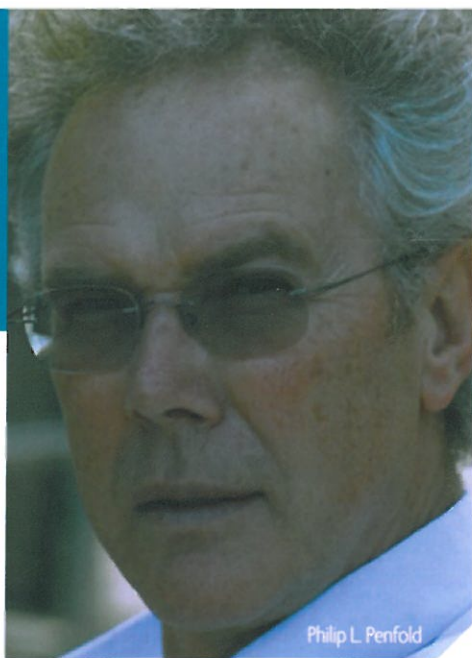


New Australian Innovations in Steroid Formulations for Retinal Disease



Philip L. Penfold PhD

Professor Penfold is Chief Scientist of EyeCo Pty Ltd: The Diabetic Eye Company, www.eyeco.com.au

He holds an adjunct appointment at the Australian National University Centre of Excellence in Vision Science (ACEVS) and is Editor of Macular Degeneration (Springer Publishing).

He patented and developed intravitreal Triamcinolone acetonide for ocular use, now approved by the USFDA for inflammatory eye conditions.

Blinding retinal disease creates a growing burden on the Ophthalmologist in Australia, and their practice managers and support teams, as low vision issues, age-related macular degeneration, and expanding incidences of diabetes related eye diseases pressure practice operations at a time of decreasing reimbursements. The retinal practice is not as 'scalable and repeatable' as the more prominent cataract and Lasik procedures; surgeons enjoy delivering the 'wow' factor achievable in laser eye procedures, and in cataract surgery (especially multifocal IOL's and RLE), and much of the improvement in patient outcomes result from high investments, and investment returns, in entrepreneurship, innovation and technology by the major drug and device companies which also leads to good commercial returns on these refractive and anterior segment procedures. What is required now is fresh thinking beyond genetically engineered drugs for vitreous and retinal disease. Surely, with all of the intellectual and innovative capabilities here in Australia, we can find a solution to this challenge, and achieve its commercial potential in the \$3B back of eye global market. As with Triamcinolone, further success has a spin off benefit of more innovative companies, more patents, more university linkages, and opportunities to cement Australia's leadership position in eye research.

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One of the strengths of ION is an innovative group of practicing doctors who also understand the importance and applications of research to improving patient outcomes.

As an immunologist I regard inflammation and related edema as the primary target for therapy in many retinal diseases, rather than established new vessels. Steroids are the agents of choice in this context since they exhibit both anti-exudative and anti-inflammatory properties.

Glucocorticoids, such as Triamcinolone, predominantly engage anti-inflammatory pathways, mineralocorticoids predominantly anti-exudative pathways. Major issues have emerged concerning the use of anti-VEGF drugs, including 'refractility' where many patients develop tachyphylaxis (reduced responsiveness) (Schaal et al., 2008) and contra indications (including stroke risk) remain a factor. It is essential that innovation in retinal treatments continues to be priority in Australia. EyeCo is pursuing a 'back to basic' re-examination of steroids and their application to back of eye disease, in particular exudative diabetic retinopathy. There are two classes of nuclear receptor mediating the steroid response, the glucocorticoid receptor (GR) and mineralocorticoid receptor (MR). To date, most ocular steroids applications (eg. Triamcinolone and Dexamethosone) have

largely triggered the GR pathway, which is, however, associated with higher IOP and promotion of cataractogenesis. The new approach aims to target exudation through MR pathways, which promises to avoid the GR mediated side effects (Albrecht, 2009). Early work in this regard at UWA (Jenny Rogers et al., 2009) was supported by a major AusIndustry grant some years back. The work has been expanded at ANU where EyeCo is a Partner Investigator to the Australian Centre of Excellence in Vision Science (ACEVS) and in early 2012 EyeCo won the prestigious "Commercialization Australia" grant to turn this innovation into a clinically applicable product. I hold a financial interest in this technology, but it is one of the most promising I have seen since my prior Triamcinolone work in Australia with Mark Gillies, Frank Billson and others.

"Many clinics see their 'procedural' based revenues grow from offering injections..."

This new 'MR' approach builds on the success of prior research on steroids in the field, including Triamcinolone, which has been validated by eminent surgeons such as (Peyman, Jonas et al). At EyeCo Pty Ltd, (and with partners to ensure proper compliance) we assist in properly supplying Triamcinolone to a growing range of eye clinics and day hospitals, and we have seen a resurgence of interest in the GR-class product, which is USFDA approved in its preservative free form. One of the key benefits in its 'staying power' is the absence

of refractility offered by preservative-free Triamcinolone. A recent study at Moorfields Eye Hospital in London in uveitis reported continued responsiveness to multiple intravitreal injections of triamcinolone (Lightman, McCluskey et al., 2011). Rather than simply applying this steroid broadly to the 'AMD market,' we see Triamcinolone used in 'segments' of that market. For example, Triamcinolone is used co-therapeutically with anti-VEGF drugs (Schaal, 2008), for intracameral use in complex cataract surgery, for surgical visualization purposes (ILM, vitrectomy), for high myopia, for uveitis, for specific pathology (BRVO), and for diabetic eye conditions. As patients exhibit refractility

to anti-VEGF drugs, introducing Triamcinolone into the pattern of treatment may offer many advantages, (in a preservative free vehicle) including sustained efficacy and cost effectiveness. Intravitreal injection has become a 'standard of care' now, with MBS, PBS and other support in Australia, as the disease burden grows. Many clinics see their 'procedural' based revenues grow from offering injections, in a scalable and repeatable way. It is my personal observation that many doctors are re-including Triamcinolone in the course of intravitreal injection treatment, as a co therapy or a mono therapy, and using the product more often during vitreous surgery. We are hopeful that the new MR product also offers additional benefits to patients, doctors, day hospitals and

busy clinics. In 2012, this Australian-developed MR technology also received its first granted patent, and new private equity investors, concurrent to the Commercialization Australia grant win.

Professor Penfold can be reached at philip@eyeco.com.au

Commercial queries about EyeCo:
The Diabetic Eye Company can be routed to
William Ardrey - qmgardrey@aol.com

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