



2007

**Nataraja Pillai Oration
Vitreo-Retinal Society of India**

Ocular Drug Delivery Systems and Their Clinical Implications



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Mussoorie, India

Dr. Nataraja Pillai

(1900 - 2000)

Dr. Subramaniyan Natarajan Pillai was born on March 1st 1900. His medical education was done in Tanjore. He moved to Madras Government Ophthalmic Hospital in 1938, and obtained his ophthalmology diploma in 1939. Col. Wright (Authority on Tropical Ophthalmology and who started the Ophthalmology museum) trained him.

He continued to serve in Madras till 1943 and shifted to the Government Erskine Hospital (Currently Rajaji Hospital), Madurai. He worked with the Government till 1951 and there after private practice. As an eye surgeon he had special passion for community work, with the help of the TVS business family.

Orators awarded the "Nataraja Pillai Oration" in the last 4 years

2003

Prof. Suresh Chandra,
Clinical Professor of Ophthalmology,
University of Wisconsin, USA.
Topic: Update in Macular degeneration

2005

Dr. John R Heckenlively
Paul Lichter Professor of Ophthalmic Genetics,
Director, Visual Physiology Lab,
Kellogg Eye Center,
University of Michigan, Ann Arbor, MI, USA
Topic: Autoimmune Retinopathy, CAR and MAR Syndromes

2006

Dr. Vinod Lakhanpal
Director of Retina Service, Eye Consultant of Maryland
Clinic Professor, University of Maryland
Chief of Ophthalmology, Union Memorial Hospital
Baltimore, USA
Topic : Prevention and Management of Massive Suprachoroidal Hemorrhage

2007

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I. Pathophysiology of DME and Corticosteroid-Based Therapies

A. The mediators that provoke the development of Diabetic Macular Edema are all impacted by corticosteroids

II. Relative Potencies of Corticosteroids

A. Not all steroids have the same potency—dexamethasone is 5 times more potent than triamcinolone

III. Maximum Vitreous Concentrations

A. Not all steroids achieve the similar maximum concentrations

B. Corticosteroid Equivalents are different between steroids—multiply the potency by the peak vitreous concentration

IV. Vitrectomy: The Effect on Ocular Pharmacokinetics

A. The elimination of drugs from the vitreous are accelerated with pars plana vitrectomy in animal studies

B. The elimination of Triamcinolone Acetonide is increased by approximately 1.5 to 2.5 fold with vitrectomy following an intravitreal injection in rabbits

V. B&L Reservoir Style Fluocinolone Acetonide Sustained Release Delivery Technology

A. Designed to last 1000 days

B. Controlled and consistent delivery

C. On-site delivery

D. Insignificant systemic dose

E. Eliminates long-term systemic side effects

F. Patient compliance not a factor

■ VI. B&L Fluocinolone Implant Uveitis Clinical Trials:

■ patients with unilateral or bilateral uveitis

■ treated with 0.5mg versus 2.0 mg FA implant

■ Tapered off systemic medications

■ Endpoints included recurrence rates, use of adjunctive therapy, visual acuity

■ Approved by FDA for this indication

■ DME Phase 3 trial using 0.5 mg implant only in implant arm (fully enrolled)

Significant efficacy seen for eyes treated with FA implant but concerns about steroid induced ocular side effects have limited approval only for the uveitis indication currently

VII. Allergan Posurdex Dexamethasone Implant

Biodegradable Dexamethasone Implant Ingredients:

■ Dexamethasone (350 or 700 g)

■ Poly [lactic-glycolic] acid

• Biodegradable copolymer

- Used in various medical products (e.g., Vicryl®)
- Hydrolyzes to lactic and glycolic acids
 - Lactic acid is metabolized to H₂O and CO₂
 - Glycolic acid either excreted or enzymatically converted to other metabolized species
- Phase 1/2 trial complete
 - Patients with persistent macular edema despite 90 days of standard therapy caused by either diabetes, vascular occlusion, post-cataract CME, or uveitic CME
 - Patients assigned to either 350mcg versus 700 mcg dexamethasone implant versus observation
 - Designed for 95 patients per arm—315 total patients enrolled
- Two Phase 3 trials underway
 - Patients with persistent diabetic macular edema
 - Patients with persistent macular edema due to vein occlusion

Summary

- Efficacy seen with triamcinolone acetonide depot injection, fluocinolone acetonide drug delivery system, dexamethasone drug delivery system
- Differences noted in duration of drug and durability of effect
- Possible differences noted in ocular side effects
- Are all steroids the same?

Challenges of Local Ocular Drug Delivery

Conclusions

- Two fundamental approaches and philosophies:
 - Longer acting reservoir implants with good long term control of disease but with potential for drug or suppressive side effects
 - Shorter acting biodegradable inserts that potentially expose eye to less drug or suppressive side effects but may control disease less well
 - However, drug potency and intraocular drug levels may have significant on control of disease beyond period of drug presence
- Possible that each approach may have preferential uses in different diseases or with different drugs

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