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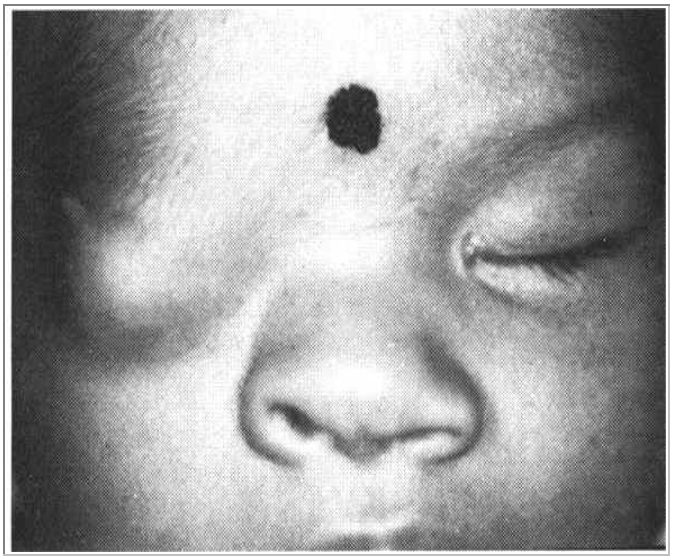
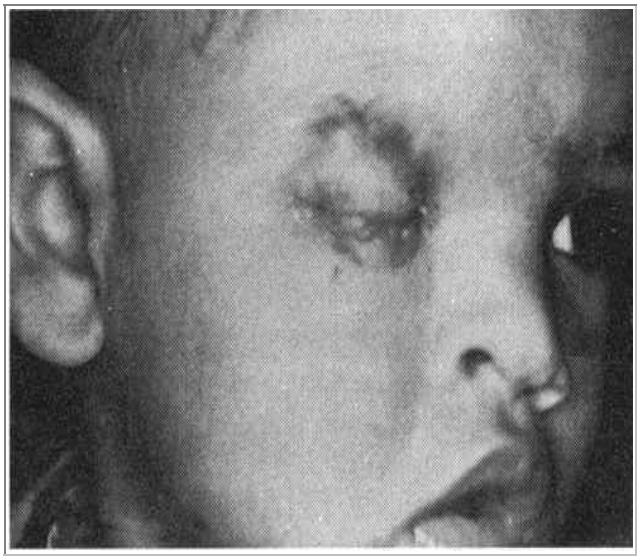


Presurgical photograph taken at 28 days of life showing complete left cryptophthalmos.



Age 13 months after skin grafting,showing no adhesions and good cosmetic outcome.

Editorial

The event of this year, some dub it as that of the century _ the unraveling of the Human Genome finds a mention in this issue of Insight also. Dr. Kumaramanickavel has lucidly written about the implications of this discovery to Medicine and in particular Ophthalmology. Scientists especially the Genetic scientists predict the end of the scalpel and the pill. He has also introduced a new term _ Predictive Medicine. The concept is interesting _ predict the onset of the disease and annul it before it occurs. No doubt the darker side of this technology is foreboding to think of,but as Dr. Kumar optimistically puts it, the positive effects will eventually prevail.

Most of us have some time or other accessed the Internet for Medical literature search. The most useful sites find a mention in Dr. Rajesh Fogla's article along with the ways of accessing them. This issue also contains interesting case reports and a perspective article on management of Malignant Melanoma of the Choroid.

Dr Mahesh P Shanmugam
Editor

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Perspective:

Treatment of Malignant Melanoma of Choroid

Mahesh P Shanmugam

The ideal treatment for malignant melanoma of the choroid is as yet unknown. Enucleation, the usual treatment for most intraocular malignancies is said to be associated with an increased mortality in malignant melanoma of choroid. This was noted, despite the lack of evidence of metastatic disease at the time of surgery.[1] Mortality has been found to be as high as 30% in the first 5 years after enucleation and 50% within 10 years.[1]

The surgical trauma of enucleation is said to increase the risk of metastasis.[1,2] Another hypothesis is that undetected subclinical hepatic metastasis exists at the time of enucleation, kept dormant by host immune response. Enucleation may remove the primary antigenic stimuli thereby allowing the metastatic foci to proliferate. Anti-tumour antibody levels have shown to increase after local treatment such as photocoagulation and irradiation while it falls after enucleation.[3] This may lead to unchecked proliferation of the metastatic disease, causing death.

In the recent years, there has been a shift away from enucleation in the management of uveal melanomas. This shift is not attributed only to the increased risk of mortality after enucleation. The recognition that spindle cell tumours are less malignant and small melanocytic tumours behave biologically dormant with little tendency to grow and metastasize has prompted physicians to conservatively manage these tumours.

Despite these controversies, enucleation has a definite role to play in the management of some malignant melanomas of the choroid, and there is agreement on performing a minimal manipulation enucleation.[2,4,5]

Current management of malignant melanoma of the choroid:

The choice of treatment for a particular patient depends on multiple factors.[6]
Visual acuity: Eyes with salvageable vision are treated conservatively, while those with no visual potential are enucleated.

Intraocular pressure: Choroidal melanomas with increased intraocular pressure are an indication for enucleation as they seldom respond to conservative treatment.

Size of the tumour: Small melanomas (2-3mm thick) are usually observed periodically for evidence of growth and other signs of malignancy. Medium (3-5 mm thick) and large (5-10mm thick) may be observed, irradiated, locally resected or enucleated depending on other factors. Extra large (>10 mm thick, 15mm in diameter) are usually enucleated.

Location of the melanoma: Tumours close to and involving the optic nerve are enucleated, while a tumour located at the equator can be irradiated and an anterior tumour can be resected depending on the size and other factors.
Growth pattern of the tumour: Diffuse tumours and those associated with large extrascleral extensions may need radical surgery.

Activity of the tumour: Documented growth on follow-up, presence of subretinal fluid, and an abrupt elevation from the Bruch's membrane suggest an active tumour, needing treatment. Drusen on the tumour surface indicates chronicity. Hazy and ill-defined orange pigment over the tumour indicates activity while well-defined pigment indicates dormancy Status of the opposite eye: In a one eyed patient, all attempts are made to manage the tumour conservatively.

Age of the patient: Enucleation may not improve the systemic prognosis in patients over 65 years of age and hence older patients are managed conservatively1.

General health of the patient: Sick patients who obviously cannot tolerate surgery or those with metastatic disease are managed conservatively.

Treatment Modalities:

Periodic observation:

Dormant, small and medium sized tumours, slow growing small and medium tumours in sick and one eyed patients may generally be observed periodically.7

Enucleation:

Large tumours producing visual loss and of a size which cannot be managed by conservative methods, small or medium sized tumours with optic nerve invasion, posterior uveal melanomas with total retinal detachment or severe glaucoma need enucleation. A minimal manipulation enucleation is advised, to prevent hematogenous dissemination of the tumour. A "no touch technique" has been advocated as also cannulation of the anterior chamber to avoid sudden fluctuations in the intraocular pressure, thereby avoiding egress of tumour cells from the eye.2,4,5

The COMS study has shown that pre enucleation radiation with 2000cGy did not alter the mortality rate (as compared to those not treated with radiation).8 Overall mortality was 57% in the enucleation only group and 62% in the preenucleation radiation group. This difference was not statistically significant. The factors statistically associated with prognosis for survival were the age of the patient and the longest basal diameter of the tumour.

Local Resection:

Indications: Tumours close to the ora serrata, not extending more than 4 clock hours of pars plicata, choroidal melanoma not greater than 15 mm in diameter, centered at the equator can be considered for partial lamellar sclerouvectomy if the retina is spared, and penetrating sclerochorioretino-vitrectomy if the retina and sclera are involved.9,10

The technique involves localisation of the tumour on the sclera, dissection of partial thickness scleral bed, resection of a thin layer of the sclera with the tumour leaving the overlying retina intact, if there is no retinal involvement. The presence of a secondary retinal detachment overlying the tumour aids resection of the tumour without damaging the retina. Preoperative barrage laser photocoagulation or cryotherapy 2-3 mm surrounding the tumour is done, if retinal involvement is noted, in an attempt to keep the retina attached postoperatively. In such a situation, the infiltrated retina with the tumour is removed with open sky vitrectomy through the scleral window. The sclera if involved is also removed and replaced with donor scleral graft.

Complications of this procedure include retinal detachment, cataract formation, vitreous hemorrhage, expulsive hemorrhage, chronic cystoid macular edema, anterior segment ischemia, tumour recurrence, hypotony, wound leak and pre retinal fibrosis. Resection is generally preferred for anterior tumours with a small base and greater height in younger patients. Resection is under a cloud in view of the COMS results which state that 55 % of tumors had scleral invasion on histopathological examination.11 If the partial thickness scleral flap contains unnoticed residual tumor this can cause local recurrence of the tumour and also increase the risk of orbital seeding.

Internal resection:

This involves preoperative photo-coagulation around the tumour followed by vitrectomy and internal removal of the tumour piece-meal, in posteriorly located tumours that are not amenable to lamellar sclerouvectomy.12 The concern is of promoting metastasis with this technique. Long term results of this procedure are awaited.

Photocoagulation:[13]

Photocoagulation has been tried for malignant melanoma of choroid but not with the same success as for retinoblastoma. (1) Small nasal melanoma (2) temporal peripheral small melanoma located away from macula and outside

the arcade can be treated with laser photocoagulation.[14] The tumours should be less than 3 mm in height and 9 to 10 mm in basal diameter without secondary retinal detachment. They should not be closer than 1 disc diameter from disc. Less than 5% of melanomas meet the criteria laid down for use of photocoagulation. Multiple treatment sessions may be necessary before satisfactory regression of the tumour.
Retinal break formation, choroido retino vitreal neovascularisation near edge of treatment, branch retinal vein occlusion, secondary macular edema and corneal and iris burns are known complications of photocoagulation treatment.

Photodynamic therapy:[15]

The combination of a tunable dye laser and a suitable photoactivated dye has been attempted in the management of malignant melanomas. Haematoporphyrin dye derivative (HPD) is the most commonly used dye. The efficacy of this treatment is still under trial.

Radiotherapy

External beam radiotherapy:

Pre enucleation radiotherapy had been advocated to decrease the mortality rate following enucleation, but the COMS and other study results have indicated othewise.[8,16] Post enucleation irradiation to the orbit has been found to decrease the mortality.[17] Regular external beam radiotherapy is not used in the management of choroidal melanoma due to the large dose involved that will invariably cause radiation related complications leading to blindness. Post enucleation irradiation may be useful in cases where extra-scleral extension is noted intra-operatively.

External beam Particle Radiotherapy:

The charged particle radiation consists of usage of helium ions and protons and the benefit lies in the fact that relatively large doses can be delivered to the tumour specifically. The high energy charged particles have minimal scatter and a well defined, finite, energy dependent range. The entire tumour can be treated uniformly, and due to the inherent Bragg peak effect, unnecessary radiation to the normal tissue is avoided.[18]

Uveal melanomas up to 24 mm in diameter and 14 mm in height have been treated with charged particle irradiation. Tumours involving the fovea, optic nerve head, those with small extrascleral extension are also manageable. The technique involves localisation of the tumour with transillumination and indirect ophthalmo-scopy and suturing four, 2.5-mm tantalum rings as localisation markers. The treatment is then planned using a computer, thereby choosing the correct direction of the beam, which entails minimum radiation to normal structures but also complete treatment of the tumour and 1.5 mm of surrounding normal tissue. Approximately 70 gray equivalents of Cobalt 60 are delivered in 5 sittings over 7 to 10 days.

The five year survival rate following proton beam radiation has been reported to be comparable with that of plaque therapy.[19] Complications include those of the surgery such as transient diplopia, intratumour hemorrhage and those related to radiation such as epilation, epiphora due to punctal occlusion, dry eye, cataract formation, rubeosis iridis, neovascular glaucoma, radiation vasculopathy, papillopathy, maculo-pathy, macular edema, neovascularisation of the retina, and vitreous hemorrhage.

The disadvantage of the current charged particle radiation systems is that they are expensive to install and maintain.

Brachytherapy

The current relative indications of plaque radiotherapy are: 1) selected small melanomas that are documented to be growing or that show clear-cut signs of activity on the first visit, 2) most medium-sized and some large choroidal and ciliary body melanomas in an eye with potential salvageable vision, 3) almost all actively

growing melanomas that occur in the patient's only useful eye. If a melanoma exceeds 15 mm in diameter and 10 mm in thickness, one should anticipate visual morbidity from radiation therapy and enucleation should be strongly advised.[20] The surgical technique of radioactive plaque application has been described in detail in the literature.[20,21] Local tumour relapse after plaque radiotherapy has been reported to occur in up to 16% of cases.[22,23,24,25] Complications of plaque therapy are similar to those of charged particle radiation.

In published literature, there is no statistically significant difference in survival between patients treated with plaque radiotherapy (cobalt 60, iodine 125) and those treated with enucleation.[26-29] One arm of the COMS study designed to evaluate enucleation vs plaque therapy in the treatment of medium sized tumours has completed patient recruitment and the results are awaited.[30]

Combined plaque radiotherapy and laser photocoagulation or thermotherapy has been used recently to increase the likelihood of complete local tumour destruction particularly in patients with tumour adjacent to the optic disc.[31] Preliminary results have shown that hyperthermia in combination with plaque radiotherapy may decrease the adverse effects of radiation to the retina, optic disc and choroid.[32]

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Prepucial Skin Graft for Fornicial and Socket Reconstruction in Complete Cryptophthalmos with Congenital Cystic Eye - A Case Report

Nirmala Subramanian, Surbhit Choudhry and Lakshmi Mahesh

Cryptophthalmos is a rare develop-mental anomaly, due to disturbance in the differentiation of surface ectoderm resulting in total ablepharon, wherein there is a complete failure of the lid folds.[1-3] Congenital cystic eye results from complete or partial failure of invagination of the primary optic vesicle.[2, 4-9] We present a case of unilateral complete cryptophthalmos with congenital cystic eye, in the absence of any associated systemic anomalies. The association of these two conditions occurring simultaneously has not been reported in ophthalmic literature. We also describe a surgical technique in this infant, wherein implantation of acrylic ball prosthesis in the eviscerated rudimentary eyeball was followed by a prepucial skin graft for fornicial reconstruction and socket expansion. Eight months follow up showed good cosmetic outcome and no complications. The use of autologous prepucial skin as an alternative graft material to the conventional mucus membrane grafts for lining fornices and sockets in recalcitrant cases of severe cryptophthalmos is elucidated.

Case Report

A 23-day-old male baby was brought to our out-patient department by his parents who noticed failure of the right eye to open since birth. The infant was delivered by lower segment caesarian section because of cephalopelvic disproportion. The child cried soon after birth, weighed 3430 g and had normal milestones for his age. There was no history of birth trauma. The mother was a healthy 21-year-old primigravida who had no serious illness or a history of drug ingestion during pregnancy. There was no consanguinity.

Examination of the infant disclosed the right globe to be hidden by a sheet of skin, passing from the forehead and dipping down over the orbit onto the cheek (Figure 1). The right eyebrow was absent nasally and displaced temporally. A small skin tag was present temporally. No eyelid fold was present. No fissure line or opening was seen in the skin. A large, spherical, cystic, compressible and transilluminant swelling measuring 25-millimeter horizontally was seen to be distending the upper lid, giving it a bluish hue. No facial asymmetry was present. Examination of the left eye and orbit revealed no abnormality. General physical examination revealed no obvious abnormalities. B-scan ultrasonography of the right orbit revealed a large cystic

eye with a globular contour, with gross thinning of the ocular coats. A moderate to high reflective membranous spike was seen dividing the smaller anterior from the larger posterior cavity, suggestive of rudimentary iris tissue compartmentalizing the cyst. There was a

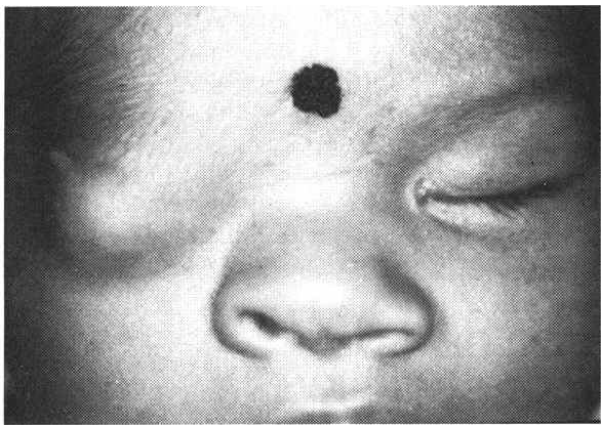


Fig. 1. Presurgical photograph *taken at 28 days of life showing complete left cryptophthalmos.*

highly reflective membranous echo extending from the posterior pole anteriorly suggestive of retinal and/or choroidal tissue in a closed funnel configuration. There was no evidence of crystalline lens. CT scan disclosed an enlarged proptotic globe with increased antero-posterior dimension and a figure of eight configuration. The bony orbit was also enlarged. There was no evidence of any intracranial abnormalities (Figure 2). Based on the clinical picture and the investigatory findings a diagnosis of right-sided complete cryptophthalmos with congenital cystic eye was made.

On the patient's ninetieth day of life, the initial set of procedures was performed to construct the socket, lids and establish conjunctival fornices. The patient underwent lid separation, with evisceration of the rudimentary eyeball and socket reformation with an acrylic ball implant. The eyeball was in the form of a large cyst showing severe degree of disorganization and thinning (Figure 3), with no differentiation into cornea or sclera. The ocular coats were replaced by vascularized fibrous tissue, which blended with the overlying skin. It was transilluminant (Figure 4). Extraocular muscles were not defined. The cyst was seen to be loculated with remnants of iris tissue compartmentalizing the cyst into two large cavities. During surgery the rudimentary eyeball was laid bare, the implant placed in-situ and the edges of the eyeball anchored to that of the newly formed eyelids. A conformer was inserted in the newly formed fornices at the end of surgery. The postoperative period was uneventful.

Histopathological studies of the contents of the cystic eye revealed dysplastic retinal and choroidal tissue and abundant glial tissue. A globular PAS positive structure was also identified, indicating the presence of a crystalline lens.

Post-operatively there was repeated dislocation of the conformer due to lid edema and shallowing of the socket. Despite the use of spring speculum, ankyloblepharon and symblepharon formed, which were released on the

twentieth post-operative day. Silicone buckle material was used to deepen the fornices and amniotic membrane graft was

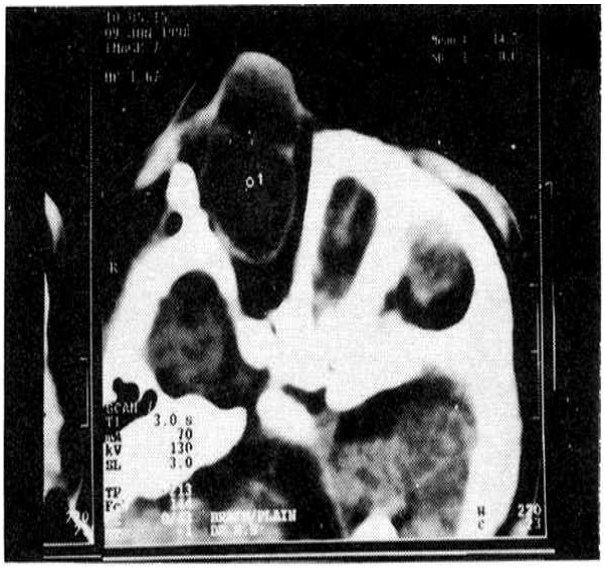


Fig. 2. Axial computed tomographic scan at age 1-month shows an enlarged proptotic globe, with increased anterior posterior dimensions and an enlarged bony orbit.

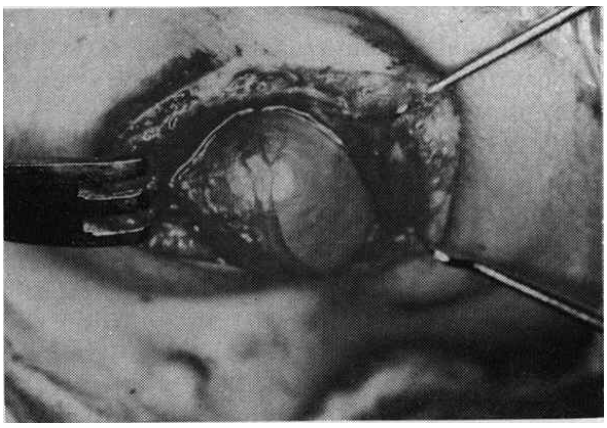


Fig. 3. Intraoperative photograph shows a large cystic eyeball with severe degree of disorganization and thinning.

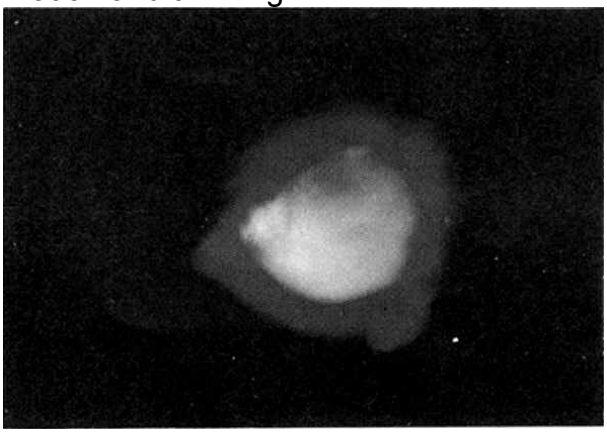
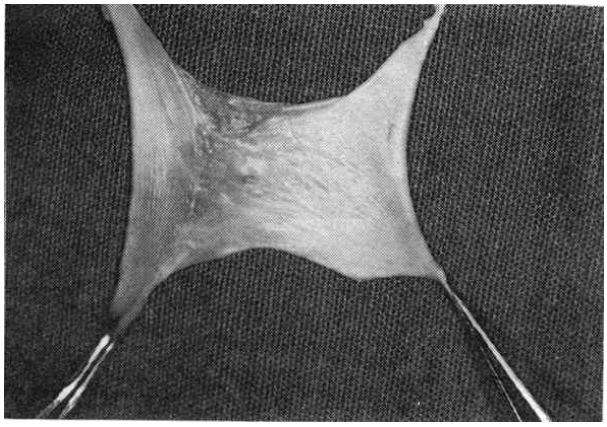


Fig. 4. Intraoperative photograph showing transillumination of the cystic eye.



5. Intraoperative photograph showing prepucial skin after circumcision.

used to line the socket following the release of adhesions. Spring speculum was used in the post-operative period.

The patient did reasonably well after this procedure until aged 5 months, when examination after administration of anesthetic showed recurrence of adhesions and socket contraction. At this stage it was decided to line the sockets with a cutaneous graft. Fifteen days later, the patient incidentally developed phimosis and was subjected to circumcision to alleviate his symptoms. The excised prepucial skin (Figure 5) was used in the reconstruction of the socket. Following the release of adhesions and deepening of the fornices, the graft was placed in the socket and sutured to the margins of the so formed eyelids. Postoperatively the graft took up well. A tarsorraphy was performed in the post-operative period to keep the conformer in place and deepen the fornices.

Eight months follow-up did not reveal the formation of adhesions but instead a good cosmetic outcome (Figure 6).

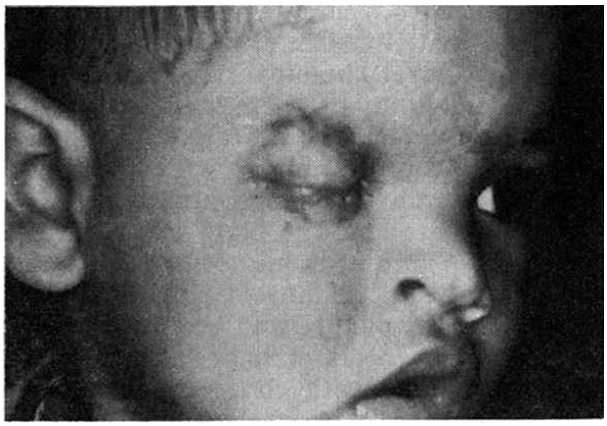


Fig. 6. Age 13 months, eight months after skin grafting, showing no adhesions and good cosmetic outcome.

Normally, the invagination of the primary optic vesicle occurs during the fourth week of gestation.2, 4, 9 Arrest in invagination at this time (2 millimeter and 7 millimeter stages) of fetal development produces a congenital cystic eye, also called ‘anophthalmos with cyst’, first described by Ida Mann.10 Once the primary optic vesicle forms, instead of the anterior part of the vesicle (the presumptive retina) involuting to lie in apposition with the posterior part (the presumptive pigment epithelium), a potential space exists between the two, forming the congenital cyst.2 This stage is followed by the formation of the lens vesicle. When the arrest in development has occurred at an early stage, a simple cyst usually occurs.2 Less commonly, the arrest may occur shortly after this stage; in such cases, when the optic vesicle has been associated with the surface ectoderm, the cyst contains a rudimentary lens and exhibits evidence of invagination of the optic vesicle.1, 2,4,11

The lid folds, both upper and lower, form in the 16-millimeter stage of the embryo. These differentiate and extend and the divisions between the upper and lower lids occur at the 31-millimeter stage. Congenital fusion of the lids is termed as Cryptophthalmos. Histopathological studies have shown diminished or absent levator muscle, orbicularis, tarsal plate and meibomian glands in these cases.3, 12-14 Mayou15 proposed that the absence of follicles in cryptophthalmos indicates that the lid folds never formed and fused, as a result of disturbance in differentiation of the surface ectoderm, probably occurring during the second month of gestation, and the condition is not a mere failure of normal separation of lids, which occurs later. Other hypothesized causes of cryptophthalmia include primary agenesis of eyelids, presence of amniotic bands, and/or ankylosis of partially formed .

Congenital cystic eye is always present at birth, is of variable size and replaces the normal eye. Like other neurogenic cysts associated with primary developmental anomalies of the globe (microphthalmos with cyst and microphthalmos with cystic teratoma), they are lined by neuroglial tissue internally, differentiating them histologically from epithelially lined cysts like the dermoid cysts or mucocele. The congenital cystic eye is histopathologically similar to the cystic portion of microphthalmos with cyst. [1,6,11]

Clinically, it is a large bluish orbital mass, which usually causes the upper lid to bulge forward in contra-distinction to a colobomatous cyst, which produces a bulge in the lower eyelid.[4, 6,11] The lack of surface ectodermal elements in congenital cystic eye is the key for correct diagnosis in difficult cases. [24] The cyst may be single or loculated, and may vary in size. The size of the cyst is believed to be related to the patency of the stalk.[6] If the lumen of the stalk remains open, fluid does not collect and the cyst remains small. If the lumen is not patent, the cyst is large, as the case presented here. Orbital ultrasound is valuable in demonstrating rudimentary ocular and cystic structures in difficult cases especially in cryophthalmic eye.

Congenital cystic eye can occur in isolation[4-9] or with other ocular or non-ocular malformations. The associated ocular malformations describe include skin tag, [5] a notch,[6] contralateral microphthalmos with cyst,[11] persistent hyperplastic vitreous and cerebrocutaneous abnormalities,[17] and periocular dermal appendages.[17-19] Cryptophthalmos is the most common finding in Fraser syndrome.[20, 24] It is a rare autosomal recessive disorder with variable penetrance characterized by cryptophthalmos, syndactyly, urogenital abnormalities, and malformation of upper airway and craniofacial structures.[20, 24] Cryptophthalmos is also associated with varied and non-consistent systemic defects including neurological anomalies[3, 24] and facial deformities.[16] None of these anomalies were seen in our case.

Fifteen cases of congenital cystic eye including our case have been published in English-literature since 1964. The association of cryptophthalmos and congenital cystic eye in combination is a rare phenomenon not previously reported in ophthalmic literature to the best of our knowledge. It is cosmetically disfiguring and socially unacceptable and its management remains challenging. Being an extensive surgical procedure, the ophthalmologist usually requires the assistance of a plastic surgeon and the procedure is attempted in stages.

Surgery to separate the skin over the globe and create eyelids for the purpose of useful visual function is not a realistic goal for most individuals with complete cryptophalmia because of the high incidence of associated severe ocular defects,[16] although the results have been encouraging in abortive and incomplete crypt-ophthalmos.[20] Different surgical procedures for reconstruction of incomplete crypt-ophthalmos have been described. Weng described a three-stage surgical procedure involving conchal cartilage "sandwich " graft, followed by mucus membrane graft and lid adjustment in the third stage.[20] Morax and associates [21] and later Dibben and coworkers [22] described a multistep procedure using buccal mucosal graft and flap reconstruction of colobomatous lid in a patient with incomplete cryptophthalmos in Fraser's syndrome with encouraging results.

Cyst evacuation and suturing its edges to the newly created eyelid margin has been tried in the past in a patient with complete cryptophthalmos and microphthalmos with subsequent severe contracture on both sides, causing difficult insertion of the prosthesis.[23] In this respect, the use of mucus membrane or skin graft is of great importance.

Mucus membrane grafts in infants are difficult to harvest due to their paucity, and are often unsuccessful following surgery due to the formation of adhesions. Partial thickness cutaneous grafts are associated with their share of demerits, which include difficulty in yielding a fat-free graft in an infants and infection and scarring of the donor site.

We describe a surgical technique in an infant with complete cryptophthalmos with congenital cystic eye wherein implantation of acrylic ball prosthesis in an eviscerated rudimentary eyeball, was followed by a prepucial skin graft for fornicial reconstruction and socket expansion. Our procedure appeared to be

advantageous, as the graft was easier to harvest and prepare owing to the absence of fat, availability of tissue in abundance and reduced chances of scarring and infection of the donor site. The cyst cavity was preserved after removal of the rudimentary tissue within the eyeball, which behaved as a bag to contain the implant, preventing its extrusion. One-year follow up showed good cosmetic outcome and no complications.

In conclusion, we present a case of complete cryptophthalmos with congenital cystic eye - a rare combination of develop-mental anomalies. Surgical management remains a challenge because of the formation of adhesions and socket contracture. The use of skin grafts - especially prepucial skin, when available, is undoubtedly advantageous over conventional graft materials.

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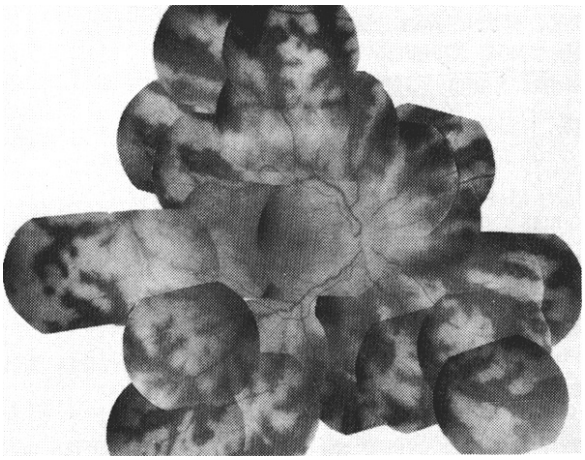
Detection of Cytomegalovirus (CMV) from Ocular Fluid of Two Patients with Progressive Outer Retinal Necrosis (PORN)

Jyotirmay Biswas, Surbhit Choudhry, K Priya and Lingam Gopal

Progressive Outer Retinal Necrosis (PORN) is a morphological variant of necrotizing herpetic retinopathy, seen exclusively in immunocompromised indi-viduals, first described by Forster and co-workers.[1] It is associated with minimal intra-ocular inflammation and has a rapidly progressive course. Initially multifocal in origin, such lesions rapidly become confluent and primarily involve the outer retina. The retinal lesions spare the retinal vasculature and ultimately become full thickness.[1,2] Often, there is development of rhegmatogenous retinal detachment with complete loss of vision in the affected eye despite antiviral therapy.[1,2,3]

We herein report two cases of PORN; the first to be described from the Indian subcontinent, in two Asian-male patients suffering from acquired immunodeficiency syndrome (AIDS). Cytomegalovirus (CMV)–DNA was detected in the vitreous fluid (VF) specimen by the polymerase chain reaction (PCR) in one eye of the patient with bilateral PORN, who had undergone vitreous surgery, and from the anterior chamber tap from one eye of the other case, indicating its possible causative role in PORN.



A 37-year-old heterosexual male with AIDS and a past history of pulmonary tuberculosis and oropharyngeal candidiasis was referred from an AIDS research center in August 1999, with a 20-day-old history of profound loss of vision in both eyes. He was detected to be HIV positive one year prior to

manifesting the ocular symptoms. His past medical history included thoracic shingles in 1998 and a recurrence of the same in July 1999. Previous investigations revealed a CD4+ T-lymphocyte count of 17 cells per cubic millimeter and blood viral load of 2,48,786 copies ten days prior to this visit.

On examination, his best-corrected visual acuity was 6/9;N6 in each eye. The anterior segments in both eyes were quiet. The intraocular pressures with applanation

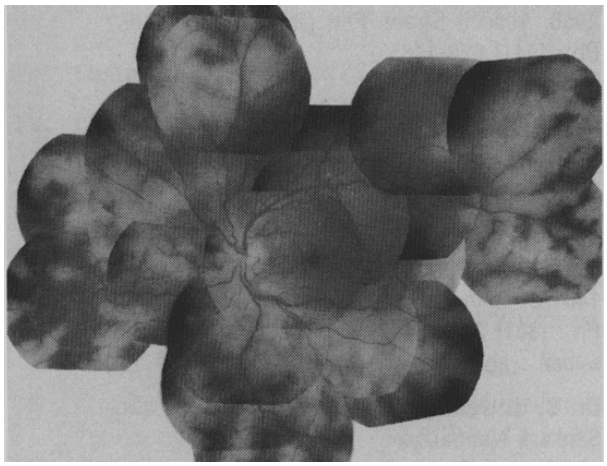


Fig.1.A, B Right and left montage fundus photograph of case1 showing bilateral swollen optic discs with numerous multifocal, deep, yellow retinal and choroidal lesions spread throughout the peripheral fundus, extending posteriorly with sparing of the periretinal vasculature

tonometery were 14 mm of Hg in either eye. Indirect ophthalmoscopic examination of the posterior segment revealed bilateral swollen optic discs with numerous multifocal, deep, yellow retinal lesions spread throughout the peripheral fundus, extending posteriorly (Fig 1A, B). There was sparing of the periretinal vasculature. The vitreous was clear with no inflammatory cells. Fundus fluorescein angiography of both eyes demonstrated peripheral, deep retinal lesions showing early blockage and late staining. There was no evidence of retinal vascular involvement. Systemic examination revealed multiple vesicles in a unilateral dermatomal distribution on the upper thorax, typical of cutaneous herpes zoster infection. Based on the characteristic picture of bilateral, deep, multifocal chorioretinitis with sparing of the retinal vasculature, a clinical diagnosis of PORN was made. The patient was treated with a two-week course of intravenous acyclovir (1500mg/square meter per day).

Enzyme-linked-immunosorbent-assay (ELISA) for antibodies to CMV & Herpes simplex virus (HSV) performed during initial examination revealed a high positive titer in serum for both Anti-HSV IgG (147 EU) and Anti-HSV IgM (172 EU). ELISA for antibodies to Herpes zoster virus (HZV) detected Anti-HZV IgG in 1:80 dilution and IgM was negative.

Despite antiviral treatment, the lesions continued to progress in both eyes rapidly to involve the posterior pole. Within four days, the entire retina was involved in both eyes. The visual acuity was reduced to hand movements and counting fingers at one meter in the right and left eye respectively.

On follow-up after a week, total rhegmatogenous retinal detachment was seen in the right eye with multiple inferior retinal breaks. The retina was thin and atrophic rendering it inoperable. Left eye revealed a similar picture, although the posterior pole remained attached. Barrage argon laser photocoagulation to the posterior pole within the vascular arcades was performed in an attempt to contain the detachment in the left eye. When reviewed fifteen days later, total combined retinal detachment was seen in the left eye. Pars-plana vitrectomy was attempted in this eye, but the procedure was abandoned owing to thin, atrophic and contracted retina.

Aqueous humor (AH) and VF specimen were collected during surgery from the left eye and were subjected to virological and PCR studies. Antigens of HZV, HSV or CMV were not detected by fluorescent antibody technique (FAT) in both these specimens. HSV was not isolated in culture in both the specimens by conventional tube culture technique using Vero cells. PCR was negative for both HSV and HZV genomes in both the specimen, while positive for CMV genome in the VF and negative for CMV genome in the AH (Fig 2).
On his last follow up, two months following the surgery, he had lost perception of light in both eyes.

A 26-year-old apparently healthy male presented with a one-month history of loss of vision in both eyes. He had no pain, redness or photophobia in either eye.

On examination, his best-corrected visual acuity was light perception with accurate projection of rays in the right eye and no perception of light in the left. Anterior segment examination revealed quiet anterior chambers in both eyes with an amaurotic

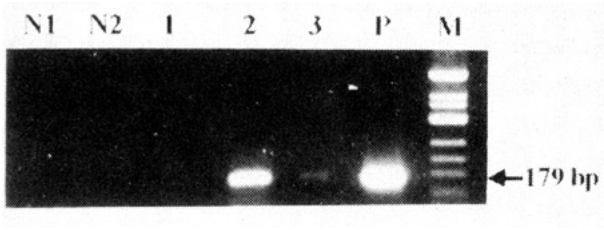


Fig.2. Agarose gel electrophoretrogram showing the PCR amplified products of the second round from intraocular specimens. Lane N1 represents negative (buffer) control, lane N2 represents the negative control, lane 1 represents the AH of the right eye of case 2 - positive, lane 2 represents the AH of the left eye of case 2 - negative, lane 3 represents the AH of case 1 - negative, lane 4 represents the VF of case 1 - positive, lane P represents the positive control and lane M represents the molecular weight marker (ÆX 174 DNA / Hinf I digest).

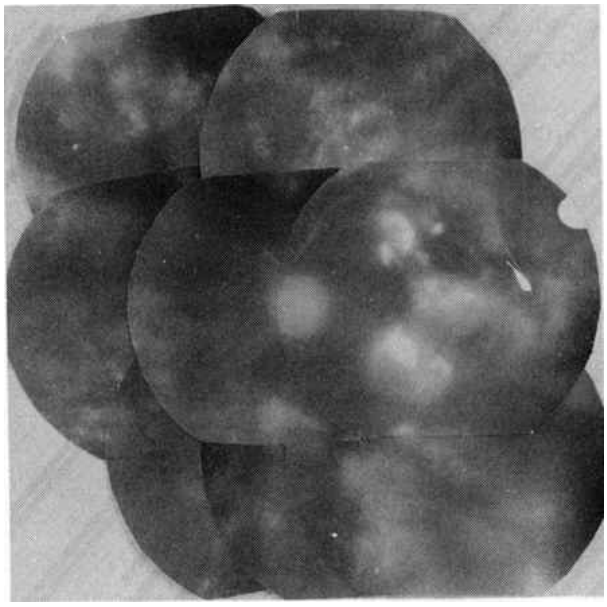


Fig. 3. Montage fundus photograph of the right eye of case 2 showing optic disc pallor, with alternating areas of peripheral, deep, yellow retinal necrosis and edema.

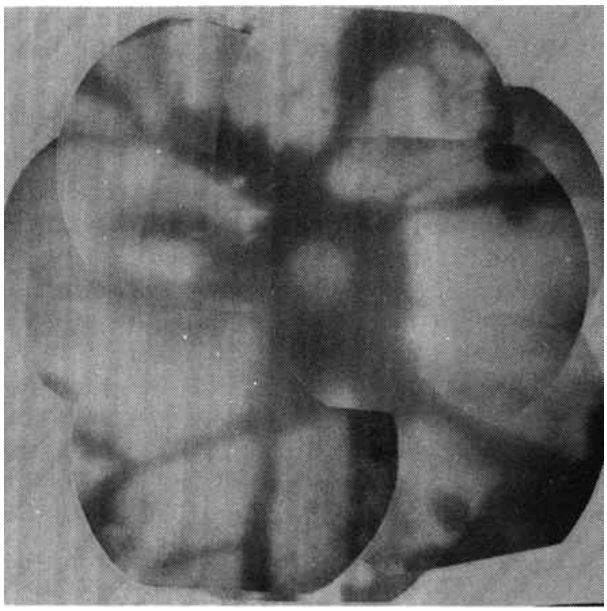


Fig. 4. Montage fundus photograph of the left eye of case 2 showed areas of deep, yellow retinal necrosis in the mid periphery extending posteriorly onto the macula with areas of scattered retinal hemorrhages.

pupil in the left eye. Intraocular pressures by applanation tonometery were 2 and 4 mm of Hg in the right and left eye respectively. Indirect ophthalmoscopy showed mild vitritis in both eyes with bilateral optic disc pallor.

In the right eye there were alternating areas of peripheral, deep, yellow-white retinal necrosis and edema. These were typically sparing the retinal vessels, extending towards the optic nerve head temporally and were associated with

prominent perifoveal edema suggestive of a diagnosis of PORN (Fig 3). Left fundus showed areas of confluent, yellow-white retinal infiltrates with discrete borders in the mid periphery extending posteriorly onto the macula with areas of scattered retinal hemorrhages (Fig 4). Based on the clinical picture, a diagnosis of acute retinal necrosis (ARN) with optic atrophy was made in the left eye. Fundus fluorescein angiogram in the right eye showed early blockage and late staining of the deep retinal lesions, very similar to the first case. There was no evidence of vascular involvement.

Following the clinical diagnosis, serology for HIV was done which was positive for Anti-HIV-1 antibody by the Immunocoomb & Tridot method. He was advised intravenous acyclovir (1,500 mg/square millimeters per day) and referred to the AIDS care center for further management.

AH was collected from both eyes at the same time and were subjected to virological and PCR studies. Antigens of HZV, HSV or CMV were not detected by FAT in both the specimens. HSV was not isolated in the culture in both the specimens. Genomes of HSV and HZV were not detected by PCR in both the specimens. CMV–DNA was detected by PCR in the AH of the right eye and was not detected in the AH of the left eye (Fig 2). CD4+ T-lymphocyte count at this stage was 154 cells per cubic millimeter.

The patient did not take treatment of any kind and was lost to follow-up.

PORN, is a recently recognized variant of necrotizing herpetic retinopathy representing a distinct form of ARN, developing in patients with AIDS or conditions causing immune compromise. It is characterized by early macular retinitis in the presence of little or no intraocular inflammation.[1,2] There is rapid progression with the development of lesions in the mid and peripheral retina with no consistent direction of disease spread unlike what is seen in cases of ARN. Unlike ARN and typical CMV retinitis, which involve full thickness of the retina, this condition is characterized by deep retinal opacification without granular borders, giving the impression of an "outer retinitis". With progression there is clearing of areas around retinal vessels, which have been described as a "cracked mud " appearance by some authors.[2] Forster and associates interpreted these findings as regions of perivascular retinal sparing.[1] However others suggested that this pattern represented early removal of necrotic debris and edema from retinal tissue adjacent to the vasculature.[2] As infected areas of retina become necrotic, large retinal breaks occur leading to rhegmatogenous retinal detach-ment in the majority of affected eyes, contributing to the overall poor prognosis.

Diagnosis of PORN is always clinical, based on its characteristic appearance as described. However it closely mimics ARN and CMV retinitis. ARN is characterized by an acute, necrotizing retinitis with associated moderate to severe vitritis and anterior chamber reaction, and classically occurs in otherwise healthy individuals.[1] Though commonly seen in immunocompetent patients, it has also been described in AIDS patients.[3] Most cases are believed to represent a viral process, with HZV and HSV implicated in most cases and proven in some by electron microscopic studies,

immunofluorescent staining, viral cultures, and PCR techniques.[3,4,5] Recently CMV has also been implicated as the cause of ARN in a report by Akpek and associates.[6]

The clinical expression of viral retinal antigen depends upon the immune status of the host, ranging from mild or classical ARN at one end of the spectrum in patients with undetectable or slight immune dysfunction, to PORN in immunodeficient patients at the other end, with intermediary forms between these two extremes. Our first patients had very low levels of CD4+ T-lymphocyte count indicative of a very poor immune status while the second had moderately reduced levels.

Our cases were unique for the fact that CMV-DNA was detected in the AH tap and the VF specimen by the PCR technique.

Previous studies indicate that HZV is the only cause of PORN.[1,2,3] Our findings suggest that PORN, which is a clinical entity, diagnosed based on morphological features, may also be caused by CMV. Our second case is intriguing in the sense that the clinical picture mimicked PORN in one eye and ARN in the other. Incidentally CMV was detected from the AH specimen of only the eye with PORN. This may reflect our inability to identify CMV in the fellow eye, or theoretically speaking, a possibility of two different viral etiologies in the two eyes of the same patient, viz. PORN in the right eye (where CMV was identified) and ARN in the left eye (where no viral DNA identified). The left eye could have been affected by HZV, HSV or CMV.

In addition, this case was unique as the diagnosis of PORN was made before the diagnosis of AIDS was confirmed. The presence of vitritis and a moderately reduced CD4+ T-lymphocyte count indicates that PORN can be an early presentation of AIDS and can develop prior to other systemic diseases related to AIDS. Only one similar case report has been described in English literature.[7] In a study by Engstrom and co-workers,[8] the median CD4+ T-lymphocyte count in patients with PORN was 21 cells per cubic millimeter (range, 0-130 cells per cubic millimeter). Ophthalmologist therefore needs to be aware of this clinical presentation and should suspect the PORN syndrome in any patient with rapidly progressive necrotizing retinopathy and investigate for the presence HIV infection.

In summary, PORN is possibly a morphological syndrome similar to ARN, but could be caused by other viral etiologies including CMV. PCR studies of the ocular fluids may aid in diagnosis.

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Unilateral Neuroretinitis following Chicken Pox - Report of A Case

Sumeet Chopra, Jyotirmay Biswas, Sudha K Ganesh and Satya Karna

Chicken pox is caused by Varicella Zoster virus, a DNA virus that can affect the eye in different ways causing conjunctivitis keratitis, episcleritis, scleritis, iridocyclitis, and glaucoma. Various retinal manifestations including necrotising retinitis, vitritis, neuroretinitis and retinal detachments have been described.[1]

We report a case of neuroretinitis following chickenpox, which resolved with a combination of treatment with oral Acyclovir and systemic steroid. This report highlights the necessity for fundus examination in cases of chicken pox who develop visual symptoms.

A 23-year-old man complained of pain behind the left eye and headache one week after developing chicken pox. Two weeks later, he noticed blurred vision in the left eye. Ocular examination showed visual acuity was 6/6;N6 in right eye and 6/9;N6 in the left eye. There was a relative afferent pupillary defect in the left eye. Slit lamp biomicroscopic examination of both eyes was

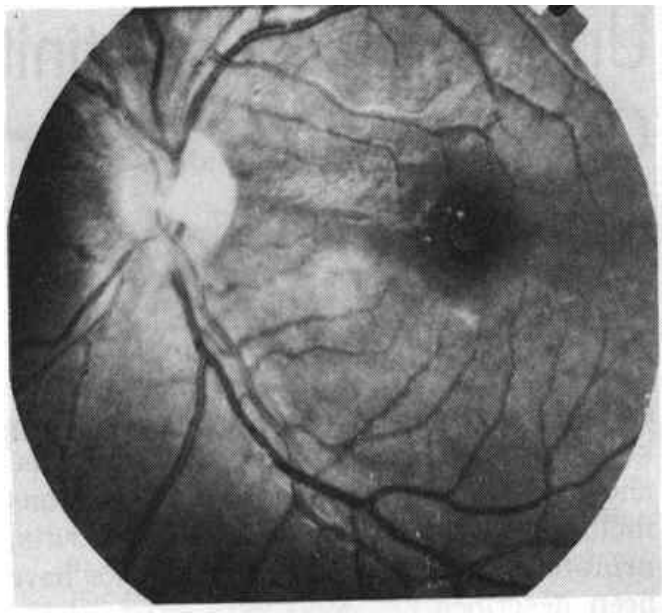

Fig. 1 Fundus photograph of the left eye showing swollen optic disc with hard exudates in the macular area

normal. Applanation tension was 15 mm of Hg in both eyes. Fundus examination revealed swollen hyperemic optic disc with elevation of the

peripapillary retina. There were few hard exudates in the macular area in a stellate configuration. (Fig.1) Automated perimetry revealed a centrocaecal scotoma in the left eye. There was a red, green color vision defect in the left eye. Systemic evaluation revealed vesicular rash typical of chicken pox on the face and extremities. (Fig.2) A diagnosis of neuroretinitis (OS) secondary to chickenpox was made. The patient was given Tab. Acyclovir 400 mg 5 times/day for two weeks and Tab.

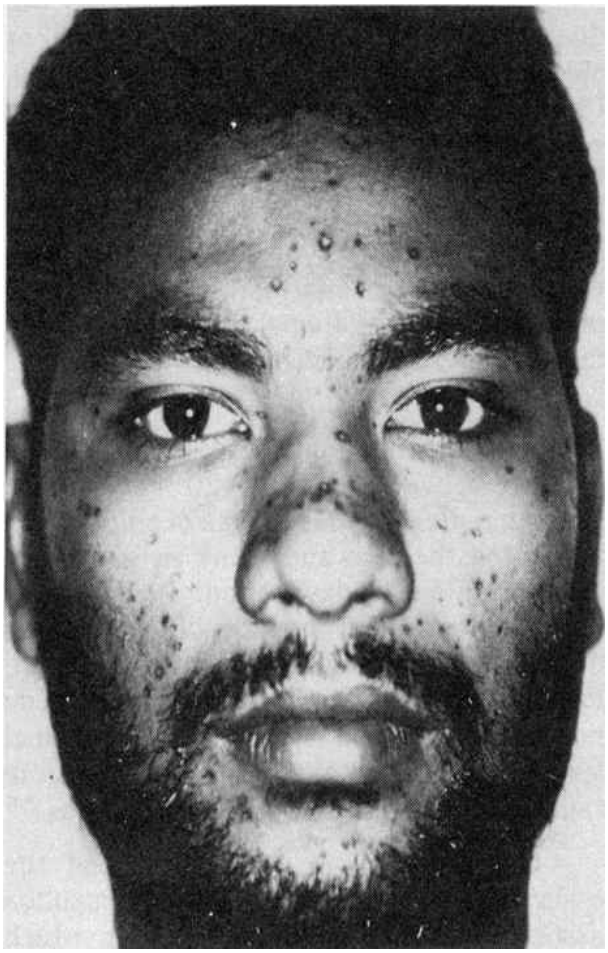

Fig. 2 External photograph showing multiple vesicular rash of chickenpox over the face of the patient

Prednisolone 40 mg/day for two weeks. Two weeks later, the patient was reviewed and the visual acuity was noted 6/6;N6 in both eyes. Fundus examination showed resolving neuroretinitis.

One month later, patient presented with pain and redness in the same eye. Visual acuity was 6/6;N6 in both eyes. Slit lamp examination showed a non-granulomatous anterior uveitis with 3 + flare and cells in the anterior chamber. Vitreous cavity was clear and fundus examination revealed a resolving neuroretinitis. The patient was treated with Predforte eye drop 8 times/day, Homatropine eye drops 2 times/day and Tab. Acyclovir 400 mg, 5 times per day for 6 weeks along with Tab Prednisolone 20 mg/day on tapering dosage. Two months later he was reviewed and examination revealed resolved

anterior uveitis and resolving neuroretinitis. (Fig.3) Vision was 6/6; N6 in both eyes.

Varicella Zoster virus (VZV) causes two distinct clinical entities; varicella or chickenpox, and herpes zoster, or shingles. Chicken pox is usually a benign, albeit highly communicable, illness primarily of childhood, that is characterized by an exanthematous, vesicular rash. With reactivation of latent VZV in sensory (dorsal root) ganglionic neurons, usually in older patients, the disease presents as a dermatomal, vesicular rash, in most cases associated with severe pain.[1]

VZV is a DNA virus of the herpes virus family. The incubation period of chicken pox ranges between 10 to 20 days. The characteristic vesicular lesions of chicken pox appear on the face and trunk in successive crops over a 2-4 day period. Ocular signs and symptoms may include blurred vision, decreased visual acuity, headache, eye pain, foreign body sensation.[2] Usually patients do not have any retinal lesions. Different retinal lesions described in chickenpox include acute retinal necrosis, retinitis and choroiditis.[3-6]

Copenhaver [3] in 1966 described the occurrence of a case of chickenpox papillitis associated with a macular lesion in which complete regression of the lesion occurred within several weeks. Several authors included chickenpox as aetiology of

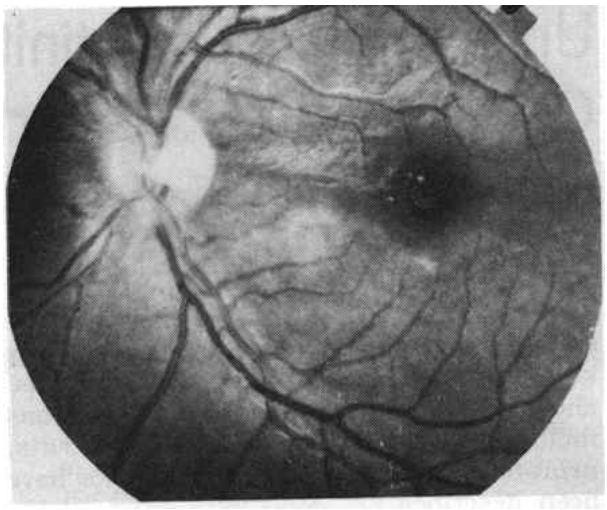

Fig. 3 Fundus photograph after two months following oral Acyclovir therapy showing complete resolution of neuroretinitis

neuroretinitis. However, there are only occasional case reports available. A mild self-limited form of necrotizing retinitis is known to develop following chickenpox.[4]

Majority of cases of retinitis following chickenpox has been reported in adults and only three cases in children.[5]

Some of these patients had some form of mild immunosuppression e.g. lung disease, prednisolone therapy and pregnancy. Choroiditis due to chickenpox is rare and only one case has been reported.[6]

Neuroretinitis is a particular form of optic neuritis characterized by swelling of the optic disc, peripapillary and macular hard exudates and often vitreous cells. Gass [7] emphasized that the condition occurred commonly in children and young adults, up to 50% of whom had an antecedent viral illness, usually affecting the respiratory tract, a few weeks before the onset of visual symptoms. It has subsequently become clear that some cases of neuroretinitis are associated with particular infectious diseases whereas others occur as apparently isolated phenomena. In the latter setting, the condition is called Leber's idiopathic stellate neuroretinitis.

Neuroretinitis is thought to be an infectious or immune mediated process that may be precipitated by a number of different agents. The most common association is with an antecedent viral syndrome. However, viruses are rarely cultured from the cerebrospinal fluid of such patients. Upper respiratory, gastrointestinal and genitourinary system symptoms with or without headache are common. Differential diagnosis of causes of neuroretinitis includes leptospirosis, cat scratch fever, influenza, mumps and chicken pox.[8] No definite guideline for management of such cases is available due to limited number of reported cases. Acyclovir has been used orally or intravenously in these patients. However, as these lesions resolve with or without Acyclovir, the precise role is not clear. In our patient despite two-week treatment with oral Acyclovir, there was recurrence of anterior uveitis. However, the inflammation was controlled with topical steroids and a repeat course of oral Acyclovir. We feel close monitoring of such patients is required and a course of oral Acyclovir can be given in case of recurrence. We also feel in a case of neuroretinitis prolonged course of oral Acyclovir (6 to 8 weeks) may be needed. The response to Acyclovir in case of varicella zoster is known to be better than in herpes simplex virus infection.

This case indicates unilateral neuroretinitis could be an ophthalmic manifestation of chickenpox. Prompt treatment with systemic antiviral agent with steroid can resolve the process and restore vision.

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Human Genome Project: A Medical Revolution

G Kumaramanickavel

From the days of Gregor Mendel till Craig Venter exactly in a century, the science of genetics has evolved to a remarkable level. Gregor Mendel described the laws of inheritance in 1866, which went without positive reception during his period. However his experiments were reborn with admirable recognition in 1900. Since then to date many scientists, particularly James Watson and Francis Crick, have contributed to the development of this science. Indian scientists like Hargobind Khurana and Kosambi have also played a major role in their contribution to this science. A new era dawned in medicine when the President of the United States Bill Clinton and British Prime Minister John Major along with renowned scientists released the draft of the human genome on 26th June 2000, nearly three years ahead of schedule.

In 1990, with advanced knowledge in genetic engineering (recombinant DNA technology), DNA and protein behavior, many scientists realized that drafting a map and sequencing the human genome (the inherited material) would be of paramount importance. This is equivalent to the quest and challenge of mapping the world or the human body (anatomy), during different stages of human history. The US Department of Energy and the National Institute of Health (NIH) initiated the human genome project (HGP). While Britain, Europe, Japan and various other countries made a concerted effort, private and public agencies like Wellcome Trust, Sanger Centre in Cambridge and Celera joined the HGP race subsequently and added a new impetus and pace to this project.

There are approximately three trillion cells in our human body. In the nucleus of each cell, the material that carries the hereditary information or the genetic material (the genome) is a chemical called the DNA (deoxy ribonucleic acid). This genetic material stores all the hereditary information, like the way a computer digitizes and stores information as ‘0’ and ‘1’, the DNA stores information in the form of four chemicals, namely ‘A’ (adenine), ‘T’ (thymine), ‘G’ (guanine) and ‘C’ (cytosine). The ATGC are the alphabets in the genetic language and like the way 26 English alphabets in different combinations produces various words, different combinations and lengths of these four DNA alphabets result in what are called genes, like the insulin or growth hormone. This four-alphabet language has a billion letter script in each of our three trillion cells and this dictates what should happen to us biologically right from conception till death. It also determines what should be our eye and skin color, height, weight, facial features etc. We basically inherit all these information from our parents, but at times we also inherit some errors called mutations. Mutation results in many inherited or genetic disorders, like sickle cell anemia or retinitis pigmentosa. This 3 billion letter inherited information is

parsimoniously packed in what are called chromosomes (like volumes in an encyclopedia) in each cell and humans have 46 of them - this number varies and is unique for each living species (Table 1). Genes are present in the chromosomes like stations on a railway track. Just as you pass through several miles of empty space in a railway track to reach a station, you have to pass through vast meaningless regions of DNA to identify a gene. It is still not very clear why advanced species' including human genome should contain huge meaningless amounts of 'Junk DNA', nearly 97% of the genome! The remaining 3% of the genome contain 50 to 60 thousand genes.

Number of chromosomes in other species

Alligator 32
Carrot 18
Chimpanzee 48
Human 46
Amoebae 50
Dog 78
Sheep 54

The HGP consisted of two major efforts, firstly to map the human genome and precisely know where each gene is present in the 46 chromosomes and secondly to read the 3 billion-letter (ATGC) DNA sequence completely from the first till the last chromosome. The project was initiated in 1990 with a $ 3 billion grant from the NIH – the biggest biological project ever. The project obtained a new fillip by the discovery of PCR (polymerase chain reaction) technique by Kary Mullis in the US; this expedited the mapping and sequencing and brought it to an early finish. In what appeared to be a small trickle of genes discovered in the early 90's, ten years later 1556 disease genes have been mapped and 36,000 'suspected' gene sites have been identified. Various genetic and molecular biological techniques are used for human genome mapping. Initially X-linked disorder genes were easily identified and later autosomal genes were also identified. Vision is a key special sense and hence mapping genes responsible for blindness was of vital importance in the HGP. Many Universities, eye hospitals and Government institutions all over the world took part in this concerted collaborative effort to map the human eye genes. More than 1000 inherited diseases affect the eye – both the anterior and the posterior compartments. In landmark events in mapping eye disease genes, Ted Dryja at Harvard and Ed Stone at the University of Iowa in the US, identified the first retinitis pigmentosa and glaucoma causing genes, respectively. Presently more than 15 genes causing congenital cataract have been identified. Of all parts of the eye, retina attracts more attention in gene mapping, probably because of its vitality in visual function. So far 122 genes causing retinal inherited degenerative diseases have been mapped and 25% of them, that is 30 in number cause retinitis pigmentosa. We at Sankara Nethralaya in this international collaborative HGP are responsible in mapping 7 eye-related genes: 5 RP genes, one stationary night blindness gene and an eye developmental gene. Besides we are also studying the genetics of age-related cataract, diabetic retinopathy and angle-closure glaucoma in the Indian population.

Human Genome Project
(List of few ocular genes mapped)

Disease	Gene	Chromosome
Cornea: Meesman dys. Reis-Bucklers dystrophy Peter's anomaly	 Keratin 3 Kerato- 5q31 epithelin PAX6	 12q13 5q31 11p13
Glaucoma: Primary congenital Open-angle	 CYP1B1 GLC1A	 2p21 1q21-31
Cataract: Pulverulent Cerulean (blue dot)	 CRYG CRYBB2	 2q33-35 22q
Retina: Retinitis Pigmentosa Retinoblastoma Stickler Stargardt	 Rhodopsin P110 COL2A1 ABCR	 3q21 13q14 12q13 1p13

Our role in Human Genome Project		
Disease	Gene	Chromosome
Retinitis Pigmentosa	Rhodopsin	3p
	RPE 65	1q
	Prominin -1-like	4p
	(Linkages)	2p, 16p
Oguchi	Arrestin	2q
Blepharophimosis	(Linkage)	7p

All this understanding could help us to forewarn and counsel these patients and families or plan some treatment or delay the degradation processes of the retina. For eye diseases many research groups are working on gene therapy by replacing defective genes with correct ones or by simply using ribozymes - the watchdogs in the cell that destroys defective or mutated proteins. Retinal cells are grown outside the body so that the degraded retina can be replaced. To stabilize the retinal degradation and ultimately the vision, neuro-regenerative growth hormones and calcium channel blocker (nifidepine) drug are being experimented. All this could be possible only because of the advances made in the HGP.

We as medical practitioners and scientists are in a new age where diseases will be diagnosed in individuals even before the symptoms appear – an emerging medical field called predictive medicine. Carrier testing, pre-implantation, prenatal and pre-symptomatic diagnoses will be the order of the day. Invasion of privacy, access of genetic information by the employer or insurance agency, patenting genes are some of the negative offshoot of this project. Ultimately the positive aspects will overweigh the negative ones. Then gene therapy and molecular surgery would be the new medical and surgical specialties without 'pills and knife'!

Yeast - a Valuable tool for differential diagnosis of glycosuria and galactosuira

S. Ramakrishnan, K. N. Sulochana, R. Punitham and S. B. Vasanthi

Occasions arise in the clinical biochemical laboratory to analyse samples of urine for sugar and confirm the presence of a particular sugar associated with a definite pathological state. For. eg. if it is glucose in urine, it may be diabetes mellitus[1] or rarely renal glycosuria[1]. It could be lactose in a normal lactating woman. Excretion of galactose is met with in galactosemia with galactosuria[2].

An ophthalmic hospital gets patients who are children with congenital cataract. The cataract could be due to galactosemia in which galactose, an abnormal constituent of systemic blood enters the lens and is reduced to galactitol by Aldose Reductase. Galactitol accumulates inside the lens, causes 'osmotic drag' and thereby cataract. In such patients the presence of galactose in the sample of biofluid has to be tested for and confirmed. There are no difficulties in detecting sugars like glucose, fructose, lactose and sucrose in urine, which are all abnormal constituents in normals. The following tests are done for identification[3]:

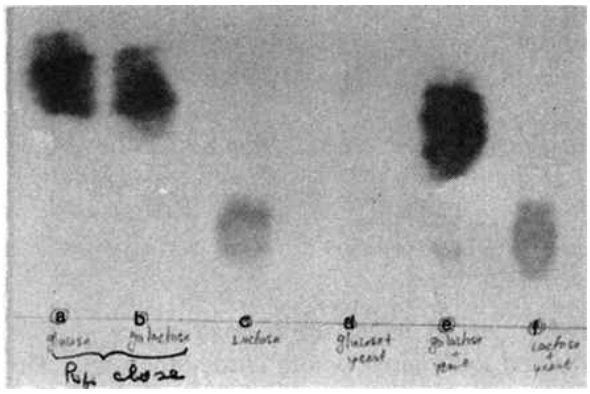

Fig.1: a and b are 10 m gm of glucose and galactose respectively. The figure indicates the close Rf (resolution factor). c 10 mg of lactose. d,e,f are a,b,c samples treated with yeast. The figure shows the disappearance of glucose while galactose and lactose are unaffected.

Glucose : Molisch (+), Benedict's (+),
Barfoed's (+), Seliwanoff's (-),
osazone and chromatography.

Fructose : Molisch (+), Benedict's (+),
Barfoed's (+), Seliwanoff's (+),
osazone and chromatography.

Lactose : Molisch (+), Benedict's (+),
Barfoed's (+), Seliwanoff's (-),
osazone test (highly
characteristic) and chromatography.

Sucrose : Molisch (+), Benedict's (-), Barfoed's
(-), Seliwanoff's (+) and
chromatography.

The Rf values of the above sugars in chromatography are sufficiently different and there is no ambiguity.

However, when it comes to galactose, there are real problems of analysis as, in most of the reactions, galactose behaves like glucose. In chromatographic technique also which helps in detection of even microgram quantities of sugars, the Rf values of glucose and galactose are so close that doubt arises about characterization (Fig 1). If the sugar is wrongly identified, it makes all the difference. One with diabetes mellitus may be branded as galactosemic and vice versa. The entire diagnosis of the disease and thereby the therapy would go wrong. Hence the necessity

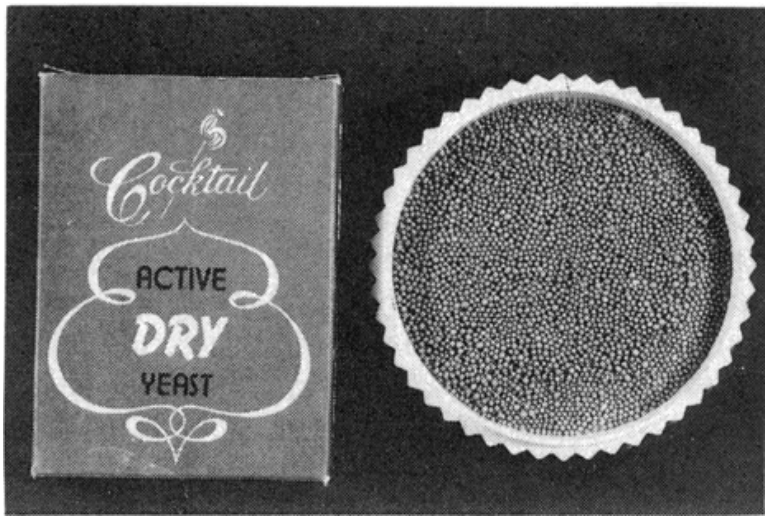

Fig. 2: Commercial Bakers' yeast

for correct identification of glucose and galactose. In this connection, yeast is very helpful in analysis and characterization.

Glucose and galactose and solvents n butanol, glacial acetic acid and aniline were of analytical grade. Aniline was distilled before use for preparing aniline hydrogen oxalate. Yeast was obtained from Sheth Enterprises, Madras (Fig 2).

Molisch test, Benedict's reaction, Barfoed's test, preparation of osazone and single dimension chromatography using n butanol, glacial acetic acid and water (4:1:1 v/v) were done for pure samples of glucose and galactose. The spraying reagent for sugar chromatogram was aniline hydrogen oxalate and

heating was done for 5 minutes at 100 - 120º C. Brown spots appeared in paper. A solution of yeast was prepared by dissolving 100 mg of dry yeast powder in 1 ml of water. 0.05 ml of the solution (= 5 mg) was added to solution of pure glucose and galactose and kept at 37º C for 16 hours.

All tests referred to above namely, Molisch, Benedict's, Barfoed's, osazone preparation and chromatography for sugars were repeated for the yeast-treated samples. The sample of glucose, treated with yeast did not answer any of the tests. This suggests that glucose has been completely destroyed by yeast, which is known to ferment it with the enzyme zymase[4] to ethyl alcohol and carbon di oxide. As yeast cannot ferment glactose[4], addition of yeast did not affect galactose. So all the tests were answered by yeast-treated galactose as a solution of pure galactose.

The above observation has a useful practical application. Diabetic urine and urine from a child with galactosuria with congenital cataract were subjected to all the tests prescribed for reducing sugars i.e. glucose and galactose. The tests were all answered by pure sample of the concerned sugars. Now 1 ml of each sample of urine i.e. glycosuric and galactosuric was separately treated with 50 ml (= 5mg)of yeast solution (100 mg/ml) kept at 37º C for overnight. All the tests referred to above were repeated for both the yeast-treated urine samples. The specimen, which does not answer any of the tests, should be glucose and patient is glycosuric (renal or diabetic). Galactose in urine even after treatment with yeast answers all the tests.

One very interesting point is the analysis of sugars by paper chromatography, which is an elegant technique and which got Nobel Prize for the twin British Scientists Martin and Synge. It is rather ticklish to differentiate galactose from glucose, as both have very close Rf values in n butanol, acetic acid, water system (4:1:1 v/v) or pyridine, isoamyl alcohol, water system (10:10:7 v/v). So there is ambiguity in characterization. Mucic acid test for galactose is not infallible. Under these circumstances, a very simple procedure is just to treat the suspected sample of urine with yeast and process as detailed above. If there is a spot for sugar in the paper chromatogram after spraying with aniline

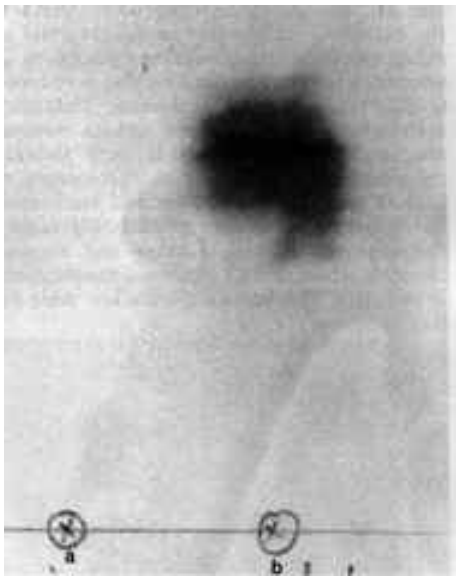

Fig.3: a) 50 ml of urine positive for glucose treated with yeast before chromatography. The figure shows no glucose spot due to fermentation of glucose by yeast. b) 50 ml urine positive for galactose treated with yeast before chromatography. The figure shows positive spot for galactose since yeast did not have any effect on galactose.

chromatogram after spraying with aniline hydrogen oxalate and heating for 10 minutes, urine contains galactose (Fig. 3) and the patient is galactosuric. If there is no sugar spot in the paper chromatogram, the urine is from a patient who is glycosuric. Thus yeast serves as a good tool for differential diagnosis of glycosuria from galactosuria.

Pure samples of glucose and galactose give all the tests for reducing sugars but yeast-treated sample does not answer any of the tests for glucose.

To have differential diagnosis of glycosuria and galactosuria, perform Molisch and Benedict's test. They are positive for both. Now treat both with yeast. The yeast-treated sample does not answer any test of glucose. So it is from the patient with glycosuria. The one, which gives positive reaction even after treatment with yeast, is from one with galactosuria.

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A NOBLE DEED WORTHY OF EMULATION

Sri A. K. Sastry of Freemont has come out with a large donation of US $ 250,000 in support of Sankara Nethralaya a renowned non-profit, non-commercial, charitable referral ophthalmic hospital located in Chennai, India. Mr. A. K. Sastry, a Mechanical Engineer, has been a resident of Chennai and he is now settled in USA after having held distinguished positions in West Africa and the United Kingdom. During his recent visit to Chennai, Mr. Sastry, was impressed with the laudable work pursued at Sankara Nethralaya towards alleviating the sufferings of indigent patients who visit the hospital in large numbers and has spontaneously donated US $ 250,000 in support of its cause. In appreciation of his kind gesture, the hospital authorities have named a floor in one of the buildings in fond memory of Sri. A.K. Sastry's beloved wife as "SMT. MANORAMA AKELLA HALL".

Mr. Sastry's kind gesture in helping a deserving institution situated in Chennai where he had his early moorings is not only commendable but also deserves emulation.

We understand from Sankara Nethralaya that they have formed a Trust in the U.S.A titled "Ophthalmic Mission Trust Inc. [OM Trust] at 14613, Pommel Drive, Rockville, MD 20850, USA, which accepts donations on behalf of Sankara Nethralaya. Such donations are IRS Tax Exempt. The contact person is Mr. S.V. Acharya, Secretary & Treasurer, Telephone No. [301] 251-0378, Fax No. 202-673-4333, and Email:omtrustusa@hotmail.com

For further details you may visit our website
http://www.sankaranethralaya.org.

Literature search on the Internet

Rajesh Fogla

Information technology has revolu-tionized modern clinical practice, with most textbooks and journals now available readily both via the internet, as well as in CD-ROM format. It is essential for the practicing ophthalmologist to be aware of the recent advances, especially in today's rapidly expanding field of ophthalmology. Most ophthalmology journals now make available the table of contents with abstracts free of cost. This has made literature search much more easier and essential for the ophthalmologist.

Entrez PubMed -
(http://www.ncbi.nlm.nih.gov/entrez)

Entrez PubMed is the National Library of Medicine's search service that provides access to over 11 million citations in MEDLINE, PreMEDLINE, and other related databases, with links to participating online journals. Medline is by far the most popular and useful computerized database available. About 30,000 new citations are added every month and coverage dates back to 1966. Abstracts are available for most of the citations. Relevant citations can be easily accessed by looking at the related articles from a single reference.

Healthgate MEDLINE -
(http://www3.healthgate.com)

Healthgate website is a dynamic integration of information and technology that is an interactive medical resource for physicians. HealthGate utilizes a technology called ReADER. ReADER lets you use your own words which are then translated automatically into the more appropriate terminology, or controlled vocabulary, to search the database you've selected. For example, ReADER automatically translates your words into MeSH, the controlled vocabulary used to describe every record found in MEDLINE.

Ophthalmology - (http://www.aaojournal.org)

Ophthalmology, journal of the American academy of Ophthalmology now provides free access to its database, allowing literature search of journal articles from September 1965. Full text is available for some selected articles in PDF format, which can be downloaded and viewed with Adobe acrobat reader. The "Reprint (PDF) (http://www.adobe.com/acrobat) Version of articles closely resembles the paper version of Ophthalmology. The table of contents of the recent issues can now be notified via email when new content goes online (eTOC).

British Journal of Ophthalmology -
(http://bjo.bmjjournals.com)

The British Journal of Ophthalmology is currently one of the highest ranked European journals in the ophthalmology category and has an impact factor of 1.908. The online version also allows eTOCs (table of contents via email), database search of the journal from July 1965, and search across multiple journals.

Sciencekomm -
(http://www.sciencekomm.at/journals/medicine/opth.html)
This website provides an alphabetical listing of 64 ophthalmic journals. Clicking on the journal of interest, links immediately to the home page of the ophthalmology journal.

Silver-Platter Information, WinSPIRIS
(CD-ROM database) -
(http://www.silverplatter.com)

Silver-Platter provides a comprehensive and seamlessly integrated database collection of scholarly reference information in electronic form - over the Internet, on campus and corporate Intranets, and on CD-ROM.

Although the presentation and search systems may vary, the underlying basic principles for performing a literature search are similar in all systems. So the basic question is -
How do you perform a search?
– In a basic search – one can search for articles using a "free text or text word".

This search traces any words in the title, abstract, author's names and the institution where the research was done, in the database.

– Enter the term or terms that you wish to search on, separating terms by spaces, and press the return key or the "search" button. This will take you immediately to the Document Summary Page, below, where you can review the results of your search.

– Placing an asterisk at the end of a term will cause Entrez PubMed to search for all terms that begin with that word; for instance "bacter*" will find all terms that begin with the letters "bacter", e.g. bacteria, bacterium, bacteriophage, etc. Phrases that have a space in the word that occurs after the asterisk will NOT be included; for instance, "infection*" will
include "infections" but not "infection control".

– Another alternative for a search is to use the medical subject heading (MeSH) terms. **MeSH Terms** includes all of the terms in the Medical Subject Headings, a controlled vocabulary of keywords used to index MEDLINE. Each MEDLINE citation is given a group of MeSH terms that relate to the subject of the paper from which it is drawn.

– Frequently, MeSH terms will have an additional term, called a "subheading", which further defines how the MeSH term relates to the article it is associated with. This subheading is appended to the MeSH term, e.g. "corneal grafting". Searching on the MeSH term (here, corneal) will retrieve all of the articles that use that MeSH term, whether they have subheadings or not.

Although MEDLINE is the best known and widely used index of the biomedical literature, it does not cover all medical publications. For example Eye News, Ocular surgery News, etc are excluded. Even then MEDLINE allows a rapid comprehensive literature search to performed rapidly with ease. This article would provide some insight into performing an effective literature search.

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