Periapical inflammatory lesion is local response of the bone around the apex of tooth that develop after necrosis of pulp tissue or extensive periodontal disease.

Most periapical radiolucent lesions heal un eventfully after endodontic treatment, however some cases may require periradicular surgery to remove pathologic tissues from the periapical area and simultaneously eliminate micro-organisms or any source of irritation that couldn't be removed by the endodontic treatment so periradicular surgery is an important part in modern endodontic practice.

The final outcome of the nature of wound healing after endodontic surgery can be repair or regeneration depending on the nature of the wound, availability of progenitor cells, signaling molecules and micro environmental causes such as adhesion molecules, extracellular matrix and associated non collagenous protein molecules. Since repair is not an ideal outcome after wound healing, regeneration approaches that aim to restore the lost tissues(bone, PDL, cementum and C,T) have been introduced.

Healing after periradicular surgery necessitates regeneration of the apical attachment apparatus and bone after disinfection of the area, so it include elimination of all

infected periapical soft tissue and microorganisms by application of combination of antibiotic drugs(metronidazole, ciprofloxacin and minocyclin)to eliminate the infection.

For optimum healing of periapical defect area after surgery, regenerative therapies like: synthetic bone graft to fill the intra bony defects with excellent bone conducting properties and platelet rich fibrin also have been used as a barrier membrane achieving the concept of guided tissue regeneration by maintaining confined space for regenerative cells for greater periapical bone.

PRF act as healing biomaterial, as it accelerate wound closure and mucosal healing due to fibrin bandage, growth factor release and it act as inter positional biomaterial which act as a barrier between the desired and undesired cells so prevent early invagination of the undesired cells.

Based upon the history in literature it was found that evaluation of different guided tissue regeneration protocols is of value.

Bacterial infection of the dental pulp may lead to periapical lesions. All inflammatory periapical lesions should be initially treated with conventional endodontic therapy and re-treatment, however failure after that calls for surgical intervention. Traditional surgical approaches to treat periapical defects include debridement of apical lesions along with reshaping of the surrounding bone, resection and retrofilling of root apex where healing is almost always by repair which does not fully restore the architecture or the function of the part. Since this is not ideal, newer approaches that aim to restore lost tissue have been introduced as follow:

I-Platelet rich fibrin

II- Bone graft materials

III- Triple antibiotic paste

I- PRF (Platelet rich fibrin)

He et al. [1] evaluated the effect of biologic properties of platelet-rich plasma (PRP)and platelet-rich fibrin (PRF) on proliferation and differentiation of rat osteoblasts.. Blood samples were collected from 14 volunteers. PRP and PRF were prepared with standard protocols. The exudates of PRP and PRF were collected at the time points of 1, 7, 14, 21, and 28 days. The levels of platelet-derived growth factor AB (PDGF-AB) and transforming growth factor 1 (TGF-1) were quantified in PRP and PRF. Then the exudates of PRP and PRF were used to culture rat calvaria osteoblasts. The biologic characteristics of osteoblasts were analyzed in vitro for 14 days.

Results showed that PRP released the highest amounts of TGF-1 and PDGF-AB at the first day, followed by significantly decreased release at later time points. PRF released the highest amount of TGF-1 at day 14 and the highest amount of PDGF-AB at day 7. Cells treated with exudates of PRF collected at day 14 reached peak mineralization. It was concluded that PRF released autologous growth factors gradually and expressed stronger

and more durable effect on proliferation and differentiation of rat osteoblasts than PRP in vitro.

Chang and Zhao et al. [(2)] evaluated the effects of PRF on periodontal ligament fibroblasts (PDLFs) and its application for periodontal regeneration. PDLFs were derived from healthy individuals undergoing extraction for orthodontic reasons. Blood collection was carried out from healthy volunteers. PRF was obtained from a table centrifuge centrifuged at 3000 rpm for 12 minutes. The effects of PRF on PDLFs were determined by measuring the expression of phosphorylated extracellular signal-regulated protein kinase (p-ERK), osteoprotegerin (OPG) and alkaline phosphatase (ALP) activity.

Results showed that PRF increase ERK phosphorylation and OPG in PDLFs in a time-dependent manner. ALP activity was also significantly up regulated by PRF. Application of PRF in infra bony defects exhibited pocket reduction and clinical attachment gain after six months. Peri apical radiography revealed radiographic defect filled in grafted teeth. It was concluded that enhancement of p-ERK, OPG and ALP expression by PRF may provide benefits for periodontal regeneration.

Goyal et al. [3] compared the healing responses related to platelet-rich plasma (PRP), PRP +a collagen sponge, and a collagen membrane used as guided tissue regeneration (GTR) materials for the treatment of apicomarginal defects. Thirty patients with suppurative chronic apical periodontitis and apicomarginal communication were selected and allocated into three groups according to the barrier technique used during periradicular surgery: the collagen membrane group, the PRP group, and the PRP + collagen sponge group. Clinical and radiographic measurements were determined at baseline and every3 months after surgery up to 1 year. Cases were defined as healed when no clinical signs or symptoms were present, and radiographs showed (scar tissue) healing.

Results showed that PRP and PRP + collagen sponge groups depicted83. 33% and 88. 89% healing, respectively, clinicaly and radiographicaly as compared with 80% in the collagen membrane group. All the three treatments showed highly significant reductions in the periodontal pocket depth (PD), the clinical attachment level (CAL), the gingival margin position (GMP), the size of the periapical lesion and periapical healing.. It was concluded that PRP may be an alternative treatment for GTR membrane in the treatment of apicomarginal defects.

Fabbro et al. [4] evaluated whether the use of platelet concentrate during endodontic surgery might have a favorable impact on pain and patient's quality of life during the first week after surgery. Eighteen patients with periapical lesion were treated with endodontic surgical procedure (control group). In another 18 patients, in adjunct to surgical procedure, platelet concentrate was applied on the root end in liquid form, within the bone defect in clot form, and over the suture in liquid form (test group). All patients completed a questionnaire for evaluation of main symptoms and daily activities during the first week after surgery. The two groups were statistically compared.

Results showed that test group showed significantly less pain and swelling, fewer analgesics taken, and improved functional activities as compared with the control group. It was concluded that the adjunct of platelet concentrate to the endodontic surgical procedure produced significant beneficial effect to patients' quality of life during the early postoperative stage.

Lekovic et al. [5] examined the ability of autologous PRF as regenerative treatment for periodontal intrabony defects in humans and to examine the ability of BPBM to

augment the regenerative effects exerted by PRF. A split-mouth design was used, 17 paired intrabony defects were randomly treated either with PRF or with PRF–BPBM combination. Re-entry surgeries were performed at 6 months. Preoperative pocket depths, attachment levels and trans operative bone measurements were similar for the PRF and PRF–BPBM groups.

Result showed that the PRF-BPBM group presented with significantly greater reduction in pocket depth, greater attachment gain and greater defect fill on buccal and lingual sites when compared with the PRF group. It was concluded that PRF can improve clinical parameters associated with human intrabony periodontal defects, and BPBM has the ability to augment the effects of PRF in reducing pocket depth, improving clinical attachment levels and promoting defect fill.

Pradeep et al. [(6)] explored the clinical and radiographic effectiveness of autologous PRF versus PRF + HA in treatment of IBDs in patients with chronic periodontitis. Ninety IBDs were treated with autologous PRF with open-flap debridement (OFD), PRF + HA with OFD, or OFD (controls) alone. Clinical and radiologic parameters, including probing

depth (PD), clinical attachment level (CAL), IBD depth, and percentage defect fill were recorded at baseline and 9 months postoperatively.

Results showed that PD reduction, CAL gain and percentage of bone fill were greater in PRF and PRF + H. A groups than the control group. It was concluded that treatment of IBD with PRF results in significant improvements of clinical parameters compared to baseline. When added to PRF, HA increases the regenerative effects observed with PRF in the treatment of 3-wall IBDs.

Zhang et al. [7] studied the effect of PRF on bone regeneration in sinus augmentation in combination with a xenograft, deproteinised bovine bone. Eleven sinuses from10 patients with posterior maxillary bone atrophy were selected for the study. As a test group, six sinus floor elevations were grafted with a Bio-Oss and PRF mixture, and as control group, five sinuses were treated with Bio-Oss alone. Clinical and radiographic examinations were performed pre- and postoperatively. After 6 months of sinus augmentation, bone biopsies were obtained from the grafted posterior maxilla, and un-decalcified ground sections were prepared..

Histological observation showed similar morphological characteristics for both the PRF and control groups. The percentage of new bone formation in the PRF group was about 1. 4 times of that in control, while the percentage of residual bone substitute in the control group was about 1. 5 times higher as that in the PRF group. No significant statistical differences between the two groups were found in these observed parameters. It was concluded that neither an advantage nor disadvantage of the application of PRF in combination with deproteinised bovine bone mineral in sinus augmentation after a healing period of 6 months.

Shivashankar et al. [8] evaluated the combined use of graft material [platelet rich fibrin (PRF) and hydroxyapatite (HA)] and barrier membrane in the treatment of large periapical lesion. A periapical endodontic surgery was performed on a 45 year old male patient with a swelling in the upper front teeth region and a large bony defect radiologically. The surgical defect was filled with a combination of PRF and HA bone graft crystals. The defect was covered by PRF membrane and sutured.

Clinical examination revealed uneventful wound healing. Radiologically the HA crystals have been completely replaced by new bone at the end of 2 years. It was concluded that the use of PRF in conjunction with HA crystals might have accelerated the resorption of the graft crystals and would have induced the rapid rate of bone formation.

Bajaj et al. [(9)] studied the clinical and radiographical effectiveness of autologous platelet-rich fibrin (PRF) and autologous platelet rich plasma (PRP) in the treatment of mandibular degree II furcation defects in subjects with chronic periodontitis. Seventy-two mandibular degree II furcation defects were treated with either autologous PRF with open flap debridement OFD(24 defects) or autologous PRP with OFD (25), or OFD alone (23). Clinical and radiological parameters such as probing depth, relative vertical and horizontal clinical attachment level and gingival marginal level were recorded at baseline and 9 months postoperatively. Results showed that all clinical and radiographic parameters showed statistically significant improvement at both the test sites (PRF with OFD and PRP with OFD) compared to those with OFD alone. Relative vertical clinical attachment level gain and relative horizontal

clinical attachment level gain were greater in PRF and PRP sites as compared to control site. It was concluded that the use of autologous PRF or PRP were both effective in the treatment of furcation defects with uneventful healing of sites.

Bölükbaşı et al. [(10)] evaluated the efficacy of PRF mixed with biphasic calcium phosphate (BCP)on bone regeneration in surgically created bone defects. Defects 5 mm in diameter were created in both tibias of 6 sheep. The defects were left empty or grafted with BCP, PRF, or BCP+ PRF. Animals were killed at 10, 20, and 40days. The specimens underwent histologic and histomorphometric analysis. Results showed that none of the groups displayed any signs of necrosis. Inflammation was observed in all groups at 10 days, at 20 days 2 specimens of PRF+BCP and all empty defects showed inflammatory cell infiltration.

During the 40-day evaluation period, the PRF+BCP group showed the highest ratios of new bone. The other 3 groups showed statistically similar results. In the BCP and PRF+ BCP groups, the residual graft ratios were decreased at consecutive time intervals. The difference between the 2 groups was not statistically significant during follow-up. It

was concluded that a histomorphometric increase in bone formation with the addition of PRF to BCP in surgically created defects in sheep tibia.

Nacopoulos et al. [(11)] compared healing properties of PRF and its combination with a ceramic synthetic material (graft) composed of hydroxyapatite and b-tricalcium phosphate in an animal model. A bone defect was surgically created in each femoral condyle of 15 New Zealand white rabbits. In each animal, 1 limb had (a) PRF only and the other (b) PRF plus synthetic graft material randomly implanted. Experimental animals were killed 3 months postoperatively.

Histological and radiological examinations were made by means of computed tomography. Results showed that Mean density of the healed bone was statistically significantly greater when synthetic material was used. Moreover, combination of PRF with the synthetic material resulted in more cortical and subcortical bone formation. It was concluded that The addition of the ceramic material significantly increased the formation of new bone, providing a better substrate for bone regeneration.

Dhiman et al. [12] evaluated the healing effect of platelet-rich fibrin (PRF) in periapical surgeries involving apicomarginal defects and to compare these results with surgeries not using any guided tissue regeneration techniques. Thirty patients with suppurative chronic apical periodontitis and apicomarginal communication were randomly assigned to either the PRF or the control group. Clinical and radiographic parameters including pocket depth (PD), clinical attachment level, gingival marginal position, size of periapical lesion, and percentage reduction of the periapical radiolucency were recorded at baseline and at an interval of 3months for a period of 12 months. Results showed that the overall success rate was 83. 33%, with a success rate of 86. 66% for PRF group and 80% for control group.

Both groups exhibited a significant reduction in previously measured parameters at 12-month period. No significant differences were observed between the 2 groups for these parameters except PD, which showed a statistically significant reduction in the PRF group. It was concluded that the adjunctive use of regenerative techniques may not promote healing of apicomarginal defects of endodontic origin.

Kobayashi et al. [13] studied how centrifugation speed (G-force) along with centrifugation time influence growth factor release from fibrin clots up to 10 days, as well as the cellular activity of gingival fibroblasts exposed to each PRF matrix. Standard L-PRF served as a control (2,700 revolutions per minute [rpm]-12 minutes). Two test groups using low-speed (1,300 rpm-14 minutes, termed advanced PRF [A-PRF]) and low-speed +time (1,300 rpm-8 minutes; A-PRF+) were investigated. Results showed that the low-speed concept (A-PRF, A-PRF+) demonstrated a significant increase in growth factor release of platelet-derived growth factor (PDGF), transforming growth factor (TGF)-b1, epidermal growth factor, and insulin-like growth factor, with A-PRF+ being highest of all groups.

Although all PRF formulations were extremely biocompatible due to their autogenous sources, both A-PRF and A-PRF+ demonstrated significantly higher levels of human fibroblast migration and proliferation compared with L-PRF. It was concluded that modifications to centrifugation speed and time with the low-speed concept favor an increase in growth factor release from PRF clots, so affecting tissue regeneration.