# insight

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Microphotograph of permanent section showing molluscum bodies (haematoxylin and eosin x 100)



#### EDITORIAL

Advances in surgical techniques and instrumentation, better understanding of the anatomy of the eye, and improved quality of intraocular lenses, have increased the safety of intraocular lens (IOL) implantation in children. As a result of this IOL's are being increasingly implanted in children. However IOL implantation is still controversial in infants & young children, and the surgical technique & tissue response is different compared to adults. Our perspective article in this issue reviews all the factors that need to be taken into consideration while implanting an IOL in children.

Accurate differentiation of herpes simplex or varicella zoster from cytomegalovirus is essential as the therapeutic agents differ. Rapid diagnosis is needed for prompt initiation of appropriate therapy and thus preserve vision. In this issue Priya and colleagues report the diagnostic value of polymerase chain reaction on intraocular specimens from patients with viral retinitis.

Most of ophthalmic surgery is performed under local anesthesia. It is not uncommon to have a difficult patient who is quite apprehensive, and claustrophobic. How do you manage these patients ? Dr Sundaraj explains it all in his article in this issue.

In the era dominated by technology, photography equipments also have undergone changes. The last page takes a brief look at digital cameras and its application in ophthalmic photography.

> Dr Rajesh Fogla DNB, FRCS (Edin) Editor

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#### **Perspective:**

## Intraocular lens implantation in children

Geetha K Iyer, Rajesh Fogla and Srinivas K Rao

improved Cataract surgery has significantly over the last two decades, with advancement in surgical techniques, instrumentation and the quality of intraocular lenses (IOL). Understanding of the pediatric ocular anatomy has improved the safety of extracapsular cataract surgery in children, and as a result of this, intraocular lenses are now being implanted with increasing frequency in the pediatric population.<sup>1-6</sup>

Optical rehabilitation of unilateral aphakic aniseikonia is difficult to tackle, as are the problems of optical distortion, compliance, and cosmesis associated with bilateral aphakic spectacle in children. Contact lens non-compliance, intolerance and possible complications associated with its use makes this modality of approach less acceptable for this age group. IOL implantation thereby offers a potentially effective means of optically correcting the eyes of children following cataract surgery, and at the same time addresses favourably the issue of amblyopia.

IOL implantation in infants and young children is still controversial with regards to IOL size, material, IOL power selection, prevention of opacification of the visual axis and long term safety of the IOL in a child's eye.

This article provides an overview of all these factors that need to be taken into consideration while implanting intraocular lenses in children.

#### 1) AGE

IOL implantation in children less than 2 years of age still remains controversial. Increased tissue reactivity, opacification of the visual axis and marked axial length and refractive changes have been cited as contraindications to the use of IOL in the first two years of life.<sup>6</sup> The eye of an adult is 40-50% larger than a newborn child's. The mean

axial length in a newborn is 17 mm as compared to 23.5mm in adults.<sup>7</sup> Implantation of a regular sized IOL in the newborn as studied in animal eyes, retards growth, indicating that pressure on the internal structures of the eye disturbs ocular growth.<sup>6</sup> The recommendation therefore is to implant downsized IOL's of approximately 10 mm diameter in infants, though this requires further evaluation.<sup>8</sup> IOL implantation in infants have been reported though the authors conclude that it is associated with a higher rate of complications including open angle glaucoma, lens reproliferation into visual axis, pupillary membranes and corectopia, as well as a large myopic shift occurring in the first 12 to 24 months (-5.49 diopters, follow up 12 months<sup>9</sup>, -6.00 diopters, follow up 41 months<sup>10</sup>). A high incidence of re-operation 23% to 92% was also noted when surgery was performed in the first year of life.9-11

Ninety percent of the crystalline lens growth occurs during the first two years of life.<sup>7,12</sup> Standard flexible IOL's of 12 mm -12.5mm diameter can be safely implanted into the capsular bag after the age of two years.<sup>12</sup>

#### 2) IOL POWER CALCULATION

Selection of the IOL power has been one of the most controversial topics related to pediatric IOL implantation. Selection of the desired postoperative refraction is challenging because of the rapid growth of the eye in infancy. Surgeons have chosen IOL powers to make the eye hypermetropic<sup>13</sup>, emmetropic<sup>14</sup>, or even myopic<sup>15</sup> in the postoperative period.

It is well known that majority of the eye growth takes place in the first 18 months of life.<sup>7</sup> Changes occur both in the axial length as well as the corneal curvature.(Fig 1,2) The increase in axial length outweighs the decrease in corneal curvature inducing a myopic shift.<sup>7</sup>



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Amblyopia and form deprivation lead to alteration in the axial length towards myopia. Significant anisometropia can lead to amblyopia. Hyperopic anisometropia has the potential to induce amblyopia more readily than myopic anisometropia. Though it would therefore seem logical to leave the eye myopic in the immediate postoperative period, it has been found that myopic shift occurs faster and is greater in myopic eyes than hyperopic eyes of the same age. Studies have shown that the myopic shift in aphakic eyes due to an increase in the axial length is greater than in pseudophakic eyes.<sup>16</sup> However, the mean quantity of myopic shift is greater in the pseudophakic eyes than in the aphakic eyes. This apparent paradox is an optical phenomenon resulting from the ever-increasing distance of the IOL from the retina as the eye grows. The higher the IOL power, the greater the myopic shift will be for pseudophakic eyes compared with aphakic eyes.

Hence it would be preferable to use a method that mimics nature, with initial hypermetropia allowing emmetropisation to occur with age, albeit sans accommodation.<sup>17</sup>

While deciding the IOL power, the following points need to be considered -

#### a) Age

Dahan has recommended that children under the age of 2 years should receive 80%



of the power need for emmetropia. (table 1) In children above 2 years of age, an under correction of 10% is sufficient and in children beyond 8 years of age, one should aim for emmetropia.<sup>17,18</sup>

Undercorrection	Age
- 20 %	1 - 2 years age
- 10 %	2 - 8 years age
- emmetropia	> 8 years age

#### Table 1

Another study evaluating the long term refractive change in pediatric pseudophakia, recommends that an appropriate IOL power can be selected based on age, (table 2) for children between 2 and 15 years of age, to yield a refraction of -1.00 diopter at the age of 20 years.<sup>19</sup> This goal should take into consideration the refractive status of the fellow eye in unilateral cases to keep induced anisometropia at a reasonable level.

Age	Target refraction (d	liopters)
3 years	+ 5.00	
4 years	+ 4.00	
5 years	+ 3.00	
6 years	+ 2.25	
7 years	+ 1.50	
8 years	+ 1.00	
10 year	s + 0.50	
13 year	s plano	

Table 2

Hence, younger the child at time of implantation, the greater is the myopic shift. To reduce the necessity of IOL exchange, these eyes should be undercorrected, with the residual refractive error corrected by spectacles that are adjusted throughout life according to refractive development. This leads to initial hypermetropia that gradually moves to emmetropia or moderate myopia in adulthood.

#### b) Axial length of the eye

Normal phakic eyes elongate rapidly in the first two years of life.<sup>7</sup> Corneal curvature decreases markedly during the first year of life and changes minimally thereafter. Large myopic shifts have been noted in infants in the first two years following IOL implantation.<sup>9,10</sup> Hence IOL power can also be calculated on the basis of axial length in the first two years of life.<sup>18</sup> (Table 3)

Axial length	IOL power
17 mm	28 D
18 mm	27 D
19 mm	26 D
20 mm	24 D
21 mm	22 D

#### Table 3

#### c) Refractive error of fellow eye

This has to be taken into consideration especially in unilateral cataracts to prevent anisometropia and aniseikonia. In these cases it seems appropriate to place the pseudophakic eye 1-2 diopters closer to emmetropia than the phakic eye.

#### d) IOL formulae

There is no significant difference in refractive calculation or average error among the SRK II, SRK-T, Holladay, and Hoffer Q formulae in children, though the Hoffer-Q formula had the lowest error.<sup>20</sup>

#### e) Facilitation of amblyopia treatment

Treatment of amblyopia following surgery is crucial because emmetropisation is a vision dependent phenomenon. The advantage of immediate postoperative emmetropia facilitating the management of amblyopia has to be weighed against the disadvantages of later onset moderate to severe myopia.<sup>6</sup> If the eye is rendered ametropic, supplemental refractive correction, either in spectacle or contact lens form is essential to ensure optimal visual development.

Finally the IOL power calculation is made on a case-by-case basis taking into consideration all the above-mentioned factors.

The maximum power available in IOL's in +30 to +34D. In eyes with shorter axial length, leaving the child with high hyperopia defeats the very purpose of IOL implantation, especially if associated with the inability of the caretaker to manage spectacles or contact lenses. Piggyback IOL's have been implanted to provide a solution to this problem by the placement of a high power IOL in the capsular bag and a low power IOL in the sulcus.<sup>11</sup> The low power IOL can be removed later, thus achieving immediate postoperative emmetropia as well as tackling the later myopic shift.<sup>11</sup>

Jacobi et al report successful implantation of zonal progressive refractive multifocal IOL in children.<sup>21</sup> However complications such as posterior capsular opacification, optic decentration and posterior synechiae can affect the final visual outcome in these cases.

#### 3) IOL BIOMATERIALS & SIZING

#### i) IOL Bio-Material

PMMA is the most commonly used IOL material in cataract surgery, as it has the longest safety record over a period of 50 years. The one piece all PMMA IOL exhibits better memory than the three piece IOL with polypropylene haptics. resisting the postoperative contraction of the capsular bag thereby retaining or even slightly increasing the diameter of the capsular bag, thus lessening the tendency towards zonular stretching that occurs with the growing ciliary ring in a child.<sup>8</sup> The flexible open loop one piece all PMMA modified C-loop capsular IOL is recommended in eyes of children two years or older due to ease of insertion and the highly flexible encircling loops.<sup>8</sup>

Heparin surface modified (HSM) PMMA IOL's are associated with decreased inflammatory cell deposits indicating a greater biocompatibility compared to the unmodified IOL's in pediatric cataract surgery.<sup>22</sup>

Since the popularization of phacoemulsification, a shift towards foldable IOL's has occurred in adults. Newer IOL's are more flexible while retaining desirable memory characteristics. Foldable hydrophilic materials (hydroxyethyl-methacrylate - HEMA) are more biocompatible than PMMA or silicone.<sup>17</sup> Both acrylic and silicone IOL's have been successfully used in pediatric cataract surgery with less astigmatism and minimal postoperative inflammation.<sup>23,24</sup>

#### ii) IOL Sizing

The crystalline lens has a mean diameter of approximately 8.4 mm at the age of 2 years which increases to 9.3 mm at the age of 16 years.<sup>12</sup> The capsular bag diameter is defined as crystalline lens diameter in mm + 1 mm.<sup>8</sup> A flexible open loop one piece all PMMA IOL with an overall length of 12 mm to 12.5 mm is recommended for children above 2 years of age with a mean capsular bag diameter of 9.5mm.<sup>8</sup> Ideal capsular bag implantation creates mild stretching and ovaling of the anterior capsulotomy bag, or both, with mild striae. Though a temporary oversizing is created, it accounts for the increase in axial length and ciliary ring diameter upto puberty. With excellent capsulotomy techniques, the capsular bag, with its high elasticity can tolerate slight oversizing.<sup>8</sup>

The adult ciliary sulcus diameter rarely exceeds 11.5 mm diameter, hence pediatric IOL 's should not exceed 12.5 mm in overall diameter. Larger diameter IOL's (13.5 mm) act like loaded springs and result in compression of ocular tissues and possibly dislocate later due to increased compression of the haptics.<sup>17</sup> Moreover if placed in the ciliary sulcus there is excessive pressure on the uveal structures resulting in a low grade chronic uveitis as well as IOL decentration due to uneven compression of the haptics.<sup>17,25</sup> An IOL diameter of 10.0 mm to 11.0 mm is recommended while implanting lenses in children less than 2 years of age.<sup>8,17</sup> These special pediatric lenses are manufactured by few companies. (1: Kidlens - IOL Technologie; La Rochelle, France, 2: Palmlens - CORNEAL; Paris, France)

#### 4) IOL POSITION

The ideal position for an IOL is the capsular bag because it is the most physiologic and has a long record of safety. Posterior chamber IOL's should be used both in primary and secondary IOL implantations.<sup>4,17</sup> Secondary in the bag intraocular lens implantation can be carried out following infantile cataract surgery without primary intraocular lens implantation. A primary anterior and posterior capsulectomy of no larger than 4-5 mm is recommended. A potential space is maintained between the fused anterior and posterior capsular leaflets for in the bag placement of the IOL, which can be reopened later as a secondary procedure.<sup>26</sup>

Primary posterior continuous curvilinear capsulorhexis (PCCC) with optic capture of the heparin coated PMMA IOL has been reported to successfully prevent secondary opacification of the visual axis.<sup>27</sup> The leaflets of the anterior and posterior capsulorhexis are apposed and sealed in front of the IOL optic except near the optic haptic junction. This prevents proliferation of the lens epithelial cells over the anterior hyaloid face. Another advantage of optic capture is in enhancing IOL centration.<sup>28</sup> Foldable acrylic IOL's also have been used successfully using similar surgical technique.<sup>23</sup> However in another study involving children younger than 5 years, it was noted that optic capture without anterior vitrectomy did not always ensure a clear visual axis.<sup>29,30</sup> PCCC is now often combined with anterior vitrectomy with or without optic capture to achieve a clear visual axis.<sup>31,32</sup> (Fig 3) Placement of a foldable acrylic lens has the advantage of a smaller incision combined with a larger optic diameter and minimal postoperative inflammation.<sup>23</sup>

Anterior chamber IOL's are best avoided in children due to lack of knowledge of long



Fig 3. Slit lamp photograph (retroillumination) showing the anterior (large arrows) and the posterior (small arrows) capsulorhexis.

term effects on angle structures and corneal decompensation, in spite of the newer flexible IOL's available, due to the long life expectancy in this group of patients.<sup>33</sup> Iris claw intraocular lenses have been successfully implanted in children.<sup>34</sup> The mean endothelial loss with these IOL's is reported to be 13.42% at the end of four years.<sup>35</sup> It is therefore possible that corneal decompensation may also occur with these IOL's in the long run.

Sulcus fixated IOL's are usually associated with secondary IOL implantation.<sup>3,36,37</sup> Although studies have reported successful outcomes with primary IOL implantation in the ciliary sulcus, this can often be associated with postoperative complications especially in eyes with traumatic cataracts<sup>38</sup>, secondary to uveal tissue irritation, which may result in fibrinous uveitis and pupillary capture.<sup>25</sup> (Fig 4)

Scleral fixated IOL's are a feasible alternative in children with unilateral aphakia unable to tolerate contact lenses and in the absence of capsular support.<sup>39-41</sup> However this procedure is technically more difficult to



Fig 4. Slit lamp photograph showing opacification of the posterior capsule, note capsulotomy – (Nd YAG) (large arrow), posterior synechiae (short arrow) and iris capture by the optic of the IOL (\*).

perform in children compared to adults and the long term risks are unknown. Besides this it is also difficult to predict the postoperative refraction. Complications associated with scleral fixation include suture erosion, elevated intraocular pressure, anterior uveitis, IOL decentration, and cystoid macular oedema.<sup>39-41</sup> Longer follow up is required to document any further complications.

#### 5) POSTERIOR CAPSULE MANAGEMENT

Posterior capsule opacification (PCO) occurs universally in younger children after cataract surgery and is a significant cause of amblyopia.<sup>31</sup> The overall percentage of PCO in patients 1 to 6 years old has been found to be more than three times that in patients 6 to 13 years old.<sup>42</sup> PCO represents a greater concern in children younger than 6 years old for several reasons. Patients this young usually require general anesthesia to undergo laser capsulotomy, and the amount of energy required to create an adequate capsular opening tends to be larger. A secondary surgical posterior capsulotomy for fibrotic membranes places stress on the capsule and the zonules, can cause intraocular bleeding and is associated with the anxiety and trauma of a second surgical procedure for the patient and the parents.<sup>29</sup> Hence primary posterior

capsulorhexis seems to be advisable for children less than six years old when cataract extraction with IOL implantation is performed.<sup>42</sup> Although this study recommends that the posterior capsule can be left intact without the need for anterior vitrectomy in children above the age of 6 years, another study by Vasavada et al<sup>43</sup> recommends PCCC and anterior vitrectomy along with optic capture of the IOL in children between 5 to 12 years of age. In his series all eyes that had vitrectomy maintained a clear visual axis at last follow up, besides significantly better low contrast visual acuity.

Cystoid macular oedema (CME) has been reported after pediatric cataract surgery with anterior vitrectomy procedure.<sup>44</sup> However with current surgical techniques, CME is not seen to occur in the early period after pediatric cataract surgery.<sup>45</sup>

The use of capsular bending  $ring^{46,47}$ , optic capture using heparin surface modified IOL's<sup>27</sup> and acrylic IOL's with sharp optic edge design<sup>23</sup> have also been evaluated as means to reduce the incidence of PCO.

#### Conclusion

In conclusion, IOL implantation in children beyond 2 years of age is less controversial, and is the treatment of choice for pediatric cataracts or aphakia. In the bag placement of the IOL is essential to minimize postoperative complications. Age and axial length have to be considered while deciding on the IOL size and power. Foldable IOL's have the advantage of a smaller incision combined with a larger optic diameter. Primary posterior capsulorhexis with anterior vitrectomy is effective in preventing opacification of the visual axis. IOL implantation in infants is associated with increased complications and needs further evaluation.

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# Molluscum Contagiosum Mimicking Lid Tumour - A Report of a Case

Dipankar Das, Jyotirmay Biswas, S Krishnakumar and Nirmala Subramaniam

Molluscum Contagiosum is common skin infection caused by DNA pox virus. Clinically it is characterized by multiple, dome shaped skin coloured nodules of varying sizes (1-3mm). Lesions are often umiblicated and yellowish cheesy material can be expressed from their centers. The lesions are usually located on the eyelid, however, when the lesion occurs at the lid margin and is single it may cause a diagnostic dilemma.

We report a case of molluscum contagiosum in a HIV negative patient wherein it mimicked a lid tumor. Subsequently, frozen section as well as histopathological examination revealed it to be molluscum contagiosum.

#### **Case report**

A 51 year old lady visited our institute in July 1993 with history of seeing flashes of light of 1 month duration and occasional pain in both eyes. She had history of myopia since childhood. On examination, her best corrected visual acuity was 6/12; N6 in the right eye and 6/9; N6 in the left eye. Slit lamp examination revealed no abnormality. Fundus examination revealed a horseshoe tear in the right eye and a pigmented lattice degeneration in the left eye. Prophylactic laser photocoagulation around the horseshoe tear and lattice degeneration was done in both eyes.

Patient was subsequently seen 8 years later with swelling on the left upper eyelid of 6 months duration and increase in size since 2 months. On slit lamp examination, a small, non tender, elevated, yellowish, umblicated swelling with loss of cilia that did not bleed on touch was seen. Ipsilateral preauricular lymphnode was palpable. Clinically a differential diagnosis of keratoacanthoma, sebaceous gland carcinoma and nodular basal cell carcinoma was entertained.

She was advised for excision biopsy of the lesion under frozen section control with eyelid reconstruction. Systemic examination revealed no evidence of malignancy. Patient underwent excision biopsy of the lid mass. Frozen section examination of the lesion revealed features consistent with molluscum contagiosum and subsequently the permanent



Fig. 1 Clinical photograph showing an umbilicated lesion in the left upper eyelid.



Fig. 2 Microphotograph showing frozen section study of excised biopsy showing acanthotic epithelium and multiple eosinophilic molluscum bodies (haematoxylin and eosin x 100)



Fig. 3 Microphotograph of permanent section showing molluscum bodies (haematoxylin and  $eosin \times 100$ )

section confirmed the findings. On light microscopy, this lesion showed acanthotic epithelium. Within the epithelium, innumerable round and oval eosinophilic intracytoplasmic inclusion bodies consistent with molluscum contagiosum was seen. Patient was assured and advised no treatment.

#### **Discussion:**

Tumors in the lid could present as a solitary nodule, with umblication in keretoacanthoma, basal cell carcinoma, sebaceous gland carcinoma, squamous cell carcinoma. Clinically occasionally it becomes difficult to make an unequivocal diagnosis of any of the above conditions. Molluscum contagiosum is usually umbilicated mostly situated on the eyelid surface and multiple in number. Molluscum contagiosum in the eyelid has been reported in patients with AIDS<sup>4</sup>. These are larger than non-HIV patients and often confluent. However, such a lesion in non HIV patient is rare. Our patient had single large eyelid lesions.

Keratoacanthoma is a specialized variant of pseudocarcinomatous hyperplasia that occurs mainly in exposed areas of the skin and usually develops in a period of weeks or few months. Clinically, а а typical keratoacanthoma appears as a dome shaped nodule with central keratin filled crater and elevated. rolled margins. Microscopic examination of а typical evelid keratoacanthoma discloses a cup shaped

nodular elevation and thickening of epidermis containing well-differentiated squamous epithelium surrounding a central mass of keratin. Frequently, the base of the lesion is rather uniform and well demarcated from the adjacent dermis by moderate inflammatory reaction. Collections of neutrophils forming microabscesses are usually present within some of the islands of squamous epithelium.<sup>1</sup>

The nodulo-ulcerative type of basal cell carcinoma appears clinically as a raised, pearly nodule, often exhibiting small telangiectatic vessels on this surface. As the nodule slowly increases in size, it may undergo central ulceration; eventually the lesion may appear as a slowly enlarging ulcer surrounded by prominent rolled border (rodent ulcer)<sup>2</sup>

Squamous cell carcinoma typically affects elderly, fair skinned individuals, most commonly it involves the margin the lower lid, but it may be located elsewhere in the eyelid. Clinically, the lesion usually manifests as an elevated, indurated plaque or nodule that tends to ulcerate and exhibits irregular borders. In well differentiated tumors, the masses of keratin may give the lesion a grayish white, granular appearance.

Sebaceous gland carcinoma consists of 1 to 3% of all lid tumors.<sup>3</sup> The disease affects elderly patients. Rarely it may occur before the age of 40. Sebaceous gland carcinoma can exhibit a broad spectrum of clinical features. Mostly commonly, it is presents as a small, diffuse plaque like thickening. It may also present as as a localized thickening of the lids associated with loss of lashes. The latter finding is caused by neoplastic involvement of the follicles of the lashes.

Though molluscum contagiosum can be seen as multiple, large and confluent lesions, it can also be seen a single large and umblicated lesion mimicking a neoplasm. Ophthalmologists and the other eye care personnel therefore should be aware of various presentations of molluscum contagiosum. We feel in such diagnositic dilemma, excision biopsy under frozen section control is advised. Electrocautery, chemical cautery, cryotherapy and surgical excision are the various treatment modalities described for molluscum contagiosum lesions.

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#### CME PROGRAMMES FOR THE SILVER JUBILEE YEAR 2002 - 2003

This Academic Year being the "Silver Jubilee Year" of Sankara Nethralaya attracts special significance and importance. Apart from the continuous efforts directed towards improvement of Patient's Care and Patient's Education on prevention and cure, the foundation has also lined up various CME Programmes for Ophthalmologists and Optometrists for updating their skill and knowledge.

Topics	Date
Uveitis & Systemic Diseases	29.06.2002
Revision Course in Ophthalmology for FRCS Exam going students	26.06.2002 to 02.07.2002
Contact Lens	31.08.2002
Update in Neuro-ophthalmology	26.10.2002 to 27.10.2002
Low Vision Aids	30.11.2002
Small Incision Cataract Surgery	14.12.2002 & 15.12.2002
Cornea	07.03.2003 to 09.03.2003
Revision course in ophthalmology for FRCS / MRCS exam going students	25.06.2003 to 01.07.2003
Paediatric Ophthalmology	05.07.2003 & 06.07.2003
Vitreo-retina	07.09.2003 & 08.09.2003
Glaucoma	06.12.2003 & 07.12.2003
	Uveitis & Systemic Diseases Revision Course in Ophthalmology for FRCS Exam going students Contact Lens Update in Neuro-ophthalmology Low Vision Aids Small Incision Cataract Surgery Cornea Revision course in ophthalmology for FRCS / MRCS exam going students Paediatric Ophthalmology Vitreo-retina

The programmes are aimed to provide continuing medical education to the practising Ophthalmologists, Residents in Ophthalmology and to the Optometrists.

#### FOR MORE DETAILS, PLEASE CONTACT

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# Multicentric trial of Intravitreal steroid implant in non-infectious uveitis affecting the posterior segment of the eye

You would be glad to know that Sankara Nethralaya is doing a project "A Multicenter, Randomized, Double masked, Controlled Study to evaluate the safety and efficacy of an Intravitreal Fluocinolone Acetonide (0.5 or 2 mg) Implant in patients with non infectious uveitis affecting the posterior segment of eye".

This 3 year global clinical trial is to evaluate the efficacy and safety of a new Intravitreal device in the management of posterior uveitis. This trial is being conducted concurrently in the United States, Australia, Europe, Canada and Singapore. The information from this trial will be part of an FDA submission for approval. In India besides our institute two other teaching institutions are involved in the trial.

#### I request you to consider referring patients who meet the following criteria:

1. Males and non-pregnant females over 6 years of age.

- 2. Uveitis of one or more years duration.
- 3. Patients who have received systemic therapy (steroids or immunosuppresants) or periocular steroids as part of their treatment for the uveitis.
- 4. Atleast 2 separate recurrences within the last six months requiring either systemic corticosteroids therapy or subtenon's injection of corticosteroids.

From a diagnostic standpoint this would mean patients with the following diagnosis:

Intermediate uveitis (parsplanitis) Sympathetic ophthalmia Vogt Koyanagi Harada Disease Behcet's disease Idiopathic posterior uveitis

We shall undertake a complete assessment of the patient at no expense to the patient and if found suitable, will receive the implant. All patients on the study are administered an informed consent prior to the study.

If your patient is found suitable for the study, I shall be sending you periodic updates of your patient. However, if the patient does not meet the inclusion criteria, I shall also inform you and the patient would be referred back to you for further treatment.

I would also like to mention that our institution has received the approval of our ethics committee and the Drugs Controller General (India) has permitted us to conduct the trial. The trial is being conducted under strict conformance to the ICMR and guidelines for good clinical practice.

I would be extremely pleased to answer any questions you may have.

**Dr J Biswas** Head of the Department of Ocular-Pathology and Uveitis Medical and Vision Research Foundations Sankara Nethralaya, 18, College Road, Chennai - 600 006 Phone: 044-8271616, Extn. 1302 / 1719 Fax : 044-8254180 E-mail: drjb@sankaranethralaya.org

#### UPDATE IN NEURO-OPHTHALMOLOGY Organized by Medical and Vision Research Foundations, Sankara Nethralaya October 26 & 27, 2002 at Hotel Ambassador Pallava, Chennai The update will include lectures, discussion, and case presentations on following topics: The optic nerve and its disorders, The efferent visual system, Neuroradiology and trauma, Ocular myopathies and Tumours of neuro-ophthalmic interest. FACULTY Dr. Robert Daroff, Cleveland, Ohio, USA Dr. B. Chidambaram, Chennai Dr. Andrew Lee, Iowa City, Iowa, USA Dr. Veena Noronha, Chennai Dr. JF Cullen, SNEC, Singapore Dr. Swatee Halbe, Chennai Dr. Sharon Tow, SNEC, Singapore Dr. Sujatha, Chennai Dr. Avertano Noronha, Chicago, USA Dr. K. Ganapathy, Chennai Dr. Vimala Menon, RP Centre, Delhi Dr. K. Rajaram, Chennai Dr. G. Natchiar, Aravind Eye Hospitals, Dr. K.C. Parvatham, Chennai Madurai Dr. A. Gajaraj, Chennai Dr. G. Arjundas, Chennai Dr. Thulasi Das, Chennai Dr. Deepak Arjundas, Chennai Dr. D. Rout, Chennai Dr. Suresh Bapu, Chennai Sankara Nethralaya faculty

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#### Contact

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# Diagnostic value of polymerase chain reaction (PCR) on intraocular specimens from patients with viral retinitis

K Priya, J Malathi and H N Madhavan

#### ABSTRACT

Since rapid aetiological diagnosis of viral retinitis is essential for institution of specific therapy, we evaluated the role of polymerase chain reaction (PCR) against fluorescent antibody technique (FAT) on intraocular specimens. One hundred and thirty intraocular specimens from 111 patients were investigated for herpes simplex virus (HSV), varicella zoster virus (VZV) and cytomegalovirus (CMV) by FAT and PCR. FAT alone detected the presence of HSV, VZV or CMV in five (3.8%) specimens from five (4.5%) patients, FAT and PCR in six (4.6%) specimens from four (3.6%) patients and PCR alone in 72 (55.4%) specimens from 66 (59.5%) patients. PCR has increased the clinical sensitivity by 55.4% and 59.5% among the specimens and patients respectively, which was statistically significant (McNemar test, P<0.001). We conclude that PCR is a rapid, absolutely specific, several folds sensitive and a more reliable diagnostic tool than FAT in viral retinitis.

**Key words:** Polymerase chain reaction, Viral retinitis, Herpes simplex virus, Varicella zoster virus, Cytomegalovirus

#### INTRODUCTION

Herpetic retinal and choroidal diseases is a problem encountered in both immunocompetent and immunosuppressed patients, but presents a greater diagnostic dilemma in the former group because of a low index of suspicion.<sup>1</sup> Accurate differentiation of herpes simplex virus (HSV) and varicella zoster virus (VZV) from cytomegalovirus (CMV) has significant therapeutic implications, as the therapeutic agents differ.<sup>2</sup> In the early stages of ocular manifestations and in patients with atypical features, it is difficult to differentiate

between CMV and other herpesvirus associated retinitis. Discrimination between viral and nonviral pathogens such as Toxoplasma gondii can be particularly difficult solely based on clinical presentations.<sup>2</sup> Rapid and accurate diagnosis of the ocular infection and prompt initiation of appropriate therapy is essential both for the preservation of sight and improved survival of the patient.<sup>3</sup> Furthermore, the personal cost of the patient and the wastage of resources associated with the use of multiple antiviral therapies prompts the development of rapid, sensitive and specific diagnostic tests for ocular pathogens.<sup>4</sup> The conventional laboratory methods of virus diagnosis include antigen detection by fluorescent antibody test (FAT) and virus isolation. Virus isolation, though the gold standard, is not a rapid diagnostic method. FAT, though rapid is adversely influenced by small sample size and low antigen threshold. Polymerase chain reaction (PCR) has been employed as a molecular biological tool in the diagnosis of viral retinitis by many investigators.<sup>2,5,6</sup> Therefore we evaluated the role of PCR in the aetiological diagnosis of herpesviral retinitis.

#### MATERIALS AND METHODS

#### Patients and specimens

A total of 130 (104 aqueous humor [AH], 26 vitreous fluid [VF]) intraocular specimens were collected from 111 patients during a period of 3 years from 1999-2001. The 111 patients included 32 acute retinal necrosis [ARN], six progressive outer retinal necrosis [PORN], 23 CMV retinitis, two herpes zoster ophthalmicus [HZO], 13 geographic hellicoid peripapillary choroiditis [GHPC], 17 viral retinitis, three choroiditis, 13 uveitis, one retinal vasculitis, one retinal sclerosis. Of the

Table 1: Specimen-wise results of fluorescent antibody test (FAT) and polymerase chain reaction (PCR) for the detection of herpes simplex virus (HSV), varicella zoster virus (VZV) and cytomegalovirus (CMV) in 130 intraocular specimens from 111 patients with viral retinitis

S No	Specimen	No. of specimens	HSV			VZV			CMV		
			FAT+	FAT/ PCR+	PCR+	FAT+	FAT/ PCR+	PCR+	FAT+	FAT/ PCR+	PCR+
1	AH	104	1	-	12	2	2	25	-	-	17
2	VF	26	-	2	4	2	2	4	-	-	10
	Total	130	1 (0.8)	2 (1.5)	16 (12.3)*	4 (3.1)	4 (3.1)	29 (22.3)*	-	-	27 (20.8)*

Numbers in parenthesis denotes the percentage

AH - aqueous humor; VF - vitreous fluid

\* - PCR has increased the clinical sensitivity by 55.4% which was statistically significant (McNemar test, P<0.001)

111, 24 patients were human immunodeficiency virus (HIV) positive. Both AH and VF were collected from 14 patients.

#### Controls

Ninety intraocular fluids (30 AH from cataract extractions, 20 VF from patients with diabetic retinopathy, 20 AH and 20 VF from culture proven bacterial or fungal endophthalmitis) collected from 90 patients were included as controls to determine the prevalence of herpesviral DNA in the intraocular fluids of patients without clinical evidence of an active viral inflammatory process.

#### Fluorescent antibody test (FAT)

Fluorescent antibody test (FAT) was done using rabbit polyclonal anti-HSV types 1 or 2 antisera for HSV, hyperimmune antisera for VZV and mouse monoclonal anti-CMV antisera. $^{3,7}$ 

#### Polymerase chain reaction (PCR)

DNA extraction and PCR were carried out as described by us earlier.<sup>8,9</sup> In brief, the DNA was extracted by proteinase K - phenol chloroform method. PCR was done using custom synthesized primers coding for the DNA polymerase gene of HSV, the immediate early gene 63 for VZV and the morphological transforming region II gene for CMV. The PCR reagents were procured from Bangalore Genei Pvt. Ltd. (Bangalore, India) and the amplification was carried out in Perkin Elmer model no. 480 and 2400 (USA) and Hybaid Omnigene model no. HBTR3CM (UK). The PCR amplified products were analyzed by gel electrophoresis using 2% agarose containing 0.5 g/ml of ethidium bromide.

The specificity of the primers was tested using various viral, bacterial and fungal DNA, human DNA and the intraocular control DNA. The sensitivity of the primers was tested using serial 10-fold dilutions of the corresponding positive control DNA of HSV, VZV and CMV.

#### Results

The primers targeting HSV, VZV and CMV were absolutely specific, as they did not amplify any of the other viruses, bacteria, fungi or human leukocyte DNA. The sensitivity of the PCRs was 0.2 pfu/ml and 0.3 pfu/ml for HSV-1 and HSV-2 respectively, and 10fg and one femtogram for VZV and CMV respectively. PCR did not detect HSV or CMV genomes in any of the 90 intraocular control fluid samples. VZV-DNA was detected in 1 (1.1%) of 90 control samples, which was a VF from a culture proven case of bacterial endophthalmitis.

The specimen-wise and patient-wise results of FAT and PCR for the detection of HSV, VZV and CMV on 130 specimens from 111 patients have been tabulated in tables 1 and 2 respectively. Of the 130 specimens from 111 patients, FAT alone detected the presence of HSV, VZV or CMV in five (3.8%) specimens from five (4.5%) patients, FAT and PCR in six

Table 2: Patient-wise results of fluorescent antibody test (FAT) and polymerase chain reaction (PCR) for the detection of herpes simplex virus (HSV), varicella zoster virus (VZV) and cytomegalovirus (CMV) in 130 intraocular specimens from 111 patients with viral retinitis

	Clinical diagnosis	No. of patients	HSV			VZV			CMV		
S. No			FAT+	FAT/ PCR+	PCR+	FAT+	FAT/ PCR+	PCR+	FAT+	FAT / PCR+	PCR+
1	ARN	32	1	1	8	3	2	9	-	-	5
2	PORN	6	-	-	-	-	-	2	-	-	3
3	CMV retinitis	23	-	-	1	-	-	2	-	-	13
4	HZO	2	-	-	-	-	-	1	-	-	-
5	GHPC	13	-	-	2	1	-	5	-	-	-
6	Viral retinitis	17	-	-	2	-	-	5	-	-	2
7	Choroiditis	3	-	1	-	-	-	1	-	-	1
8	Uveitis	13	-	-	1	-	-	1	-	-	1
9	Retinal vasculitis	1	-	-	1	-	-	-	-	-	-
10	Retinal sclerosis	1	-	-	-	-	-	-	-	-	-
	Total	111	1 (0.9)	2 (1.8)	15 (13.5)*	4 (3.6)	2 (1.8)	26 (23.4)*	-	-	25 (22.5)*

Numbers in parenthesis denotes the percentage

\* - PCR has increased the clinical sensitivity by 59.5%, which was statistically significant (McNemar test, P<0.001)

(4.6%) specimens from four (3.6%) patients and PCR alone in 72 (55.4%) specimens from 66 (59.5%) patients. Thus PCR has increased the clinical sensitivity by 55.4% and 59.5% among the specimens and patients respectively, which was statistically significant (McNemar test, P<0.001).

Of the 14 patients with dual specimens of AH and VF, herpesviral DNA was detected in AH alone in one (7.1%), VF alone in five (35.7%) and both in five (35.7%) patients. Overall, herpesviral DNA was detected in 56 (52.8%) of 106 AH and 22 (84.6\%) of 26 VF.

#### Discussion

In 1995, before the introduction of PCR, we implicated herpesviral aetiology in 44.4% of ARN patients (2 HSV and 2 CMV) by FAT.<sup>3</sup> In 1999, we implicated herpesviral aetiology in 18.8% of ARN patients (1 HSV 2 VZV and 3 CMV) by FAT.<sup>10</sup> Today in this study, the herpesviral aetiology was implicated by FAT in 3.6% of viral retinitis patients. This decrease in the antigen detection rate by FAT over the

years is probably attributed to the decreasing antigen threshold due to the high load of antivirals before the patients reach the referral centres. With the application of PCR herpesviral aetiology was implicated additionally in 59.4% of these patients. This implies the remarkable increase in the rate of aetiological diagnosis of viral retinitis. In five specimens from five patients, HSV or VZV antigens were detected by FAT alone while their corresponding genomes was not detected by PCR. This positivity was considered as false due to the high relative subjectivity of the microscopic observations involved in the interpretation of fluorescence tests. This was further confirmed by the exclusion of the presence of PCR inhibitors in these specimens by spiking them with the least amount of known positive control DNA.

PCRs for the detection of HSV, VZV and CMV were absolutely specific and highly sensitive. VZV-DNA was detected in one patient with post-operative bacterial endophthalmitis. It is likely that in this patient activation of VZV could have been triggered during the episode of bacterial endophthalmitis with a spill over of the virus-laden leukocytes into the vitreous cavity. The absence of HSV, VZV and CMV genomes in the intraocular fluids of patients undergoing cataract extraction and patients presenting with non-viral retinal inflammations indicate that the detection of herpesvirus DNA by PCR implicates an active infection. Other investigators have also shown similar findings,<sup>5,11,12</sup> except in one report by Fox et al6 who detected CMV-DNA in one of eight vitreous fluid tested from normal persons.

Comparing the detection rate of AH and VF, our findings indicate that AH is as good as VF in the detection of the herpesviral aetiology. Therefore, being a simple and safe office procedure, AH is an ideal specimen for the detection of the viral aetiological agent by PCR.

In the context of an established diagnostic virology laboratory in India, the approximate working (recurring) cost to detect these three viruses per specimen of conventional virological methods (FAT and virus isolation) is Rs. 1200/ - while that of PCR is Rs. 750/-. The expertise of the personnel involved is equally expensive for both the tissue culture and PCR work.

In this study we have been able to attribute herpesviral aetiology in 72/113 (63.7%) patients with viral retino-choroiditis. Thus, PCR has been extremely helpful as a rapid, absolutely specific, highly sensitive and a more reliable diagnostic tool for the detection of the herpesviral agents in patients with viral retinitis.

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## Managing the unco-operative patient under Local Anaesthesia - How We Do It

Ian Sundararaj

A patient undergoing ophthalmic surgery under local anaesthesia may become uncooperative after entering the operation theatre due to "needle phobia" or may pull out the sterile drapes after being draped, due to suffocation or claustrophobia.

Sometimes it is possible to assuage the fears of the unco-operative, anxious patient and convince him to undergo surgery under local anaesthesia. In the occasional patient however, it may be necessary to reassess the patient's fitness to undergo a general anaesthesia and return for surgery at a later date.

General anaesthesia has its own disadvantages when compared with a local or a regional anaesthesia. Furthemore, several patients who present for cataract surgery have co-existing medical diseases like ischaemic heart disease, hypertension, diabetes, asthma, liver, renal or endocrine disease. Special investigations such as an echocardiogram or serum electrolytes may also be required and this may further delay surgery.

Local anaesthesia acts by blocking pain sensation without producing total unconsciousness. There is less 'insult' to the various systems and less release of stress hormones.<sup>1</sup> The problems of postoperative nausea and vomiting, laryngospasm and other complications related to general anaesthesia can also be avoided.

Sometimes patient's relatives are unwilling for a patient to undergo the risk a general anesthesia for cataract surgery. So left with no choice a local anaesthesia will have to given.

How can you convince a patient to cooperate and help him to overcome his fear of needles, suffocation and claustrophobia? How to convince him to stay still during surgery ? Is it possible ? We have been confronted with the "difficult patient" many a time and we have found it worth while helping both patient and surgeon under such circumstances.

#### **CLAUSTROPHOBIA & SUFFOCATION**

The patient suffering from claustrophobia refuses to be draped after administration of the local anaesthetic. If we are aware that the patient suffers from claustrophobia we try a "trial draping" pre-operatively after explaining to the patient the manner in which he will be draped in the operation theatre. It helps to ask the patient how he feels with the drapes covering his face. If the patient feels uncomfortable we lift up the drape from the face and give sufficient space till the patient feels comfortable.

We have also asked the patient's relatives to try draping the patient at home. This is especially useful in the mentally retarded patient (eg. The patient with Down's Syndrome.)

On the operation table also we try the same technique providing the patient with enough space by lifting the drapes away from the face. We use a special stainless steel arch that is placed across the patient's chest which helps to lift the drapes preventing them from falling on the patient and causing a feeling of suffocation. This also gives enough room for the patient to breathe easily.

Oxygen is administered via a twin bore nasal oxygen catheter and the flow may be increased till the patient feels comfortable. Sometimes allowing sufficient light to enter under the drapes seems to help the claustrophobic patient.

#### DEMENTIA

#### Alzheimer's Disease

After obtaining intravenous access (which can sometimes prove difficult!), the patient maybe sedated with midazolam<sup>2</sup> ( a short acting benzodiazepine) in the dose of 1mg intravenously and propofol<sup>3</sup> (a short acting intravenous agent) given in 10mg incremental doses. After the patient is just asleep and quiet, the local anaesthetic block is given. Recovery from propofol is quick and uneventful.<sup>4</sup>

#### ANXIETY, APPREHENSION

Injection midazolam in a dose of 0.5 -1mg intravenously followed by propofol in 10 mg incremental doses have both been tried with success in many of our patients. Propofol can be used in intermittent doses till the patient is made calm but is still conscious and responding to commands.

The patient recovers completely and quickly soon after the last dose.

We have found it helpful to allow the patient's close relative to be with the patient in the operation theatre to hold his hand during surgery and talk to him.

## INTERSTITIAL LUNG DISEASE, COPD, KYPHOSCOLIOSIS

Patients with chronic lung disease will find it difficult to lie supine for long periods of time. A careful detailed history will be helpful to ascertain the correct position in which the patient can lie comfortably without any respiratory insufficiency. The position in which the patient sleeps at night, (eg. supported by pillows etc) maybe tried on the operating table. After positioning the patient the surgeon should focus the operating microscope and see if he is able to perform surgery in a position other than the usual. The patient should be supported using a pillow to maintain that posture without moving.

#### HARD OF HEARING

If the patient is hard of hearing and does not use a hearing aid and if he has some vision

in the eye he is shown the syringe, needle etc and using hand signs the local anaesthetic procedure is explained to the patient.

When the surgery is over and when we remove the drapes we often find a smiling satisfied face filled with gratitude!

#### UNDERSTAND THE PATIENT'S PROBLEM

Some times the patient may have problems which could be the cause for restlessness such as a distended bladder, water entering the ear while cleaning, severe back pain or pain in the leg, tight BP cuff etc. In such situations the cause should be ascertained and appropriate measures taken to alleviate the patient's discomfort.

These are some of the simple but important measures by which we have been able to successfully anaesthetize and operate on our patients.

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# Macular Changes associated with Hyper Histidinemia

Nitin S Shetty, S. Lakshmi and K. N. Sulochana

#### INTRODUCTION

Amino acids are known to be associated with retinal degenerative disorders. Hyper homocystinuria is associated with retinal vein occlusion<sup>1</sup>. Ornithinemia is seen in patients with gyrate atrophy<sup>2</sup>. Few cases of glycinuria<sup>3</sup> and cystinuria<sup>4</sup> have also been reported to be associated with retinal degenerative diseases. Hyperthreoninemia is associated with blindness, nystagmus and variable opthalmoscopic appearance<sup>4</sup>. In this article we report for the first time the association of macular abnormalities seen in patients with elevated levels of histidine.

#### CASE REPORTS

**Case 1 :** This patient was first seen here in 1981 as a 7-year-old child who was brought for examination with complaints of defective vision in both eyes and squinting of eyes. At that time he was noted to have scanty, hypopigmented scalp hair. The antenatal history was unremarkable. He was born of a full term, forceps assisted delivery. There was no history of any birth injuries. His younger brother was having similar complaints. History of consanguinity was noted amongst the parents. The child had undergone investigations to detect antibodies against toxoplasmosis the tests were negative. X-ray of the skull had been done elsewhere and was normal.

His best-corrected visual acuity was noted to be 6/18; N 6 and 6/18; N 18 in the right and left eye respectively. A refractive correction of -1.75 diopter spherical was required in both eyes. Fundus examination in both eyes showed a large well-demarcated atrophic lesion involving almost the entire macula. Pigment clumping was noted within the lesion. The optic nerve head and the retinal blood vessels were normal. Tests for toxoplasmosis were repeated and were again found to be negative.

The patient was being followed up on a regular basis here and complained of fluctuating vision in both eyes. At his last checkup here, his visual acuity was 6/24; N10 and 6/60; N10 in both eyes. Clinically the extent of the atrophic fundus lesion was the same; however the pigmentation within the lesion was found to be progressively increasing.

Electroretinogram test carried out in February 1999 showed marked reduction in both the cone and rod responses, indicating a more generalized involvement of the retina. The test repeated two years later showed further reduction in the rod and cone responses.

Color vision was found to be grossly affected as tested with Ishihara's test plates.

Examination of the patient's brother showed similar fundus lesions.

**Case 2** : A 35-year-old female patient presented with history of decreased vision and nystagmus in both eyes since early childhood. Vision was more or less stable and the patient did not complain of progressive loss of vision. Past and family history was unremarkable except for history of consanguinity amongst her parents. She gave history of having scanty hypopigmented hair since early childhood. Her best-corrected visual acuity was noted to be 3/ 60;N6 in both eyes. A refractive error of -11.0 Dsph and -9.00 Dsph was noted in the right and left eye respectively. Fundus examination in both eyes showed mild pallor of the optic nerve head. A broad annular atrophic ring was noted in the central macular region. Rest of the posterior pole had a tessellated appearance. The retinal blood vessels and the peripheral retina were normal. Fluorescein angiography showed a central annular band of transmission



defect. An ERG test showed reduction in both the rod and the cone amplitudes.

#### **BIOCHEMICAL METHODS:**

Amino acid and homocystine analysis in plasma sample was done in acid citrate dextrose anticoagulated blood sample and fasting urine sample. The clear supernatant obtained after precipitating the plasma with 10%TCA was used for the analysis.

The amino acid analysis was carried out using HP-HPLC by the method of pre-column OPA derivatization. The detection was carried out at 338nm using variable wavelength detector. The gradient elution was performed using acetate buffer (A) and acetate buffer with 40% of acetonitrile and methanol each (B) of pH  $7.2^5$ .

Homocystine analysis was performed isocratically using phosphate buffer of pH 3.5 with C18 RP column and the detection was done at 190 nm (UV detector)<sup>6</sup>.

#### **RESULTS & DISCUSSION**

The amino acid analysis revealed increase in plasma histidine. In case 1 it was 106.56 and in case 2 - 60.05. (normal 26.34  $\pm$  3.98) nm/ml and normal levels of other amino acids in both plasma and urine. In case 2, the homocystine was found to be increased to 50 $\mu$ M from a normal of 0-19 $\mu$ M in urine and normal levels in plasma.



Histidine, an imidazole containing amino acid is catabolised to glutamate and in this process, it contributes a carbon atom to one carbon metabolism. The enzyme involved is histidase. An error in this metabolism leads to increase in histidine levels leading to histidinemia. This is a rare genetic disorder that is inherited in an autosomal recessive<sup>7</sup> pattern. Histidinemia cases often have impaired intellectual speech development. However our cases appeared to be intelligent. In one of the article published by the Dhir SP etal have reported the association of histidinemia<sup>8</sup> with reduced visual acuity, nystagmus and hypopigmentation of the maculae. In our cases also we have similar clinical findings like degeneration, reduced visual typical RPE acuity and hypopigmentation of hair etc.

The mechanism behind histidinemia may be due to a disorder in the enzyme histidase. The disorder or deficiency of histidase enzyme may be due to a mutation in the gene coding for the protein histidase . This enzyme is necessary for the conversion of histidine to transurocanic acid. This intermediate product is reported to undergo photoisomerisation when it absorbs UV light. It is also believed that the enzyme histidase has a role in mediating UV protection via the transurocanic acid. Thus when there is impairment in the enzyme histidase, there may be possibility of hypopigmentation in the patients with histidinemia<sup>9</sup>.



Fig: 1 Plasma Amino acid profile from a Normal individual

Plasma Histidine level : 30.32 (normal : 26.34 ± 3.98)

Alternatively the cause of histidinemia may be due to deficiency of vitamin folate that is involved in the histidine metabolism. It is suggested that for such patients intake of vitamins or plenty of vegetables and fruits with low histidine diet can be given.

In case 2 an increase in homocystine in urine along with histidinemia was observed. The increase in level of homocystine is reported to be a marker for the diagnosis of the deficiency of vitamin B12 and folate<sup>10</sup>. Homocystinemia is also reported to be a risk factor for nonarteritic anterior ischemic optic neuropathy, central retinal artery occlusion and central retinal vein  $occlusion^{11}$ . This deficiency may also be due to defective absorption or availability of the vitamins.

Even though both conditions had changes restricted to the posterior poles, the characteristics of the lesions were quite different. Factors other than just histidine abnormality may be playing a role. These need to be further investigated. The ERG findings in both cases were however more or less similar with marked reduction in both the cone and rod responses. Progressive loss of the ERG amplitudes as seen in Case 1 suggests that this is likely to be a progressive condition.



Fig: 2 Plasma Amino acid profile of case 1 with Macular changes

Plasma Histidine level : 102.56 (normal : 26.34 ± 3.98)

The mode of inheritance in these patients could not be exactly determined. The history of consanguinity in the parents in both the cases could suggest a autosomal recessive inheritance. However the other family members need to be examined both clinically and by biochemical tests, in order to detect any 'subclincal' cases.

In the 2 cases we have reported the increase of histidine is association with the clinical findings of macular dystrophic changes. In such cases of macular dystrophy, the measurement of plasma amino acid. histidine in particular, may be useful in the differential diagnosis. Readymade diet low in histidine may be used with regular monitoring of histidine levels in blood and urine.

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microscope to record intra-operative photographs. The camera can also be used to take photographs of CT Scan, MRI, X Ray plates attached to the view box. Some of these cameras also have a facility to record video for a short duration besides still photographs. This also is useful to record observations such as nystagmus, essential blepharospasm, etc. Attached to the slit lamp one can also record procedures such as tear film break up time, siedel's test for leaking wounds etc. Which camera to buy ? Well there are several cameras available in the market today.(Nikon, Kodak, Sony, Canon, Fuji, Minolta) Most of these cameras are priced between 600 to 800 US \$. One should choose a camera that gives a minimum resolution of 2 million pixels. This is essential to have printouts comparable to standard photographic quality. The Nikon coolpix 995 with a resolution of 3.34 million pixels is a good buy and proves useful in ophthalmic photography.

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## COME, GIVE THE GIFT OF SIGHT

## Last Page Digital Photography

#### Rajesh Fogla

Photographic documentation is an essential component of clinical ophthalmology, to document interesting cases, assess treatment outcomes and collect data for teaching and research. It has played a crucial role in many successful research projects to determine the effectiveness of newer treatment procedures, to obtain knowledge about eye diseases and their effect on vision. It also proves useful as a teaching tool, to describe various ocular diseases to residents in training, as well as ophthalmologists at various continuing medical education sessions.

Majority of the clinical imaging in ophthalmology is related to the posterior segment ie retinal photography and fundus fluorescein photography. This is followed by external photography of the eye and adnexa, and slit lamp photography of the anterior segment.

Most of these photographs are usually taken with the conventional 35mm camera with macrolenses of long focal length, and electronic flash equipment. With recent advances in technology, many sophisticated products using computers and imaging technology are currently available in the market for ophthalmic photography. These latest digital cameras offer many advantages over the standard 35 mm equipment, and allow instant availability of results besides adjustment of image parameters.

Digital cameras have a chip or CCD that images the photograph. A digital camera with a high density 3.34 million pixels CCD chip, gives a maximum image resolution of 2048 x 1536 pixels. This is essential for good quality colour prints. How are the images stored ? Well the images are instantly stored onto the hard disk or memory card in the camera. Compact flash card of different storage capacity are available (16 / 32/ 64 / 128 Mb) and the number of pictures it can store depends on the resolution selected. These images can be transferred to the computer and stored on compact discs. The images can also be viewed on the large screen of the computer monitor.

Digital workstations though expensive, provide a variety of options for ophthalmic photography. The images taken can be immediately reviewed on the large monitor at different magnifications. Various image enhancement techniques can also be applied to these images. The images can be stored or transferred to a different computer over the network.

Photography with the handheld digital camera is fairly simple. Most of the images can be taken in the autofocus mode. These images can be instantly reviewed on the inbuilt monitor of the camera and taken again if not satisfactory. External macrophotographs of the eye and adnexa are easy to shoot in ambient room illumination. Slit lamp photography of the anterior segment needs a little patience and practice. The camera lens needs to be held or attached to the evepiece of the slit lamp. Excellent photographs can be taken with diffuse illumination, slit illumination and retroillumination. One can also attach the camera to the eyepiece of the operating (contd. on page 27)

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