

OPHTHALMOLOGY AND THE HISTORY OF PENICILLIN: A TALE OF FOUR CITIES

By **John D. Bullock, MD, MPH, MSc***

Purpose: To review the history of penicillin (PCN) and to highlight the importance of ophthalmology / ophthalmologists

Methods: [1] Literature search; [2] Site visits

Results: Alexander Fleming's discovery of penicillin was one of the defining moments of the twentieth century and the contributions of ophthalmology / ophthalmologists to this endeavor were highly significant. An ophthalmologist advised Alexander Fleming to study medicine. Fleming discovered lysozyme's presence in tears and later recognized the same antibacterial effect (lysis) of PCN on *Staphylococcus aureus*. Fleming proved the non-irritancy of crude PCN by irrigating the human conjunctiva Q1Hx24 hours. The first extraction of PCN was by a future ophthalmologist. The first documented clinical successes of (crude) PCN were in cases of ophthalmia neonatorum. The first instance of a presumed PCN-resistant staphylococcal organism occurred in an ocular infection. Fleming's only clear-cut cure with crude PCN was in a case of pneumococcal conjunctivitis. The first PCN treatment of a post-traumatic infection was for an intraocular foreign body. The first use by Florey and Chain of injectable extracted PCN was for a case of endophthalmitis / orbital cellulitis. Six of ten cases in the original series of Florey and Chain, treated with extracted PCN, were ophthalmic patients. In the first spectacular life-saving cure, PCN was co-given by a future ophthalmologist.

Conclusion: Ophthalmology and ophthalmologists were instrumental in the inauguration of this new era of scientific therapeutic medicine.

THE RELATIONSHIP BETWEEN COMBINED POSITRON EMISSION TOMOGRAPHY / COMPUTED TOMOGRAPHY FINDINGS AND LIGHT MICROSCOPIC FINDINGS IN CASES OF CHOROIDAL MELANOMA

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Purpose: To investigate the correlation between gross and light microscopic features of choroidal melanoma with combined PET/CT scanning findings.

Methods: Fourteen eyes of fourteen patients with choroidal melanoma underwent combined PET/CT scanning and enucleation. Combined PET/CT scan findings were then correlated with the light microscopic findings in the enucleated eyes. No authors have any financial interests to disclose.

Results: All fourteen eyes showed uptake on the combined PET/CT scan. Mean patient age was 62 years old (SD 12.5 years). There were six women and eight men. Mean tumor thickness was 9.3 mm (range 3 – 23 mm). Histopathology showed choroidal melanoma in all fourteen patients: six tumors were mixed cell type, seven were spindle cell type, and one was epithelioid cell type. By combined PET/CT scan, the average Standardized Uptake Value (SUV mean) was 3.7 (range 1.7 – 12.8). A correlation was found between the SUV mean and lesion thickness ($r=0.85$; $p<0.01$) and with the largest tumor base diameter ($r=0.65$; $p=0.01$). Melanomas associated with focal necrosis ($p=0.03$) or of mixed cell type ($p<0.01$) appeared to have higher SUV means. No correlation was found with the presence of complex microvasculature or number of mitotic figures.

Conclusion: The majority of choroidal melanoma in this series had low to medium mean SUVs. Lesion thickness accounted for a significant portion of the variation seen in the SUV mean, though the largest tumor base diameter, focal necrosis, and cell type were other factors associated with higher SUV means. In this study, no other histological findings showed correlation with PET/CT uptake.

THE INCIDENCE OF CENTRAL SEROUS CHORIORETINOPATHY IN OLMSTED COUNTY, MINNESOTA, FROM 1980 TO 2002

By Anna S. Kitzmann, MD*, **Jose S. Pulido, MD, MS, MPH, MBA**, Nancy N. Diehl, BS, David O. Hodge, MS, James P. Burke, PhD

Purpose: To determine the incidence of central serous chorioretinopathy (CSC) in Olmsted County, Minnesota from 1980 to 2002. The secondary *Purpose* of this study was to determine the associated risk factors for CSC based on previously reported risk factors and to investigate for any new risk factors not previously reported.

Methods: We conducted a population-based, retrospective cohort study using the resources of the Rochester Epidemiology Project. Medical records of all potential cases of CSC residing in Olmsted County, MN from 1980 to 2002 were reviewed. Controls were selected from the same general population. Control group 1 patients were matched for age, sex, length of medical follow-up, and index

date (corresponding with date of diagnosis for cases). Control group 2 patients were matched for all the same criteria as control group 1, and, in addition, they had a documented normal eye exam.

Results: There were 74 cases (63 men, 11 women) of CSC. The mean annual age-adjusted incidence per 100,000 was 9.9 (95% confidence interval (CI), 7.4-12.4) for men, 1.7 (95% CI, 0.7-2.7) for women. The incidence of CSC was approximately 6 times higher in men than women ($p < 0.001$). There were no significant risk factors identified for CSC.

Conclusion: The incidence of CSC has not previously been reported in a population-based study. In accordance with previous studies, we found that CSC occurs more frequently in men than women.

COMPARISON OF ANGLED AND STRAIGHT IRIS HOOKS

By **John C. Merriam, MD***, Adrian Brügger, Lei Zheng, MD

Purpose: To evaluate the effect of the angle of attack of straight iris hooks on displacement of the pupil and to design an angled hook to minimize displacement of the iris.

Methods: A finite element model of the human iris, created with the algorithm LARSA 2000, simulated the effect of four iris hooks on displacement of the pupil margin at attack angles of 5, 25, and 45 degrees (relative to the plane of the iris) and a horizontal enlargement of the pupil of 2.5 mm. With the aid of the model, an angled iris hook which minimized iris displacement was fabricated and compared with straight hooks in human and animal globes.

Results: As the approach angle of the straight hook increases, the pupil margin is lifted: 0.22 mm with a 5 degree attack angle, 1.17 mm with a 25 degree angle, and 2.5 mm with a 45 degree angle. In human and animal globes, the performance of the straight and angled hooks is similar when the hook is parallel or nearly parallel to the iris plane. As the attack angle of the hook increases, it is easier to grab the iris with the angled hook and the iris is less displaced.

Conclusion: With straight hooks, deformation of the iris increases with the angle of attack. Tests in animal and human globes suggest that the angled hook may facilitate surgery when the pupil is small or the iris is floppy.

Financial Disclosure: Dr. Merriam and Dr. Zheng are named on a preliminary patent issued to Columbia University.

INITIAL STUDIES OF THE USE OF OCULAR VIBROACOUSTOGRAPHY

By **Jose S. Pulido, MD, MS, MPH***, Randall R Kinnick, Cheryl Hann, James F. Greenleaf, PhD

Purpose: Ultrasonography is critical in the diagnosis and follow-up of intraocular tumors. Vibroacoustography, a recently developed technique demonstrates not only the ultrasonic findings but also incorporates the recordings of low frequency vibrations induced by the ultrasound waves. This gives an indication of the elasticity of the tissue, a finding not found by classic ultrasonography. Recent studies have evaluated the use of vibroacoustography in determining presence of liver metastases and the development of breast cancer being able to determine microcalcifications of 110microns. The transverse spatial resolution of vibro-acoustography is in the sub-millimeter range, making the technique suitable for high-resolution imaging

We have performed preliminary studies on the use of vibroacoustography for imaging intraocular tumors.

Methods: Following IRB approval, eyes that had undergone enucleation were evaluated by vibroacoustography using a saline bath, a 9MHz confocal transducer and 50kHz frequency separation. The scans were 30mm x 24mm x 0.1mm/pixel. Comparisons were made to 10 MHz Bscan ultrasonography and gross pathology

Results: 9 eyes were imaged. Four had ciliochoroidal melanomas and 3 had choroidal melanomas. One had a regressed choroidal melanoma with a dense vitreous hemorrhage and painful neovascular glaucoma and one had a retinoblastoma. Vibroacoustography demonstrated edges very well and had superb depth of field. In addition, calcium was well-visualized in the case of retinoblastoma. Internal structures were not readily seen though occasionally vascular channels appeared to be visualized.

Conclusion: Vibroacoustography as presently used determines calcification very well. In addition, imaging has more depth of field than traditional ultrasonography. Evaluation of internal structure is challenging and further studies are ongoing.

Financial Disclosure: Dr Greenleaf has a financial interest in vibroacoustography.

EVIDENCE FOR CORNEAL GLUTAMATE RECEPTOR EXPRESSION AND FUNCTION

By S. Shippy, PhD*, **J.S. Pulido, MD**, H. Qian PhD, J.D. Nelson, MD, M.-J.Lu, and **J.C. Erie, MD**

Purpose: Glutamate signaling is crucial for normal function of the nervous system. Its dysfunction has been linked to a number of pathologies. The presence of glutamate signaling machinery, especially N-methyl-D-aspartate-type glutamate receptors (NMDA R), has been detected in many tissues. This work explores the presence of glutamatergic signaling in normal and diseased corneas.

Methods: Immunohistochemistry was performed with cryosections of rat cornea tissues and NMDA R1 subunit antibody. Levels of mRNA expression in the cornea were determined by real-time RT-PCR with NMDA R1 subunit specific primers. Cultured rat corneal cells were used to measure glutamate-elicited responses. Intracellular calcium levels were measured with the calcium indicator Oregon Green. Human tears were collected from 3 normal and 1 dry eyes patient for amino acid analysis by capillary electrophoresis.

Results: Positive staining by NMDA R1 antibody was detected in both the corneal epithelium and endothelium. Similarly, PCR demonstrated the presence of NMDA R1 subunit mRNA in corneal tissues. Glutamate applications on cultured corneal cells elicited a fast and repeatable enhancement of the intracellular calcium level. Neither N-methyl-D-aspartate in the presence of glycine nor kainate mimics the glutamate-elicited calcium signal. The amino acid analyses confirmed the presence of 5-30 microM glutamate.

Conclusion: The presence of NMDA receptors in normal cornea tissue is demonstrated by using immunocytochemical and RT-PCR. Intracellular calcium responses elicited from individual corneal cells indicates metabotropic receptors under cultured conditions. Tear glutamate may play signaling roles at the corneal epithelium and be involved in dry eye syndrome or diabetic keratopathy.

NODULAR DEGENERATION

By **Thomas O. Wood, MD***, Ellen E. Williams, MBA, Danielle L. Hamilton, Bryan L. Williams, PhD

Purpose: Recent studies suggest that Salzmann nodular degeneration can be treated effectively and safely using the excimer laser. However, while describing the clinical symptoms of nodular degeneration, this study will also explain a simple, office procedure for removing the nodules and present the post operative outcomes associated with the described surgical technique.

Methods: The study sample consisted of 36 eyes among 30 consecutive patients who presented with symptomatic nodular degeneration. Twenty-five of the patients were female. Discomfort and decreased vision was observed in 25 of the eyes; only discomfort was observed in 6 eyes; and only decreased vision was observed in 5 eyes. Patients underwent removal of the nodules using topical anesthesia and toothed forceps at the slit lamp; this entire procedure required only 10 to 15 minutes to complete.

Results: Thirty-two of the 36 eyes have follow-up averaging 10.5 months. Thirty-one had improvement in discomfort, vision, or both. One patient has had improvement in pain and vision but occasionally experiences watering. Two of the 31 eyes that had initial improvement through 12.75(A) and 9(B) months have had asymptomatic recurrences at 27(A) and 17.25(B) months. Patient B has keratoconus and wears a hard contact lens which created the recurrence that was removed before symptoms developed.

Conclusion: Simple dissection is an effective treatment for Salzmann nodular degeneration.

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Bold type indicates AOS member.