Guest Editorial

Shaken not Stirred

On numerous occasions in modern history, the world has been the beneficiary of significant contributions from Great Britain in fields such as literature, music, and science. Ushered in by Sir William Bowman and catapulted by the great works of Sir Stewart Duke-Elder, modern British ophthalmology has similarly made many great advances in [illegible]

cellular membranes at the vitreoretinal subretinal space. The membranes are (primarily Müller cells and astrocytes), ges and lymphocytes).[2] Contraction of by counteracting the therapeutic effects as the end result of anomalous wound osing factors that lead to the two main tinal pigment epithelial cells and release The presence of large retinal breaks and ctors for retinal pigment epithelial cell ent and choroidal detachment, cryopexy ,[5] introducing serum components into e extreme case of blood–ocular barrier nomodulators such as T and B lympho- and have also been implicated in the d is the hyalocyte, resident macrophage ls to be exposed to the noxious stimuli hyalocytes are capable of eliciting the ause these cells are entwined within the hyalocytes, along with the other cells in he retina in PVR.[8] Furthermore, as the membranes migrate and proliferate, the elopment and course of PVR.[9]

ly in the surgical arena, where vitreous PVR. In the 1970s and early 1980s the %, with reattachment in less than 20% of ces in surgical technique and instrumen- de C3 PVR but were still less than 60% ches to treat this disease have failed.[12,13] s in London and Liverpool, England, and -1183) showed statistically and clinically nt as that used in the previous attempts lecular weight heparin. Vitrectomy was etinal detachment with half of the cases ion infused during surgery, whereas half

genic disease is characterized by the development of interface, vitreous base, and, less commonly, in the composed of retinal pigment epithelial cells, glial cells fibroblasts, and inflammatory cells (mostly macropha these membranes induces recurrent retinal detachment of scleral buckling and retinopexy. Best characterized healing,[3] PVR is the consequence of several predisp pathogenic process of this disorder: the dispersion of re of chemoattractant serum components into vitreous.[4] the use of excessive cryopexy are the major risk fa dispersion.[4] As is the case for extensive retinal detachm also induces breakdown of the blood–ocular barrie vitreous. Of course, vitreous hemorrhage represents t breakdown and, additionally, introduces cellular immu cytes, which are important in normal wound healing pathogenesis of PVR.[6] Of recent interest in this regar in the posterior vitreous cortex.[7,8] Among the first ce attendant to retinal detachment and its surgical repair type of immune response that characterizes PVR.[7] Be dense collagen matrix of the posterior vitreous cortex, these membranes, could readily mediate traction to t extracellular matrix on which constituent cells in PVR posterior vitreous cortex can greatly influence the dev

To date, attempts to treat PVR have succeeded on microsurgery has increased the reattachment rate for reported surgical success rates were no better than 40% severe cases.[10] At the close of the 20th century, advan tation increased the reattachment rates to 70% for gra for grade D3 PVR.[11] Until now, pharmacologic approa However, the study performed by Asaria and colleague published in this issue of *Ophthalmology* (pages 1179- significant efficacy using 5-fluorouracil, the same age that failed, but this time in combination with low mo performed in 174 cases of primary rhegmatogenous r receiving the "British PVR cocktail" as part of the solu

received a placebo infusion solution. Combination therapy with 5-fluorouracil and heparin decreased the incidence of postoperative PVR by more than 50% ($P = 0.02$). As a secondary result, final visual acuity was substantially better in the group that did not develop PVR ($P < 0.001$).

The principal reason for the success of this is the fact that each of the two major components in the pathogenesis of PVR are treated by the "British PVR cocktail": the antimitogenic properties of 5-fluorouracil prevent the proliferation of cells within vitreous, whereas heparin reduces the effects of inflammation by binding postoperative fibrin and growth factors. Furthermore, because the cells responding to the chemoattractant and mitogenic stimuli of inflammation do so within the extracellular matrix of the vitreoretinal interface,[9,14] heparin can have additional beneficial effects by interacting with extracellular matrix components at this interface, likely rendering the scaffold less suitable for cell migration and proliferation. Moreover, this study randomly assigned only patients determined to be at risk for PVR on the basis of selected clinical criteria previously found to have high discriminant power (Kon et al. Br J Ophthalmol, in press). A companion article in this issue of *Ophthalmology* (pages 1184–1186) describes the results of a prospective study of 212 patients that were classified as low or high risk for PVR on the basis of this discriminant analysis. The incidence of PVR was 9.2% in the "low-risk" group vs. 28% in the "high-risk" group ($P < 0.001$). The use of this approach to increase the prevalence of PVR in the combination drug therapy study increased the "signal-to-noise" ratio in this population, amplifying the beneficial effects of preventive therapy to a statistically and clinically significant level.

As a result of these two landmark studies, ophthalmologists throughout the world can now identify which of their patients are at risk of developing PVR and serve them the concoction of 5-fluorouracil and heparin as effective prophylaxis. Thus, from the folks who brought us "tonic" for malaria, we now have the "HEPURA" cocktail for PVR.

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