

# INTRODUCTION

Proliferative vitreoretinopathy (PVR) is a complex process that appears with some types of retinal detachment (RD) having many similarities to a wound – healing response with inflammation, cell migration, proliferation and extracellular matrix (ECM) production leading to growth of membranes within the hyaloid, the retina and on both retinal surfaces (*Machemer, 1988; Kaufmann et al., 1994; Kosnosky et al., 1994; Pastor, 1998*).

Contraction of these membranes exerts traction and may cause traction on the retina that reopens otherwise successfully treated retinal breaks, creates new retinal breaks, distorts the macula, or directly detaches the retina (*Ryan, 1993; Regillo et al., 2004*).

However, PVR cannot be understood as a specific clinical entity; rather, it is considered the end point of a number of intraocular diseases with various stimuli. Retinal detachment and the associated vitreal alterations are important factors, but not the only ones, in the development of PVR. Several experimental studies have confirmed the hypothesis that PVR is a reparative process induced by a retinal break that causes RD. The most important factor is probably the excessive inflammatory reaction that occurs in some clinical situations that predispose to PVR (*Martini, 1992; Ayelward, 2004*).

Although refinements in surgical techniques and equipment have improved the success rate of surgery to repair RD in recent years up to 90% or more, recurrence due to proliferation is not uncommon and remains the leading cause of failure of surgeries to repair rhegmatogenous retinal detachment (RRD) (*Kon et al., 2000; Regillo et al., 2004*).

Various studies suggest that pharmacologic adjuvant therapy can modify the proliferative disease process and improve the success of surgery. There are a number of studies showing potential benefit of a variety of pharmacologic interventions including retinoic acid *Araiz et al., (1993)*, dexamethasone *Tano et al., (1980)*, colchicines *Lemor et al., (1986)*, Taxol *Van Bockxmeer et al., (1985)* and daunomycin (*Weidemann et al., 1991*).

5-Fluorouracil (5-FU) is a synthetic pyrimidine analogue that acts by irreversibly inhibiting the enzyme thymidylate synthetase thus inhibiting DNA synthesis & more importantly modifying protein synthesis by its incorporation in RNA substituting for uracil. 5-FU has a greater effect on proliferating cells than resting cells (*Blumenkranz et al., 1982*).

In earlier experimental trials, prolonged drug exposure methods were used. Recent work showed that short term exposures result in long term comparable effects on cell proliferation in vivo & in vitro. Using 5-FU in the intraocular infusion during surgery for single 30-minutes exposure can significantly inhibit collagen gel contraction and retinal pigment epithelium proliferation and in a lower & safer concentration than a single higher bolus dose at the end of surgery. It also delivers drug from the beginning of surgery that may resulting treatment of cells at time of activation i.e. at time of surgical trauma (*Asaria et al., 2001b*).

Low molecular weight heparin (LMWH) is a multipotent drug useful in treatment of PVR. LMWH has been shown to reduce postoperative fibrin formation after vitrectomy and to result in fewer hematological complications (*Iverson et al., 1991*).

Therefore it is believed that an intravitreal infusion of 5-FU & LMWH combination intraoperatively may have a significant synergistic anti-proliferative effect *Asaria et al. (2001b)* it also allows using 5-FU at subtoxic levels, which doesn't produce morphologic or electrophysiologic changes according to experimental studies (*Stern et al., 1983*).

The following are believed to be clinical risk factors of postoperative PVR, in which 5-FU & LMWH combination can be tried to prevent PVR. They include: aphakia, pseudophakia with open posterior capsule, preoperative PVR, size of detachment, large or multiple retinal breaks, the use of extensive cryotherapy or laser photocoagulation, anterior uveitis, prolonged duration of detachment, vitreous hemorrhage, presence of choroidal detachment and hypotony (*Kon et al., 2000*).