



Footprints



International Uveitis Study Group meeting with the 2nd Uveitis Society (India) [US(I)] meeting, Chennai, 2001. In the photograph, among other prominent Specialists, the Patrons and Founder members of the US (I) are seen. Top row, 4th from right, Prof. Dr. Jyotirmay Biswas, 6th from right, Dr. Carl P. Herbort, 7th from right, Dr. Virender S. Sangwan. Middle row, 3rd from left, Padmashri Prof. Amod Gupta. Front row, 4th from right, Prof. Narsing Rao, first from left, Prof. Dr. Sudha K. Ganesh, second from, left Prof. Dr. S. R. Rathinam.





President uveitis society (india)

Dr. Kalpana Babu, DO FMRF MRCOphth(Lon), MNAMS Head of the Department, Uveitis and Ocular Inflammation Prabha Eye Clinic and Research Centre & Vittala International Institute of Ophthalmology, Bengaluru kalpanababumurthy@gmail.com

Dear friends,

25 years ago, uveitis specialists in India were very few and the uveitis practices were sporadic, largely driven by individual interests and experience. The Uveitis Society of India was formed because of the efforts of these passionate individuals and continues to be a forum for discussions, learning and motivating research in this field. Since its formation, the society has inspired a whole generation of young ophthalmologists who have taken up uveitis practice as their specialty of choice.

As we celebrate the 25th year of the Uveitis Society of India, I thank the editorial team for having come out with the silver jubilee edition of the newsletter so aptly titled "Footprints". This newsletter captures the impressive journey of the uveitis practice in India, highlighting the advances in the uveitis practice over the last 25 years as recounted by some of the pioneers in uveitis in India. Each article in this newsletter is a testimony to the years of experience and the progress in this field. I am sure this newsletter will leave an impact on the mind of the readers.

I congratulate and thank all the authors for having contributed to this special edition. A big thanks to the editorial team for having brought out this edition in such a short time and in such a wonderful manner, team Hallmark and the industry support for their coordinated efforts in bringing out this silver jubilee edition of the USI newsletter for all of us

Regards,

Dr. Kalpana Babu



200000

Secretary uveitis society (india)

Dr. Sudharshan Sridharan, DO DNB Senior Consultant, Department of Uveitis Sankara Nethralaya, Chennai *drdharshan@gmail.com*

Dear Friends

Greetings!

As we all celebrate the silver jubilee year of Uveitis society of India this year, we have our special edition coming out for the same. This edition is like no other because we have our founders, past presidents, stalwarts and best in the business sharing their knowledge on various topics of prime importance.

Not only that, there are many nostalgic events described, heartfelt notes and many more.

Who best to coordinate and compile all these than our own editor in chief, Dr. Abhilasha and her team.

Grateful, as always to all those who have contributed to this for their valuable time and effort.

Am sure this will be a prized possession for all of us and we are looking forward to hearing from you all

With best wishes

Dr. Sudharshan Sridharan





www.indianuveitis.org

Editor-in-Chief, Newsletter UVEITIS SOCIETY (INDIA)

Dr. Abhilasha Baharani, DNB, FRCS, FICO Senior Consultant, Neoretina Eyecare Institute, Hyderabad. drabhilashabaharani@gmail.com

"The journey of a thousand miles begins with a single step." - Lao Tzu

The year Two Thousand and twenty four, the quadricente nnial year of the Uveitis Society (India) [US(I)], we celebrate the journey and reminisce about the path that has led us here. Uveitis was and to some extent is still the road less taken and therefore a road had to be built, a path had to be created. We trace the footprints in the sands of time and gratefully acknowledge the contribution of the patrons and founders of the Society and all the past Presidents who have been great teachers and continue to be the torch bearers. Their footprints or so to say their clinical acumen, passion for uveitis, research, academics and teachings over the years have guided all of us in the clinic and life in general. This issue of the Newsletter, titled "Footprints" attempts to bring together the wisdom of all past Presidents of the Society. It contains a treasure trove of articles from the best of the US(I) in the chronological order of their Presidential terms.

The Newsletter opens with the article titled "Clinical pearls in the management of uveitis" by Padmashri Prof. Amod Gupta. The article begins with the three most important words in medicine, "mindful clinical examination". It is a generously illustrated gist of the most important points one must know while practicing uveitis. Needless to say, it's not to be missed.

Next, Prof. Dr. Jyotirmay Biswas elegantly describes his 35 year old journey in uveitis in the article titled, "My Journey in Uveitis: From steroids to biologics". His writing style is unique, lucid and simple that you can almost hear him speak. One key take away that I



wish to quote, "I diligently maintained a register of all cases and analyzed respo nses to steroids, immunosuppressives, and biologics across various diseases." His experience of using newer agents in the management of uveitis has guided us in using these drugs in our population. I requested him to share photographs of the register he still maintains and he graciously obliged. There's nothing more enduring than learning from your own patient out -comes.

The article titled, "When will we start diagnosing Leptospirosis" by Prof. Dr. S. R. Rathinam is something to ponder. The enormous global burden despite this underreporting of widespread zoonosis is well documented in literature. This sentence from the article reveals the sheer volume of patients with leptospirosis associated uveitis and I quote, "One of the largest retrospective population studies on ocular leptospirosis was done at our institute using of the data of over 27 years with 1268 seropositive leptospirosis patients." It also gives us an idea of the numbers that we might be missing! Dr. Rathinam's lifetime of work and publications on leptospiral uveitis is a story of determination and resilience which shines through in the article.

"Epidemiology of Uveitis in India: Changing trends" by Dr. Virender S. Sangwan takes us on a time machine. The article comprehensively describes the trends in etiological diagnosis, diagnostic modalities and treatment options in uveitis over the decades. A rewarding sentence for those who have worked passionately and tirelessly for the subspecialty and I quote, "No longer is idiopathic the most common cause of uveitis, approximately 70% of the times, we can find a cause as opposed to 30% of the times, about 20 years back."

The next article by Prof. Dr. Sudha K.

Ganesh is an exemplary piece of writing on "Cataract Surgery in Pediatric and Cataracts: Challenges Adult Uveitic and Lessons". It is meticulously written just like her surgery. Every aspect of cataract surgery in uveitic eyes including preoperative assessment and preparation and post operative complications and management is covered in depth and detail. Prof. Ganesh has not only included some excellent clinical images, she has also generously provided video links for those interested in learning the intraoperative techniques. One key take home and I quote, "All inflammatory cells both in the anterior chamber and vitreous must be eliminated before surgery. It is recommended to check the inflammation a few days before surgery to avoid complications." For those facing challenges in uveitic cataract surgeries, this is your manual.

"Fundus camera to chat GPT: The journey of imaging in Uveitis" by Prof. Vishali Gupta cohesively describes the evolution of imaging in uveitis, which is now an indispensable part of clinical practice. The references include some landmark articles on imaging and the final section on artificial intelligence (AI) discusses the journey of AI so far and the future possibilities. Prof. Gupta, the first Asian President of the IUSG has kept pace with the times and her zeal and philosophy of positivity is brought out in her words and I quote, "World remembers contributors and not critics: and I strongly believe in that".

Finally, we have an eye opener article, "Publishing original data but don't know where to publish: Lessons learned from a life without mentors to guide" again by Padmashri Prof. Amod Gupta. Now before anyone of you reading this editorial, credits me for giving such a pertinent topic to Prof. Gupta, let me clarify that he has written this article voluntarily, in addition Isn't it! That is the mark of an enormously generous mentor-teacher. As I said in my previous editorial, he's still on the road less traveled and this time he has even gone the extra mile. The key sentence that hits hard and I quote, "You might throw your manuscript into the wastebasket if others cannot retrieve the content." Upon reading his article, I requested him to share his irretrievable articles, the precious full texts of which are available in the final section titled, "Lost and Found" of this very fortunate issue.

The silver jubilee year is special and to encourage contribution from all members of the US(I), an initiative called, "Heartfelt and Handmade" was conducted where interested members contributed clinical images, photographs, sketches and paintings commemorating 25 years of the US(I). Members have also shared handwritten notes/poems for their teachers and important clinical cues or quotes they learnt during fellowship. I express my sincere gratitude for the contribution and efforts of the members that has added warmth and given a very personal touch to the newsletter. These heartfelt joys can be found throughout the newsletter intervening the articles.

I'm filled with gratitude to the Founders and past Presidents of the Society who graciously agreed to write for the newsletter. Their footprints of wisdom and knowledge make our paths richer and this issue a special souvenir.

I sincerely thank the President, Dr. Kalpana Babu Murthy, Secretary, Dr. Sudharshan Sridharan, Vice President Dr. Padmamalini, Joint Secretary Dr. Soumyava Basu and Treasurer Dr. Parthopratim Dutta Majumdar for their support and guidance.

Cheers to the Hallmark team, Mrs. Veidhehi, Mr. Sampath and Mr. Vinay, without whose creative efforts this would not have been possible.

Though this newsletter has been put together with a lot of heart, there might have been oversights and flaws and there's always scope for improvement. Nevertheless, I hope everyone will enjoy reading this special issue and will gain from the wisdom it encapsulates. Please feel free to mail in your comments and critique.

Sincerely, Abhilasha

CONTENTS

<i>Clinical pearls in the management of uveitis</i>	PADMASHRI PROF. AMOD GUPTA	01
My Journey in Uveitis: From steroids to biologics	PROF. DR. JYOTIRMAY BISWAS	13
When will we start diagnosing Leptospirosis	PROF. DR. S. R. RATHINAM	23
Epidemiology of Uveitis in India: Changing trends	DR. VIRENDER S. SANGWAN	32
Cataract Surgery in Pediatric and Adult Uveitic Cataracts: Challenges and Lessons	PROF. DR. SUDHA K GANESH	42
Fundus camera to chat GPT: The journey of imaging in Uveitis	PROF. DR. VISHALI GUPTA	55
Publishing original data but don't know where to publish: Lessons learned from a life without mentors to guide	DADMACHDI DDOF, AMOD, CUDTA	69
	PADMASHKI PKOF. AMOD GUPIA	00
Lost and Found	PADMASHRI PROF. AMOD GUPTA	77

Clinical pearls IN THE MANAGEMENT OF UVEITIS

Padmashri Prof. Amod Gupta

President US(I) 1999-2002



Padmashri Prof. Amod Gupta, MS, DSc (Hon.), FAMS

Emeritus Professor Advanced Eye Centre, PGI, Chandigarh dramodgupta@gmail.com

- 1 Mindful clinical examination-The key to success in uveitis care and management is a mindful ocular examination and review of systems. No eye examination is complete without a slit lamp and dilated fundus examination (Figure 1)
- 2. The presence of intraocular white cells is inflammation which may be immunemediated or caused by infectious (endogenous or exogenous) agents including bacteria, viruses, fungi, and parasites. Important to remember that malignant cell infiltration in ocular tissues and intraocular spaces simulates inflammation, especially at extremes of age. (Figure 2)
- 3. All inflammations do not need treatment. Fuchs' uveitis is the most overtreated anterior uveitis that often presents to general ophthalmologists with unilateral cataracts who on finding KPs, and some vitreous opacities/cells immediately jump to starting treatment with corticosteroids. All must familiarize themselves with stellate KPs scattered over the back of the cornea with atrophy of iris crypts, loss of pupillary ruff, and transillumination defects, and no posterior synechiae. These patients eventually require cataract would surgery. Look out for raised IOP in such patients. (Figures 3-5)

4. Hypopyon in the eye should prompt a search for systemic associations. Look for its mobility.

hypopyon -favors lympho a. Mobile blastic leukemia in young children and lymphoma in the elderly (Figures 6a and 6b). You will be able to save a life if you think of masquerades at extremes of age. In young adults, it indicates the presence of Behcet's disease. Don't forget to ask history of oral and genital ulcerations to confirm your suspicion of Behcet's disease. It needs longterm corticosteroid/immunosuppressive/ biological therapy to prevent blindness. (Figure 6c)

b. Fibrinous non-mobile hypopyon in young male adults with acute onset pain and redness is highly suggestive of HLA-B27+ associated acute anterior uveitis. Ask for a history of morning stiffness that gets better on moving around. These patients need a referral to a Rheumatologist. Unrecognized/ untreated these patients will develop severe skeletal deformities. The inability of the patient to put his chin on the slit lamp's chin rest and increasing wall to occiput distance are pointers to ankylosing spondylitis. The asymmetric involvement of the proximal interphalangeal joints and /or keratoderma blennorrhagica indicate Reiter's disease (Figures 7 a-d)).

c. Fibrinous hypopyon with severe anterior



chamber/ vitreous cells may be caused by endogenous or exogenous bacterial or fungal infection. Ask for a history of trauma/ surgery or a visit to a healthcare facility for any interventions. Fundus media haze must be graded and photographed, if possible, to not only look for any retino-choroidal abscesses but also to look for a response to treatment. A high index of suspicion is needed to diagnose endophthalmitis as these patients require urgent surgical interventions for diagnostic and therapeutic purposes. Beware of focal fungal retinitis.

- 5. Beware of starting oral/periocular or intravitreal corticosteroids in patients with post-cataract surgery hypopyon (Figure 8a and b)
- 6. If you do not look for IOP, corneal sensations, or corneal edema/scars, you may miss Herpes uveitis.70-80% of the eyes may show granulomatous KPs. Herpes patients respond dramatically to oral antiviral therapy but show recurrences and require long-term prophylactic treatment.
- Focal iris atrophy is best examined on retro illumination. 50% of HSV and only 10% of VZV uveitis may show focal iris atrophy. Diffuse iris atrophy is less common (Figure 9)
- 8. Mutton fat KPs, Koeppe and Busacca nodules, and broad posterior synechiae aresigns of granulomatous inflammation. Rule out Sarcoidosis, tuberculosis, and VKH disease (Figure 10).
- 9. Even a single mutton fat KP must prompt a dilated fundus examination. Especially look at the inferior periphery for any nummular scars that indicate a VKH disease.
- 10. If the inflammation is localized primarily

in the vitreous cavity (intermediate uveitis), rule out TB, Sarcoidosis, or Syphilis before labeling it as idiopathic. Always look at the inferior periphery for pars plana exudates or peripheral vasculitis. The latter may indicate multiple sclerosis.

- 11. When you see a lesion in the fundus, always ask a question – Is it retinitis or choroiditis? With exceptions like Behcet's disease, retinitis is invariably infectious while choroiditis is immune-mediated (Yes, even TB choroidal granulomas are MTB-driven immune responses). (Figures 11)
- 12.The use of corticosteroids alone is disastrous for toxoplasma and viral retinitis.
- 13.In bilateral necrotizing retinitis always rule out HIV infection or an immunosuppressive setting (Figure 12).
- 14.A very rapidly progressive necrotizing retinitis in young persons, without many inflammatory signs, think of subacute sclerosing panencephalitis (SSPE), a fatal disease.
- 15. Choroidal granulomas caused by TB are fewer in number, larger, and may or may not have exudative retinal detachment. The presence of even a tiny intraretinal hemorrhage is highly suggestive of TB etiology (Figures 13,14). Sarcoidosis granulomas are usually smaller and multiple (Figure 15).
- 16.On OCT, choroidal granulomas remain limited to the choroid while TB granulomas tend to infiltrate the outer retina (Figure 16).
- 17.If you see unilateral or bilateral optic disc edema, must look for signs of



inflammation. It may be caused by Sarcoidosis or VKH disease.

- 18.Optic disc edema with new vessels and signs of inflammation is highly suggestive of Sarcoidosis
- 19. All lesions that look inflammatory may not be uveitis. Think of primary vitreoretinal lymphoma in old age (Figure 17).
- 20. Mistaking subretinal fibrin for choroiditis and treating it with corticosteroids can be disastrous. The clear-dot sign is highly suggestive of exudative CSCR. Do FFA when in doubt. FFA in these patients is diagnostic.
- 21.Most of the patients of TB serpiginouslike choroiditis will show paradoxical worsening on initiating anti-TB drugs and oral corticosteroids.
- 22.The most common mistake in treating autoimmune uveitis like VKH disease and JIA-associated uveitis is inadequate corticosteroid/ immuno

suppressive therapy.

- 23. Look at the hands of all scleritis patients. 33% of all scleritis are due to rheumatoid arthritis. Necrotizing scleritis may be seen in up to 50% of the granulomatosis with polyangiitis (GPA) a life-threatening ANCA-positive vasculitis.
- 24. Infectious scleritis, often unilateral, with a history of trauma or surgery may be caused by Ps aeruginosa, Nocardia, S aureus, or fungal. Infectious scleritis besides pain and chemosis shows purulent discharge. In TB-endemic countries think of TB as a possible etiology. Deep debridement and biopsy may be needed in infectious scleritis (Figure 18).
- 25.In autoimmune uveitis, never stop corticosteroids abruptly. Taper. Start at the highest dose and taper. Start immunosuppressive agents at low doses and increase gradually. Taper slowly.





Figure 1. While the presence of flare and cells is suggestive of inflammation, these patients require complete ocular examination including binocular indirect ophthalmoscopy.



Figure 2. Must differentiate between grey RBCs, inflammatory cells (a), and the large-sized malignant cells (b)



Figure 3. Patients with Fuchs 'uveitis often present with symptoms of unilateral cataract without a history of trauma.



Figure 4. Unlike other cases of uveitis, wherein KPs are distributed in Arlt's triangle, stellate, or glassy KPs are seen across the post-corneal surface.





Figure 5a, b. Look at the loss of Iris crypts in Fuchs uveitis (a) compared with the normal iris pattern (b).



Figure 6a, b. Acute lymphoblastic leukemia presenting as a mobile hypopyon in a 4-yearold child (a). Lymphoma in a 70-year-old man presenting as a mobile hypopyon (b).



Figure 6c. Mobile hypopyon in a patient with Behcet's disease.



Figure 7a. Fibrinous hypopyon in acute anterior uveitis (a). Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Red Eyes— Conjunctivitis, Corneal Ulcers, Dry Eye Disease, and Acute Uveitis. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi.org/10.1007/978-981-99-7923-3_17 with permission of the publishers.



Figure 7b,c: Sudden onset pain, redness, and dimness of vision in the left eye of a patient with a history of morning stiffness of the lower back, with cellular reaction in the anterior chamber as acute anterior uveitis (b). Formation of filiform posterior synechiae and anterior fibrinous deposit (c). Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Red Eyes— Conjunctivitis, Corneal Ulcers, Dry Eye Disease, and Acute Uveitis. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi.org/10.1007/978-981-99-7923-3_17 with permission of the publishers.



Figure 7d. Pigment on anterior lens surface in acute anterior uveitis (AAU) in quiescence stage (d). Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Red Eyes— Conjunctivitis, Corneal Ulcers, Dry Eye Disease, and Acute Uveitis. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi.org/10.1007/978-981-99-7923-3_17 with permission of the publishers.



Figure 8a, b. The patient presented with fibrinous hypopyon two weeks after small incision cataract surgery (a). She had received oral corticosteroids to control inflammation. Fundus showed fungal endophthalmitis (b).



USI Desits Society (India)

www.indianuveitis.org

Figure 9. Sectoral iris atrophy is seen in iris transillumination in the case of HSV anterior uveitis. Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Red Eyes— Conjunctivitis, Corneal Ulcers, Dry Eye Disease, and Acute Uveitis. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi.org/10.1007/978-981-99-7923-3_17 with permission of the publishers.



Figure 10. Busacca nodules (a and b) in two different patients with VKH disease. They always indicate an underlying granulomatous process.



Figure 11a-f: The retinal vessels over a retinitis lesion (a) are generally obscured while they run a normal course over a choroidal lesion (b). On FFA, the retinitis lesions show staining of the retinal vessel walls running through the lesion (c), while the choroidal lesion shows initial hypofluorescence (d). In the late frames of FFA, extensive hyperfluorescence of the retinal

lesion with indistinct borders (e) is seen, and the choroidal lesion shows hyperfluorescence not as intense as retinitis with dye pooling due to a localized exudative retinal detachment (f). Note that the example in (b, d, and f) represents a case of chorioretinitis. The intense staining in (f) is due to retinal inflammation. Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Retinal and Choroidal Infections and Inflammation. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi. org/10.1007/978-981-99-7923-3_10 with permission of the publishers.



Figure 12. Tongue-like areas (red arrows) of necrotic retinal opacification in the periphery of the right eye with vitreous haze, suggestive of acute retinal necrosis (ARN). Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Retinal and Choroidal Infections and Inflammation. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi. org/10.1007/978-981-99-7923-3_10 with permission of the publishers.



Figure 13a, b. A case of TB choroidal granuloma with intraretinal hemorrhage (a). Fluorescein angiography shows the classical retinal angiomatous proliferation feeding the granuloma. Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Retinal and Choroidal Infections and Inflammation. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi. org/10.1007/978-981-99-7923-3_10 with permission of the publishers.



Figure 14a, b. Tubercular retinal vasculitis (blue arrows) with periphlebitis, retinal hemorrhages, and perivascular cuffing (a). Fluorescein angiography shows extensive capillary non-perfusion (*) (b). Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Retinal and Choroidal Infections and Inflammation. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi. org/10.1007/978-981-99-7923-3_10 with permission of the publishers.



Figure 15. A 59-year-old male was a known case of skin sarcoidosis, had calcified mediastinal lymph nodes, and presented with bilateral choroidal granulomas (black arrows). On OCT, the sarcoid choroidal granulomas are uniformly hyporeflective (blue arrow) and

occupy the choroid's total or partial thickness. Increased light transmission is seen posterior to these hyporeflective spaces. Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Retinal and Choroidal Infections and Inflammation. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi. org/10.1007/978-981-99-7923-3_10 with permission of the publishers.



Figure 16. On OCT, Choroiditis lesions (granulomas) are associated with exudative subretinal fluid (blue arrow) with a bumpy elevation of the (yellow arrow) of the RPE-Bruch's complex. Note infiltration of the outer retina from the choroidal granuloma. Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Retinal and Choroidal Infections and Inflammation. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi. org/10.1007/978-981-99-7923-3_10 with permission of the publishers.



Figure 17. A 66-year-old man was symptomatic for 6 months and had received PST Kenalog injections in the left eye for presumed posterior uveitis without any response(a). He was suspected to have primary vitreoretinal lymphoma (PVRL) and was subjected to vitreous surgery. The subretinal fluid aspiration cytology showed CD 20+ positivity (b). He was diagnosed with B-cell lymphoma and received a course of intravitreal methotrexate. Nearly 6 months later, shows complete resolution of the lymphoma (c). He was monitored on an MRI brain for the development of CNS lymphoma. While 80% of PVRL will go on to develop Primary CNS lymphoma, 20% of Primary CNSL will develop PVRL.



Tubercular Figure 18. anterior nodular scleritis (a) in a patient with multiple discrete mediastinal lymph nodes and retroperitoneal lymphadenopathy on the CECT chest/abdomen (b). He underwent scleral biopsy (c) which revealed multiple epithelioid cell granulomas (c). ZN staining showed acid-fast bacilli (AFB), suggestive of Mycobacterium tuberculosis (red arrows, d). Anti-tubercular therapy (ATT) was initiated. Three months after starting ATT, scleritis was completely healed (e). Reproduced from Gupta, A., Bansal, R., Sharma, A., Kapil, A. (2023). Episcleritis, Scleritis, and Peripheral Corneal Ulceration. In: Ophthalmic Signs in Practice of Medicine. Springer, Singapore. https://doi.org/10.1007/978-981-99-7923-3_18 with permission of the publishers.





Prof Amod Gupta

He is a "Guru" and "teacher of teachers" for majority of the uvea specialists in our country. He is an encyclopedia of uveitis and I have always approached him before reading a book whenever I was lost and confused regarding my patient. His words of wisdom come from the vast experience and passion for the subject.

Prof. Gupta always said that never be bothered about the number of patients standing outside your clinic door and always give full time and attention to the patient you are seeing. These golden words are engraved in my mind and made me a better clinician.

He has taught us to focus and passionately follow your path irrespective of what the world says. This principle followed by him led to pioneering research and knowledge on ocular tuberculosis. We have no words to thank him enough for the same as it has helped us manage so many of our patients.

Despite retiring we still long to hear him, as we know that the knowledge we get may not be available in the best of the books.

Wishing him a happy healthy life with his family and my pranams to this great teacher.....

Hope his words of wisdom and blessings always remain with us.

Regards **Manisha Agarwal** Director of Vitreo Retina,Uvea and Clinical Research Dr Shroff's Charity Eye Hospital, New Delhi. Hon General Secretary-VRSI





Left Eye : Anterior segment shows stellate keratic precipitates(blue arrow), iris heterochromia (blue star) and fundus examination revealed Vitritis with vitreous membranes(white arrow)

Don't miss the anterior segment findings

Dr. Nitin Kumar Menia

Assoc. Professor, AIIMS, Jammu.

A 20-year-old male presented to us for a second opinion. He was diagnosed elsewhere as left eye intermediate uveitis and was on oral corticosteroids. Anterior segment examination at our center revealed stellate keratic precipitates, iris heterochromia and early posterior subcapsular cataract. Fundus examination revealed vitreous cells and membranes. A diagnosis of Fuch's heterochromic uveitis was considered and oral steroids were stopped.



Dr. Rajwinder Kaur Professor and Head Adesh Institute of Medical sciences and Research Bathinda, Punjab



My Journey in Uveitis FROM STEROIDS TO BIOLOGICS

Prof. Dr. Jyotirmay Biswas

President US(I) 2003-2006



Prof. Dr. Jyotirmay Biswas, MS. FMRF, FNAMS, FIC Path., FAICO, MNAsc, FRCS (Ed), FACS Director of Uveitis & Ocular Pathology Department, Sankara Nethralaya *E-mail: drjb@snmail.org*

Let me start this article with a story from 1989. Fresh from my fellowship at the Doheny Eye Institute, University of Southern California, under the mentorship of Prof. Narsing A Rao, I returned to India. It was then that a 12-year-old boy from Patna, fascinated by the Mahabharata serial airing on TV, accidentally injured his left eye while playing with a bow and arrow alongside his brother.

The injury left his left eye sightless and phthisical. Tragically, a month later, his good right eye also lost vision abruptly. Diagnosed with sympathetic ophthalmia by a local ophthalmologist, he was prescribed oral prednisolone, but his vision remained limited to counting fingers at a mere meter's distance. Seeking further treatment, the patient arrived in Chennai at Sankara Nethralaya.

I initiated treatment for him at Sankara Nethralaya with an immunosuppressive regimen combining Azathioprine and Prednisolone. Remarkably, the patient's vision in his right eye improved to 6/6, N6. Though initially under follow-up, he eventually lost touch with us. Twenty-five years later, a heartwarming email arrived from him, revealing he was pursuing a postdoctoral fellowship in Finland. This success marked a deeply gratifying milestone, being the first patient where I employed immunosuppressive agents.

Since first experience with my immunosuppressive agents, I have come a long way. I joined Sankara Nethralaya as a uveitis consultant in 1985, around the time when Dr. Rajinikantha had recently established the Uvea Department. Following Dr. Rajinikantha's departure from Sankara Nethralaya in 1989, I assumed leadership of the Uvea Department. During that period, our treatment protocols included the use of Betamethasone eye drops and administering subconjunctival injections of Hydrocortisone.

I transitioned to prednisolone acetate eye drops for their superior bioavailability and adopted the technique of posterior subtenon injection of triamcinolone, which I learned during my fellowship. During those years, systemic steroids were administered in divided doses. I implemented a regimen of a single morning dose after breakfast, starting at 1 mg/kg of body weight, gradually tapering the dosage, and achieved favorable outcomes. Back then, we lacked experience intravenous methylprednisolone. with After consulting with our physician and anesthesiologist, I began using intravenous



methylprednisolone under their supervision.

I began achieving excellent results treating Vogt-Koyanagi-Harada disease and sympathetic ophthalmia. Introducing azathioprine for the first time at our institute, I initiated a regimen starting with a dosage of 2.5 mg/kg of body weight, administering a 50 mg tablet of azathioprine thrice a day. Initially, I monitored total white blood cell (WBC) counts, platelet counts, and liver function tests every two weeks due to my initial concerns, later adjusting to once every four weeks.

In addition to azathioprine, I utilized cyclosporine for Behçet's disease and refractory non-infectious uveitis cases. For challenging instances of sympathetic ophthalmia Vogt-Koyanagiand Harada disease, we implemented tripleagent immunosuppression combining Prednisolone. Azathioprine, and Cyclosporine, resulting in significant vision recovery for all treated cases.^{1, 2}

During one of my visits to an international uveitis study group meeting in Yokohama, Japan, I discovered that some members were using a new drug called Mycophenolate Mofetil. Back then, Mycophenolate Mofetil was primarily used by nephrologists in India. I initially prescribed it at 500 milligrams twice a day but soon realized this dosage was insufficient. I adjusted the regimen to one gram twice a day.

In India, we reported for the first time the use of Mycophenolate Mofetil in eight patients with recalcitrant uveitis, treated alongside oral Prednisolone. Initially, we observed no side effects from its use.³ However, several years later, a 34-year-old male patient treated with Mycophenolate Mofetil for recurrent bilateral posterior uveitis due to sarcoidosis developed extensive herpes zoster in the right upper thoracic region, occurring 10 months after starting the treatment.⁴ Т began utilizing optical coherence tomography to monitor Vogt-Koyanagi-Harada patients treated with steroids and immunosuppressive agents. For cases of non-infectious intermediate uveitis, rather than following Kaplan's four-step approach, I initiated treatment with Mycophenolate Mofetil and Prednisolone from the outset. Our publication on the efficacy of Mycophenolate Mofetil in intermediate uveitis demonstrated favorable outcomes. I observed that early introduction of immunosuppressive agents aided in the long-term control of intermediate uveitis.⁵

Initially, I was treating patients with serpiginous choroiditis with immuno suppressive agents and corticosteroids, and I was getting good results, but the patients experienced recurrence of inflammation a few months later. Therefore, I switched to anti-tubercular treatment with corticosteroids after reports from the uveitis group from the PGIMER Chandigarh.

The intravitreal dexamethasone implant became available in 2012. We participated in its trial and subsequently began using it for non-infectious intermediate uveitis patients who had either cystoid macular edema or vitritis unresponsive to standard treatments. Our experience with the intravitreal dexamethasone implant (Ozurdex) has demonstrated excellent outcomes.

We also successfully treated an HIVpositive patient on antiretroviral therapy for posterior uveitis due to ocular syphilis using two intravitreal dexamethasone implants. The patient presented with cystoid macular edema, which resolved without infection reactivation during long-term follow-up.⁷ However, we encountered a case of a 64-year-old male diabetic patient who developed toxoplasma retinitis two months after receiving an intravitreal triamcinolone acetonide injection.⁸ Recently, in 2023, we published the 3-year results of a randomized



trial conducted in India. This study aimed to assess the long-term efficacy and safety of an intravitreal fluocinolone acetonide implant delivering 0.2 micrograms per day in 155 patients with non-infectious posterior uveitis lasting more than 2 years, conducted across 15 centers in India. The results with fluocinolone acetonide implant were remarkable: 101 eyes treated showed a reduced recurrence rate of uveitis, longer median time to recurrence, and fewer eyes with residual macular edema (24.21). However, as expected, there was a higher incidence of cataract requiring surgery (70.5%) and intraocular pressure elevation (22.8%) compared to sham-treated eyes.9 Additionally, we conducted a prospective study involving 43 patients who underwent a detailed interview for quality-of-life assessment using the National Eye Institute (NEI) Visual Function Questionnaire. It revealed significant improvements in psychological well-being and general health mean scores following immunosuppressive therapy.¹⁰

When biologic agents became available, we started using mainly Infliximab and Adalimumab, with a few cases treated using Golimumab and Tocilizumab. In 2020, we published an analysis of 18 patients with refractory uveitis and scleritis that did not respond to steroids and conventional immunosuppressive agents but showed positive response to biologic agents.¹¹ I found biologic agents particularly effective in treating Behcet's disease.¹² Patients with juvenile idiopathic arthritis-associated uveitis (JIA) also achieved good uveitis control with subcutaneous injections of adalimumab every 15 days. However, the drug was considerably more expensive at that time. Recently, the cost has decreased with the introduction of biosimilars.

For infectious uveitis, I implemented a new regimen. In cases of Toxoplasma retinochoroiditis, the standard treatment protocol for lesions involved pyrimethamine and sulfadiazine. I introduced clindamycin 300 mg four times daily for six weeks, which yielded positive outcomes. Starting from 1995, we began treating AIDS patients presenting with cytomegalovirus retinitis. Due to the high cost of intravenous therapy, administered ganciclovir Т intravitreal ganciclovir alone. Since 1990, cases of acute retinal necrosis have been observed. I initiated polymerase chain reaction testing of anterior chamber aspirates and administered intravenous acyclovir, with patients typically admitted for seven days.¹³

My journey in uveitis began modestly with steroids approximately 34 years ago. Currently, immunosuppressive agents. biologics, and Janus Kinase Inhibitors are more frequently utilized. We first reported on the Janus Kinase Inhibitor Tofacitinib in two cases of refractory scleritis.14 Throughout my career in uveitis, I diligently maintained a register of all cases and analyzed responses to steroids, immunosuppressives, and biologics across various diseases. We encountered adverse reactions to biological agents as well; for instance, one patient with juvenile idiopathic arthritis-associated uveitis developed choroidal tubercles, and another developed tuberculous ascites following Adalimumab therapy.¹⁵

My journey in uveitis spans 35 years of continuous learning and the adoption of new treatment regimens in India. I have gleaned invaluable insights from patients and esteemed mentors, particularly Prof. Narsing Rao, Prof. Amod Gupta, and colleagues from the International Uveitis Study Group.



References:

- 1. Agarwal M, Ganesh SK, Biswas J. Triple agent immunosuppressive therapy in Vogt-Koyanagi-Harada syndrome. Ocul Immunol Inflamm. 2006;14(6):333–9.
- Ganesh SK, Narayana KM, Biswas J. Peripapillary choroidal atrophy in sympathetic ophthalmia and management with triple-agent immunosuppression. Ocul Immunol Inflamm. 2003;11(1):61–5.
- 3. Rathore VM, Agrawal R, Chaudhary S, Biswas J. Mycophenolate mofetil therapy in uveitis: analysis of eight cases in a tertiary ophthalmic care centre in India. Int Ophthalmol. 2009;29:117–22.
- 4. Hegde S, Annamalai R, Biswas J. Extensive herpes zoster involvement following mycophenolate mofetil therapy for sarcoidosis. J Ophthalmic Inflamm Infect. 2012;2:47–8.
- 5. Ali S, Kharel Sitaula R, Biswas J. Efficacy and safety of mycophenolate mofetil in the treatment of recalcitrant intermediate uveitis. Ocul Immunol Inflamm. 2019;27(5):851–7.
- Palla S, Biswas J, Nagesha CK. Efficacy of Ozurdex implant in treatment of noninfectious intermediate uveitis. Indian J Ophthalmol. 2015;63(10):767–70.
- Majumder PD, Mayilvakanam L, Palker AH, Sridharan S, Biswas J. Intravitreal sustainedrelease dexamethasone implant for the treatment of persistent cystoid macular edema in ocular syphilis. Indian J Ophthalmol. 2019;67(9):1487– 90.
- 8. Ahmed A, Sudharshan S, Gopal S, Majumder PD, Biswas J. Toxoplasma retinitis following intravitreal injection of triamcinolone acetonide: A case report and review of literature. Indian J

Ophthalmol. 2018;66(8):1205-8.

- Biswas J, Tyagi M, Agarwal M. The 0.2-µg/day Fluocinolone Acetonide Intravitreal Implant in Chronic Noninfectious Posterior Uveitis: A 3-year Randomized Trial in India. Ophthalmol Sci. 2024;4(1):100403.
- 10. Kaleemunnisha S, Sudharshan S, Biswas J. Quality of life in non-infectious uveitis patients on immunosuppressive therapy. Middle East Afr J Ophthalmol. 2014;21(3):225–31.
- Sadhu S, Majumder PD, Biswas J. Biological therapy in refractory cases of uveitis and scleritis: an analysis of 18 cases from a tertiary eye care center from South India. Indian J Ophthalmol. 2020;68(9):1929–33.
- 12. Ramdoss J, Singh P, Ahmed AS, Biswas J. Clinical profile and management with immunosuppressants and biologics in Behcet's uveitis: A cohort of 25 patients from a tertiary eye care center in South India. Indian J Ophthalmol. 2023;71(5):1972–6.
- Mohan S, Dhanurekha L, Janani M, Biswas J. Correlation of quantitative polymerase chain reaction with clinical characteristics of patients with viral retinitis. Indian J Ophthalmol. 2022;70(6):2090–3.
- 14. Pyare R, Kaushik V, Majumder PD, Biswas J. Tofacitinib in recalcitrant scleritis: First case report from India. Indian J Ophthalmol. 2020;68(9):1988–90.
- 15. Vaidya H, Majumder PD, Biswas J. Presumed tubercular choroidal nodule following adalimumab therapy for juvenile idiopathic arthritis. Indian J Ophthalmol. 2019;67(3):399– 400.





Figure 1: Photograph of Dr Jyotirmay Biswas examining a patient in 1985 (A) and 2024 (B) at Sankara Nethralaya



Figure 2: A 12- year old boy from Patna, Bihar accidentally lost his vision in his left eye following bow and arrow injury.

Right eye slit lamp photo showing multiple keratic precipitates, fundus photo showing disc edema with serous retinal detachment. (Permission taken for the photographs)



Figure 3: After treatment with azathioprine and steroid got back 6/6 vision in the sympathizing right eye



...Today

Figure 4: After 20 years he informed that he is doing post-doctoral fellowship in Finland. (Permission taken for the photographs)



Figure 5: A 16-year old girl from West Bengal presenting a frame with a sketch of me drawn by her. She recovered full vision after treatment for her uveitis. (Permission taken for the photographs)



Figure 6: The same sketch drawn and framed by her was given to me



é «.							gr: 5323
21/01/2 21/01/2 21/01/2	1 Avril Vashutha 1 Mario Rama Büsch Sullah S	4790205 479020	Tox'o. Interectale work	12/02/21	VIMAL RANKA	47949.61	Pnkylonng spordylitis weitj
22/01/21	Aakrla Praveen J Himarish Dinish Ahup	2555846	Chorotatra. Intumediale wetti	RELOTI	Deva kumaizv	4794967-	T gbuloma.
83/1121 29/1121 29/1121 29/1121	Shefdet Janaki B Rahul Kumar agarwal	4790469 4790469 4791214 3967169	Anterior uncita	2312524. 25/2/21 25/2/21	Sudali NavPriet Kaur Shibdar Dana.	4795217 4795217 4715274	TB TU TU chesoiditu.
20/1/21 -30/1/21	Mittua s Logunaria	4789914	Corneal Scar Choroidad ganulon	01/3/21	Glanush Ramani Samuvel E	4795510	Panuvcitu. Toxo Plasmosu
4/2/21 4/2/21 4/2/21	Shamina Aktu Pradup G Mastu Shawwa Tara	4792094	Multifocal choicelin Internediale unicity Toxocare	01/3/21 01/3/21 02/3/21	Sub Prable Kondar Agnes Brintha	4795871 4794362 4796058	Seepigmous TOXO Intermedicate United
5/2/21 8/2/21 8/2/21	Gopal VG Mu. Subbia Gosh Rabbi chabiatorny	4792229 4792563 4558158	Antiner weiri.	05/3/21 05/3/21 05/3/21	Nity Kumasi Partuk Siddharth Jain Divyani Patodia	4796334	Anturn uverta Nonti quanta
8/2/21 8/2/21 11/2/21	Kusum Kumai ^o Malaskodi Sharni Naupma TOPPO	4792574 4792683 4792891	TB Lucitie. DU: Anturer works	08 22121 05 2121 09 12 121	Shahnaz Regum Dyvisay Visma Vikram Dhambolinia	4796908	Antures uvertu Non-granuformites Antuiet uveita
12/2/21	Rommi Plavalika Rahul Rajni Sont	4792918 4793331 4793390	Intermediate with Selfiginous chorch	11/3/21 11/3/21 12/3/21	Mr. S. K. Hishra Dolan Shaema Giamay Singh	4797458	Anturoj Liveris ERUS Contecto Superinous
18/2/21 18/2/21 19/2/21	Snighte Sabat Glokul	4794156 4794314	Intermediate uverte Intermediate uverte	18/3/21 16/3/21 19/3/21	HBU Basal MPBaumi Swind Ray D Manish Kumal	479850	T Sallord uverte Anterior uverte Internetiation
20/21 01 20/2/21 22/2/21	Divya Strigh Jornob Nega Jotni B	4794342 4794516 4794620	Petthal valida	23/3/21	Raja kanan K Sanjay Kumat Amaint Sanyayi Kumat	47935	6 Anterior Uverri. I IV VKH.
23/2121	SUGANDHA SINGH	4394392	Retinidis.	16/3 hi	Mir Wahand Klam	4759703	Pundate inner Chandate inner

Figure 7: Photographs of the uveitis registers meticulously maintained, sharing on the Editor's request.



Always examine the retinal periphery in patients with anterior uveitis

Dr. Nitin Kumar Menia

Assoc. Professor, AIIMS, Jammu

My teachers at PGIMER, Chandigarh and Sankara Netralaya Chennai, always emphasized the importance of posterior segment examination in patients with anterior uveitis. A patient with viral retinitis may present with spill-over anterior uveitis. Peripheral viral retinitis patches may be missed if posterior segment examination is omitted. So, "Always examine the retinal periphery in patients with anterior uveitis."



Picture Courtesy: Dr. Manohar Babu B

Heartfelt

and Handmade

Diamond in the Dark

Dr. Divya Ganesan Medical Officer Aravind Eye Hospital, Salem

Diamond like deposits on Posterior Chamber Intraocular lens in a case of Propionibacterium acnes Endophthalmitis.

When will we start diagnosing LEPTOSPIROSIS

Prof. Dr. S. R. Rathinam

President US(I) 2007-2009



Prof. Dr. S R Rathinam, FAMS, PhD Principal, Prof. of Ophthalmology and Head of Uveitis service, Aravind Eye Hospital & PG. Institute of Ophthalmology, Madurai *rathinam@aravind.org* **Dr. E. Rajashree**, MS Uveitis Fellow, Aravind Eye Hospital, Madurai

eptospirosis, also known as the 'ratfever' is a serious multisystem waterborne zoonotic disease which could be life-threatening if not promptly diagnosed or treated. It is estimated to cause 58,900 deaths annually worldwide [1] The major cause of death being pulmonary haemorrhagic fever (Weil's disease) or renal failure. The alarming factor about this disease is the underestimation of numbers and its non-inclusion in the 'notified disease' in many countries. When a patient presents to the hospital with an acute febrile illness, the suspicion of Leptospirosis arises only when all other causes of fever have been ruled out. This diagnostic delay is mainly due to the lack of specific clinical signs pointing towards definite leptospirosis. But an ophthalmologist has the advantage of identifying ocular leptospirosis with the help of certain confirmed clinical signs as diagnostic indicators which we would be discussing in this article.

The Initial Struggle

Until 1993, ocular manifestations of Leptospirosis remained to be an undiscovered entity about which ophthalmologists did not have any slightest clue. It was during this time, when Madurai experienced an unusually high rainfall and flooding following which there was an outbreak of fever. But this febrile illness was treated by the physicians like any other seasonal flu. A few months later, a large proportion of people starting walking into our department with uveitis which included non-granulomatous panuveitis with hypopyon, retinal vasculitis, membranous vitreous opacities and disc hyperemia. Detailed history from these patients revealed that all of them belonged to the flooded low lying areas of Madurai. After ruling out all other possible causes of fever through various laboratory investigations, the puzzle remained unsolved and the etiology remained to be Idiopathic.

A total of about 300 patients had come to our department with the same complaints and similar findings over 4 months. With limited resources and without internet search engines at that period, accessing information relevant and literature was a great challenge. After a detailed discussion with a lot of clinicians. scientists. corporation government officials and hospital microbiologists, physicians in and around Madurai, we were quided to approach Prof. Ratnam at Chennai, a humble veterinary surgeon who had done his PhD on leptospirosis in animals. The



courier service or land line phone connection was not even in concept level in those days! It was sheer determination and curiosity which motivated the author to carry the serum samples of these patients to Chennai all alone to hand it over to Prof. Ratnam for microbiological examination. Following a brief discussion about the possible etiology of leptospirosis, there was finally light at the end of the dark tunnel when the bright spirochetes shining under the dark field microscope were killed by antibodies of the patients. It was indeed leptospirosis! The results were confirmed with high possible titres in samples by Micro agglutination test (MAT) which was the gold standard test at that point of time.

The results obtained from the regional laboratory at chennai were confirmed by cross reference with other World reference laboratory like Center for Disease Control (CDC) in Atlanta, USA, Royal Tropical Institute, the Netherlands and Monash University at Australia. We characterized the clinical manifestations of leptospiral uveitis, and ultimately came up with our first International Publication in the American Journal of Ophthalmology and received one of the highest citations among all our publications.^[2]

The large disease population and the lack of reference laboratory motivated us to the establishment of a regional leptospirosis laboratory at Aravind Medical research Foundation, Madurai in 1999 with the help of Welcome funds and National Leptospirosis Reference Center, Royal Tropical Institute, Amsterdam, Netherlands. We also strived hard to find the veterinary seroprevalence by isolating leptospires from large and small animals like field rats and bandicoots, which were collected from nearby villages with the help of veterinary surgeons from Netherlands. Urine and Kidney samples of these animals were cultured, thus proving that field rats were a major infectious source of leptospirosis in and around Madurai [3][4

Mode of spread:

Other mammalian reservoirs for this disease-causing spirochete include cows, horses, pigs and goats. The leptospires present in the infected urine of these animals can enter humans through intact mucous membrane or abraded skin. These spirochetes can also survive in stagnant water. Thus, paddy field workers, veteneraians, water sports adventurers (fresh water swimming, kayaking) are more prone for acquiring leptospirosis.

This disease has a wide geographical distribution, especially the low-lying, densely inhabited coastal areas where frequent flooding or waterlogging occurs during the monsoon season. In India, Andhra Pradesh (64.7%), Kerala (60.6%), Orissa (52.3%), Tamil Nadu (45%), and Andaman and Nicobar (42.15%) have the highest prevalence of leptospirosis ^[5].

Pathogenesis:

Leptospirosis has a biphasic illness with an early leptospiremic phase and a later immune phase which occurs 3-6 months later.

- * The **early/anicteric phase** could be asymptomatic or associated with symptoms like:
- » Fever
- » Arthralgia
- » Myalgia
- » Muscle tenderness
- » Vomiting
- » Abdominal pain
- » Cough
- * The icteric phase is known as the 'Weil's disease' and affects about 10% of the patients and involves
- » Hepato-renal failure
- » Multiorgan haemorrhage
- » Meningitis or meningoencephalitis
- » Pulmonary haemorrhage with respiratory failure



- Leptospirosis uveitis is a late immune reaction and takes months to manifest in the eye. This time delay is also another important reason for underestimation of ocular leptospirosis. But veterinary science has extensive literature on this topic especially in horses. Molecular mimicry between leptospiral proteins and horse ocular antigens has been suggested as a possible cause ^[6]. Leptospiral Sph2 has been found to be an important virulence factor triggering the inflammatory cascade and causing endothelial cell damage. Further activation of coagulation factor -III leads to delayed coagulation time causing multiorgan failure [7].
- We found specific antibodies directed against leptospiral lipoprotein LruA and LruB in >65% of sera from MATpositive and MAT-negative patients with leptospiral uveitis. The sequences of genes encoding LruA and LruB are known to be highly conserved among the pathogenic serovars of *L. interrogans* ^{[8].}

Ocular presentation:

One of the largest retrospective population studies on ocular leptospirosis was done at our institute using of the data of over 27 years with 1268 seropositive leptospirosis patients ^[9]. These patients had a systemic past history of fever, headache, joint pain, severe fatigue, diarrhoea, and jaundice.

- Farmers/ sewage workers/ veterinary workers/ anyone exposed to contaminated water
- Acute non granulomatous uveitis
- Hypopyon
- Vitreous membranes
- Absence of chorioretinitis
- Retinal Vasculitis
- Disc hyperemia
- Rapidly maturing cortical cataract



Figure 1: Hypopyon and pearly white cataract in leptospiral uveitis in a young female patient.



Figure 2: Retinal vasculitis in a leptospiral uveitis patient.



Figure 3: Vitreous inflammatory reaction with freely floating veil like vitreous membranes and a string of pearls appearance below and hazy view of hyperaemic disc in the background.

Uveitic cataracts are mostly posterior subcapsular in nature but the interesting reason behind the rapidly maturing



cortical cataract in leptospirosis was the cross reaction between the leptospiral antibodies in the patient's serum and the multiple lens proteins which are involved in maintaining the transparency of the lens. Retinal dehydrogenase 1 and crystallins (α -B, α -A2, β -B2), were recognized in the serum of leptospiral uveitis patients. It is homologous to the leptospiral protein, betaine aldehyde dehydrogenase. This cross reaction was found to be the reason cataractogenesis. Histopathological for examination of the extracted lens material also showed globular degeneration in contrast to parallel fiber arrangement of senile cataract controls.^[10] Spontaneous absorption of cataract was also found in a few patients.^[11]

Laboratory investigations

- Microscopic agglutination testing (MAT): It is a highly specific gold standard test for sero-diagnosis of leptospirosis. This test involves detecting antibodies in the patient's serum using a darkfield microscope after incubating them with positive serovars containing live leptospires. The highest dilution of serum that yields 50% agglutination is reported as the final titre.Inspite of good specificity this test lacks sensitivity because of the globally changing serovars. This test also requires live leptospirs to be maintained, hence only certain highly equipped laboratories can maintain the panel.
- ELISA: This test detects the IgM antibodies which are found in the patient's serum immediately after the onset of symptoms and lasts up to 5 months. They also have the advantage of being conducted as rapid tests as it is commercially available as rapid test kits.
- Polymerase Chain Reaction: PCR testing is helpful in the early/acute phase of illness and are commercially available

Over the years leptospirosis has slowly shifted from an epidemic outbreak to becoming an endemic disease with newer serovars coming into action. The positivity rate has dropped from 92% (in 1992) to as low as 35% ^[12]. In our studies *L. Autumnalis, L. Icterohaemorrhagiae*, and *L. Australis* were the predominantly found serovars ^[13]. The emergence of new serovars has declined the sensitivity of tests like MAT and ELISA. Updating the panel with commonly found isolates of the locality would enhance the sensitivity rates.

Recent Advances

- Early-stage detection of Lip32, an outermembrane protein present only on pathogenic leptospira species by lateral-flow immunoassay has been found to be superior to real-time polymerase chain reaction technique ^[14].
- Metagenomic next generation sequencing is also gaining importance in detecting various challenging infections which are usually missed by the standard culture or PCR techniques. In the diagnosis of leptospirosis also, this culture independent method helps in detecting the pathogen by core genome analysis by using urine or blood samples

Treatment

Topical, periocular and/or or al Corticos teroids remain the mainstay treatment of ocular leptospiros is. A course of doxycycline also helps to reduce the infective load in the early phase of the disease.

Challenges in Diagnosis

 The National Reference Laboratory for leptospirosis is placed in Andaman Islands thus making the shipping of patient's serum a great challenge. It is high time that the concerned authorities understand the endemicity and fatality of this disease and plan to build a reference laboratory in the mainland of India.
- Ophthalmologists must know about the global burden of the disease, its prevalence, demographic risk factors, relevant history clinical signs and recent advances in laboratory investigations to confirm on the diagnosis. We had also published a (Knowledge, Attitude and Practice) study about the lacunae of knowledge on this topic among ophthalmologists, undergraduates and postgraduates ^{[16][17]}.
- Public awareness campaigns are a must to inform people about the severity and prevalence of the disease and to educate them about the safety measures that could be followed to avoid acquiring this disease.
- The contaminated water source should be identified and regular environmental surveillance must be deployed.
- One -Health' type of holistic approach encompassing human, animal and environmental health needs to be practiced effectively controlling this infection.

Uveitis clinic, Aravind eye hospital, Madurai.

It started in 1992 with a single medical officer, SR Rathinam, now it has four medical officers and several fellows from India, Nepal and short-term fellows from several countries. It has treated over 1,00,000 new uveitis patients so far. The uveitis clinic celebrated its 25th anniversary in 2017. Author got her PhD for her work in leptospirosis in 2005 and FAMS in 2011. She has 151 publications to her credit including Book chapters. Total citations of these publications received are 4121, h-index-37, i10-index- 67. Maximum citation received by the land mark paper on epidemiology is 462. (As on 2/8/2024) She has contributed

chapters for books published in India, United Kingdom, Germany, Korea and the United States of America, Co Editor for Wills eye manual uvea atlas, USA and authored a manual on Ocular Pharmacology.

References

- Costa F, Hagan JE, Calcagno J, et al. Global Morbidity and Mortality of Leptospirosis: A Systematic Review. PLoS Negl Trop Dis 2015;9:e0003898
- Rathinam SR, Rathnam S, Selvaraj S, Dean D, NozikRA, Namperumalsamy P. Uveitis associated with an epidemic outbreak of leptospirosis. Am J Ophthalmol. 1997 Jul;124(1):71-9. doi: 10.1016/ s0002-9394(14)71646-0. PMID: 9222235.
- 3. Batmanabane V, Chidambaranathan GP, Rathinam S. Spectrum of Leptospira species identified in patients with leptospiral uveitis in an ophthalmological institute in South India. Indian J Med Microbiol. 2011 Oct-Dec;29(4):444-5. doi: 10.4103/0255-0857.90198. PMID: 22120817.
- Priya CG, Hoogendijk KT, Berg M, Rathinam SR, Ahmed A, Muthukkaruppan VR, Hartskeerl RA. Field rats form a major infection source of leptospirosis in and around Madurai, India. J Postgrad Med. 2007 Oct-Dec;53(4):236-40. doi: 10.4103/0022-3859.37511. PMID: 18097111.
- Choudhary S, Choudhary RK, Kumar M, Singh S, Malik YS. Epidemiological status of Leptospirosis in India. J Pure Appl Microbiol. 2023;17(4):1968-1977. doi: 10.22207/JPAM.17.4.44
- Che R, Ding S, Zhang Q, Yang W, Yan J, Lin X. Haemolysin Sph2 of Leptospira interrogans induces cell apoptosis via intracellular reactive oxygen species elevation and mitochondrial membrane injury. Cell Microbiol. 2019 Jan;21(1):e12959. doi: 10.1111/cmi.12959. Epub 2018 Oct 19. PMID: 30278102.
- Wollanke B, Gerhards H, Ackermann K. Infectious Uveitis in Horses and New Insights in Its Leptospiral Biofilm-Related Pathogenesis. Microorganisms. 2022 Feb 7;10(2):387. doi: 10.3390/microorganisms10020387. PMID: 35208842; PMCID: PMC8875353.



- Verma A, Kumar P, Babb K, Timoney JF, Stevenson B. Cross-reactivity of antibodies against leptospiral recurrent uveitis-associated proteins A and B (LruA and LruB) with eye proteins. PLoS Negl Trop Dis. 2010 Aug 3;4(8):e778. doi: 10.1371/journal.pntd.0000778. PMID: 20689825; PMCID: PMC2914785.
- Rathinam, SR; Kohila, Jeya G.1; Sundar, Balagiri K2; Gowri, Chidambaranathan P2; Vedhanayagi, Rajesh2; Radhika, Manoj2; Nadella, Venu3. Utility of demographic and clinical signs as diagnostic predictors for leptospiral uveitis: A retrospective study. Indian Journal of Ophthalmology 72(6):p 869-877, June 2024. | DOI: 10.4103/IJO. IJO_1376_23
- Rathinam SR, Rathakrishnan S. Rapid maturation of unilateral cataract in leptospirosis. Indian J Ophthalmol. 2020 Sep;68(9):1977-1979. doi: 10.4103/ijo.IJO_535_20. PMID: 32823447; PMCID: PMC7690476.
- 11. Rathinam SR, Namperumalsamy P, Cunningham ET. Spontaneous cataract absorption in patients with leptospiral uveitis. Br J Ophthalmol 2000;84:1135–1141.
- 12. Rathinam SR, Vedhanayagi R, Radhika M, Balamurugan MS, Balagiri K, Priya CG, Kohila GJ. Why do Doctors Miss the Diagnosis of Leptospiral Uveitis? Emergence of New Serovars and Challenges in Diagnosis. Ocul Immunol Inflamm. 2023 Dec 21:1-6. doi: 10.1080/09273948.2023.2291477. Epub ahead of print. PMID: 38127787

- Rathinam SR, Kohila GJ, Gowri PC, Balagiri KS. Leptospiral uveitis- "Transition 'from epidemic to endemic form" difficulties in laboratory confirmations. Indian J Ophthalmol. 2023 Aug;71(8):3031-3038. doi: 10.4103/ IJO.IJO_61_23. PMID: 37530277; PMCID: PMC10538821.
- 14. Deenin W, Yakoh A, Kreangkaiwal C, et al. Integrated Lateral Flow Electrochemical Strip for Leptospirosis Diagnosis. Anal Chem 2022;94:2554–2560.
- Agampodi SB, Vinetz JM. Next-Generation Sequencing Analysis of Pathogenic Leptospira: A Way Forward for Understanding Infectious Disease Dynamics in Low/Middle-Income, Disease-Endemic Settings. Am J Trop Med Hyg. 2021 Mar 22;104(5):1625-1627. doi: 10.4269/ ajtmh.20-1518. PMID: 33755589; PMCID: PMC8103479.
- Sivakumar RR. Ocular leptospirosis: lack of awareness among ophthalmologists and challenges in diagnosis. Curr Opin Ophthalmol. 2022 Nov 1;33(6):532-542. doi: 10.1097/ ICU.00000000000896. Epub 2022 Sep 8. PMID: 36206109.
- 17. Rathinam S, Thundikandy R, Balagiri K. Knowledge, Attitude, and Practice Towards Leptospirosis among Undergraduate and Postgraduate Medical Students in India. Ocul Immunol Inflamm. 2021 Jul 4;29(5):951-956. doi: 10.1080/09273948.2019.1705988. Epub 2020 Feb 14. PMID: 32058828.





Dr. Leenu Jeris Medical Consultant Aravind Eye Hospital, Madurai

Look at the patient when the patient enters the consultation room. Listen, touch the patient, examine meticulously. Don't get obsessed with previous diagnosis. treat the patient as a whole". I am indebted to my mentor, teacher, stalwart, Dr. S.R. Rathinam Madam, for teaching me the nuances of uveitis. I hope to imbibe her valuable teachings and become good uvea practitioner.

Heartfelt A. Humble Reverence For My Teacher and Handmade Dr. Anuradha V.K HEAD OF UVER SERVICES ARAVIND EYE HOSPITAL , COIMBATORE Beyond the eye, humanity's call, Health and heart, you've taught it all. To collaborate buyond name and fame To play the risks - and - benefits game. The xpirit, the value of trust's embrace your windom helps me find my place. With humility and grace so pure, so true Ma'am, I'm Jorever grateful to you With a heart full of gratite de Dr. Vandance Pradeep

Dr. Vandana Pradeep Uvea Consultant, Ophthalmic Surgeon SUT Academy of Medical Sciences, Trivandrum

Epidemiology of Uveitis in India: CHANGING TRENDS

Dr. Virender S. Sangwan

President US(I) 2010-2013



Dr. Tanya Jain, MS Consultant Vitreoretina and Uvea services Dr. Shroff's Charity Eye Hospital, New Delhi

Dr. Virender Singh Sangwan, MS Director Innovations Translational research Consultant Cornea and Anterior Segment Dr. Shroff's Charity Eye Hospital New Delhi drsangwan.lvpei@gmail.com

Introduction

Uveitis is a significant cause of ocular morbidity worldwide. It may lead to irreversible visual loss if not treated adequately and timely. Around 5%–20% of cases of legal blindness in developed countries and 25% of blindness in the developing world are due to uveitis.¹ The incidence in India has been reported to be as high as 1 in every 140 people.²

The epidemiology of uveitis varies worldwide and can be influenced by a host of factors like environmental, socio-economic, autoimmune, geographical and ethnic factors, among others.³ The final visual outcome of the disease is also influenced by the access to medical care, which varies across populations.⁴ Delays in diagnosis, untreated diseases, and longer durations of diseases account for poor visual outcomes.

The pattern of uveitis can be vivid and vary from country to country and region to region. Various reports are available from the different areas of India regarding the epidemiology of uveitis.^{4,5} Several demographic and ethnic factors also influence the changing pattern of uveitis. Moreover, the latest advancement in diagnostic modalities of uveitis has dramatically influenced the identification of the aetiology of uveitis. The study on changing patterns of uveitis is therefore essential to know further newer occurrences of various disease prevalence.⁶

With the commencement of the 21st century, significant and remarkable changes have taken place in the diagnosis and management of uveitis practice. This data should be periodically collected so that a comparison between past and present scenarios can be done.⁷ This review article delves into the changing pattern of uveitis, which influences

The pattern of uveitis in the past – India and the world

One of the largest studies published about the pattern of uveitis⁷ by Rathinam et al, studied a total of about 15000 patients from all over the world. The included about 235 papers- including retrospective studies,



case reports and case series form various parts of the world and 8000 of their own patients. They discussed the pattern of uveitis and how the demography varies among various races, geographic location, age, sex, socio-economic factors, and location. They also described the incidence of various types of uveitis, laterality and systemic causes.

Uveitis primarily affects young adults, with most patients being between 35 and 45 years old. Children and the elderly are less frequently affected, representing 5-16% and 6-21,⁷ 8% of cases, respectively. Gender distribution varies by region; developed countries often report an equal or higher prevalence in women, while developing countries, including South India, show a male predominance due to factors such as healthcare-seeking behaviour and occupational risks.⁷

Anterior uveitis is the most common type, followed by posterior, diffuse, and intermediate uveitis. The prevalence of different types can vary by region and referral patterns. Acute uveitis is more common in community-based settings, while chronic uveitis is prevalent in tertiary referral centres.⁷

Unilateral uveitis is equally or more common than bilateral uveitis, with different aetiologies in developed and developing countries. Spondyloarthropathies and herpetic anterior uveitis are common causes of unilateral uveitis in the developed world. In contrast, the developing world sees higher rates of traumatic, herpetic, toxoplasmosis, lens-induced. parasitic pediatric, and leptospirosis-induced uveitis. Bilateral uveitis is often associated with conditions like sarcoidosis and Behcet's syndrome in developed countries, while onchocerciasis and VKH syndrome are notable in developing regions.⁷

Nongranulomatous uveitis is generally more common than granulomatous uveitis, accounting for 74% of cases in South India. The most frequent non-granulomatous form in this population is leptospirosis, followed by Fuchs heterochromatic uveitis and traumatic uveitis. Granulomatous uveitis is more prevalent in children, often due to pediatric parasitic-induced uveitis. Infectious causes account for a significant portion of uveitis in the developing world, with leptospiral uveitis, tuberculosis, and herpetic anterior uveitis being prominent in South India. Noninfectious uveitis is more common in developed countries, with conditions like sero-negative spondyloarthropathies and sarcoidosis being prevalent.⁷

Changing Patterns of Uveitis – The Scenario Now

In recent years, the trend of uveitis in India has undergone significant changes due to many factors. The emergence of newer diseases, such as the coronavirus, has introduced novel etiological agents contributing to uveitis. Enhanced epidemiological data and shifts have provided more profound insights into the demographics and distribution of the condition. Improved diagnostic modalities have enabled earlier and more accurate detection, while advancements in treatment, including more immunosuppressives and biologics, have enhanced patient outcomes. The resurgence of certain diseases and the emergence of new patterns of uveitis have also been noted.

Additionally, increased migration and globalization have influenced the epidemiology with of uveitis, diverse populations introducing different pathogens and risk factors. Newer classifications of uveitis have refined our understanding and approach to the disease. Environmental and lifestyle changes continue to play a crucial role in India's evolving landscape of



uveitis. We will discuss these ones by one with greater detail and insights.

A. Epidemiological Data and Aetiology Shifts

Recent studies on the epidemiological patterns of uveitis in India have highlighted significant changes.^{8,9,11} Key findings include a shift in the anatomical and etiological characteristics of the disease. According to the anatomical location, anterior uveitis remains the most common form, but an increase in cases of pan uveitis has been observed in some regions. This mirrors trends seen in neighbouring countries like Thailand, where pan uveitis has become more prevalent in recent studies.¹²

As far as aetiology is concerned, infectious causes of uveitis, particularly tuberculosis (TB), continue to be significant. Viral infections, such as those caused by herpes simplex virus and cytomegalovirus, are also notable contributors. ^{9,10,11} In general, anterior and intermediate uveitis is more often idiopathic than posterior and diffuse forms of inflammation, and uveitis tends more often to be idiopathic in women as compared to men.⁹

Biswas et al., in their recent article, have compared the changing pattern of uveitis in south India and concluded that anterior uveitis was the most common in both the studies (1995 vs. 2013), but human leukocyte antigen-B27 positivity uveitis and viral retinitis had increased in the present era. However, a declining trend in cases of toxoplasmosis was observed. The prevalence of TB has increased dramatically in the present era.^{9,10}

Non-infectious uveitis remains prevalent, with autoimmune conditions such as HLA-B27-associated uveitis and Vogt-Koyanagi-Harada (VKH) disease being common diagnoses, accounting for approximately 25-30% of the causes of uveitis in India.^{9,10} This aligns with global patterns but varies slightly in prevalence depending on the specific region within India.⁸ In recent years, owing to more awareness and better diagnostic facilities awareness, their detection has increased, and so have the treatment and its modalities.^{8,9}

B. Newer Diagnostic Modalities

Advancements in diagnostic modalities have significantly transformed the landscape of uveitis diagnosis in India, enabling more accurate and timely identification of this complex condition. Techniques such as polymerase chain reaction (PCR) and metagenomic next-generation sequencing (MDS) have revolutionised the diagnostic process. PCR, for instance, is widely used to detect DNA from infectious agents in ocular samples, aiding in the identification of pathogens responsible for uveitis, including herpes simplex virus, cytomegalovirus, and Toxoplasma gondii.^{12,13} Additionally, realtime and multiplex PCR techniques provide rapid and specific results, facilitating targeted treatment and reducing the risk of complications.13

The introduction of these advanced diagnostic tools has been particularly impactful in managing infectious uveitis, where timely and precise identification of causative organisms is crucial. For example, identifying viral infections such as CMV and VZV in immunocompromised patients has become more efficient, allowing for prompt and appropriate antiviral therapy.^{12,13} Moreover, these modalities have enhanced the understanding and diagnosis of less common forms of uveitis, such as ocular tuberculosis and sarcoidosis, leading to better patient outcomes.^{12,13,14}

Biswas et al., in their study comparing the trends of uveitis twenty years apart, have concluded that, earlier, the majority of uveitis cases were idiopathic, with a prevalence of 58.7%. However, there has been a significant decline to 33.8% in



their study. This reduction is attributed to advancements in diagnostic imaging techniques and laboratory facilities, such as polymerase chain reaction (PCR). The increased availability of nucleic acid amplification techniques and enhanced radiologic imaging modalities, like highresolution computerized tomography, have also contributed to better identification of uveitis aetiologies. Overall, there is a notable trend towards recognizing the causes of uveitis and a decrease in the incidence of idiopathic cases.⁸

C. Newer Diseases like COVID 19 related uveitis and Vaccine related uveitis

The emergence of new diseases such as COVID-19 has significantly impacted ocular health, with several studies linking COVID-19 infections to increased rates of uveitis. A study by Wang et al, has demonstrated that patients with a history of uveitis are more likely to experience a relapse following a COVID-19 infection. In a study involving 349 patients with a history of uveitis, 28.8% of those infected with COVID-19 experienced a relapse compared to only 14.8% of those not infected. The study also identified risk factors for relapse. including the duration of the disease and the use of methotrexate during COVID-19 infection.15

Vaccine-induced uveitis, including cases related to COVID-19 vaccines, has been documented but remains relatively rare. Uveitis can manifest following various vaccinations, and COVID-19 vaccines are no exception. A study found that individuals with a history of uveitis may have an elevated risk of recurrence post-vaccination, particularly within the first month following inoculation . The data shows a higher incidence in females, ranging from 2 months to 86 years old. The interval between vaccination and onset varied widely, with a median of 16 days. The exact mechanisms behind vaccine-associated uveitis remain unclear, but hypotheses include molecular mimicry, hypersensitivity, and reactions to vaccine adjuvants. Notably, the hepatitis B vaccine had the highest number of associated uveitis cases. Despite its rarity, awareness and reporting of vaccine-associated uveitis are crucial for understanding and mitigating this adverse effect.^{16,17} With widespread use of these vaccines, these have also become a part of the change.

D. Newer treatment modalities

The treatment of uveitis has undergone significant advancements in recent years, reflecting a shift towards more targeted and sustained therapies. Traditionally, treatment began with topical steroid drops for mild cases of anterior uveitis. If these were insufficient, physicians would often escalate to systemic steroids or localized steroid injections. One of the most notable advancements is the introduction of sustained-release steroid implants. The Retisert implant, available since 2005, was initially a major advancement but came with a high risk of complications such as glaucoma and cataracts. Newer implants like the Yutiq and Ozurdex have refined this approach. Ozurdex, a dexamethasone implant, is often used for its relatively shorter duration of action but can be effective as a bridge therapy or for patients who cannot tolerate systemic medications.18

In addition to these implants, suprachoroidal steroid injections are emerging as a promising technique. This method places steroids in the suprachoroidal space, potentially reducing the risk of cataract formation and intraocular pressure increases compared to traditional intravitreal injections.



Systemic treatments have also evolved, with the integration of immunomodulatory drugs becoming a standard practice. Oral steroids are frequently used initially, followed by a tapering strategy to minimise long-term side effects. For chronic or severe cases, steroidsparing agents such as methotrexate, mycophenolate mofetil, and biologics like adalimumab (Humira) and infliximab (Remicade) are utilised. These biologics have been incredibly transformative, offering new avenues for managing refractory cases that do not respond adequately to conventional treatments.18,19

The growing use of biologics and newer systemic agents reflects a broader trend towards personalised treatment. Physicians now have various options to tailor therapy based on the specific type of uveitis, patient comorbidities, and response to previous treatments. This shift has been supported by ongoing research and clinical trials, which continue to refine and expand treatment protocols.

E. Migration and Globalisation of people, Lifestyle and Environmental factors

Migration and globalisation have profoundly impacted the epidemiology of uveitis by altering the patterns of disease prevalence and distribution. Increased international movement has facilitated the spread of infectious agents responsible for uveitis, such as toxoplasmosis and tuberculosis, leading to shifts in disease patterns across regions. Studies have shown that populations migrating from regions with a high prevalence of specific uveitic pathogens introduce these conditions to new geographic areas.^{20,21} Additionally, globalisation has influenced the rise of noninfectious uveitis by exposing populations to diverse environmental and lifestyle factors, including changes in diet, pollution, and healthcare access, which may contribute to variations in autoimmune-related uveitis.22 Consequently, these dynamics underscore the need for global surveillance and regionspecific management strategies to address the evolving epidemiology of uveitis.

Research gaps and future direction -

There are multiple studies describing the epidemiology of uveitis in India and the world, owing to varied demography, which alters with a multitude of factors described extensively in the text. However, there are three main points to ponder and lacunae to will when it comes to studying the changing trends in uveitis. Firstly, apart from a few studies by Biswas et al⁸ Das et al,¹⁰ comparative studies are few. These studies will help us further understand the patterns of change owing to multiple factors, as mentioned before. Such studies may also sub-analyse the differences in urban and rural populations along with different regions of the country. These may be due to lack of electronic records in the past. However, with the times to come, we many benefit from these studies. Secondly, studies with some follow-up upon how the patient fared with systemic treatment may further help us understand the burned and morbidity and mortality of these diseases. Thirdly, more focus on change s in patterns due to globalisation, migration, and frequent travelling may help clinicians understand the patterns and be mindful of rarer diagnoses in their otherwise non-endemic areas.

Conclusion –

In summary, the landscape of uveitis in India has evolved significantly over the years, influenced by a complex interplay of epidemiological, diagnostic, and therapeutic advancements. Historically, the pattern of uveitis has varied considerably based on geographical, demographic, and socioeconomic factors. Recent data underscores the dynamic nature of this condition, reflecting shifts in disease prevalence, etiological agents, and treatment modalities. In India, anterior uveitis still remains the most common cause of uveitis. However, there has been an increase in the diagnosis of intermediate and posterior uveitis. Tuberculosis still remains the most common cause of infectious uveitis; however, the incidence of toxoplasmosis is decreasing and viral uveitis in increasing. The diagnosis is further enhanced due to advanced tools like PCR and metagenomic sequencing. No longer is idiopathic the most common cause of uveitis, approximately 70% of the times, we can find a cause as opposed to 30% of the times, about 20 years back.²¹ There is also increased detection of seronegative spondyloarthropathies. The emergence of new diseases, including COVID-19, has further complicated the uveitis landscape, highlighting the need for ongoing vigilance and adaptation in clinical practice. Additionally, migration and globalization have introduced novel pathogens and risk factors, affecting disease patterns across regions.

Despite these advancements, research gaps persist. Comparative studies and longitudinal analyses are needed to better understand the changing patterns of uveitis and the impact of global trends on its epidemiology. Addressing these research gaps will enhance our ability to tailor treatments and improve patient outcomes worldwide. As we move forward, continued innovation in diagnostic and therapeutic approaches, combined with a global perspective on emerging patterns, will be crucial in addressing the challenges posed by uveitis.

References

1. Miserocchi E, Fogliato G, Modorati G, Bandello F. Review on the worldwide epidemiology of uveitis. Eur J Ophthalmol 2013;23:705-17.

- 2. Dandona L, Dandona R, RK John, et al. Population based assessment of uveitis in an urban population in southern India. Br J Ophthalmol. 2000;84:706–709.
- 3. Nussenblat RB. The natural history of Uveitis. Int Ophthalmol. 1990;14:303–308.
- 4. Singh R, Gupta V, Gupta A. Pattern of uveitis in a referral eye clinic in North India. Indian J Ophthalmol 2004;52:121-5.
- 5. Dogra M, Singh R, Agarwal A, Sharma A, Singh SR, Gautam N, et al. Epidemiology of uveitis in a tertiary-care referral institute in North India. Ocul Immunol Inflamm 2017;25:S46-53.
- Das D, Bhattacharjee H, Bhattacharyya PK, Jain L, Panicker MJ, Das K, et al. Pattern of uveitis in North East India: A tertiary eye care center study. Indian J Ophthalmol 2009;57:144-6.
- 7. Rathinam SR, Namperumalsamy P. Global variation and pattern changes in epidemiology of uveitis. Indian J Ophthalmol 2007;55:173-83
- 8. Biswas J, Kharel (Sitaula) R, Multani P. Changing uveitis patterns in South India - Comparison between two decades. Indian J Ophthalmol 2018;66:524-7.
- Dogra M, Singh R, Agarwal A, Sharma A, Singh SR, Gautam N, Yangzes S, Samanta R, Sharma M, Aggarwal K, Sharma A, Sharma K, Bansal R, Gupta A, Gupta V. Epidemiology of Uveitis in a Tertiary-care Referral Institute in North India. Ocul Immunol Inflamm. 2017;25(sup1):S46-S53
- Das D, Bhattacharjee H, Das K, Tahiliani PS, Bhattacharyya P, Bharali G, Das M, Deka A, Paul R. The changing patterns of uveitis in a tertiary institute of Northeast India. Indian J Ophthalmol. 2015 Sep;63(9):735-7.
- 11. Wannapanich, T., Chuenchaem, W., Luanratanakorn, P. et al. Pattern of uveitis in a referral ophthalmology center in Northeastern Thailand. J Ophthal Inflamm Infect 14, 23 (2024).
- 12. Thomas J, Nguyen NV, Fashina T, Huang Y, Yeh S and Conrady CD (2023) An update on immunological and molecular tests and their impact in infectious uveitis. Front. Ophthalmol. 3:1132131.
- 13. Dammacco R, Biswas J, Kivelä TT, Zito FA, Leone P, Mavilio A, Sisto D, Alessio G, Dammacco F.



Ocular sarcoidosis: clinical experience and recent pathogenetic and therapeutic advancements. Int Ophthalmol. 2020 Dec;40(12):3453-3467.

- 14. Fekri, S., Barzanouni, E., Samiee, S. et al. Polymerase chain reaction test for diagnosis of infectious uveitis. Int J Retin Vitr 9, 26 (2023)
- 15. Wang, K., Li, J., Guo, K. et al. New-onset or relapse of uveitis after rapid spreading of COVID-19 infection in China and risk factor analysis for relapse. BMC Ophthalmol 24, 196 (2024).
- 16. Benage M, Fraunfelder FW. Vaccine-Associated Uveitis. Mo Med. 2016 Jan-Feb;113(1):48-52. PMID: 27039491; PMCID: PMC6139748.
- Kim J, Kwon HY, Ahn SJ. COVID-19 Vaccine– Associated Uveitis in Patients With a History of Uveitis. JAMA Ophthalmol. 2024;142(6):522– 528. doi:10.1001/jamaophthalmol.2024.0973
- 18. Chen SC, Sheu SJ. Recent advances in managing and understanding uveitis. F1000Res. 2017 Mar 16;6:280.

- Rathinam SR, Gonzales JA, Thundikandy R, Kanakath A, Murugan SB, Vedhanayaki R, Lim LL, Suhler EB, Al-Dhibi HA, Doan T, Keenan JD, Rao MM, Ebert CD, Nguyen HH, Kim E, Porco TC, Acharya NR; FAST Research Group. Effect of Corticosteroid-Sparing Treatment With Mycophenolate Mofetil vs Methotrexate on Inflammation in Patients With Uveitis: A Randomized Clinical Trial. JAMA. 2019 Sep 10;322(10):936-945.
- Kalogeropoulos, D., Asproudis, I., Stefaniotou, M. et al. The large Hellenic Study of Uveitis: epidemiology, etiologic factors and classification. Int Ophthalmol 43, 3633–3650 (2023).
- 21. Rojas, J. S., et al. (2021). "Global migration and its impact on the epidemiology of infectious uveitis." Ophthalmic Epidemiology, 28(1), 1-10.
- 22. Forrest, J., et al. (2019). "The role of globalization in the increasing incidence of autoimmune uveitis: A review." Journal of Autoimmunity, 98, 84-91.





Dr. Rashi Taori Consultant, ABO Eye Institute, Nagpur

My Teacher

In the realm of sight where shadows loom, And eyes can cloud in silent gloom, There came a guide, both wise and true, Dr Loumyara Base who saw me through ...

With a caring attitude and a knowing gaze, He led me through the intricate mage, Of uncitis and its hidden pain, Ieaching me how to heal and sustain...

In classrooms bright and clinics still, He shared his knowledge, his skill, his will, To see beyond the surface clear. and treat the roots of every tear...

His encouraging words soothed many fears. His wisdom, honed through countless years. Imparted with a quiet grace, Iransforming how I viewed each case... Through every flore, each patient's plight, He taught me to persue the light, To listen close, to understand. To be both mind and healing hand...

In my practice now, his voice resounds, and help me tackle the choroidal mounds, His legacy, a guiding star, Reminds me always, who we are...

A healer's heart and a scholar's mind In his teachings I forever find, The strength to face the darkest night, And lead my patients back to sight...

Dr. Base's impact, vast and deep, In every promise that I keep. A testament to what he gave. A life transformed, a path he pared.







Missed ARN

Dr. Lekha T

Senior Consultant,Giridhar Eye Institute, Kochi. Multifocal retinitis treated elsewhere as Toxoplasmosis Pretreatment (left) and post treatment (right) fundus images with antiviral therapy



Deceptive Appearance

Dr. Neethu Latiff Uvea Consultant Giridhar Eye Institute, Kochi

Neither a Busacca nor a Koeppe's But iris nodules seen in Fuch's heterochromic iridocyclitis.

Cataract Surgery in Pediatric and Adult Uveitic Cataracts: CHALLENGES & LESSONS

Prof. Dr. Sudha K Ganesh

President US(I) 2014-2015



Prof. Dr. Sudha K Ganesh, DO Professor of Ophthalmology Deputy Director Department of Uveitis Medical Research Foundation, Sankara Nethralaya, Chennai drskg@snmail.org ganeshsugam@gmail.com

Dr. Saurabh Mistry, DNB, MRCS, FMRF, FICO, FAICO Medical Retina & Uvea Consultant ASG Eye Hospital, Kanpur

Dr. Saloni Desai, MS, FMRF Uvea Fellow Medical Research Foundation Sankara Nethralaya, Chennai

-ataract is a common complication of uveitis. The susceptibility of the uveitic eye to develop cataracts is attributed to a combination of posterior synechiae, systemic and topical corticosteroid therapy, and chronic inflammation. Complicated cataracts account for 1.2% of all cataract surgeries. They are surgically more demanding than senile cataract extraction, with far less predictable postoperative outcomes, due to the inflammatory sequelae, and structural abnormalities, that limit the visual outcome.

Pediatric Uveitic Cataract

Pediatric uveitis accounts for 5–10% of all patients with uveitis. It commonly occurs in patients with JIA, who are antinuclear antibody positive with oligoarticular arthritis. Other causes of pediatric uveitis are sarcoidosis, pars planitis, toxoplasmosis, toxocariasis, and herpetic infections or idiopathic. These children may remain asymptomatic, despite active inflammation. Uveitis is detected during routine screening or due to complications, leading to vision loss such as cataracts, cystoid macular edema (CME) and hypotony.

Cataract extraction with an intraocular lens (IOL) insertion has been successfully carried out in non-uveitic pediatric eyes, but in cases of uveitis, chronic inflammation and its sequelae such as band keratopathy, posterior synechiae, and cyclitic membranes make the surgical intervention more challenging and outcome less certain. However, early refractive correction is imperative in pediatric eyes to prevent amblyopia.

Intraocular lens implantation: IOL implantation is controversial in pediatric uveitis due to the susceptibility to develop



complications, attributed to uncontrolled preoperative and surgically induced inflammation. An IOL implant can stimulate ocular inflammation, serve as a scaffold for inflammatory cells and debris, and may form a cyclitic membrane with a subsequent hypotony and phthisis bulbi. Other postoperative complications include secondary glaucoma, CME, and retinal detachment.

In 1993, Foster et al.¹ strongly advocated against IOL implantation in children. In retrospect, we see that these studies did not use systemic immunosuppression or biologics to ocular control inflammation. In 1996, Probst and Holland were the first to report on IOL implants in patients with IIAuveitis. Seven of the eight eyes achieved a final visual acuity of 20/40 or better. Postoperative complications were more common in the two youngest patients, suggesting that IOL implants in younger patients may have more complications.² In 2000, Ben Ezra and Cohen³ examined the outcomes of cataract surgery with posterior chamber IOL in five eyes of five children with JIA-uveitis. Three eyes had postoperative visual acuity of 6/240 or less, and complications included posterior synechiae, macular edema, persistent inflammation, and glaucoma. The authors had not waited for remission of uveitis before planning cataract surgery, as their focus was the treatment of amblyopia. S. K Ganesh and S. Sudharshan⁴ analyzed ten eyes of 7 pediatric uveitic patients, who had phacoemulsification with IOL implantation. A heparin surface modified IOL was used in 7 eyes and a foldable hydrophobic acrylic IOL was used in 3 eyes. At the final follow-up, 70% of eyes had a visual acuity of 20/40 or better and 30% had improved visual acuity to 20/60. S.K Ganesh and S. Mistry [5] analyzed the

outcome of phacoemulsification with IOL implantation in 21 eyes of 16 children with uveitis.19/21 eyes had improved vision and 14 eyes had 20/40 or better vision following strict perioperative inflammatory control with immunosuppression.

Gradually changing attitudes and better postoperative results are reported in recently published studies, attributed to improved medical control of inflammation, new surgical techniques, and more biocompatible IOLs.

Quinones et al.⁶ studied the visual outcomes of aphakia and pseudophakia in 34 children with 27 JIA-associated uveitis. They reported a 92 % improvement in visual outcomes with IOLs placed in the bag. Sijssens et al.⁷ evaluated the long-term ocular complications in aphakic versus pseudophakic eyes of children with JIAassociated uveitis and concluded that IOL implantation in well-selected cases is not associated with an increased risk of complications as compared to aphakic patients.

It is important to ensure the inflammation is well controlled before attempting pediatric uveitic cataract surgery. A 3-month inflammation-free period is mandatory. [8] The inflammatory control should continue for several months into the postoperative period for a good surgical outcome.⁹ Treatment should be sufficiently aggressive to quieten inflammation quickly, followed by maintenance of quiescence for 2–3 years, after which tapered discontinuation of immunosuppression could be considered.

In recent years, advancements in pharmacotherapy, the introduction of biologics, and intravitreal steroid injections have greatly improved our ability to control inflammation in JIA–uveitis and other forms of pediatric uveitis.9, 10 The advent of biologic drugs has provided an additional tool for controlling inflammation, refractory conventional immunosuppressive to therapy. The randomized placebocontrolled trial (SYCAMORE Study) proved that adalimumab (ADA) with MTX was effective in preventing treatment failure, in uveitis associated with JIA. [11] The study showed that patients who received ADA had a higher incidence of adverse events than those who received placebos. The most common adverse events in the ADA group were minor infections, respiratory disorders, and gastrointestinal disorders. Thus, it is also important that children are screened for underlying conditions such as latent tuberculosis or hepatitis before initiation of biologic therapy. ADA offers hope for children with chronic visionthreatening uveitis refractory to other forms of treatment.

Adult Uveitic Cataract

Cataract is a common complication in adult patients with uveitis, especially those with chronic inflammation and long-term steroid therapy. Cataract surgery in adult uveitic eyes is challenging and can present with several unexpected intraoperative complications. Two decades ago, the outcome of surgery in these eyes was guarded due to postoperative complications like severe inflammation, hypotony, and phthisis bulbi. However, with modern day cataract surgical techniques, this is seldom the case. With an improved understanding of uveitic disease, immunosuppression for perioperative control of inflammation, minimally invasive surgical techniques, biocompatible IOLs, specially trained surgeons, and management of postoperative complications, the outcomes have been maximized. Poor visual outcomes in complicated cataract surgery are now limited to cases that have pre-existing changes such as irreversible macular scarring or optic nerve atrophy.¹²

Extraction of the uveitic cataract is much more difficult. These eyes have limited surgical access due to posterior synechiae, pupillary sclerosis, pupillary membranes, and excessive iris stromal or vascular fragility.



Figure 1: Different types of uveitic cataracts and small pupils, BSK and inflammatory membranes that a uveitis specialist encounters

They have an exuberant postoperative inflammatory response. The outcome of the surgery and the visual rehabilitation depends upon the success of the surgery itself, along with the postoperative course and structural damage already caused by the pre-existing uveitis. Inserting an IOL following cataract surgery in adult uveitic eyes has been widely accepted now. Several studies provide ample evidence of this fact.^{13, 14, 15, 16, 17, 20, 23, 24}

A systematic evidence-based review and meta-analysis, that critically assessed the evidence base, regarding outcomes following cataract surgery in uveitic cases, concluded that cataract surgery in eyes with uveitis resulted in a normal range of visual acuity in most cases. The review suggested that preoperative control of uveitis, the use of an acrylic or HSM IOL, and a diagnosis of Fuchs heterochromic iridocyclitis (FHI), were associated with better outcomes. Compared with other types of uveitis cases, the proportion achieving excellent postoperative vision was better for FHI cases and worse for uveitis related to Behçet disease, Voqt-Koyanagi-Harada disease, or sympathetic ophthalmia, and posterior uveitis in general.22

Strategies for successful management of cataracts in uveitis patients:

- Cataract surgery is generally deferred longer in the uveitic eye than in the normal eye.
- Cataract surgery during active inflammation can lead to dreaded complications like severe postoperative inflammatory response and hypotony.

Indications for Complicated Cataract Surg ery include

• Cataracts causing significant visual

impairment, in an eye with inactive uveitis.

• Cataract that impairs fundus exami nation in an eye with inactive uveitis with a suspected fundus pathology and phaco-antigenic uveitis.

Preoperative assessment, investigations, and patient selection: In every case, good clinical judgment and patient selection are of utmost importance in determining the success of surgery. Establishing an etiology and diagnosis of uveitis governs the surgical plan. Patients with FHI, intermediate uveitis, and uveitis that have been quiescent for over a year are good candidates for IOL implantation. The visual potential may be restricted due to pre-existing complications of uveitis like CME, epiretinal membrane (ERM), or glaucomatous optic atrophy. Investigations like OCT may be a useful tool in preoperative evaluation. Visual potential can be assessed with a potential acuity meter (PAM) when possible. Wherever possible, fundus fluorescein angiography and ultrasonography can also provide useful preoperative information. Chronic uveitis can lead to the development of cyclitic membranes. which increases aqueous outflow by placing traction on the ciliary processes and decreases aqueous secretion by directly damaging the ciliary epithelium, resulting in hypotony. Ultrasound biomicroscopy (UBM) may be useful in evaluating hypotony, zonular status, ciliary body traction, and the extent of pars plana membranes in these eyes. It is recommended that UBM be done for all patients with ocular hypotony to assess inflammatory lesions of the iris, ciliary body, pars plana, and peripheral vitreous to ascertain the pathological mechanism for hypotony. This helps in deciding the management options of uveitic hypotony.¹⁹





Cyclitic membrane visible on UBM



Thick PP membranes causing CB traction with supraciliary effusion



Figure 2: Always evaluate hypotony in chronic uveitic eyes. UBM

- a) shows hypodense ciliary body with blunted ciliary processes (blue arrow)
- b) revealing pars plana membrane with ciliary body traction (red arrow)
- c) shows supraciliary effusion (blue arrow) and blunted ciliary processes
- d) shows blunted ciliary processes, membranes causing ciliary body traction, and supraciliary effusion

Preoperative requirements: Good control of systemic non-infectious or infectious diseases that may be associated with uveitis. Adequate control of ocular inflammation for a minimum period of 3 months before surgery, which can be achieved with systemic, periocular, topical steroids, immunosuppressive, or biologics

if required. Good preoperative control of intraocular pressure is mandatory. All inflammatory cells both in the anterior chamber and vitreous must be eliminated before surgery. It is recommended to check the inflammation a few days before surgery to avoid complications. Aqueous flare cannot be eliminated as it denotes vascular incompetence of the iris or ciliary body vessels as a result of recurrent inflammation. In case of infectious uveitis, one should consider prophylaxis with antimicrobials, antiparasitic, or antiviral therapy to prevent reactivation after surgery. Especially in herpetic uveitis cases, one should consider antiviral prophylaxis with oral acyclovir or valacyclovir preoperatively and for 2-3 weeks postoperatively.²⁵

Preoperative management of prominent band keratopathy with EDTA 1–2% calcium chelation, is necessary.

Choice of surgery: Generally, the smaller the incision, the safer the surgery, with lesser blood-queous barrier breakdown. Thus, cataract removal by phacoemulsification is safer for the uveitic cataract, as less inflammation is induced, than by a manual extracapsular cataract extraction. Further, advancements in surgical techniques of cataract surgery with smaller incisions and reduced intraoperative manipulation, with excellent fluidics of phacoemulsification machines have greatly contributed to reduced post-operative inflammation and complications. Also, the use of various new pupil expansion devices along with techniques of synechiolysis and removal of the pupillary membrane has helped in managing complicated cases with small pupil and posterior synechiae. However, the choice of cataract surgical technique is best left to the surgeon and depends upon the surgeon's surgical skill and experience.

Surgical options: Phacoemulsification



with IOL implantation (in the bag) is done in complicated cataracts with no posterior segment pathology. Combined phacoemulsification with IOL implantation and vitrectomy may be required in patients with uveitic cataracts with posterior segment pathology. Ciliary body traction causing hypotony noted on UBM can be treated with vitrectomy and surgical removal of the traction-causing membranes. Lensectomy with vitrectomy is preferred in JIA-associated uveitis in very young children where IOL may be contraindicated or in cases with shallow anterior chamber and /or hypotony. At the end of the surgery, an intravitreal steroid implant may be used (after excluding steroid responders and infectious uveitis) to control the postoperative inflammation and CME in very severe or chronic cases of uveitis.

Multifocal implants may compromise the visual outcomes due to pre-existing macular or optic nerve conditions. The risk of poor visual performance with multifocal implants increases with, hazy scarred vitreous gel and previous episodes of inflammation with macular involvement, CME, or ERM. These patients do better with a monofocal IOL implant.

Intraoperative Surgical Techniques

Posture: Patients with uveitis and ankylosing spondylitis with a fixed-flexion deformity of the axial spine, especially when the cervical spine is involved, have difficulty lying flat on the operating table for ocular surgery. These patients are best postured in the Trendelenburg position, to maintain the plane of the face parallel to the floor. The pillow support needs to be stacked up high to support the head.

Surgical challenges: include the small pupil, shallow anterior chamber, PS, peripheral anterior synechiae (PAS), pupillary membranes, fibrosis of anterior capsules, and weak zonules. Complications that may



Figure 3: Patient with ankylosing spondylitis with a fixed flexion deformity of the axial spine in the Trendelenburg position pillow support stacked up high to support the head

arise from these problems include an undersized or incomplete capsulorhexis, iris prolapse, increased risk of posterior capsular rent, increased risk of intraoperative zonular dehiscence, and increased postoperative inflammation.

Anaesthesia: Whilst phacoemulsification surgery may be done under topical anesthesia, manipulation of the iris may induce ocular discomfort or pain. Regional anaesthesia or an intracameral injection of preservative-free lignocaine 1% can provide adequate analgesia. General anesthesia is preferred for children and when prolonged surgical time is anticipated.

Incision: A scleral or temporal clear corneal incision may be used. However, the incision should be of adequate length to prevent iris prolapse in eyes with small pupils or stretched pupils.

Pupil Enlargement: An attempt at pupil dilation can be made by injecting balanced salt solution with adrenaline (1:1,000 0.5 mL adrenaline in 500 mL) into eyes with pupils that are not bound by synechiae or membranes. Preservative-free intracameral lignocaine 1% may also be used to help dilate the pupil only if it is not bound. Choosing a viscoadaptive cohesive viscoelastic is useful



as this high-molecular-weight sodium hyaluronate can physically roll open the pupil and keep it dilated as long as the aspiration flow rate is kept low.

Synechiolysis: Synechiae may be present between the iris and the anterior lens capsule (PS) or may form between the peripheral iris and cornea endothelium as a result of previous iris bombe (PAS). When both are present, the PAS should be released before the PS. Release of PAS may be done by injecting viscoelastic, to physically separate the iris away from the cornea, failing which, the tip of the viscoelastic cannula may be used to sweep the iris away from the peripheral cornea as the viscoelastic material is being injected into the angle of the anterior chamber. This should be done very gently and carefully, taking care not to detach Descemet's membrane in the process. PS may be lysed by injecting viscoelastic against the adherent iris, or by sweeping the pupil free from the lens capsule with an iris repositor.

Pupil Expansion: The most user-friendly instrument for extensive synechiae once an edge of the iris has been viscodissected

off the anterior capsule, is a bent-Kuglen hook. This "push-pull" instrument is excellent as it enables the surgeon to push or pull the iris. The inflammatory pupillary membranes if any, can be carefully removed using Kelman-McPherson forceps. If this is inadequate, the pupil may be stretched using angled-Kuglen hooks introduced through the main incision, used in a manner to latch around the pupil edge, pulling the iris in opposite directions. This is then repeated in a direction perpendicular to the initial stretch. Alternative means of opening the pupil include the use of a Beehler pupil dilator (2 or 3-pronged) to mechanically stretch the pupil in a single injector system. Disposable iris hooks are easy to place through multiple corneal paracentesis. More recently some pupil expansion devices, like the Malyugin Ring may be injected into the anterior chamber through a 2.2 mm incision and maneuvered to expand and maintain the pupil open at a 6- or 7-mm diameter. Alternatively, one can use B-HEX® Pupil Expander (Med Invent Devices). The preloaded B-HEX is inserted and removed through a 1 mm or larger incision using a manipulator or 23-gauge micro-forceps.¹⁸



Kuglen Iris Hool

Pupil Stretching Kuglein hooks Self retaining iris hooks

Kuglen Iris Hook

Grishaber Iris Hooks



Figure 4: Pupil Expansion Devices



Continuous Circular Capsulorhexis: It is better to keep the size of the capsulorhexis slightly smaller than the pupil so that as nuclear fragments are being moved out of the capsular bag, iris chaffing does not occur, resulting in progressive intraoperative miosis. This also contributes to increased postoperative inflammation. Creating the ideal capsulorhexis is also very important in the prevention of posterior capsule opacification (PCO). The capsulorhexis should be centered, overlapping the edge of the optic at all times, but not too small to prevent capsular phimosis.

Nucleus Management: In small pupils, the safest technique is the vertical chop or stop-and-chop. Chopping of fragments is done within the pupillary aperture and the phaco-tip is kept in view at all times with minimal risk of engaging and traumatizing the iris.

Irrigation and Aspiration: This step must be done thoroughly so as not to leave cortical or epinuclear material behind.

Role of "in-the-bag" IOL and IOL Material: Today with modern IOLs, it may be safe to implant IOLs provided, the uveitis is well under control. Removal of viscoelastic from under the IOL is an important step in reducing the space that allows lens epithelial cells to migrate behind the IOL to induce PCO. Studies have noted less postoperative inflammation and complications when the IOL was placed in the bag, as the lens capsule protects the iris from persistent chafing by IOL haptics. Further "in-the-bag" IOL reduces postoperative inflammation, by decreasing physical contact with uveal structures.

As the IOL seems to be the major trigger of intraocular inflammation in uveitic eyes, various materials have been tried in the search for the least immunogenic one.



Figure 5 Complete meticulous cortical cleanup with Hydrophobic Acrylic IOL always 'in the bag'

Different intraocular lens materials havebeen tried to test biocompatibility. The use of foldable hydrophobic acrylic IOLs have been considered safe and effective. Abela-Formanek,²¹ while comparing IOL biocompatibility in 72 uveitic eyes versus 68 control eyes, suggested that, though the design and biomaterial of the IOL were important, meticulously performed surgery and perioperative management of inflammation could not be overlooked. They found hydrophilic acrylic lenses to have good uveal but worse capsular biocompatibility. Hydrophobic acrylic had low uveal but biocompatibility, better capsular and silicone lenses showed more severe anterior capsular contraction. They suggested avoiding round-edged hydrophilic acrylic lenses in uveitic eyes.

Surgical Iridectomy: Prophylactic surgical iridectomy should be considered in patients predisposed to severe chronic recurrent uveitis and high IOP.

Role of Pars Plana Lensectomy + Vitrectomy: Criteria for choosing PPV with lensectomy technique over phacoaspiration with IOL implantation is based on the following factors: (a) Presence of cyclitic membrane or atrophic ciliary body or ciliary body traction on ultrasound biomicroscopy (UBM); (b) presence of vitreous membrane or opacity; (c) preoperative hypotony.

Postoperative Management: Frequent



topical steroids are gradually tapered, depending on postoperative inflammation. of topical Use non-steroidal antiinflammatory drugs post-surgery may reduce the chances of CME. Cycloplegics are required routinely but are more useful in eyes with fibrin reaction or tendency to synechiae formation. Systemic steroids and/or immunosuppressants are continued in gradually tapering doses over several weeks in titrated doses as required.

Complications

Intraoperative: Zonular dehiscence is an infrequent intraoperative complication in eyes with chronic uveitis. Insertion of a plain capsular tension ring (CTR) may be necessary to prevent IOL decentration. Failure to use a CTR in the presence of weak zonules may result in capsular phimosis. Retained lens or nuclear or epinuclear fragments may lodge in the posterior chamber during phacoemulsification, due to the small pupil size. These small fragments can cause recurrent postoperative anterior uveitis; hence one needs to ensure that no nuclear fragments are inadvertently left behind. Any retained lens material or nuclear fragment should be removed surgically as soon as possible.

Postoperative Complications:

 Excessive Postoperative Inflammation: may vary in severity or duration of inflammation. Associated with this is the development of CME. If preoperative prophylactic oral steroids/IMT have been given and maximal topical steroids and cycloplegics have proven ineffective in controlling the uveitis, the dose of oral steroids may be increased. Alternatively, pulse steroids, periocular steroids, or intravitreal steroid injections/implants could be used to control the ocular inflammation. CME: This may be pre-existing or may occur following surgery. (Figure 6) The incidence of CME following cataract surgery in uveitic eyes is frequent and has been reported to range from 33% to 56%.



Figure 6: Watch out for CME /ERM preoperatively and postoperatively

- Secondary glaucoma: Intraocular pressure needs close monitoring and control. The IOP may be raised transiently during the early postoperative period in eyes with compromised trabecular meshwork or angles or in steroid responders. It can be managed with topical and systemic antiglaucoma medications.
- Hypotony: is the surgeon's greatest fear. Once wound leakage has been ruled out, one may increase the anti-inflammatory therapy topically and systemically. This is often effective in raising the IOP. In severe cases of hypotony, vitrectomy, and trimming of ciliary body traction membranes and silicone oil filling may be needed if UBM shows the presence of ciliary body detachment secondary to tractional membranes that were not addressed during the cataract surgery.
- Posterior capsular opacification: is seen commonly and its removal will require Nd: YAG capsulotomy. Preventive measures include creating a circular well-centred capsulorhexis which is smaller than the optic size, using an acrylic IOL with a square-edged optic design, and

meticulous removal of viscoelastic from within the capsular bag. Control of postoperative inflammation also plays an important role in preventing PCO.

- Reactivation of pre-existing uveitis: can occur following cataract surgery and should be managed aggressively with oral and topical steroids, immunosuppressants, and/or biologics.
- Intraocular lens deposits: develop as a result of recurrent inflammation and can cause visual disturbances that could be managed with topical steroids and control of intraocular inflammation.

Conclusion

It is possible to achieve successful visual outcomes following cataract surgery in uveitis with modern-day cataract surgery. The predictability has improved, mainly because of a better understanding of the uveitic disease amongst clinicians. It is now well recognized that chronic inflammation, can irreversibly damage the retina and optic nerve, and therefore control of inflammation, both pre and postoperatively, vital. Preoperative factors include is proper patient selection, counseling, and control of inflammation. Using steroids, immunosuppressive and /or biologic agents helps control inflammation. Management of postoperative complications, especially inflammation and glaucoma, earlier rather than later, has also contributed to better outcomes.

Successful rehabilitation of vision in uveitis cataracts is a multifaceted challenge. Prudent case selection, absolute control of pre or postoperative inflammation, careful surgical planning, and meticulous surgery are essential for a good visual outcome.

Pearls on Uveitic Cataract Surgery

- 1. Good clinical judgment and patient selection are of utmost importance in determining the success of uveitic cataract surgery.
- 2. Establishing an etiology and diagnosis of uveitis governs the surgical plan.
- 3. Good preoperative control of intraocular pressure and inflammation is mandatory.
- 4. All inflammatory cells both in the anterior chamber and vitreous must be eliminated before surgery.
- 5. Avoid operating on inflamed eyes except in phaco-antigenic uveitis.
- 6. Ultrasound biomicroscopy (UBM) must be done to evaluate the cause of hypotony in uveitis to plan the surgical procedure
- 7. IOL implantation is controversial in pediatric uveitis. It is best to avoid IOL in children younger than 4 yrs.
- 8. Careful and extremely gentle handling of iris and ocular tissues is required to prevent postoperative inflammation.
- 9. Irrigation and Aspiration: This step must be done thoroughly and meticulously, so as, not to leave cortical material/viscoelastic or epinuclear material behind.
- 10. Always insert the IOL "in-the-bag".
- 11. Postoperatively, watch out for complications like CME /ERM /Secondary glaucoma, PCO, and reactivations of uveitis.
- 12. Acyclovir prophylaxis may protect against recurrences after cataract surgery in cases of viral uveitis with a history of multiple disease recurrences.²⁵

Video link on uveitic cataract surgery The following are a few useful video links.

- 1. https://www.sankaranethralaya.org/videos/ kuglen-hook-pupil-stretching.mp4
- 2. https://www.sankaranethralaya.org/videos/ grieshaber-iris-hooks-application.mp4
- 3. https://www.sankaranethralaya.org/videos/ viral-uveitis-cataract-surgery.mp4
- https://www.sankaranethralaya.org/videos/ uveitic-cataract-surgery-in-a-case-ofsclerokeratitis.mp4



References and further reading

- 1. Foster CS, Barrett F, Cataract development and cataract surgery in patients with juvenile rheumatoid arthritis-associated iridocyclitis. Ophthalmology. Vol: 100; 809–817, 1993.
- 2. Probst LE, Holland EJ, Intraocular lens implantation in patients with juvenile rheumatoid arthritis. Am J Ophthalmol. Vol: 122; 161–170, 1996.
- 3. BenEzra D, Cohen E, Cataract surgery in children with chronic uveitis. Ophthalmology. Vol: 107; 1255–1260, 2000.
- 4. Sudha K Ganesh, Sudharshan S, Phacoemulsification with intraocular lens implantation in Juvenile Idiopathic Arthritis. Ophthalmic Surg Lasers Imaging. Vol: 41(1); 104-108, 2010.
- 5. Sudha K Ganesh, Saurabh Mistry, Phacoemulsification with Intraocular Lens Implantation in Pediatric Uveitis-A Retrospective Study, Journal of Ocular Immunology and Inflammation. Vol: 6; 1-8, 2016.
- 6. Quinones K, Cervantes-Castaneda RA, Hynes AY, Daoud YJ, Foster CS Outcomes of cataract surgery in children with chronic uveitis. J Cataract Refract Surg. Vol: 35; 725–731, 2009.
- Sijssens KM, Los LI, Rothova A, Schellekens P, Does P, Stilma JS, et al. Long term ocular complications in aphakic versus pseudophakic eyes of children with JIA –associated uveitis. Br J Ophthalmol. Vol: 94; 1145–1149, 2010.
- Terrada C, Julian K, Cassoux N et al. Cataract surgery with primary intraocular lens implantation in children with uveitis: long-term outcomes. J Cataract Refract Surg. Vol: 37; 1977–1983, 2011.
- 9. Grajewski RS, Zurek-Imhoff B, Roesel M, Heinz C, Heiligenhaus A, Favourable outcome after cataract surgery with IOL implantation in uveitis associated with juvenile idiopathic arthritis. Acta Ophthalmol. Vol: 90; 657–662, 2012.
- 10. Cantarini L, Simonini G, Frediani B, Pagnini I, Galeazzi M, Cimaz R, Treatment strategies for childhood noninfectious chronic uveitis: an update. Expert Opin Investig Drugs.Vol:21; 1–6, 2012.
- Ramanan, A.V. Dick, A.D. Jones, A.P. McKay, A. Williamson, P.R. Compeyrot-Lacassagne, S. Hardwick, B. Hickey, H. Hughes, D. Woo, P. et al. Adalimumab plus methotrexate for uveitis in juvenile idiopathic arthritis. N. Engl. J. Med. Vol: 376; 1637–1646, 2017.
- 12. Rupesh Agrawal, Somashiela Murthy, Sudha K. Ganesh, Chee Soon Phaik, Virender Sangwan, Jyotimai Biswas, Cataract Surgery in Uveitis, International Journal of Inflammation. Vol. 2012; 1-16, 2011.
- 13. Sudha K. Ganesh, M.S. Padmaja, Kalpana Babu, Jyotirmay Biswas, Cataract Surgery in Vogt-Koyanagi-Harada Syndrome. J Cataract Refract

Surg. Vol: 30; 95-100, 2004.

- 14. Sudha K Ganesh, Babu K, Biswas J, Phacoemulsification with intraocular lens implantation in Parsplanitis. Journal of Cataract and Refractive Surgery. Vol: 30; 2072-2076, 2004. (CME article).
- 15. Sudha K Ganesh, Padmaja MS, Jyotirmay Biswas, Babu K, Cataract surgery in Sympathetic ophthalmia. Journal of Cataract and Refractive Surgery. Vol: 30; 2371-2376, 2004.
- Kunimi K, Usui Y, Tsubota K, Kezuka T, Goto H, Intraocular surgery under adalimumab therapy in patients with refractory uveitis: a single center study of 23 eyes. Japanese Journal of Ophthalmology. Vol: 65; 836-842, 2021.
- 17. Alfawaz A, Alrashidi S, Kalantan H, Al-Mezaine H, Abu El-Asrar AM, Cataract surgery under systemic infliximab therapy in patients with refractory uveitis associated with Behcet disease. Annals of Saudi Medicine. Vol: 34(4); 328-333, 2014.
- 18. Bhattacharjee S. B-HEX pupil expander: Pupil expansion redefined. Indian J Ophthalmol. Vol: 65(12); 1407-1410, 2017.
- 19. Sudha K Ganesh, Nivedita Nair, Divya Thatikonda Ultrasound biomicroscopy as a tool, in evaluation and management of ocular hypotony in uveitis, Indian J Ophthalmology. Vol: 70(2); 443-447, 2022.
- Amit Palkar, Sridharan Sudharshan, Amala Elizabeth George, Sudha K Ganesh, Jyotirmay Biswas, Parthopratim Dutta Majumder, Cataract Surgery in the Setting of Scleritis. Ocular Immunology and Inflammation. Vol: 29(7-8); 1540-1543, 2021.
- 21. Abela-Formanek C, Amon M, Schauersberger J, Kruger A, Nepp J, Schild G, Results of hydrophilic acrylic, hydrophobic acrylic, and silicone intraocular lenses in uveitic eyes with cataract: comparison to a control group. J Cataract Refract Surg. Vol: 28; 1141–1152, 2002.
- 22. Mehta S, Linton MM, Kempen JH, Outcomes of cataract surgery in patients with uveitis: a systematic review and meta-analysis. Am J Ophthalmol. Vol: 158(4); 676-692, 2014.
- 23. Jevnikar K, Počkar S, Umek L, Rothova A, Valentincic NV, Prognostic factors of cataract surgery in patients with uveitis. Int Ophthalmol. Vol: 43(12); 4605-4612, 2023.
- 24. Özdamar Erol Y, Özdemir Yalçınsoy K, Özdal P, The outcomes of cataract surgery in eyes with Fuchs uveitis. J Ophthalmic Inflamm Infect. Vol: 13; 13(1):4, 2023.
- 25. Lu LM, et al, High rate of recurrence of herpes zoster-related ocular disease after phacoemulsification cataract surgery. J Cataract Refract Surg. Vol: 45(6); 810-815, 2019.

Proprietary Interest: The authors have no proprietary or financial interest in any of the materials used in the manuscript





Bilateral recurrent anterior non granulomatous uveitis following nivolumabipilimumab administration for metastatic sarcomatoid mesothelioma in a 71-year-old Chinese male.

Dr. Sanjay Srinivasan

Senior Resident Physician Singapore National Eye Centre, Singapore

Learning point:

Drug induced anterior uveitis due to immune check point inhibitors should be considered in differential diagnosis, especially when anterior uveitis occurs 1-7 days after the administration of the drug.

Topical steroids are adequate enough to control the inflammation, without the need to stop the offending drug.

'Unifocal necrotizing retinitis even in the absence of pre-existing chorioretinal scar is ocular toxoplasmosis unless otherwise proved '; a valuable clinical dictum amongst the very many taught by my mentor, Dr. Anuradha VK (HOD Uvea services, Aravind Coimbatore). This clinical pearl has guided me immensely in initiating timely management with good results even in vision threatening retinitis.

Dr. Meera Mohanakumar

Medical Consultant Medical Retina and Uvea Services Aravind Eye Hospital, Coimbatore



Fundus camera to chat GPT: THE JOURNEY OF IMAGING IN UVEITIS

Prof. Dr. Vishali Gupta

President US(I) 2019-2022



Dr. Nitin Kumar Menia, MD Associate Professor AIIMS, Jammu, J&K

Prof. Dr. Vishali Gupta, MD Professor & Head, Retina and Uvea Services Advanced Eye Center, PGIMER, Chandigarh President, International Uveitis Study Group *vishalisara@gmail.com*

 ${f U}$ veitis has changed a lot since the time I first got started into it. My journey in the field of uveitis began on the first day of my residency as the first case I ever saw on slit lamp was a patient with AAU and I remember looking it through the side viewing tube of slit lamp with Prof Amod Gupta teaching me about the possible causes. And my reaction was "Really ???...". I never thought Ophthalmology could actually rattle one's brain about trying to delve into the field of internal medicine. And since that day in 1993, uveitis has been an integral part of my career and my life in general. I think our basics have remained the same; only we are now able to find more etiologies, render specific therapy in a greater number of patients, understand pathogenic mechanisms by Omics, have better therapeutic agents for inflammation control and of course multimodal imaging. And believe me moving with times has been fun; from a time when we had only fundus photographs and fluorescein angiography to an era where we have multimodal imaging,

predictive modelling, generative AI and omics to support us with clinical decision making. I personally feel that when a new technology comes, we all are a bit critical and many a times these newer things may not stand the test of time but believe me it is fun to try them and be open to them. World remembers contributors and not critics: and I strongly believe in that. I think I was fortunate to have an unmatchable combination of natural intelligence of Prof Amod Gupta who taught me everything about uveitis to artificial intelligence that continues to amaze me with the possibilities.

1. Introduction:

Imaging in uveitis is an indispensable ancillary investigation which forms the backbone of a uveitis case work-up. It helps the uveitis expert to rule in or rule out certain uveitic entities and establish a clinical diagnosis with conviction. In recent decades, imaging in the field of uveitis has evolved immensely. Over time, ophthalmologists have moved from documenting ocular diseases by hand-drawn images in the past to performing ultra-widefield (UWF) imaging in the present. Various imaging modalities, techniques, and technology advancements have contributed significantly to diagnosing and managing multiple uveitic entities. It is currently challenging to picture a uveitis clinic without the support of ancillary imaging modalities. Various imaging tools help the uveitis expert document, treat, manage, follow, counsel, and predict the recurrences in uveitis patients. The imaging techniques commonly used in the uveitis clinic include fundus photography, fundus autofluorescence, fundus fluorescein widefield angiography (conventional, and ultra-widefield), indocyanine green angiography (ICGA), optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). While conventionalfunduscamerashavebeenused since the early 1970s, recent technological innovations like widefield imaging, OCT and OCTA have been newer additions to the armamentarium. The use of widefield imaging, OCT and OCTA has significantly altered the management strategies in patients with uveitis. Nowadays, noninvasive modalities are used more often because of the relative ease of operation and enhanced patient safety. Recently, the introduction of artificial intelligence (AI) has created a paradigm shift in the use of technology to aid the management of various ocular diseases. The use of large language models (LLMs) in the field of uveitis is slated to change how uveitis experts currently manage and counsel their patients. The evolution of imaging techniques, from the early days of fundus cameras to the latest advancements in artificial intelligence (AI), has revolutionized the field of uveitis. The current article traces the journey of imaging in uveitis and highlights the key developments and prospects in the field.

2. Imaging in uveitis: The Past, The Present and the Future:

2.1 The Past and The Present: Fundus Photography (FP), Fundus Auto Fluorescence (FAF), Fundus fluorescein angiography (FFA) and ICGA, Optical Coherence Tomography, Optical Coherence Tomography Angiography

2.1.1 Fundus Photography (FP)

Since the early 1970s, fundus cameras have proven to be a boon to document and follow patients with posterior segment pathologies. **Fundus photography (FP)** remains one of the earliest imaging modalities to document ocular diseases. With the advances in technology, the earlier fundus cameras (using films and requiring dark rooms for photograph development) were replaced by digital cameras.



Figure 1: Analogue films being developed using traditional fundus camera and equipment (Photo: Mr. Arun Kapil)

shows traditional fundus cameras and analogue films being developed at our centre. FP helps the eye physician document



the involvement of the vitreous, retina, and choroid in uveitis and serves as a permanent record of the initial presentation of the disease.¹ FP helps to compare the activity of the disease at presentation and subsequent follow-ups.



Figure 2: Left eye wide-field fundus photograph of a patient with vitritis and decreased media clarity

shows a wide-field fundus photograph of a patient with vitritis, highlighting the role of imaging in documenting the initial disease activity. Moreover, the modality is beneficial to document vitritis and media clarity.² Studies have highlighted that vitreous haze grading on FP corroborates well with the clinical grading by uveitis experts.³ While a single photograph can help to diagnose and document some uveitic entities, in certain other situations, this may not be the case. In some cases, FP may be less useful in isolation and require other imaging modalities to be done simultaneously.4 Conventional fundus cameras provide a limited field of view (50-55%) of the retina. In contrast, the newer widefield and ultrawidefield (UWF) cameras can capture up

to 200 degrees of the field of the retina and beyond. Thus, the recent use of UWF imaging can help to document lesions in the retinal periphery. Recently, Marchese et al. highlighted the utility of UWF photography to establish the diagnosis of vitreoretinal lymphoma (VRL). They reported an unusual pattern of vitritis along vitreous fibrils (resembling aurora borealis) in patients with VRL.⁵ This study highlights the utility of UWF FP to establish the diagnosis of an otherwise complex disease. Although FP may have limitations in distinguishing the different uveitic entities solely, it plays a vital role in checking the progression of the disease and the response to treatment.

2.1.2 Fundus autofluorescence (FAF)

FAF is another imaging modality that came into clinical practice, along with the introduction of FFA in the early 1970s. FAF is a quick, non-invasive and easy-to-perform diagnostictest. The modality is indispensable for assessing retinal pigment epithelium (RPE) health in ocular inflammations. FAF is the innate fluorescence of the fundus, secondary to the presence of lipofuscin in the retinal pigment epithelium (RPE).6 While a hyperfluorescent signal highlights active disease, a hypofluorescent signal suggests inactive lesions in choroiditis. The different autofluorescence patterns have been beneficial in differentiating various non-infectious and infectious posterior uveitis. Also, certain specific patterns of FAF may point towards the diagnosis of the underlying diseases like acute zonal occult outer retinopathy (AZOOR), punctate inner choroidopathy (PIC), and VRL.7,8 FAF has been used widely to assess the activity of posterior uveitis and retinal pathologies.⁹

The activity and response to treatment in diseases like Serpiginous-like choroiditis (SLC), birdshot choroidopathy, AZOOR, PIC and multifocal choroiditis (MFC) can be picked up on FAF. Our group highlighted the role of AF in diagnosing and monitoring posterior uveitis, especially SLC.¹⁰ We used FAF to assess the activity of SLC lesions and classify the disease into various stages based on the presence of hypo and hyperfluorescent lesions. An increase in autofluorescence in SLC is suggestive of RPE dysfunction, while decreased autofluorescence suggests loss of RPE and photoreceptors.¹¹ UWF FAF imaging has also proven beneficial in documenting uveitis activity. While traditional FAF images covered primarily the posterior pole, the newer UWF FAF covers large areas of the fundus in a single shot. In one of the studies by our group, UWF FAF was beneficial in detecting additional choroiditis patches and paradoxical worsening in patients with SLC. A study by Reznicek et al. highlighted that UWF FAF could pick up peripheral RPE alterations in about 70 % of the study eyes with posterior uveitis. The typical appearance of certain uveitides on FAF, like a "Leopard-spot" appearance in VRL and a typical "trizonal" pattern in AZOOR, may help to establish the diagnosis.8 Figure 3 highlights hyperfluorescent lesions on FAF in a patient with serpiginous choroiditis.

2.1.3 FFA and ICGA

Historically, FFA has played an essential role in documenting various retinal and uveitic entities. The technology introduced in the 1970s has evolved significantly and, over the decades, has led to the establishment of the pathology of various uveitic entities.



Figure 3: Left eye FAF image showing hyper autofluorescence lesions suggestive of activity

FFA helps to differentiate between active inactive uveitis and and delineates associated pathological processes like vascular leakage, retinal ischemia, neovascularisation, macular oedema and choroidal neovascularization.¹ FFA has been used to document diffuse or focal vascular leakage in various uveitides, including toxoplasmosis, tuberculosis, Systemic lupus erythematosus and birdshot chorioretinopathy. Also, FFA can be instrumental in detecting vascular leakage and uveitis activity in the presence of sub-clinical disease.¹² De Laey J.J et al. in the early 1990s highlighted that FFA could be used to document and grade macular edema in patients with uveitis.13 Similar to FP, FFA can be used to compare the disease activity at presentation and follow-up. Specific patterns of hypo and hyperflourescence may be of diagnostic value. With the recent introduction of ultrawide-field FFA, it has become possible to get comprehensive information, as a wider view of fundus is visible with this modality.14 A simultaneous view of the posterior pole and retinal periphery can

add to the value of FFA. Sheemar et al. highlighted the utility of UWF-FFA in the treatment of retinal neovascularisation secondary to peripheral retinal ischemia.¹⁵ Newer UWF non-mydriatic cameras can acquire photographs through a small pupil, which may be expected in uveitic eyes secondary to posterior synechiae.¹⁶ This allows the uveitis expert to view the posterior segment even when a clinical examination may be difficult. Also, the quick acquisition of the images in the current machines adds to the utility of these imaging modalities and enhances patient comfort. UWF FFA can sometimes provide excess information, and the physician should be cautious while interpreting the angiograms. A study by Laovirojjanakulet al. showed that in a cohort of uveitis patients, about 50% of the eyes had asymptomatic peripheral capillary leakage.17 This leakage did not affect the visual acuity or require any treatment. Also, FFA is an invasive, less repeatable, and less quick procedure than fundus photography or OCT. Using a fundus camera depends on a skilled photographer and may have a learning curve.

ICGA is a gold standard imaging modality for assessing choroid.¹⁸ It plays a crucial role in analyzing the choroidal inflammation and characterizes the different uveitic entities.¹⁹ Specific patterns on ICGA are diagnostic for specific uveitic entities. Choriocapillaropathies are characterized by geographic hypofluorescent "dark" patches in the late phases of the angiograms. These findings indicate hypoperfusion or nonperfusion at the level of choriocapillaris.18 Meanwhile, the typical findings in stromal choroiditis include granulomatous involvementofchoroidasseeninVKHdisease, Sympathetic ophthalmia and Birdshot choroidopathy. The ICGA shows multiple hypofluorescent dots associated with leaky stromal vessels in these diseases.²⁰ ICGA provides valuable information regarding the pathology of diseases like SLC, VKH disease and MEWDS.²¹ ICGA leads to a precise estimate of the involvement of the choroid and plays a vital role in assessing the response to therapy. Figure 4 shows the hypofluorescent lesions on wide-field ICGA in a patient with serpiginous choroiditis.



Figure 4: Left eye wide-field ICGA shows hypofluorescent lesions in a patient with serpiginous choroiditis

2.1.4 Optical Coherence Tomography:

OCT provides an optical cross-section of the various coats of the eye and is indispensable for documenting vitreous, retinal, and choroidal pathologies. Since its introduction in the 1990s, OCT has revolutionized diagnosing and managing patients with uveitis. Being a non-invasive modality, OCT has replaced FFA as the investigation of choice to document macular edema. Studies comparing FFA and OCT showed that both imaging modalities are comparable in diagnosing macular oedema.²² OCT has rapidly evolved from time-domain to Fourier domain, spectral domain and swept-source technologies. It is central to detecting and documenting macular abnormalities like macular edema and Vitreo-macular interface abnormalities in uveitic eyes.^{23,24,25} Innovations in technology, such as enhanced depth imaging (EDI), have allowed for a better understanding of the retinochoroidal involvement in posterior uveitis. Several OCT biomarkers have recently been identified to differentiate between infectious and non-infectious uveitis.²⁶ Similarly, OCT has played a crucial role in characterizing various disease entities based on typical findings and the involvement of various layers. While multiple serous detachments with bumpy RPE may be a feature of Vogt-Koyanagi Harada disease, outer retinal layer involvement on OCT may point towards diagnosing AZOOR, PIC or Serpiginous choroiditis.²⁷ Spaide et al., in 2008, introduced the concept of EDI-OCT.²⁸ It has played an essential role in studying various pathologies in the choroid. Ivernizzi et al. highlighted the role of EDI-OCT in differentiating choroidal granulomas in various uveitic entities.²⁹ It has an inherent role in monitoring uveitic entities, too. Our group established the role of EDI-OCT in monitoring the treatment response tubercular Multifocal Serpiginoid of Choroiditis.³⁰ In addition to the qualitative assessment, OCT allows quantitative in the form of various assessment (retinal measurements and choroidal thickness), aiding in monitoring the response to treatment.³¹ OCT has been primarily used to diagnose and manage uveitic entities involving the posterior segment.³² However, some authors have also studied the potential role of OCT in diagnosing and quantifying anterior segment inflammation. Agarwal et al. reported that cells in the anterior chamber could be visualized as hyper-reflective dots on OCT.33 Another innovation in the field of OCT is the ability of newer platforms to acquire scans of the peripheral retina.34 Advances in UWF imaging have now made it possible to image peripheral lesions that otherwise were not amenable to imaging previously. Another recent advance is the integration of OCT into the operating microscopes. This has revolutionized Vitreo-retinal surgery in patients with uveitis. Intra-operative OCT can assist the surgeon in identifying the pathologies at the time of surgery with precision and improve surgical outcomes.³⁵

2.1.5 Optical Coherence Tomography Angiography:

In 2015, Spaide et al. introduced OCTA, a revolutionary imaging modality that could assess the retinal and choroidal vascular functionality without injecting the dye.³⁶ OCTA allows uveitis specialists to individually study the vascular supply of various retinal layers and the choroidal circulation.³⁷ OCTA is indispensable in diagnosing and treating posterior uveitis and several retinal pathologies. This is a relatively newer, non-invasive, repeatable imaging modality that highlights blood flow in the choroid and retina without a dye. Using OCTA has led uveitis specialists to reconsider the pathogenesis of certain entities like Multiple Evanescent White Dot Syndromes (MEWDS). The OCTA in MEWDS has highlighted the relative non-involvement of choriocapillaris contrary to previous beliefs. The inflammation of photoreceptors has now been postulated as a cause of the disease.³⁸ Our group highlighted that flow deficits on OCTA corresponded to the dark areas on ICGA in patients with SLC.³⁹ We also highlighted that the quantitative assessment of the flow-deficit areas could be an essential biomarker and help

monitor patients with SLC.40 OCTA has now been used to differentiate uveitic entities and inflammatory choroidal neovascular membranes from other inflammatory lesions.⁴¹ In 2019, our group defined a new entity based on findings on OCTA in patients with Dengue maculopathy.⁴² While the older platforms could image a limited fundus area, the newer widefield OCTA has revolutionized the management of uveitis and other retinal diseases. There may be some constraints, such as difficulty capturing images due to small pupils, vitreous haze, and vitritis. With continuous technological advances, we may soon be able to overcome these hurdles. Figure 5 highlights subretinal hyper-reflective material on OCT B scan and an inflammatory CNVM on OCTA in a patient with healed choroiditis.



Figure 5: OCTA scan showing inflammatory CNVM complex in a patient with healed choroiditis, OCT B scan shows sub-retinal hyper-reflective material



3. The future: Use of Artificial Intelligence (AI)

It would be an understatement to say that "AI" is the future; the reality is that 'It' has already arrived. AI has been used in the management of a variety of retinal and uveitic entities. Integration of AI with retino-choroidal imaging modalities is the latest frontier in uveitis management. Al algorithms have been trained on vast datasets of retinal images. These can assist in the automated detection and classification of uveitic lesions. The systems can analyse and identify patterns and subtle changes that the human eye may otherwise miss. ChatGPT and other AI-driven platforms have offered exciting possibilities. By leveraging natural language processing and machine learning, these tools can provide real-time assistance to clinicians, answer queries, and even suggest differential diagnoses based on imaging findings. This synergy between imaging and AI can enhance diagnostic precision and streamline clinical workflows. LLMs can be trained to augment appropriate decision-making in the field of uveitis.43 The possible role of AI chatbots in research has also been studied.⁴⁴ Many publications have recently compared AI chatbots with uveitis specialists to establish the correct uveitis diagnosis. Carabali et al. showed that human experts were slightly superior to AI chatbots in establishing uveitis diagnosis. Regarding the adoption of Al, a surveybased study highlighted that the uveitis specialists favoured AI integration into clinical practice.⁴⁵ Another study by Carabali et al. compared two chatbots (ChatGPT 3.5 or 4.0 and Glass1.0) with uveitis experts.

While ChatGPT achieved an accuracy of 66%, Glass1.0 achieved 33% accuracy compared to the 100% accuracy achieved by uveitis experts in establishing the correct diagnosis.⁴⁶ These studies highlight that chatbots are currently less accurate in diagnosing uveitis. There are exciting possibilities for integrating chatbots into clinical practice. However, LLMs are rarely trained on uveitis-specific data. If such training can be taken up in the future, this will improve the efficiency and accuracy of AI chatbots and help them perform better. Considerations like ethical use of patient data, regulatory approvals, biases and lack of transparency may be potential hurdles in integrating AI in healthcare.

4. Conclusion

To conclude, the journey from the fundus to ChatGPT camera highlights the remarkable evolution of imaging in uveitis. Advances in technology and the introduction of newer modalities have contributed to a deeper understanding of the disease processes and effectively managing this complex condition. The uveitis experts have embraced the newer non-invasive modalities in clinical practice. Regarding the imaging modalities, UWF imaging tools have become available and are being used more commonly. The integration of AI promises to revolutionize the field further, offering new avenues for research and clinical practice. The potential of LLMs to assist uveitis specialists is immense. However, further extensive studies are required to establish the reliability and repeatability of this technology.
References:

- 1. Gupta V, Al-Dhibi HA, Arevalo JF. Retinal imaging in uveitis. Saudi J Ophthalmol. 2014;28:95-103.
- 2. Gupta V., Gupta A. Fundus photography. In: Gupta A., Gupta V., Herbort C.P., Khairallah M., editors. Uveitis text and imaging. Jaypee Brothers Medical Publishers; 2009. pp. 50–60. Chapter 4.
- 3. Dickson D, Agarwal A, Sadiq MA, et al. Assessment of vitreous haze using ultra-wide field retinal imaging. J Ophthalmic Inflamm Infect 2016; 6: 35.
- 4. Hsieh J., Honda A.F., Suarez-Faririas M. Fundus image diagnostic agreement in uveitis utilizing free and open source software. Can J Ophthalmol. 2013;48:227–234.
- 5. Marchese A, Miserocchi E, Giuffre C, et al. Aurora borealis and string of pearls in vitreoretinal lymphoma: patterns of vitreous haze. Br J Ophthalmol 2019; 103: 1656–1659.
- 6. Delori FC, Dorey CK, Staurenghi G, Arend O, Goger DG, Weiter JJ. In vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics. Invest Ophthalmol Vis Sci. 1995;36:718–29.
- 7. Yeh S, Forooghian F, Wong WT, et al. Fundus autofluorescence imaging of the white dot syndromes. Arch Ophthalmol 2010; 128: 46–56.
- 8. Ishida T, Ohno-Matsui K, Kaneko Y, et al. Fundus autofluorescence patterns in eyes with primary intraocular lymphoma. Retina. 2010;30:23-32.
- 9. Bansal R., Kulkarni P., Gupta A., Gupta V., and Dogra M. R., High-resolution spectral domain optical coherence tomography and fundus autofluorescence correlation in tubercular serpiginouslike choroiditis, Journal of Ophthalmic Inflammation and Infection. 2011;4: 157–163
- 10. Gupta A, Bansal R, Gupta V, Sharma A. Fundus autofluorescence in serpiginouslike choroiditis. Retina. 2012;32:814-825.
- 11. Meleth AD, Sen HN. Use of fundus autofluorescence in the diagnosis and management of uveitis. Int Ophthalmol Clin. 2012;52:45-54.
- 12. Atmaca L.S. Fundus changes associated with BehÇet's disease. Grafe's Arch Clin Exp Ophthalmol. 1989;227:340–344.
- 13. De Laey J.J. Fluorescein Angiography in posterior uveitis. Int Ophthalmol Clin. 1995;35:33–58.
- 14. Marchese A, Agarwal A, Moretti AG, et al. Advances in imaging of uveitis. Ther Adv Ophthalmol. 2020;12:2515841420917781.

- 15. Sheemar A, Temkar S, Takkar B, et al. Ultrawide field imaging characteristics of primary retinal vasculitis: risk factors for retinal neovascularization. Ocul Immunol Inflamm 2019; 27: 383–388.
- 16. Tripathy K, Chawla R, Venkatesh P, et al. Ultrawide field imaging in uveitic non-dilating pupils. J Ophthalmic Vis Res 2017; 12: 232–233.
- 17. Laovirojjanakul W, Acharya N, Gonzales JA. Ultra-widefield fluorescein angiography in intermediate uveitis. Ocul Immunol Inflamm 2019; 27: 356–361.
- 18. Hochheimer BF. Angiography of the retina with indocyanine green. Arch Ophthalmol. 1971;86:564–65.
- 19. Bouchenaki N, Cimino L, Auer C, Tran VT, Herbort CP. Assessement and classification of choroidal vasculitis in posterior uveitis using indocyanine green angiography. Klin Monatsbl Augenheilkd. 2002;219:243–9.
- 20. Chan CC, Ben Ezra D, Hsu SM, Palestine AG, Nussenblatt RB. Granulomas in sympathetic ophthalmia and sarcoidosis. Arch Ophthalmol. 1985;103:198–202.
- 21. Agrawal RV, Biswas J, Gunasekaran D. Indocyanine green angiography in posterior uveitis. Indian J Ophthalmol. 2013 Apr;61(4):148-59.
- 22. Tran T.H., deSmet M.D., Bodaghi B. Uveitic macular oedema: correlation between optical coherence tomography patterns with visual acuity and fluorescein angiography. Br J Ophthalmol. 2008;92:922–927
- 23. Hunter RS, Skondra D, Papaliodis G, Sobrin L. Role of OCT in the diagnosis and management of macular edema from uveitis. Semin Ophthalmol. 2012;27:236–41. doi: 10.3109/08820538.2012.708813.
- 24. Markomichelakis NN, Halkiadakis I, Pantelia E, Peponis V, Patelis A, Theodossiadis P, et al. Patterns of macular edema in patients with uveitis: qualitative and quantitative assessment using optical coherence tomography. Ophthalmology. 2004;111:946–53. doi: 10.1016/j.ophtha.2003.08.037.
- Dysli M, Rückert R, Munk MR. Differentiation of underlying pathologies of macular edema using spectral domain optical coherence tomography (SD-OCT) Ocul Immunol Inflamm. 2019;27:474– 83. doi: 10.1080/09273948.2019.1603313.



- 26. Invernizzi A, Agarwal AK, Ravera V, et al. Comparing optical coherence tomography findings in different aetiologies of infectious necrotising retinitis. Br J Ophthalmol. 2018;102(4):433-437. doi:10.1136/ bjophthalmol-2017-310210
- 27. Onal S, Tugal-Tutkun I, Neri P, Herbort CP. Optical coherence tomography imaging in uveitis. Int Ophthalmol. 2014;34:401–35. doi: 10.1007/ s10792-013-9822-7.
- 28. Spaide RF, Koizumi H, Pozonni MC. Enhanced depthimaging spectral-domain optical coherence tomography. Am J Ophthalmol. 2008;146:496– 500. doi: 10.1016/j.ajo.2008.05.032.
- 29. Invernizzi A, Mapelli C, Viola F, et al. Choroidal granulomas visualized by enhanced depth imaging optical coherence tomography. Retina. 2015;35(3):525-531. doi:10.1097/ IAE.00000000000312
- Moharana B, Bansal R, Singh R, Sharma A, Gupta V, Gupta A. Enhanced Depth Imaging by High-Resolution Spectral Domain Optical Coherence Tomography in Tubercular Multifocal Serpiginoid Choroiditis. Ocul Immunol Inflamm. 2019;27(5):781-787. doi:10.1080/09273948.20 18.1465101
- Sugar EA, Jabs DA, Altaweel MM, Lightman S, Acharya N, Vitale AT, et al. Identifying a clinically meaningful threshold for change in uveitic macular edema evaluated by optical coherence tomography. Am J Ophthalmol. 2011;152:1044–. e5. doi: 10.1016/j.ajo.2011.05.028.
- 32. Gallagher MJ, Yilmaz T, Cervantes-Castaneda RA, et al. The characteristic features of optical coherence tomography in posterior uveitis. Br J Ophthalmol 2007; 91: 1680–1685.
- 33. Agarwal A, Ashokkumar D, Jacob S, et al. High-speed optical coherence tomography for imaging anterior chamber inflammatory reaction in uveitis: clinical correlation and grading. Am J Ophthalmol 2009; 147: 413–416.e3.
- 34. Agarwal A, Ashokkumar D, Jacob S, et al. High-speed optical coherence tomography for imaging anterior chamber inflammatory reaction in uveitis: clinical correlation and grading. Am J Ophthalmol 2009; 147: 413–416.e3.
- 35. Ehlers JP, Goshe J, Dupps WJ, et al. Determination of feasibility and utility of microscope-integrated optical coherence tomography during ophthalmic surgery: the DISCOVER Study RESCAN Results. JAMA Ophthalmol 2015; 133: 1124–1132.
- 36. Spaide RF, Fujimoto JG, Waheed NK. Optical coherence tomography angiography. Retina. 2015;35:2161–2. doi: 10.1097/ IAE.00000000000881.

- Tugal-Tutkun I, Herbort CP Jr, Mantovani A, Neri P, Khairallah M. Advances and potential new developments in imaging techniques for posterior uveitis. Part 1: noninvasive imaging methods. Eye (Lond). 2021;35(1):33-51. doi:10.1038/ s41433-020-1063-1
- 38. Yannuzzi NA, Swaminathan SS, Zheng F, et al. Swept-source OCT angiography shows sparing of the choriocapillaris in multiple evanescent white dot syndrome. Ophthalmic Surg Lasers Imaging Retina 2017; 48: 69–74.
- 39. Mandadi SKR, Agarwal A, Aggarwal K, et al. Novel findings on optical coherence tomography angiography in patients with tubercular serpiginous-like choroiditis. Retina 2017; 37: 1647–1659.
- 40. Agarwal A, Corvi F, Kumar Menia N, et al. Choriocapillaris Flow Deficit in Tubercular Serpiginous-Like Choroiditis with and without Paradoxical Worsening. Ocul Immunol Inflamm. Published online November 3, 2022. doi:10.1080 /09273948.2022.2140296
- 41. Astroz P, Miere A, Mrejen S, Sekfali R, Souied EH, Jung C, et al. Optical coherence tomography angiography to distinguish choroidal neovascularization from macular inflammatory lesions in multifocal choroiditis. Retina. 2018;38:299–309. doi: 10.1097/ IAE.000000000001617.
- 42. Agarwal A, Aggarwal K, Dogra M, et al. Dengueinduced inflammatory, ischemic foveolitis and outer maculopathy: a swept-source imaging evaluation. Ophthalmol Retina 2019; 3: 170–177.
- 43. Tan Yip Ming C, Rojas-Carabali W, Cifuentes-González C, et al. The Potential Role of Large Language Models in Uveitis Care: Perspectives After ChatGPT and Bard Launch. Ocul Immunol Inflamm. Published online August 10, 2023. doi: 10.1080/09273948.2023.2242462
- 44. Sallam M. ChatGPT utility in healthcare education, research, andpractice: systematic review on the promising perspectives andvalid concerns. Healthcare (Basel). 2023;11(6):887.
- 45. Rojas-Carabali W, Cifuentes-González C, Wei X, et al. Evaluating the Diagnostic Accuracy and Management Recommendations of ChatGPT in Uveitis. Ocul Immunol Inflamm. Published online September 18, 2023.
- 46. Rojas-Carabali W, Sen A, Agarwal A, et al. Chatbots Vs. Human Experts: Evaluating Diagnostic Performance of Chatbots in Uveitis and the Perspectives on AI Adoption in Ophthalmology. Ocul Immunol Inflamm. Published online October 13, 2023. doi:10.1080/ 09273948.2023.2266730







My fortunate venture into the challenging field of uveitis was given firm roots by my respected mentor Dr.Anuradha VK(HOD Uvea services, Aravind Coimbatore).'Teaching is more than imparting knowledge; it is inspiring change. Learning is more than absorbing facts; it is acquiring understanding' - a quote I dedicate for her unconditional guidance in marking my journey in this field.

Dr. Meera Mohanakumar

Medical Consultant Medical Retina and Uvea Services Aravind Eye Hospital, Coimbatore



FFA in APMPPE

Dr. Devi Priya V Consultant Medical Retina Sankara Eye Foundation, Coimbatore

FFA in APMPPE - early hypofluorescence (blockage) corresponding to the placoid lesions followed by late, irregular hyperfluorescent staining

Early hypofluorescence represent poor perfusion of the choriocapillaris or signal attenuation from overlying outer retina and/or RPE thickening.

Late hyperfluorescence due to vascular leakage







The Tell-Tale Granuloma of Trematode Induced Uveitis

Dr. Meera Mohanakumar

Medical Consultant Medical Retina and Uvea Services Aravind Eye Hospital, Coimbatore

Trematode granuloma is a rare, yet newly recognized cause of granulomatous intraocular inflammation in children living in tropics ,caused by a presumed water born trematode infection.



Fibrillary Material Mimicking Fungal

Dr. Neethu Latiff Uvea Consultant

Giridhar Eye Institute, Kochi A case of PXF with wrinkled capsule mimicking low grade endophthalmitis.

Publishing original data but don't know where to publish: LESSONS LEARNED FROM A LIFE WITHOUT MENTORS TO GUIDE

Padmashri Prof. Amod Gupta

President US(I) 1999-2002



Padmashri Prof. Amod Gupta, MS, DSc (Hon.), FAMS Emeritus Professor Advanced Eye Centre, PGI, Chandigarh dramodgupta@gmail.com

 ${\mathcal T}$ he immediate provocation for writing this series of stories is a paper by Dr Jyoti Biswas in the Indian Journal of Ophthalmology, "Evolution of research in diagnosis and management of uveitis over four decades in India".1 He and his colleagues have summed up very elegantly the highlights of uveitis research in India from the 1990s to the present day. This is a landmark paper and will be a historical document. The stories I write in this paper are not a criticism of Dr Biswas but to highlight the challenge future researchers will face if they publish their original data/ observations in fly-by-night journals that often disappear without a trace. I quote the authors, "Studies before the 1990s predominantly consisted of case reports and epidemiological studies conducted within a tertiary hospital or an institute." If the past researchers, long gone from this earth, could be resurrected, they would also share several such stories where their original contributions, not merely 'case reports' have been lost to history.

If they are impactful, published papers are still counted as a measure of excellence. Papers fetch recognition, prestige, fame, and awards to the authors. If we intend to say something new, original, or different for the first time, we all wish to claim the priority of 'me first'. The proceedings of the Royal Society of London have been published since 1660 to settle this 'me first' claim and accord due priority, and ever since, thousands of scientific journals worldwide have continued to publish millions of original papers every year.

Although our papers do not provide the final answers, they generate new ideas, streams of thoughts, and hypotheses. Truly pathbreaking research becomes increasingly relevant with time. The half-life of poorly conducted science is very short, and up to one-third of the published papers may be stillborn, i.e., these may manage to get published but remain largely ignored by the scientific community and never get cited.

How about papers that are written and published but have not been seen? On April 5, 1884, a reader, S.A.H., posted a question to the Scientific American, a science weekly magazine published in New York, "If a tree were to fall on an uninhabited island, would there be any sound". The answer was No. Only when the vibrations of the falling tree



are perceived at our nerve centres do these become sound.

Likewise, if you publish a paper that does not get seen, read, or noticed, it simply does not exist. Further, the readers need to retrieve a full-length article or its abstract to ensure it exists. In these events, you may rather throw your paper in a trash bin than claim priority in your claims.

I lost nearly twenty of my initial academic years, needing to figure out how and where to publish my original observations. I had teachers but no mentors; perhaps they too needed mentors to guide them on where to publish their precious work. Through this write-up, I share a few stories to warn the next generation of authors to seek guidance from their mentors before embarking on a path to becoming authors.

Long before the surge of predatory journals that abound these days, publishing journals had once become a popular pastime of some eminent academic personalities in India. I believe such journals and their editors were no better than modern-day 'fly-by-night' operators. The journals and the papers they published vanished without leaving a physical or digital footprint. Even today, some novice authors fall prey to such operators who follow the pay-to-publish model.

Story # 1 of the first description of culture positive Herpetic Uveitis from India

In 1979, I published the first paper on Herpetic Uveitis from India and described the now well-known clinical signs for the first time.²

The patients were seen in 1977. The work was carried out in our institute's virology lab. We cultured HSV on the chorioallantoic membrane (C.A.M.) of 11-day-old chick embryos from aqueous humour in two of the three patients with suspected herpetic uveitis. The formation of HSV pox on the C.A.M. at 72 hours was standard virological practice in those days. None of the control aqueous samples obtained from cataract patients (n=21), healed herpetic keratitis (n=6), herpetic keratouveitis with raised I.O.P. (n=6), or acute glaucoma (n=6) were culture-positive. The following is a screenshot of the clinical signs from our paper

- (a) Evidence of past corneal herpes affection in the form of healed corneal lesions with dull sensations. Very often, these healed corneal opacities are associated with a fine pigment on the PCS (Jain, 1972).
- (b) Only a mild ciliary congestion.
- (c) Corneal oedema depending on the level of IOP.
- (d) Medium to large sized (Mutton fat) white or pigmented KPs.
- (e) Mild flare and only few cells in the anterior chamber.
- (f) Koeppe nodules at the pupillary border.
- (g) Middilated, sluggishly reacting pupil and pupillary border atrophy.
- (h) Raised intra ocular pressure.

These are classic signs of HSV uveitis described almost 45 years ago by us, for which we did not get any credit. The reason was straightforward: an error of judgment in publishing our paper in a journal that anyone worldwide would ever notice.

Anti-climax of the story: Most unfor tunately, we published it in the Eastern Archives of Ophthalmology, where it was unnoticed by the rest of the world. Remarkably, in the same year, an experimental model of HSV eye disease was reported by injecting HSV into the autonomic ganglia of rabbits. Herpetic eye disease or virus isolation was reported in 18 of the 27 animals, and 94% of the eyes developed anterior uveitis, besides conjunctivitis and dendritic ulcer.³ This study, too, went unnoticed and received just 3 citations to date. Previously, injecting



live HSV into the vitreous cavity of rabbits produced primary herpes uveitis.⁴ Just 13 citations to date led to significant work on the immunopathology of herpes uveitis that emerged following this paper.

Postscript-1: Eastern Archives of Ophthalmology, a journal edited by one of the tallest luminaries of Ophthalmology, was published by C.B.S. publishers, Darya Ganj, New Delhi. To further confound the matter, in 1973, Eastern Archives of Ophthalmology published Volume I as a book, contributed by the Asia-Pacific Academy of Ophthalmology, printed by Oriental Medical Publications, and claimed to be originally from the University of California. A total of six volumes were published till 1978. It was claimed that it was digitized in 2008.⁵ Both the books and the journal or its digitized versions have disappeared and are not retrievable.

Postscript-2: It is another matter that the Asia-Pacific Academy of Ophthalmology launched its journal named 'Asia Pacific Journal of Ophthalmology' in 2012 without any reference to its previous incarnation.⁶

Postscript-3: Dr S Choudhury, who performed the lab tests, had been trained in Germany and was so excited by the results of our study that he wrote a big grant to expand the work. The then H.O.D. of the Virology department refused to forward the project. Disgusted, Dr. Choudhury decided to leave the institute, and I lost contact with him. No wonder path-breaking research is a significant challenge in India.

Story # 2 of a case of HSV uveitis we followed for 22 years⁷

This article is searchable on Scopus and a Weblink, but no abstract/ full text⁸ is available.

The male patient had been seen at the age of 20 years with a dendritic ulcer in his left eye. His records in our department revealed that the ulcer healed with two weeks of idoxuridine (I.D.U.) therapy, the only topical antiviral available in 1968. Nine years later, this patient was seen by me in March 1977 with acute uveitis with mid-dilated pupil, granulomatous K.P.s, and 7-8 Koeppe nodules. The I.O.P. was 29mm of Hg. He had dull corneal sensations. He is one of the patients described above in whom we had grown HSV pox on C.A.M. of chick embryo described in Story #1. He was treated with I.D.U., topical corticosteroids, and Diamox. His I.O.P. and inflammation resolved in one week, albeit with focal iris atrophy. He was next seen in 1982 with an episode of hypertensive uveitis and subsequently had 6 more recurrences of uveitis. In Nov.1989, I saw him with a large geographical ulcer following treatment elsewhere with topical steroids. By this time, topical acyclovir ointment was available, and despite its use, it evolved into a meta herpetic ulcer that necessitated a bandage contact lens. Eventually, it healed, gaining a visual acuity of 6/12 in this eye.

This was perhaps the longest-ever followup of an HSV culture-positive patient with a complete spectrum of ocular herpes disease ever reported in the literature, but it was lost to the world because we fell into the trap of submitting this case to another fly-by-night journal.

Story # 3 of HLA B 27+ Acute anterior uveitis

Association of HL-A27 with acute anterior uveitis was first noted by D.A. Brewerton in 1973.9 Until then, nearly 90% of patients with Ankylosing spondylitis had been noted to have HL-A27 versus 4-5% of the Caucasian population. Brewerton et al. first found HL-A27 in 55% of the 44 Caucasian patients with acute anterior uveitis versus 4% of normal controls.9 In the same issue of Lancet, Brewerton et al. reported that 25 of the 33 (75%) patients with Reiter's disease had HL- A27 positive versus 3 of 33 with non-specific urethritis and 2 of 33 normal controls. Soon after, a Greek study found HLA-B27 in 12 out of 33 (36.36%) patients with acute non-granulomatous anterior



uveitis vs. 4.72% in controls.¹⁰

My chief, Dr I S Jain, published the firstever report on the association of HLA B27 with acute anterior uveitis in the Indian population.¹¹ Unfortunately, this paper is not retrievable from the journal's website. However, the article's abstract, published in the Bull P.G.I., is still available.¹²

They reported 24 cases (22 Males) of uveitis with ankylosing spondylitis. Nearly half of the patients were in the age group of 31-40 years. Male female ratio was 22:2. Significantly in 18 of the 24 patients, the sentinel sign of Ankylosing spondylitis was acute uveitis. Ankylosing spondylitis was diagnosed later. Anterior uveitis was present in 87.5% and panuveitis in 12.5% of cases. HLA. phenotyping was done in 14 cases of uveitis with ankylosing spondylitis and compared with patients with only ankylosing spondylitis and normal controls. HLA-B 27 was present in 3.3% of control, 94% in ankylosing spondylitis, and 100% in uveitis with ankylosing spondylitis. The difference was found to be statistically highly significant.

I expanded the series from 24 to 44 patients. $^{\rm 13}$

I share screenshots of some of the salient features we described in the 1984 paper.

Recurrence

Twenty of the 44 patients (45.9 per cent) had recurrent uveitis in either the same eye or the other eye at intervals varying from eight months to 18years (average 3.5 years). Majority of the patients, however, suffered recurrence within one to two years.

Onset of uveitis

The onset of uveitis was acute and dramatic in 40 patients and subacute in four. All patients had unilateral uveitis at the onset and the other eye became involved in 15 patients (34 per cent) at an interval varying from one to 18 years (average four years).

Clinical signs

In the first attack of uveitis, visual acuity was reduced to hand motions counting fingers. At least in three patients, light projection was inaccurate. The recurrent attacks of uveitis, however, were less dramatic at the onset and visual acuity was always 6/24 or better. Uveitis was characterized by a marked ciliary injection, a heavy aqueous flare and cells in all the cases. Nearly one-third of the eyes presented with a fibrinous exudative reactions in the anterior chamber. Fine keratic precipitates were seen in 61.4 per cent of cases. Other clinical signs noted were tenous posterior synechiae (69.2 per cent) hyphaema (4.54 per cent) hypopyon (2.27 per cent) vitreous cells (29.5 per cent) macular oedema (22.2 per cent) and hypotony (43.2 per cent).

The readers will note that the clinical signs and pattern of uveitis in HLA B27+ uveitis have remained the same in the last 40 years since our pioneering studies from India.

Postscript-1: A new guarterly journal, "Afro-Asian Journal of Ophthalmology", was launched on June 1, 1982. It was edited by the then most well-known luminaries of Indian Ophthalmologists (I will let the readers quess the names!) with an announcement by Dr John H Dobree, a renowned name in the field of Retina (He contributed to volume 10, diseases of the Retina and Vitreous, System of Ophthalmology by Sir Stewart Duke-Elder in 1967) in the March 1983 issue of the Br J Ophthalmology. With these credentials, anyone would fall prey and submit their original observations to the journal. Only years later, we realized, to our horror, that the journal with our precious papers had vanished without a trace. Among several other papers that I lost to this journal, my biggest regret is that a still unresolved, mysterious case of my life also got sacrificed at the altar of this journal. This was a young girl who had frequent episodes of bloody sweat oozing out of the skin of her lids even while we watched. The skin biopsy showed extravascular red blood cells but without any pathology accounting for it.14



Story # 4 of the first description of T.B. uveitis from India, which accrued us no credit

Most people worldwide identify me and my group with TB Serpiginous-like choroiditis (2003) and other manifestations of intraocular tuberculosis. It was believed then, for good reasons, that uveitis is rarely seen in patients with active pulmonary tuberculosis. I want to share our 10-year data (1977-1986) of 16 patients with active pulmonary tuberculosis who developed uveitis during their disease. I presented this data at the Xth Asia-Pacific Academy of Ophthalmology meeting held in Kuala Lumpur in 1987 in an almost empty hall where it went unnoticed. Unfortunately, we published our paper in Bull P.G.I. in 1987.¹⁵, and it was also lost to the rest of the world.

Of these 16 patients (10 men and 6 women), five had pulmonary T.B., three had cervical T.B. lymphadenitis, and eight had hilar lymphadenitis with pulmonary infiltrates. All patients were either sputumpositive or histopathology-positive for MTB. All patients had an Mx test +>10mm, and 11 of 16 had \geq 35mm. These were the times when hardly anybody in the world, and least in India, believed that TB was the cause of uveitis. Fourteen patients had bilateral involvement. Twenty-two eyes showed granulomatous uveitis, while eight eyes showed a non-granulomatous pattern. The clinical signs included mutton fat K.P.s (n=22), small to medium K.P.s broad-based synechiae (n=8), (n=14), multiple fine synechiae (n=16), Koeppe and Busaca's nodules (n=8), choroiditis (n=14; central in 2, 1-2 lesions in 6 and >2 in 8), exudative retinal detachment (n=4). All patients received the then-standard anti-TB drugs, including Inj Streptomycin, isonex, rifampicin, ethambutol, and thioacetazone. They did not receive oral corticosteroids but, when needed, were given periocular steroids in addition to topical steroids and atropine. Interestingly, as a classic example of 'eyes don't see what the mind does not know',

we did not see any case of periphlebitis or serpiginous-like choroiditis.

Postscript-1: Bulletin, Post Graduate Institute of Medical Educational and Research began in 1966 (The official website claims it started in 1970) as an in-house quarterly journal to publish preliminary reports of research, editorials, review articles, etc. by the faculty and students at the institute. In 2012, it appeared in a new incarnation as 'Journal of Postgraduate Medicine, Education and Research (JPMER)'. Since 2012, it has been an open-access journal published by Jaypee Brothers, New Delhi. Contents before 2012 are not retrievable. To date, contents are not searchable on PubMed. You might throw your manuscript into the waste basket if others cannot retrieve the content.

Postscript-2: Although this work did not fetch us any recognition, it led to my highly productive collaboration for the next more than 20 years with Prof Pradeep Bambery, Professor of Medicine and a rheumatologist at our institute, who suggested that we start looking for evidence of MTB infection and not necessarily a clinical TB disease in our patients with uveitis. Rest, as they say, is history.

Epilogue-1: Let me end this series of my untold stories with an interesting an ecdote from the pre-internet and the quick spell-check era. In 1992, we published the first-ever reported case of retinal pigment epitheliopathy and retinal vasculitis caused by microfilaria.¹⁶ In our manuscript, while we correctly spelt the name of the microfilaria as 'Wuchereria bancrofti', the reviewer/ editor of Acta Ophthalmologica insisted that we had spelt it incorrectly and if we wished to have our paper published, we had to spell it their way, 'Wucheria Bancrofti'. See reference 15 for the funny spellings. The to-and-fro correspondence with the editors in the snail mail era can only be imagined. Dr. Anita Agarwal, my student then, even suggested that we withdraw our paper from



the journal if the editors insisted on using the wrong terminology. Not with standing the incorrect spellings, it fetched at least 10 citations, including a recent paper by Dr Jyoti Biswas and in the prestigious "Whitcup and Nusseblatt's Uveitis: Fundamentals and Clinical Practice" edited by Whitcup SM, Sen HN and Palestine A in 2021.

References:

- 1. Biswas J, Jadhav S, Eswaran BV. Evolution of research in diagnosis and management of uveitis over four decades in India. Indian J Ophthalmol 2024;72:809-15.
- Gangwar DN, Jain IS, Gupta Amod, Choudhury S, Pal SR. Herpetic uveitis. East Arch Ophthalmol 1979; 7:104-109). (Please note, it is not abstracted by PubMed but available on Scopus as a reference)
- Mintsioulis G, Dawson CR, Oh JO, Briones O. Herpetic eye disease in rabbits after inoculation of autonomic ganglia. Arch Ophthalmol. 1979 Aug;97(8):1515-7. doi: 10.1001/ archopht.1979.01020020177019. PMID: 223532.
- 4. Oh JO. Primary and secondary herpes simplex uveitis in rabbits. Surv Ophthalmol. 1976 Sep-Oct;21(2):178-84. doi: 10.1016/0039-6257(76)90097-7. PMID: 185739.
- 5. (https://www.google.co.in/books/edition/_/Li-FA AAAIAAJ?hl=en&sa=X&ved=2ahUKEwjA6Mj0k 60HAxWAQ2cHHVIjAOsQ7_IDegQIDxAD)
- Lam DS, Ritch R, Rao SK, Leung CK. Aspire to Inspire: The Launch of the Asia-Pacific Journal of Ophthalmology. Asia Pac J Ophthalmol (Phila). 2012 Jan-Feb;1(1):1-2. doi: 10.1097/ APO.0b013e3182413b60. PMID: 26107008.
- 7. Gupta A, Khandalawala B. Disease spectrum in

a case of ocular herpes: Twenty-two year follow up. Afro-Asian J Ophthalmol IX Dec 1990; 93-94.

- 8. https://experts.nebraska.edu/en/publications/ disease-spectrum-in-a-case-of-ocular-herpestwenty-two-years-foll
- Brewerton DA, Caffrey M, Nicholls A, Walters D, James DC. Acute anterior uveitis and HL-A 27. Lancet. 1973 Nov 3;302(7836):994-6. doi: 10.1016/s0140-6736(73)91090-8. PMID: 4127279.
- Zervas J, Tsokos G, Papadakis G, Kabouklis E, Papadopoulos D. HLA-B27 frequency in Greek patients with acute anterior uveitis. Br J Ophthalmol. 1977 Nov;61(11):699-701. doi: 10.1136/bjo.61.11.699. PMID: 563238; PMCID: PMC1043100.
- Sen Gupta, S., Jain, I.S., Jain, G.C., Deodhar, S.D. 1979. HLA antigens in acute anterior uveitis in North Indians. Indi-an Journal of Ophthalmology; 26(4): 26-29.
- 12. Jain, I.S., Jain, G.C., Sen Gupta, S. 1979 Uveitis and ankylosing spondylitis. Bulletin, Postgraduate Institute of Medi-cal Education and Research, Chandigarh. 13(3), pp. 140-145.
- 13. Jain IS, Gupta A, Dogra MR, Singh S. 1984. Uveitis with ankylosing spondylitis. Afro-Asian J Ophthalmol vol III, pp62-63.
- Gupta, A., Grewal, S.P.S., Khandalvala, B. Idiopathic episodic palpebral hemorrhage: An enigma.1992. Afro-Asian Journal of Ophthalmology, 11 (3), pp. 223-225.
- 15. Jain IS, Ram J Gupta A. Tubercular UveitisBull. P.G.I.,21, Special issue, 1987, pp 45-48.
- Gupta A, Agarwal A, Dogra MR. Retinal involvement in Wucheria bancrofti filariasis. Acta Ophthalmol (Copenh). 1992 Dec;70(6):832-5. doi: 10.1111/j.1755-3768.1992.tb04896.x. PMID: 1488896.





Dr. Rajeev Gupta Consultant Vitreoretina and Uvea Sangam Netralaya, Mohali



The Eklavyas of uveitis

Dr. Shahana Mazumdar

Consultant Retina and Uvea, ICARE Eye Hospital and PG Institute, Noida

Prof Amod Gupta is the doyen of uveitis and for us Indians- the Drona of uveitis. And being Drona to the (PGI) Pandav-GIs he has of course superbly trained the Arjuns and Yudhishthirs whom we all know very well. But where there is a Drona-there will always be an Eklavya...or even many Eklavyas!

Cut to a long-ago meeting, maybe 2008- when I was so intrigued by an 'Entire conference on Uveitis!!!' at Hyderabad that I decided to attend it. As I entered the small classroom like hall, I noticed that the attendance was pretty thin with little fanfare and trappings of an AIOC that I started thinking what had I got myself into! The misgivings only lasted till I heard the first lecture by Sir- which had me completely riveted! I was stunned...at his grasp of the subject, his enthusiasm, logic, curiosity that I couldnt get enough! I was completely hooked.

From then on, I would scour every conference to see if sir was speaking and attend it for sure. And this is how I fell in love with uveitis and learnt it vicariously (like Eklavya). I lapped up every word, hunted him down with all my questions, sent him email after email with queries about patients or sent the patients to him. He not only gave the answer but taught me how to think.

On sharing my Eklavya status- I found that I was not alone! In fact, there were so many-that dare I say we by ourselves could have beaten the kauravs!

On behalf of Dr Soumavya Basu and myself and all the eklavyas

Heartfelt and Handmade

Lost and Found

This section contains the full text of the irretrievable articles mentioned in "Publishing original data but don't know where to publish: Lessons learned from a life without mentors to guide" by **Prof. Amod Gupta.**



East. Arch. Ophthal., 7 : (1979) 104-109

HERPETIC UVEITIS

D.N. GANGWAR, I.S. JAIN, AMOD GUPTA, S. CHOUDHURY* AND S.R. PAUL*

Postgraduate Institute of Medical Education and Research, Chandigarh-160012. (INDIA)

Summary :— A group of three patients of presumed herpetic uveitis with raised intra ocular pressure were studied. Clinical picture of granulomatous uveitis due to replicating HSV as shown by positive aqueous culture in 2 out of 3 patients has been described. The pathogenesis of herpetic uveitis in the light of current literature is discussed. An interesting observation following paracentasis in the relief of uveitis and control of tension has been made.

Keywords :- Herpetic Uveitis.

The occurence of iridocyclitis in association with active herpetic keratitis is well known. Almost all cases of herpetic epithelial disease are accompanied by a uveal reaction in the form of a mild aqueous flare and cellular reaction without any keratic precipitates (KPs) (Thygeson, 1957). Stromal keratitis on the other hand, may be associated with a severe uveal reaction in the form of ciliary injection, heavy aqueous flare, medium sized KPs and in about 50% of these cases intra ocular pressure (IOP) is raised (Thygeson, 1957). However, uveitis may also occur in the absence of any active corneal lesion. Clinical picture of such cases has varied from non-specific acute iridocyclitis, haemorrhagic iridocyclitis, recurrent iridocyclitis to hypersensitive uveitis (Favalaro, 1949; Cavara, 1954; Hewson, 1957; Postic and Jelesic, 1958. Pavan-Langston, 1969; Bock, 1972; and Dhir et al, 1974).

Material and Methods

We studied clinical picture and course

Departments of Ophthalmology and Virology.

of the disease in three patients of presumed herpetic uveitis and aqueous humour was cultured for isolation of HSV. Simultaneously, a control blind study was undertaken to find out if the HSV could be isolated from aqueous humour of normal human eyes, healed herpetic keratitis, acute herpetic keratouveitis with ocular hypertension, and acute glaucoma. All patients studied were selected at random. For the control study following groups were made :—

- (a) Normal control: 21 patients of mature senile cataract without any evidence of past ocular disease.
- (b) Healed herpetic keratitis: 6 patients.
- (c) Acute herpetic keratouveitis with ocular hypertension : 6 patients.
- (d) Acute glaucoma : 6 patients.

0.25 ml. of aqueous was aspirated into a sterile syringe through a paracentasis incision and transferred to a vial contain-



GANGWAR ET AL

Vol. 7, May 1979

ing Hank's balanced salt solution with 0.5% geletin and transported immediately to the laboratory in an ice-flask and stored at -70°C. Culture for HSV was done on the chorio-allantoic membrane (CAM) of eleven days old chick embryo and membranes examined for the presence of HSV specific pocks after 72 hours of incubation.

Results

Results are shown in Table I.

- A. Presumed herpetic uveitis : HSV could be isolated in two out of three patients.
- B. Controls : In none of the samples, HSV could be isolated.

fluoresceint. Corneal sensations were dull. Posterior corneal surface (PCS) was studded with medium to large sized K Ps. sluggishly Pupil was middilaled and reaction Pupillary border showed 7-8 koeppe nodules. Mild flare was present. Fundus showed macular oedema. Tension Schiotz was 29 mm. of Hg. Clinical diagnosis was granulomatous uveitis of suspected herpetic actiology. He was put on local Betnesol, atropine, and IDU drops thrice a day, in addition to Tab. Diamox thrice a day. Two days later, his IOP in the affected eye was 12 mm. of Hg. but the rest of the ocular condition was same as before.

Paracentesis of the affected eye was done on 25.3.77 and HSV could be isolated from the aqueous humour.

	Table I
To show results	of HSV isolation from aqueous humour on chick embryo in various groups

	Group	Eyes	Positive HSV isolation
1.	Presumed herpetic uveitis	3	2
2.	Healed herpetic keratitis	6	Nil
3.	Active herpetic kerato-uveitis with ocular hypertension	6	Nil
4.	Acute Glaucoma	6	Nil
5.	Normal control (senile cataract)	21	Nil

Case Reports

Salient clinical features and result of treatment are shown in Table II.

Case 1

B.S. 20 years male, was seen by us with 2 weeks history of pain, redness, watering and diminution of vision from left eye. 9 years earlier, he had been treated by us for herpetic keratitis in the left eye and had not sufferred any recurrence in the intervening period.

On examination, right eye was normal. Left eye visual acuity was 6/12 unaided. Mild ciliary congestion was present. Cornea showed fine nebular opacity in the pupillary area, which did not stain with Post-operatively, Diamox was stopped and only local therapy continued. Within 2 days of paracentasis, koeppe nodules disappeared, KPs were much less in number and became pigmented with crenated borders. Macular oedema had almost subsided. Tension Schiotz was 7 mm. of Hg. Subsequently, this eye has remained quiet with 6/9 vision. A few old fine pigmented KPs are present and pupillary border shows atrophy from 2 to 5 O'clock. Tension Schiotz at the last followup 3 months later, was 12 mm. of Hg. A repeat paracentasis at this stage was not successful for the isolation of HSV.

Cass 2

105

S.K. 29 years male came to us on



East. Arch. Ophthal.

HERPETIC UVEITIS

	T	abl	le	п
--	---	-----	----	---

w	result of treatment in herpetic granulomatous	uvenus
To show salient clinical features and	result of design	1.20

Patient Age and Sex	BS 20 M	SK 29 M	38 M
Salient clinical signs : Visual acuity in the affected eye Corneal lesion Keratic precipitates Flare Koeppe nodules Pupil Iris Fundus Intraocular pressure (Schiotz mm of Hg)	6/12 Healed herpetic Medium to large size white Mild 6-8 Mid dilated sluggish reaction Sphincteric atrophy Macular oedema	6/36 Healed herpetic Medium to large pigmented Mild 3-4 Dilated fixed Sphincteric atrophy Macular oedema	6/24 Healed herpetic Medium to large white Mild Nil Mid dilated fixed Posterior synechiae Nil 35
Paracentasis : Intraocular pressure response (a) Immediate (b) Late HSV isolation Final result : Inflammation Intraocular pressure	controlled + controlled Normal	raised controlled controlled Normal	raised controlled +

Absconded. No follow up available.

4.4.77 with 10 days history of pain, redness and watering from left eye for which he was using IDU drops one hourly without any relief. 11 years earlier, he had been treated for herpetic keratitis in the same eye. On examination, his right eye was normal. Left eye visual acuity was 6/36 unaided. Mild ciliary congestion was present. Cornea showed a nebular opacity in the lower half. Corneal sensations were dull. PCS was studded with multiple medium to large sized KPs, heavily pigmented and more numerous in the lower third of cornea. Pupil was dilated and fixed and showed spincteric atrophy from 1 to 6° clock. 3-4 Koeppe nodules were seen from 9 to 11° clock. Mild aqueous flare and few cells were present in the anterior chamber. Lens showed posterior cortical changes. Fundus revealed macular oedema. Tension Schiotz

was 29 mm of Hg. He was diagnosed as a case of granulomatous uveitis of presumed herpetic etiology. He was put on local Betnesol and atropine.

CNI

Paracentasis was done on 5.4.77 but HSV could not be isolated from the aqueous.

2 days later, tension was still 29 mm of Hg. (Schiotz). KPs had decreased in number but Koeppe nodules were still present. Tab Diamox one tab. 6 hourly was started. In next 2 days the tension was reduced to 10 mm of Hg. (Schiotz). Only mild flare and cells persisted and Koeppe nodules disappeared. On 5th day Diamox was ommited. 2 weeks later, his vision had improved to 6/12. PCS showed only fine pigment. Ocular tension was 10 mm.



Case 3

S.N. 38 years male, was admitted on 2.6.77 with history of redness in left eye 7 years back and complained of diminution of vision in this eye for the last 2-3 years.

On examination, right eye visual acuity was 6/12 unaided and showed few nebular corneal opacities. Corneal sensations were dull. Left eye visual acuity was 6/24 unaided. Cornea showed multiple fine nebulae with dull sensations. PCS was studded with medium sized white KPs. Pupil was middilated with multiple posterior synechiae. Only mild flare was present. Tension in this eye was 35 mm. of Hg. (Schiotz). He was diagnosed as a case of presumed herpetic uveitis in left eye.

Paracentasis was done on 3.6.77 and HSV isolation was positive.

Next day to paracentasis, ocular tension was very high (51 mm of Hg. Schiotz), with moderate corneal oedema, though KPs had regressed. He was put on Tab. Diamox 6 hourly and within next 3 days, tension came to normal. KPs had almost disappeared and only a minimum flare was present. 2 days later, patient abscomded and did not report for follow up.

Comments

Uveitis associated with active herpetic keratitis poses no difficulty for etiological diagnosis. But in the absence of active corneal lesion, uveitis is a definite diagnostic problem. There is fairly a close resemblence in the clinical picture of all of our three patients. The first two patients presented with complaints of mild pain, redness and watering for the first time after suffering from herpetic keratitis in the past. In the 3rd case, symptoms were so mild that he was unaware of the onset of the uveitis process, though he showed a strong evidence of old corneal herpes. Clinically, all the three patients were diagnosed as cases of granulomatous uveitis with ocular hypertension of presumed herpetic etiology. In 2 of these

patients herpetic etiology of the granulomatous uveitis was confirmed by isolation of HSV on CAM of chick embryo. The three cases reported by Dhir et al (1974) had also nearly a similar presentation.

No definite clinical picture of herpetic uveitis is described in literature. In case of recurrent herpetic uveitis, onset is saids to be usually abrupt and accompa nied by a high rise of IOP. Course of di^Sease is often prolonged and cells and flare persist in the anterior chamber for months after subsidence of acute symptoms (O'Connnor, 1976). On the other hand Sugar (1971) suspects his cases of herpetic uveitis without active keratitis, when the cornea is anaesthetic, but the eye is painfull because of raised IOP rapid deposition of KPs and ease with which they resolve following use of steroid drops.

We believe, that the herpetic uveitis patients, where in viral replication is responsible for the inflammatory process presents features of granulomatous uvitis with raised IOP. This is in contradistinction to an acute non-granulomatous type of herpetic uveitis where a hypersestive reaction to the virus is implicated (Duke-Elder, 1966). From the study of our own patients we find the following clinical signs helpful in suspecting a granulomatous herpetic uveitis :--

- (a) Evidence of past corneal herpes affection in the form of healed corneal lesions with dull sensations. Very often, these healed corneal opacities are associated with a fine pigment on the PCS (Jain, 1972).
- (b) Only a mild ciliary congestion.
- (c) Corneal oedema depending on the level of IOP.
- (d) Medium to large sized (Mutton fat) white or pigmented KPs.
- (e) Mild flare and only few cells in the anterior chamber.
- (f) Koeppe nodules at the pupillary border.
- (g) Middilated, sluggishly reacting pupil and pupillary border atrophy.



East. Arch. Ophthal.

HERPETIC UVEITIS

(h) Raised intra ocular pressure.

Of these sight, evidence of past herpetic keratitis is of prime importance and any uveitis in such a patient should be considered herpetic unless proved otherwise (Pavanlangston, 1975).

Presence of a middilated, sluggishly reacting or fixed pupil is another important observation in such cases and has been noted clinically (Dhir et al, 1974) as well as in experimental work (Tokomaru and Wilentz, 1975). Response to paracentasis in these patients is interesting. Intially, the response may be unpredictable, as we found in 2 of our patients where the IOP either remained unaltered or increased following paracentasis. This rise of IOP, however, could be easily and permanently controlled with Diamox therapy for 3-5 days. Paracentasis did help in greatly reducing the number of KPs which became pigmented and crenated. Koeppe nodules disappeared and aqueous flare and cells minimized within 48 hours of paracentasis. Within a week, the inflammation had almost subsided and IOP normalised. Similar reduction in the severity of herpetic keratouveitis was observed by Jones et al (1968).

Pathogenesis of herpetic uveitis remains speculative (O 'Connor, 1976). Some workers have been able to isolate HSV from non-specific iridocyclitis (Cavara, whereas others (Thygeson and 1954) Kimura, 1957 and Kimura, 1962) have not succeeded in doing so in presumed herpetic uveitis. It is again controversial whether replication of virus or hypersensitive reaction to its antigen is responsible for the uveitis process, despite the fact that the virus has been demonstrated in the uveal tissues of such a patient (Witmer and Iwomoto, 1968).

Invasion of the uvea by HSV sensitizes this tissue. In any future attack by the virus, the local immune mechanism in the uvea would fix the virus and produce a hypersensitive type of uveitis. Isolation of HSV from the aqueous humour of such cases would be impossible using routine procedures. A similar mechanism may exist for the uveitis process associated with severe herpetic keratitis, which explains why we were unable to isolate HSV from the aqueous humour of any of the 6 cases of acute herpetic keratouveitis.

Isolation of HSV from 2 out of 3 cases of presumed herpetic uveitis, who showed features of granulomatous uveitis is strongly suggestive of a replicating HSV responsible for the inflammatory process in these patients. We have observed first attack of uveitis (history was definite in first two patients) who had sufferred from herpetic keratitis in the same eye in the past. Obviously, the uveal tissues in these patients were not sensitized to the HSV antigen. Uveal tissues in all eyes suffering from herpetic keratitis may not become sensitized as Patterson et al (1968) were able to demonstrate HSV antigen in the aqueous humour of only 2 out of 6 eyes suffering from herpetic keratitis. Our hypothesis is amply supported by an experimental work (Oh, 1976) where the author was able to isolate HSV from uvea and vitreous of most of the eyes of Primary herpetic uveitis but none of the eyes of secondary herpetic uveitis. Pathological studies of herpes simplex keratitis have shown a granulomatous reaction around the Descemet's membrane (Green and Zimmerman, 1967). This further supports our observation that HSV can produce a granulomatous reaction in eyes which have not been sensitized previously by HSV antigen. Isolation of HSV in a case of recurrent iridocyclitis (Bock et al, 1972) may be explained by the inability of the sensitized uvea to fix the invading virus due to a low immune competence.

From our study, we feel that the primary attacks of HSV uveitis show features of granulomatous reaction whereas in the subsequent attacks the clinical picture would change to an non-granulomatous type of uveitis. Clinically, these patients would also be considered as cases of herpetic uveitis though with a different clinical picture. This would also explain why some workers have failed to isolate the virus despite a strong clinical suspicion of herpetic aetiology.

GANGWAR ET AL

Vol. 7, May 1979

One possibility which has not been considered seriously is the chance isolation of HSV in cases of uveitis. Trigeminal ganglia have been shown to be the site of latent HSV (Barringer and Swoveland, 1973; Bastian et al, 1972). Surgical stimulation of trigeminal ganglia in infected animals has lead to peripheral shedding of HSV in 80% of animals (Nesburn, 1976). Thus it may be speculated that under conditions of stress, there might be

a stimulus for the virus to travel down the ciliary nerves into the uvea and the aqueous humour. In the control group studies we have not been able to isolate HSV either from the normal aqueous humour of patients undergoing senile cataract surgery or from patients of healed herpetic keratitis, acute herpetic keratouveitis and acute glaucoma, where a condition of ocular stress exists.

REFERENCES

- Baringer, J. and Swoveland, P. (1973) N. Engl. J. Med. 288 : 648.
- Bastian, F.O., Rabson, A.S., Yee, C.L. and Tralka, T.S. (1972) – Science, 178 : 306.
- Bock, J., Fanta, J., Soltz-Szots, C. Zehetbaver, G. and Gebhart, W. (1972) – Arch. Klin. Exp. Ophthal. 185 : 349.

Cavara, V. (1954)-Concilium Ophthal. 2: 1232.

- Dhir, S.P., Jain, I.S., Schgal, S. and Paul, S.R. (1974)-East. Arch. Ophthal 2:255.
- uke Elder. S. and Perkins, E.S. (1966)-System of Ophthalmology, Vol. 1X, Henry Kimpton, London, p. 336.
- Favalaro (1949)—Atti Cong. Soc. Oftal. Ital. 11:3.
- Green, W.R. and Zimmerman, L.E. (1967)-Amer. J. Ophthal. 64: 555.
- Hewson, G.E. (1957) Irish. J. Med. Sci. 6: 372.

Jain, I.S. (1972)-Personal communication.

- Jones, B.R., Patterson, A. and Rice, N.S.C. (1968) - Trans. Ophthal, Soc. U.K. 88 : 235.
- Kimura, S.J. (1962)-Trans. Am. Ophthal. Soc. 60: 440.

- Nesburn, A.B., Cook, M.L. and Steven, J.G. (1972)-Arch. Ophthalmol. 88: 412.
- Nesburn, A.B., Dickinson, R., Rad Noti, M. and Green M.J. (1976)-Surv. Ophthalmol. 21: 185.
- O'Connor, G.R. (1976)-Surv. Ophthal. 21: 165.
- Oh, J.O. (1976)-Surv. Ophthal. 21 : 178.
- Patterson, A., Somerville, R.G. and Jones, B.R. (1968) – Trans. Ophth. Soc., U.K. 88: 243.
- Pavan-Langston, D. and Brockhurst, R. (1969)-Arch. Ophthalmol. 81: 783.
- Pavan Langstan, D. (1975)-Int. Ophth. Clin. 15(4): 31.
- Postic and Jelesic (1958)-Bull. Soc. Franc. Ophthal. 71: 202.
- Sugar, H.S. (1971)-Ann. Ophthal. 3: 356.
- Thygeson, P. and Kimura, S.J. (1957) Amer. J. Ophthal. 43: 109.
- Thygeson, P., Hogan, M.J. and Kimura, S.J. (1957)-Trans. Am. Ophthalmol. Soc. 55: 333.
- Tokomaru, T. and Wilentz, J. (1975)-Canad. J. Ophthalmol. 10: 193.
- Witmer, R. and Iwamoto, T. (1968)—Arch. Ophthal. 79: 331.

Afro-Asian J. Ophthatmol. IX Dec. 1990

DISEASE SPECTRUM IN A CASE OF OCULAR HERPES : TWENTY TWO YEARS FOLLOW UP

-Amod Gupta and Birgit Khandalavala Department of Ophthalmology, Postgraduate Institute of Medical, Education and Research, Chandigarh 160 012, India

ABSTRACT

A 42 year old male was seen twenty two years ago when he presented with herpes simplex keratitis of the left eye. Nine years later, he presented with uveitis and aqueous tap was cultured for the virus which was isolated on chorioallantoic chick membrane. During the subsequent twelve years he had recurrent bouts of uveits, with and without hypertension, unassociated with keratitis. In 1989, he presented with a geographical corneal ulcer which evolved on treatment into a metaherpetic ulcer. The final visual acuity in the involved eye is 6/12. There has been no involvement of the fellow eye. It is interesting that no episode of uveitis or keratitis coexisted together. The factors responsible for recurrences and their morphology remain speculative.

Key words : Herpes simplex keratitis, uveitis, metaherpetic uveitis, geographical corneal ulcer.

Herpes simplex keratitis is the single most frequent cause of corneal pathology resulting in considerable visual impairment. Active infection with replicating virus is responsible for the production of dendritic and geographical epithelial ulceration, while infection and immunity are responsible for stromal and uveal disease. Abnormal tear function, decreased corneal sensation and antiviral toxicity may all contribute to the development of post infectious ulceration.¹ We report the entire spectrum in a patient observed over twenty two years.

CASE REPORT

A 42 years old male first presented in January 1968 when he was 20 years old with a dentritic epithelial ulcer in the left eye. He recovered uneventfully within two weeks of Idoxuridine therapy, leaving a cantral nebular opacity.

Correspondence to : Dr Amod Gupta, Additional Professor and Head Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012 India Nine years later, in March 1977, he was seen with pain and redness in the left eye. On examination, the right eye was normal. Visual acuity was 6/12 in the affected eye. Mild ciliary congestion was present. Cornea showed a faint opacity which did not stain with fluorescein. Corneal sensations were dull. Posterior corneal surface was studded with medium to large sized keratic precipitates. Pupil was mid-dilated, sluggish in reaction and showed 7.8 Koeppe's nodules. Mild aqueous flare was noted. The intraocular presure was 29mm of Hg. Topical corticosteroids and Idoxuridine with tablet Acetazolamide thrice a day was instituted. The intraocular pressure normalized within two days. Paracentesis of the affected eye was performed on 25.3.1977 and herpes simplex virus was isolated on chorioallantoic membrane of eleven day old chick embryo. The uveitis settled in a week's time with maintenance of normal intraocular pressure and residual iris atrophy.

In March 1982 five years later, the patient had a recurrence of hypertensive uveitis in the same eye and was managed with topical steroids alone. Subsequently, he had six episodes of recurrent uveitis in the same eye with or without hypertension and responded to topical steroids each time.

In November 1989, he presented with a large geographical defect with underlying stromal inflammation (Fig 1). He had been treated elsewber the the previous two weeks with topical steroids alone. There was no associated uveitis. After ten days of treatment with topical Acylovir olatment five times a day, the lesion evolved into a metakerpetic ulcer. A soft bandage conteclens was inserted, but an initial improvement was followed by recarreninfective lesion necessitating lens removal and institution of topical antivini therapy. Two weeks later, the ulcer had healed (Fig. 2) and the antiviril







Fig 1. Initial presentation of the patient at the most recent recurrence showing a large central, fluorescein-staining geographical ulcer. medication was tapered off. He achieved a final visual acuity of 6/12 in this eye.

DISCUSSION

Ocular herpes

Herpes simplex involvement of the eye is characterized by recurrences. Twenty five percent following the first attack develop a recurrence within two years.¹ Stromal disease behaves similarly. The virus responsible for the varied lesions remains the same, there is no fresh infection.² If the initial virus that infects the host is of low virulence or nonpathogenic, the incidence of serious disease is negligible. In fact the individual may be protected from the more virulent strains.² In our case, the virus was particularly active and was isolated.³ The clinical course of this patient has been especially interesting, with episodes of uveitis preceded and followed by epithelial lesions, and no episode of uveitis associated with an epithelial lesion. Fig 2. Present appearance of the patient with a healed metaherpetic ulcer and final visual acuity of 6/12.

The precise sites of dormant virus, the factors responsible for reactivation and the clinical morphology it can evolve into remain matters of conjecture. The viral strain, viral antigens, modification of host antigens and the immune response of the host all are alleged to play varying roles in the phenomenon of recurrences,¹ the precise mechanism and appropriate management of which are yet to be elucidated.

REFERENCES

- 1. Hyndiuk RA, Glaser DB. Infections of the Eye. 343-368, 1986.
- Kaufman HE, Centifano-Fitzgerald YM, Varnell ED. Ophthalmology. 90:700-706, 1983.
- Gangwar DN, Jain IS, Gupta A, et al. Eastern Arch Ophthal, 7:104-109, 1979.



Afro-Asian J. Ophthalmol., III/September/62

UVEITIS WITH ANKYLOSING SPONDYLITIS

I.S. Jain, Amod Gupta, M.R. Dogra and Surat Singh Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh

Abstract

In a study of uveitis with ankylosing spondylitis, 41 of the 44 patients were males. Uveal inflammation in these patients was typically acute at onset, unilateral and responded dramatically to steroid therapy. Nearly 46 per cent of the patients had recurrent attacks of anterior uveitis. HLA-B 27 was positive in all the 14 patients with uveitis and ankylosing spondylitis, who were subjected to histocompatibility test.

Key words: Ankylosing spondylitis, HLA-B 27, uveitis.

Ankylosing spondylitis constitutes a major factor in the aetiology of acute anterior uveitis and accounts for 16.6 to 37.7 per cent of all anterior uveitis cases in males.1 Acute non-granulomatous uveitis occurs in between one-third and one-fifth of patients with ankylosing spondylitis.³ Uveitis may be the presenting symptom of the disease complex and may indeed antedate arthritic complications by 10-12 years.³ Precise aetiology of ankylosing spondylitis is still in debate but convincing evidence of a genetic mechanism has been presented by showing a close link of histocompatibility antigen HLA-B 27 with ankylosing spondylitis and anterior uveitis.4 The purpose of this study was to determine the clinical picture, response to treatment, prognosis and frequency of HLA antigens among the patients of uveitis with ankylosing spondylitis.

Material and Methods

Patients attending the uveitis clinic of the Postgraduate Institute of Medical Education and Research, Chandigarh were the subjects of this study. Patients suspected of ankylosing spondylitis

Request for reprints: Dr. I.S. Jain, Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh-160012 (India). were subjected to x-rays of sacroiliac joints. Seventeen patients of ankylosing spondylitis, 14 patients of ankylosing spondylitis with uveitis and 60 healthy normal controls were referred to the histocompatibility laboratory for HLA typing.

Criteria for diagnosis of ankylosing spondylitis

Ankylosing spondylitis was diagnosed in the presence of bilateral sacroilitis with one of the following five clinical criteria:

1) Pain in the lower back and stiffness for more than three months.

- 2) Pain and stiffness in the thoracic region.
- 3) Limited motion in the lumbar spine.
- 4) Limited chest expansion, and
- 5) Positive history of iritis.

A diagnosis of preankylosing spondylitis was considered if typical symptom complex of spondylitis was present in a case of uveitis with equivocal or minimal x-ray changes in the sacroiliac joints.

Results

Uveitis was associated with ankylosing spondylitis in 44 patients. Of these 41 were males and three females with ages varying from 14 to 60 years.



Uveitis with ankylosing spondylitis

Seventy-seven per cent of patients were seen in the third and fourth decades of their life. Thirty-four of the 44 patients first presented with uveitis while 10 patients were already known cases of ankylosing spondylitis. In eight patients uveitis was associated with symptom complex typical of preankylosing spondylitis.

Onset of uveitis

The onset of uveitis was acute and dramatic in 40 patients and subacute in four. All patients had unilateral uveitis at the onset and the other eye became involved in 15 patients (34 per cent) at an interval varying from one to 18 years (average four years).

Recurrence

Twenty of the 44 patients (45.9 per cent) had recurrent uveitis in either the same eye or the other eye at intervals varying from eight months to 18 years (average 3.5 years). Majority of the patients, however, suffered recurrence within one to two years.

Clinical signs

In the first attack of uveitis, visual acuity was reduced to hand motions counting fingers. At least in three patients, light projection was inaccurate. The recurrent attacks of uveitis, however, were less dramatic at the onset and visual acuity was always 6/24 or better. Uveitis was characterized by a marked ciliary injection, a heavy aqueous flare and cells in all the cases. Nearly one-third of the eyes presented with a fibrinous exudative reactions in the anterior chamber. Fine keratic precipitates were seen in 61.4 per cent of cases. Other clinical signs noted were tenous posterior synechiae (69.2 per cent) hyphaema (4.54 per cent) hypopyon (2.27 per cent) vitreous cells (29.5 per cent) macular oedema (22.2 per cent) and hypotony (43.2 per cent).

R esponse to treatment

Topical and subconjunctival injections of steroids and atropine showed a dramatic response and the vision acuity improved within hours. Once the eye became white, there were only minimal or no sequelae. All patients recovered 6/18 or better visual acuity and nearly 61 per cent achieved acuity

11.35

1 Tiursh

of 6/6. Vitreous cells and hy otony were the last to disappear after treatment.

Histocompatibility antigens

HLA-B 27 was positive in 3.3 per cent of normal controls as compared to 94 per cent of ankylosing spondylitis and 100 per cent of ankylosing spondylitis with uveitis.

Comments

Uveitis associated with ankylosing spondylitis presents a fairly characteristic, if not pathognomonic, picture. Uveal inflammation is typically unilateral, dramatic at the onset with rapidly deteriorating vision. It is accompanied by a marked cilliary injection and an exudative reaction in the anterior chamber which is often fibrinous. The pupil is miotic with a tendency to form thin posterior synechiae. Keratic precipitates when present are always fine cellular deposits on the posterior corneal surface. Hypopyon or hyphaema may be present when uveitis may be mistaken for endophthalmitis. Response to treatment with steroids is equally dramatic and in a large majority visual acuity would return to normal level and no sequalae may be left behind in the eve.

Uveitis may be the presenting symptom of ankylosing spondylitis disease complex and an ophthalmologist may be first to diagnose the systemic disease as is evident from this study. It is important to consider this disease in the aetiology of uveitis of sudden onset in young male adults.

Precise aetiology of ankylosing spondylitis is uncertain. However, the presence of HLA-B 27 in 94 per cent of patients with ankylosing spondylitis and 100 per cent of those associated with uveitis is convincing evidence for genetic mechanisms in the pathogenesis of this disease complex.

References

- 1. Duke Elder, S. and Perkins, E.S. (Ed.), System of Ophthalmology Vol. X. Disease of the uveal tract, Henry Kimpton, p. 549, 1966.
- 2. Hart, F.D., In Ankylosing spondylitis, Ed. Moll, J.M.H., Churchill Livingstone, New York, p. 63, 1980.
- 3. Jain, I.S., Jain, G.C. and Sen Gupta, S., East Arch. Ophthalmol., 7: 118-122, 1979.
- 4. Brewerton, D.A., Caffrey, M., Nicholls, A. et al., Lancet, 2: 994, 1973 a.



Bull. P.G.I., 21, Special Issue, 1987

14.00

TUBERCULAR UVEITIS

stalloused fragments

and the states and

Harahoradus.

I.S. JAIN, JAGAT RAM and AMOD GUPTA (Department of Ophthalmology)

Endogenous tuberculosis of the uvea is undoubtedly secondary to a systemic infection (Sorsby, 1963). Report of uveitis in active systemic tuberculosis are scarce in the literature (Duke Elder, 1966). In most of the cases diagnosis of tubercular uveitis remains presumptive or speculative in the presence of a healed focus, a positive tuberculin reaction, a past history of tuberculosis or a therapeutic response to antitubercular treatment. We describe 16 patients of uveitis seen over a period of ten years who suffered from active systemic tuberculosis during the course of uveitis. Some and the second se

Patients and Methods

Trete use interesting Patients of uveitis who fulfilled one of the following criteria (a) active pulmonary tuberculosis or (b) hilar, lymphadenopathy with pulmonary infiltration. (c) histopathologically proved tubercular lymphadenopathy were included into this study. A detailed systemic and radiological examination was carried out in all cases. Lymph node biopsy was performed in suspected cases. A PPD test was performed in all cases. Detailed ocular examination was carried band were the root in many area's one to out.

Patients of uveitis with active systemic tuberculosis were put on topical therapy (a) steroids (b) mydriatics and cycloplegics like atropine 1% or cyclopentolate 1% (c) periocular steroids mydriatic-cycloplegic wherever required. Systemic therapy included antitubercular regime on three of the following : Inj. streptomycin, isonex, rifampicin, ethambutol thiacetazone. Systemic steroids were given in patients of uveitis with exudative retinal

Tubercular Uveitis

detachment, papillitis, bilateral choroiditis or severe uveitis. These patients were followed from 6 months to 5 years.

Observations

There were 10 women and 6 men from 11-50 years of age who had active focus of systemic tuberculosis. Eight of the patients showed hilar lymphadenopathy with pulmonary infilteration; three cervical tubercular lymphadenopathy and five had pulmonary tuberculosis. Mantoux test was over 10 mm x 10 mm in all the cases. 11 of the 16 patients showed 16 mm - 35 mm size of induration. 14 of the 16 cases had bilateral involvement. Twenty two eyes showed characteristic granulomatous uveitis and eight eyeshad nongranulomatous picture. The keratic precipitates were muttonfat in 22 and fine to median size in 8 eyes. Nerarly 2/3rd of the eyes showed 1 + to 2 + flareand cells in anterior chamber. There were multiple fine posterior synechiae in 16 eyes and broad based in 14. Koeppe's and Busaca's nodules were seen in eight eyes. Anterior vitreous activity was seen in 22 eyes. Choroiditis was seen in 14 eyes. It was central in two, one to two patches in six and more than two patches in six eyes. Four case showed exudative retinal detachment which was unilateral in one and bilateral in three cases. Two patients with bilateral exudative retinal detachment also had papillitis in addition. Pigmented and fibrotic subretinal bands were observed in many area's on resolution of exudative retinal detachment. During the course of the disease 10 eyes developed complicated cataract and four had secondary glaucoma. Two eyes showed atrophia bulbi. Nearly 1/3rd eyes recovered 6/18 or better visual acuity. 22 eyes showed a low grade activity for a long period. Till the end of follow up. 11 eyes had suffered a

USU

I.S. Jain et al

single recurrence and 9 eyes had multiple recurrence. In most of the recurrences (60%) uveal inflammation was non-granulomatous in nature.

Discussion

Patients with healed focus of tuberculosis are common but it is rare to find active systemic tuberculosis in patients with unveitis during its course. We treated 16 such patients of tubercular uveitis over a period of 10 years. Nearly half of our cases had lymphadenopathy with pulmonary infilteration. All of our cases showed a positive mantonx test (over 10 x 10mm). Nearly 2/3rd cases showed highly positive mantoux test. Most of our cases showed bilateral granulomatous reaction. Choroiditis and exudative retinal detachment was a common features in these patients. Nearly half of the cases showed choroditis and one fourth cases showed exudative retinal detachment. These patients showed pigmented sub-retinal bands on resolution of choroitis and exudative retinal detachment with antitubercular and steroid therapy. It is interesting to observe that over 60% cases showed nongranulomatous reaction in recurrences. Majority of our cases showed good response to antitubercular treatment. Systemic tuberculous focus healed in all cases.

Summery

Sixteen cases of tubercular uveitis in patients of active systemic tuberculosis are described. Most of the patients had a bilateral granulomatous picture. Posterior segment involvement in the from of choroiditis and exudative retinal detachment was seen in majority. Topical steroids antitubercular treatment and systemic steroids in selected cases effectively contolled the disease process. Recurrences of non-granulomatous nature were seen in sixty percent of the eyes. 48 Tubercular Uveitis

References

- Duke Elder, S. and Perkins Es.(EDs) System of Ophthalmology, Vol IX, 246-285. Henry Kimpton, Lond, 1966.
- Wood, A.C. : In : Sorsby A (ED), Modern Ophthalmology, Vol II, Ocular Tuberculosis, 116-153, Buttersworth, London, 1963.



Afro-Asian J. Ophthalmol Vol. XI No.3 December 1992

IDIOPATHIC EPISODIC PALPEBRAL HEMORRHAGE : **AN ENIGMA**

Amod Gupta, S.P.S. Grewal, Birgit Khandalvala,

Department of Ophthalmology, Postgraduate Institute of Medical Education & Research, Chandigarh 160 012 (India)

ABSTRACT

A nine -year -old girl complained of sudden bouts of spontaneous bleeding from the right upper lid of one month duration. This occurred during waking hours and lasted a few minutes, 1-6 times a day. There were no aggravating or precipitating factors. No local or systemic abnormality could be detected. Coagulation studies were normal. Psychiatric and paediatric evaluations were non-contributory. Skin biopsy revealed focal dermal haemorrhages. The other structures were essentially normal. We consider this to be a unique case of inexplicable spontaneous episodic palpebral haemorrhage.

KEY WORDS : Idiopathic palpebral haemorrhage, histopathology.

Secretion of blood from the eye is not unusual. Bloody tears have been reported in conjunctival lesions including haemangioma, telangiectasis and inflammatory granulomas. Lacrimal gland and sec tumours, bleeding disorders and local trauma may also be associated with bloody tears. 1 Bloody sweat 2 is an extremely rare condition where blood is mixed with the normal secretions of the sweat glands. We report an exceptional case of spontaneous recurrent bleeding from the right upper lid with perplexing dinical presentation and histopathology.

CASE REPORT

We saw a nine-year-old girl in August, 1988, with the complaint of recurrent episodes of bleedings from the right upper lid for the past one month. Each episode lasted for a few minutes and stopped as abruptly as it would start. The attacks were more common during school time. No episode was known to occur during sleep. There was no history of bleeding from any other part of the body. listory of easy bruising, joint swelling, malena or haematuria was bsent. There was no family history suggestive of bleeding asorders. The child is the youngest of three sisters, and has a hother younger to her. She has an average performance at school indhas a congenial home environment with good parental support. The child has not attained menarche till date.

The child was closely observed on numerous occasions in the outpatients department and was admitted to the hospital for 24 hour

Reprint requests to : Dr. Amod Gupta, MD

Additional Professor and Head, Department of Ophthalmology. Postgraduate Institute of Medical Education & Research, Chandigarh - 160 012 (India)

observation under strict surveillance. In between attacks the skin of the right upper lid appeared completely normal (Fig 1 A). There were no nodules, telangiectatic vessels, scars or ecchymosis and was comparable in all aspects to the uninvolved left eyelid.



Fig. 1 (A) Normal appearance of the right upper eye lid skin before the onset of episode.

We observed each episode to be identical in nature and have examined entire episodes through the microscope of the slit lamp. The onset was unpredictable. The child would be sitting in a chair or in bed and without any change in the perception of the child, a sanguinous fluid would suddenly appear on the right inner canthus (Fig 1 B). This red ooze would then coalesce to form a fine haze and the blood would clot in a few minutes to form a dark red film over the eye lid and the skin medial to the inner canthus (Fig 1 C&D). When seen under magnification the bleed appeared to

Amod Gupta. MD



Fig 1 (B) Magnified view of the first appearance of a bead of red sweat. (arrow)



Fig 1 (C) Increase and coalescence of the bleed from the skin of right upper lid and an area nasal to the medial canthus. (arrow heads)

come directly out of the skin. Each attack lasted barely a few minutes and occurred 1-6 times a day during the periods of observation. The child remained oblivious of the onset or duration of bleeding. There was no change in behaviour preceding or during the bleed. We were unable to induce bleeding by the Valsalva manoeuvre, rubbing the skin or putting the patient in a situation of mental stress. No episode occurred during sleep. Sweating in the involved area was otherwise normal. Parasympathetic stimulation by intradermal injection of pilocarpine in the affected lid failed to elicit any bleedings.



Fig 1. (D) Dried film of blood over the affected area at the conclusion of the episode



Fig 2. Abundant focal dermal haemorrhages (arrow) and few nonspecific inflammatory cells (250 x) (H&E)

Hemogram, leukocyte count, erythrocyte sedimentation rate, bleeding time and clotting time were within normal limits. Platelet count was 1,85,000/mm and Hess test was negative. Prothrombin time was 14 seconds and the prothrombin index was 100 per cent. Assays for factor VIII and XIII were normal. Platelet adherence and aggregation were normal.

A thorough systemic evaluation by paediatricians and dermatologists revealed a normal healthy child for her age withno detectable abnormalities. On psychiatric evaluation, the child was found to have a normal personality with average intelligence and an expected quantity of sibling rivalry. A skin biopsy was taken from the right upper lid under general anaesthesia. The wound healed well to form a fine scar. Histopathology revealed focal dermal haemorrhages with few nonspecific inflammatory cells. uppathic Episodic Palpebral Hemorrhage : An Enigma

The distribution of these haemorrhages did not indicate the source of bleed. The sweat glands were normal. (Fig 2)

During a period of observation of fifteen months, the frequency and quantity of bleedings has decreased to once in 2-3 months at present. No treatment was instituted at any time.

DISCUSSION

Bleeding disorders, particularly purpura, manifest as spontaneous bleeding from the skin³. The localised nature of bleeding and the sck of clinical or histopathological evidence in our case eliminates his possibility. Vicarious menstruation cannot be entertained in his case as the child has not attained menarche and the stopathology has failed to reveal any aberrant endometrial issue. Self inflicted injury was initially considered a possible etiological factor. However, the child was under careful scrutiny a many occasions under the watchful eyes of upto twelve bervers at times. There was no wound or scar and the eyelid werted to its normal appearance on the cessation of bleeding, nee the dried blood was removed. Histopathology did not show ay distortion of tissues or evidence of scarring. In addition, entire isodes could be seen to occur in the sequence described above ith the slit lamp magnification.

te absence of bleeding during sleep implies a functional element dit may be postulated as a likely cause, more so as a modulator some unknown mechanism causing the strange histopathology. milar bleeding during hysteria or religious fervour has been scribed (Stigmatization)⁴. This entails a considerable alteration behaviour preceding the event and has been described in scrific areas as the palm, sole, chest or around the head, and is d to result in scarring of the affected area. Behavioral changes I cutaneous scars were notably missing in our case.

tereas the clinical presentation was confounding, the topathology was enigmatic. The predominant feature was the indant dermal haemorrhages, a unique phenomenon. There is no red blood cells in the sweat glands. The epidermis, blood sels and sweat glands were normal. No significance could be ched to the few inflammatory cells. No clue as to the origin and te of bleeding could be revealed. The mechanism and ifestation remain speculative. We conjecture that the blood sels demonstrate a localized hyperpermeability due to an nown stimulus, probably modulated by a functional element, that allows the red blood cells to escape and accumulate in the dermis. From the dermis the red blood cells probably enter the glandular openings and are extruded out as tiny droplets that we observed. To confirm this we would have liked to have taken a biopsy at the time of actual bleeding. The need for general anaesthesia and the fleeting nature of bleeding made this task impossible to achieve. Another route of exit could be epidermis itself and though breaks were noted in the epidermis on histopathology, these were considered artifactual in origin.

Another factor to be considered in the interpretation of the histopathology is that the biopsy was taken during a period of inactivity. The dermal haemorrhages may just be accumulation of residual cells that participated in diapedisis of red bood cells through the layers of skin and having failed to be extruded, were showing degeneration. They may be considered the source of the bleeding or probably, the effect of bleeding.

Unfortunately there exists no histopathological work of cases described as stigmatives that would have allowed a comparison, for in these cases too, there is spontaneous and localized bleeding that does not follow the usual norms. In addition, dermal haemorrhages have not been previously described in any condition. This confounds the case further.

In conclusion, we admit that this patient's clinical protocol and biopsy findings defy rational explanation within the confines of current scientific knowledge and remains an enigma that we have labelled as idiopathic episodic palpebral haemorrhage.

The authors wish to thank the Armed Forces Institute of Pathology, Washington, DC, USA for the histopathological work.

REFERENCES

- Krohel G.B., Duke M.A., Mehu M.: (1987), Arch Ophthalmol, 105:1489-1490
- Duke-Elder S Haematohydrosis. In : System of Ophthalmology. Ist ed. London; Henry Kimpton, 19074; 13 (1):25
- Champion R.H. Disorders of sweat glands In : Rook A, Wilkinson D.S., Ebling FJG, eds. Text book of Dermatology. Oxfort : Blackwell Scientific Publications, 1979:1698.
- Klauder J.V. (1938), Arch Dermatol 37:650-659.

ACTA OPHTHAL MOLOGICA

Retinal involvement in Wucheria bancrofti filariasis

Amod Gupta, Anita Agarwal and Mangat R. Dogra

Department of Ophthalmology, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Abstract. We report the first case of inflammation of the retinal pigment epithelium and tetinal vasculities presumably caused by microfilaria of Wucheria bancrofti and discuss its possible pathogenesis. Therapy with diethyl carbamazine citrate resulted in rapid resolution of the inflammation.

Key words: Wucheria bancrofti - microfilaria - acute multifocal placoid pigment epitheliopathy - retinal vasculitis diethyl carbamazine citrate.

Microfilarial disease due to Onchocerca volvulus is a common cause of blindness in certain parts of the world such as Central America, Tropical Africa and Saudi Arabia (Bird et al. 1976). There are only isolated case reports of other larvae - microfilaria, loa loa, Schistosoma mansoni - affecting the eye and causing ocular morbidity (Toussaint & Danis 1975; Dickinson et al. 1990). We report the first ever case of inflammation of the retinal pigment epithelium and retinal vasculitis presumably caused by the microfilaria - Wucheria bancrofti.

Case Report

A 22-year-old male presented with sudden diminution of vision in the right eye of twelve days duration. He had visited South India (an endemic zone for Wucheria bancrofti) a year earlier, following which he had fever, chills and swelling of the

left leg, which subsided without any specific therapy. Presently, he was receiving prednisolone 40 mg orally for his visual symptoms without any improvement. Visual acuity of right eye was 6/24 and left eye 6/5. Left eye examination was unremarkable. Biomicroscopy of the right eye showed one + vitreous cells. Fundus examination revealed optic disc oedema, venous dilatation and perivenous cuffing of the upper temporal vein. There were multiple grey-white placoid lesions both discrete and confluent deep to the retinal vessels in the posterior pole. On fundus fluorescein angiography, the placoid lesions were hypofluorescent during dye transit and became hyperfluorescent in the late phase. Systemic examination was normal. An initial diagnosis of acute posterior multifocal placoid pigment epitheliopathy with retinal vasculitis was made. Two weeks later, he developed neovascularisation of the optic disc with occlusion of the upper venous trunk and multiple superficial haemorrhages confined to the upper half without any change in the appearance of the placoid lesions (Figs. 1 and 2). Investigations revealed haemoglobin 13.5 g/100 ml, total leucocyte count 6050 mm³, neutrophils 64, lymphocytes 30, monocytes 2, eosinophils 4 and ESR 2 mm. Peripheral blood smear showed numerous microfilariae of Wucheria bancrofti (Fig. 3). Chest X-ray was normal. Rheumatoid factor, VDRL, LE cell, ANF and Mantoux test were negative.

He was treated with diethylcarbamazine citrate







Early phase fundus fluorescein angiogram showing neovascularisation of optic disc and multiple areas of hypofluorescence.

Fig. 2. Late phase fundus fluorescein angiogram showing leakage of dye from the optic disc neovessels and peripheral staining of the patches seen in Fig. 1.

200 mg thrice daily for 3 weeks. Visual acuity improved to 6/12 within one week, vitreous cells disappeared and the placoid lesions on FFA showed only transmission defects. Subsequently, night blood samples became negative for microfilaria. Three months later he developed vitreous haemorrhage from neovessels on the optic disc for which he underwent an uneventful vitrectomy in the right eye. A year and a half later, the visual acuity was RE 6/9 and LE 6/5. There was residual preretinal gliosis without evidence of the neovessels on the optic disc and pigmented and depigmented scars corresponding to the placoid lesions (Fig. 4).

Discussion

The clinical manifestation of bancroftian filariasis is caused by the adult worm and is almost always confined to the lymphatic system. The early phase of the disease is characterised by fever, chills, lymphagitis and regional lymphadenitis. Painful orchitis, epididymits and funiculitis may also occur. These features subside spontaneously in a few days and can recur at irregular intervals till slow progressive lymphatic obstruction develops, resulting

53 Acta Ophthal. 70.6

in elephantiasis. Rarely, other organs reported to be involved by the adult worm include the orbit, anterior chamber of the eye and joint space (Manson & Bell 1987). Microfilaremia is generally considered asymptomatic. Tropical pulmonary eosinophilia, however, is a syndrome believed to be type I, II and IV immune reaction to microfilaria.



Fig. 3. Peripheral blood smear showing microfilaria of Wucheria bancrofti.





Fig. 4.

Composite fluorescein angiogram 18 months later showing multiple hypo and hyperpigmented lesions consistent with pigmented scars in the fundus. Note glial scar on the optic disc from regression of optic disc neovessels.

Mesangio-proliferative and diffuse proliferative glomerulonephritis in bancroftian filariasis have been reported and an immune mediated mechanism has been suggested (Chugh & Sakhuja 1990; Chugh et al. 1978). Microfilariae have also been demonstrated in the glomerular capillaries (Date et al. 1979). Haemorrhagic pericardial effusion containing microfilaria (without microfilaraemia) which responded dramatically to diethylcathamazine suggests a pathogenic role for the microfilaria (Manson & Bell 1987).

The cause of placoid lesions in acute posterior multifocal placoid pigment epitheliopathy is due to an immune complex mediated vasculitis and obstruction of the choriocapillaris and subsequent ischemia of retinal pigment epithelium (Young et al. 1980). Circumstantial evidence suggests that the retinal periphlebitis and placoid lesions in our patient were caused by obstruction of the chorioca-

pillaris and retinal veins. It is probable that the microfilaria induced a hypersensitivity or an immune complex mediated reaction which resulted in vasculitis of both retinal vessels and the choriocapillaris. Alternatively, the microfilaria could have lodged in the retinal and choroidal circulation and excited a granulomatous reaction similar to tropical pulmonary eosinophilia. This hypothesis is supported by histopathological evidence of finding numerous intravascular microfilariae of loa in the retina, retinal blood vessels and choroidal vessels in a patient (Toussaint & Danis 1965). More recently, a patient similar to ours presumably caused by Schistosoma mansoni has been reported (Dickinson et al. 1990).

Our patient showed a progressive inflammatory disease despite systemic steroids for 4 weeks but responded dramatically to diethylcarbamazine, a response typically seen in tropical eosinophilia

syndrome. However, the patient went on to develop optic disc neovascularization secondary to upper trunk venous occlusion, and a vitreous haemorrhage which cleared after vitrectomy. The creamy placoid lesions healed and the visual acuity improved from 6/24 to 6/9. The absence of an exaggerated immediate hypersensitivity response to diethylcarbamazine suggests the probable cause of the vascular occlusion to be mechanical blockade of the retinal vessels and choriocapillaris by the microfilaria (with or without local inflammatory reaction), which was relieved by the death of microfilaria following therapy.

References

- Bird A C, Anderson J & Fuglsang H (1976): Morphology of posterior segment lesions of the eye in patients with onchocerciasis. Br J Ophthalmol 60: 2-19.
- Chugh K S & Sakhuja V (1990): Glomerular diseases in the tropics. Am J Nephrol 10: 437-450.
- Chugh K S, Singhal P C, Tewari S C, Nath I V S & Datta B N (1978): Acute glomerulonephritis associated with filariasis. Am J Trop Med Hyg 27: 630-631.

- Date A, Gunasekharan V, Kirubakaran M G et al. (1979): Acute eosinophilic glomerulonephritis with bancroftian filariasis. Postgrad Med J 55: 905-907.
- Dickinsin A J, Rosenthal A R & Nicholson K G (1990): Inflammation of the retinal pigment epithelium: A unique presentation of ocular schistosomiasis. Br J Ophthalmol 74: 440-442.
- Manson P E C & Bell D R (1987): Manson's tropical diseases. Filariasis, p 363. Bailliere Tindall, London.
- Toussaint D & Danis P (1965): Retinopathy in generalised Loa-Loa filariasis - a clinicopathological study. Arch Ophthalmol 74: 470-476.
- Young NJ A, Bird A C & Sehmi K (1980): Pigment epithelial diseases with abnormal choroidal perfusion. Am J Ophthalmol 90: 607-618.

Received on April 2nd, 1992.

Author's address:

Dr. Amod Gupta, Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012, India.

Reproduced from Gupta A, Agarwal A, Dogra MR. Retinal involvement in Wucheria bancrofti filariasis. Acta Ophthalmol (Copenh). 1992 Dec;70(6):832-5. doi: 10.1111/j.1755-3768.1992.tb04896.x. PMID: 1488896 with permission of the publishers

53*



Onwards and Together Against Inflammation Dr Sanjays

Dr. Sanjay Srinivasan

Senior Resident Physician, Singapore National Eye Centre, Singapore



Address for Communication



C/O Hallmark Events, Maruthi ' 688, 1st Floor, 6th Main 3rd Block, BEL layout, Vidyaranyapura, Bangalore - 560097

Ph: 080 - 23646880 | Mob: 9591732274 | 9845671462

Email: uveitissociety@gmail.com



www.indianuveitis.org