Therapies

- **Stem Cell Therapies –** is the use of stem cells to treat or prevent a disease or condition.
- Embryonic, Mesenchymal, Adiposal, Organic (Cardiac, Cartilage)



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Types of Autologous Therapies

- **Hematopoietic stem cell** transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood.
- It may be autologous (the patient's own stem cells are used)
- allogeneic (the stem cells come from a donor) or
- syngeneic (from an identical twin)

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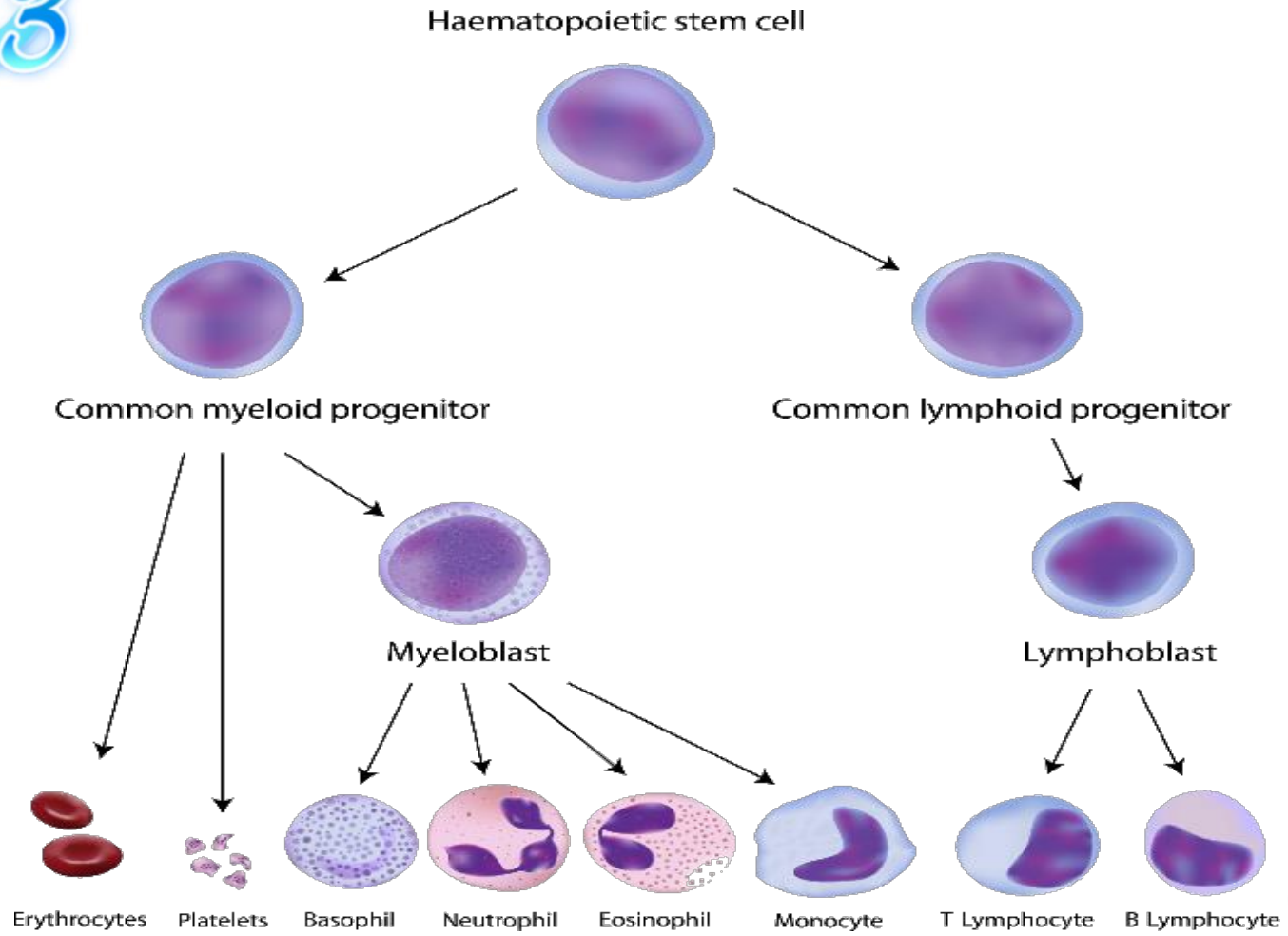
Hematopoietic stem cell



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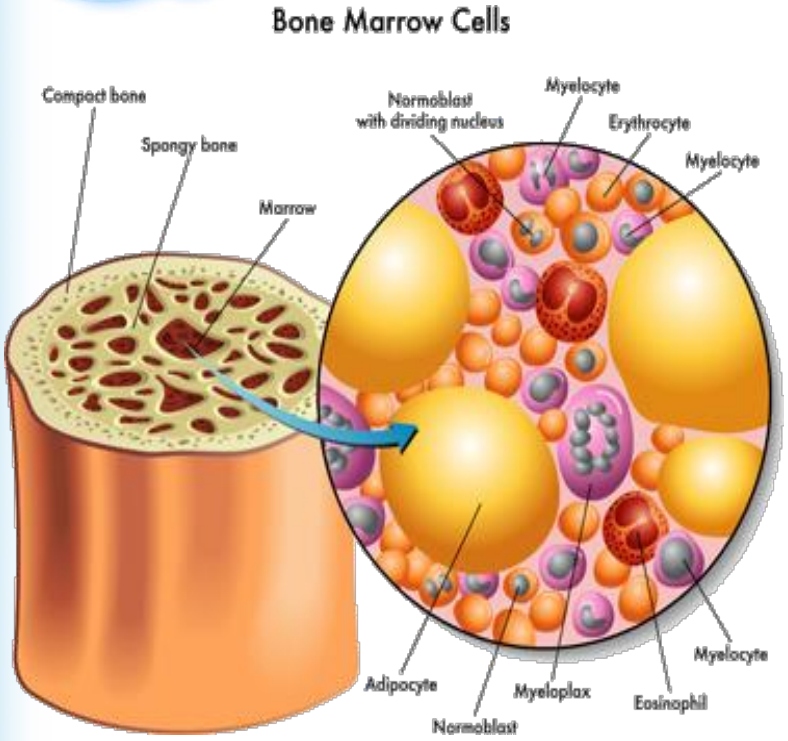
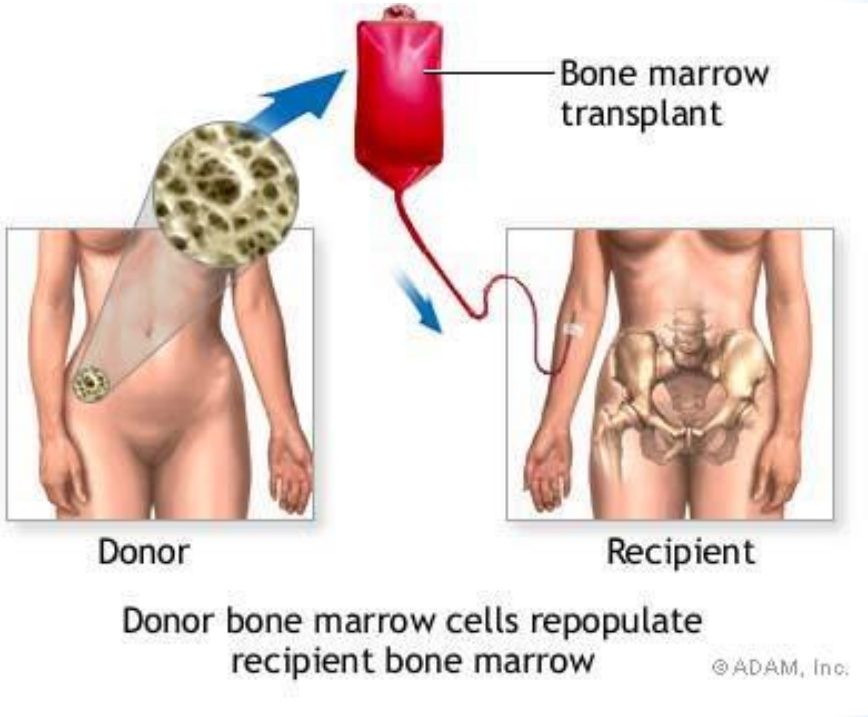
Bone Marrow





- Bone Marrow Transplantation

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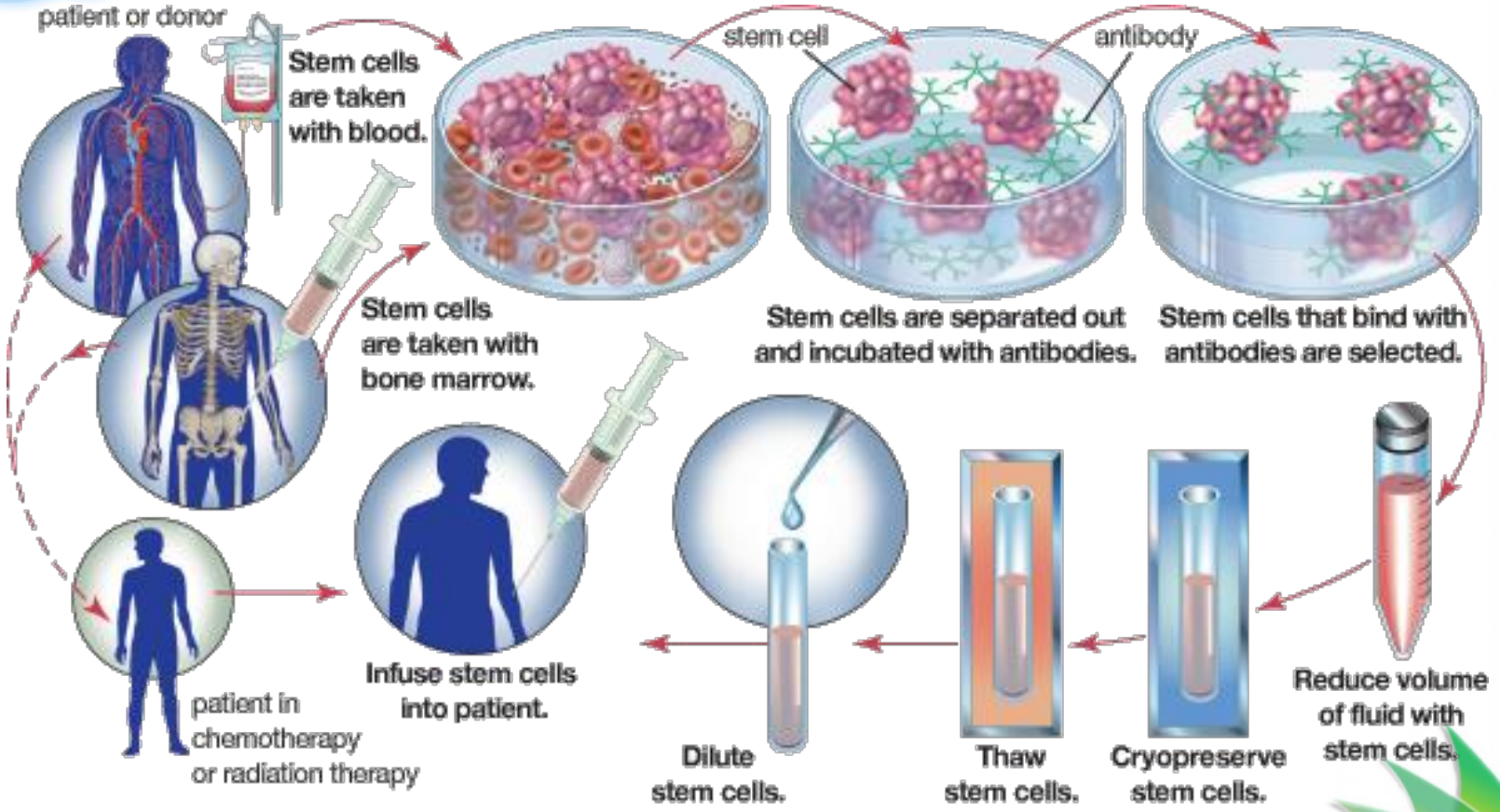
Bone Marrow



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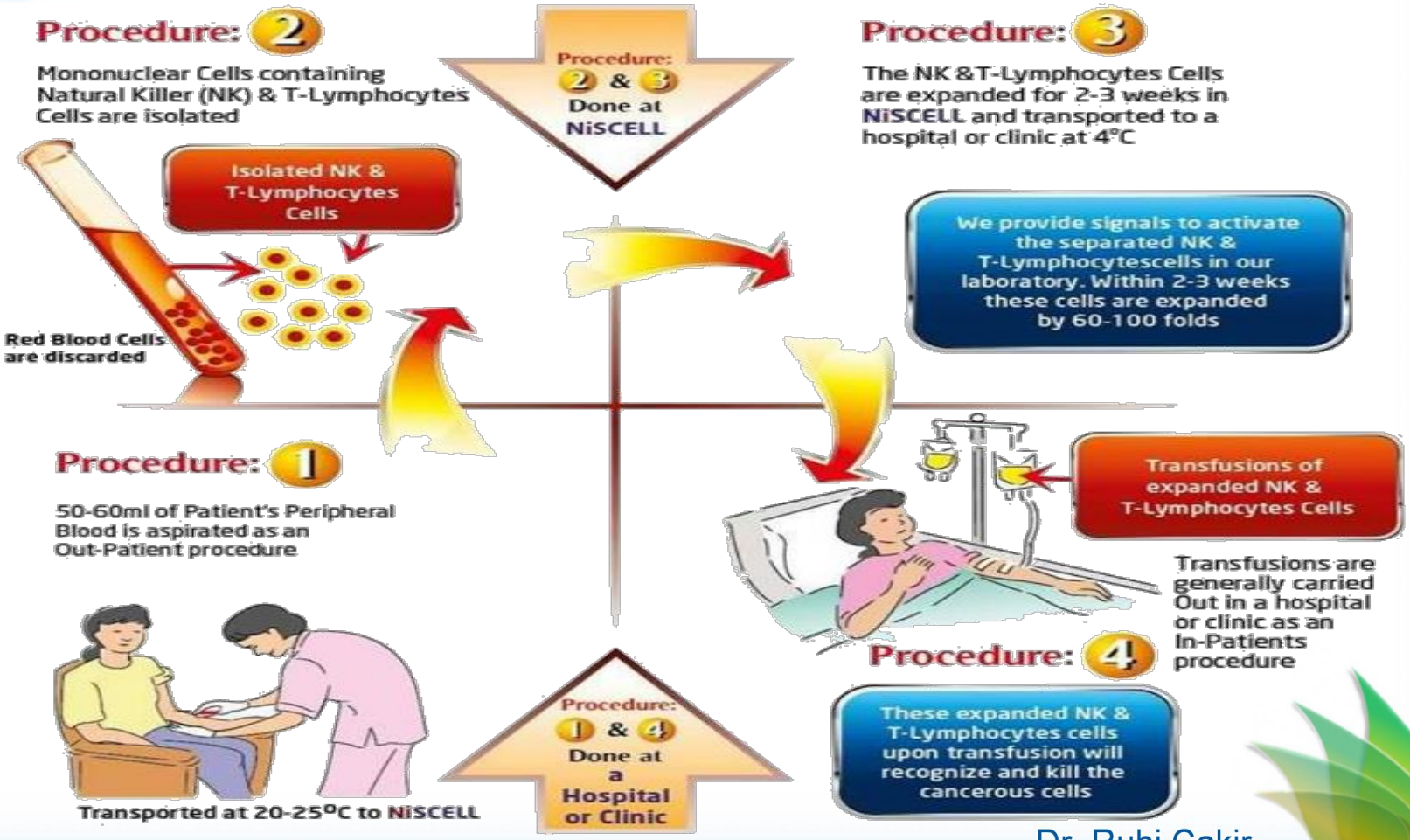
Autologous immune enhancement therapy (AIET)



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Growth Factor

Figure 1: Growth factors acting on 'healing cascade'

Factor	Name	Principal source	Effects
PDGF aa PDGF bb PDGF ab	Platelet derived growth factors	Activated thrombocytes Activated thrombocytes	Mitogenes of mesenchymal stem cells promote the synthesis of the extracellular matrix
TGF-alpha TGF-beta	Transforming growth factors	Activated thrombocytes	Stimulation of DNA synthesis, proliferation of various types of cells. Favours the synthesis of collagen
IGF-I IGF-II	Insulin-like growth factors	Activated thrombocytes	Stimulates proliferation and differentiation of osteoblasts
EGF	Epidermal growth factor	Activated thrombocytes	Stimulates proliferation and differentiation of epidermis cells, co-stimulating angiogenesis
VEGF	Vascular endothelial growth factor	Leucosytes and endothelial cells	Stimulates angiogenesis and chemo-attraction of osteoblasts

In addition, the activated thrombocytes have on their surface a multitude of signalisation molecules, for example: CD9, CD-W17, CD31, CD41, CD42a-d, CD51, CD-W60, CD61, CD62P, CD63

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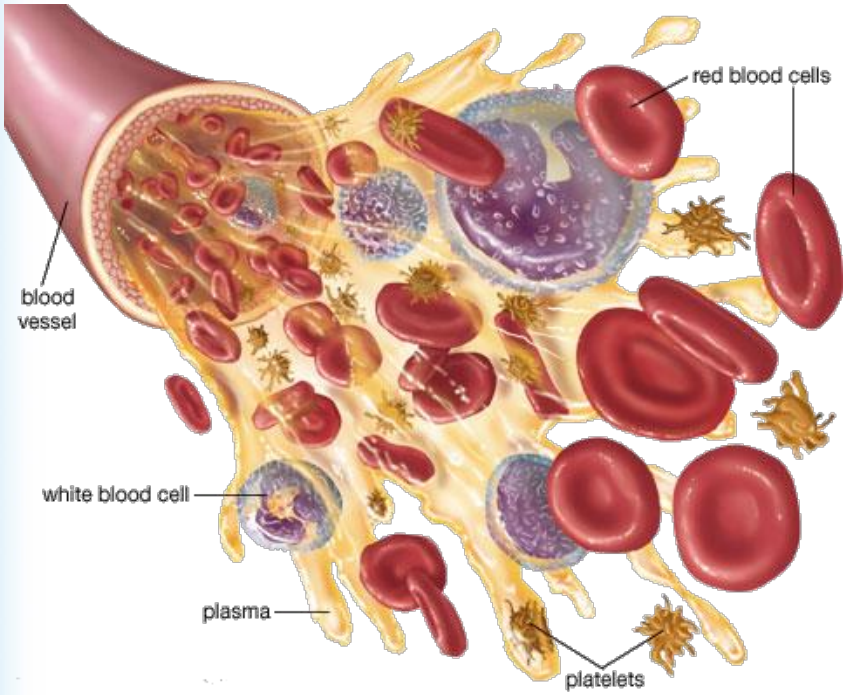
Simple Office Procedures



- PRP (Platelets Rich Plasma)
- CGF (Concentrated Growth Factors)
- PRF (Platelets Rich Fibrin)
- PRGF®-Endoret® (Plasma rich in Growth Factors)
- Blood Ozonation
- Blood UV Therapies

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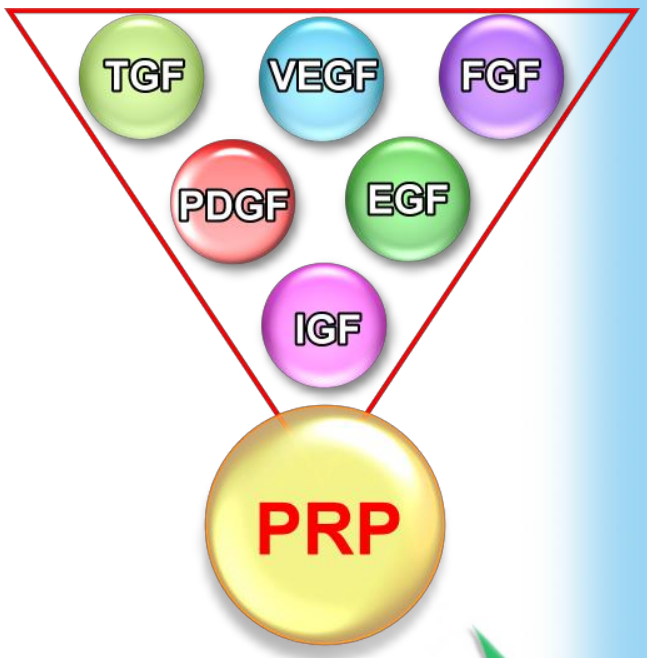
Synopsis Of Growth Factors Present in PRP

Growth Factor	Source	Function
Transforming Growth Factor-beta,TGF-ß	Platelets, extracellular matrix of bone, cartilage matrix, activated TH_1 cells and natural killer cells, macrophages/ monocytes and neutrophils	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	Platelets, macrophages, mesenchymal cells, chondrocytes, osteoblasts	Promotes growth and differentiation of chondrocytes and osteoblasts; mitogenetic for mesenchymal cells, chondrocytes and osteoblasts
Platelet Derived Growth Factor,PDGFa-b	Platelets, osteoblasts, endothelial cells, macrophages, monocytes, smooth muscle cells	Mitogenetic for mesenchymal cells and osteoblasts; stimulates chemotaxis and mitogenesis in fibroblast/glial/smooth muscle cells; regulates collagenase secretion and collagen synthesis; stimulates macrophage and neutrophil chemotaxis
Epidermal Growth Factor,EGF	Platelets, macrophages, monocytes	Stimulates endothelial chemotaxis/angiogenesis; regulates collagenase secretion; stimulates epithelial/mesenchymal mitogenesis
Vascular endothelial growth factor,VEGF	Platelets, endothelial cells	Increases angiogenesis and vessel permeability, stimulates mitogenesis for endothelial cells
Connective tissue growth factor,CTGF	Platelets through endocytosis from extracellular environment in bone marrow.	Promotes angiogenesis, cartilage regeneration, fibrosis and platelet adhesion



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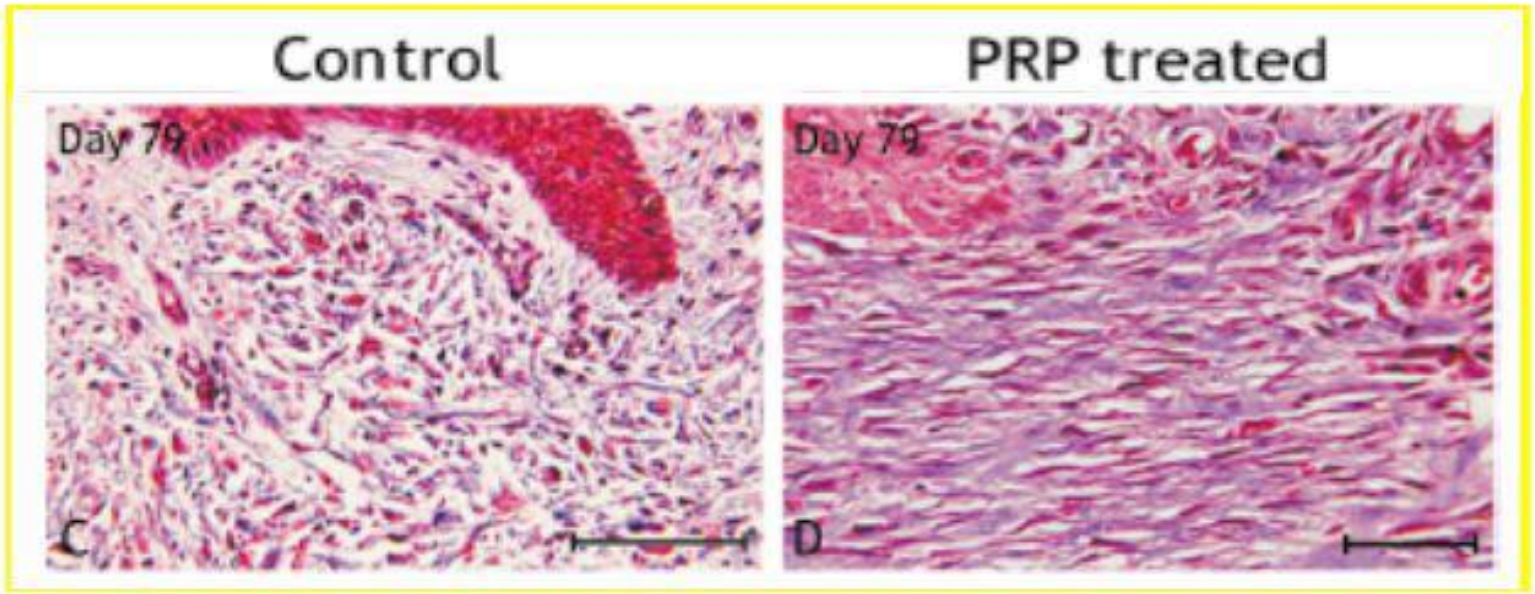
COLLAGEN ORGANIZATION
79 days after treatment



random, dispersed

oriented, organised

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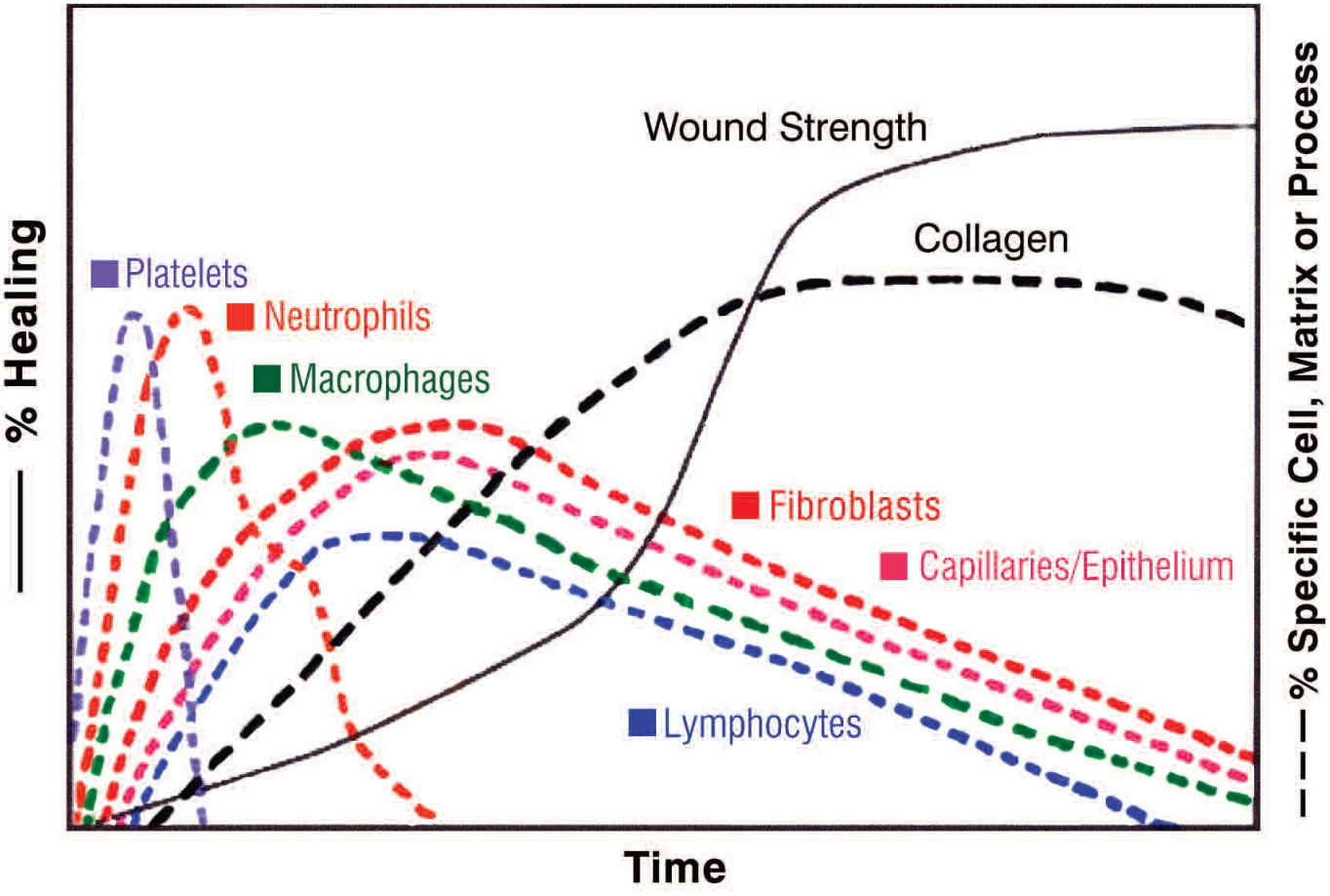
The physiology of Healing of the chronic wound



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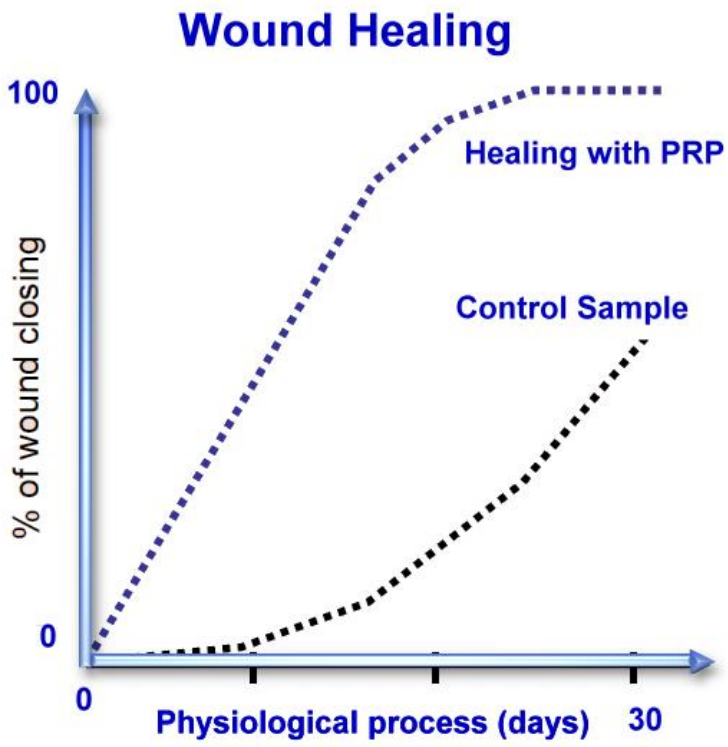
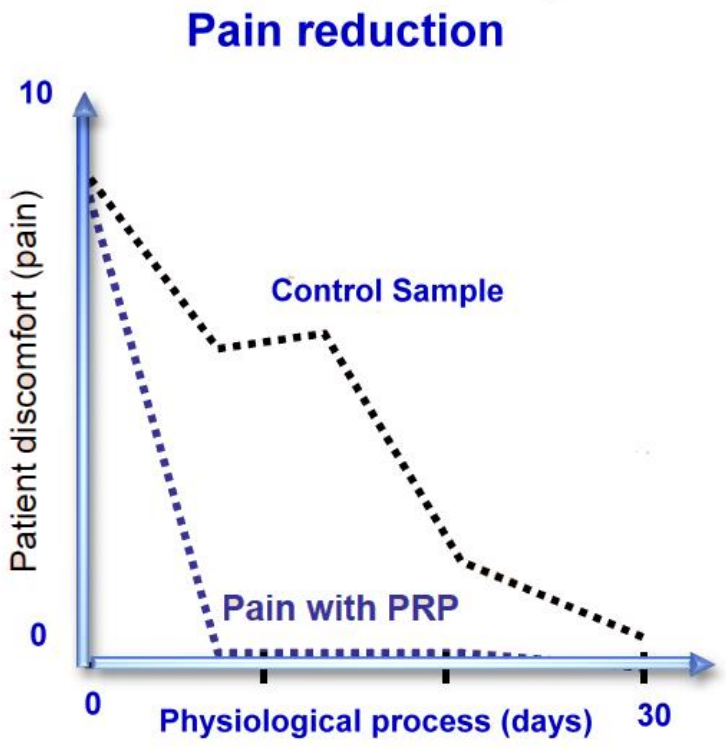
Visible effect in time of Healing and Discomfort





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CGF-LPCGF – General Applications

- Orthopedic surgery
- Oral surgery
- General Surgery
- Dermatology
- Ophthalmology
- Maxillofacial surgery
- Cosmetic Surgery
- Sport medicine
- Gynecology

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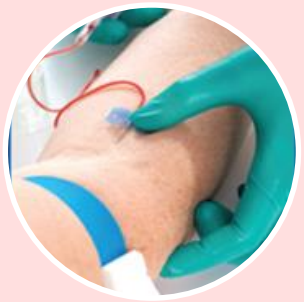
Procedures of LPCGF



1.

Collect 18 ml of blood sample.

2.

Separate & extract LPCGF by centrifugation.

3.

Extract LPCGF from the tube.

4.

Inject LPCGF where needed.

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