Eye Banking in India: A Road Ahead.

VS Sangwan[*], U Gopinathan[**], P Garg P[*], GN Rao[*]

[*]*Cornea and Anterior Segment Service, L. V. Prasad Eye Institute &*

[**]*Ramayamma International Eye Bank, L. V. Prasad Eye Institute, Hyderabad, Andhra Pradesh, India*

Abstract*: Clear transparent cornea is essential for normal vision. The corneal transparency is lost by trauma, dgenerations, dystrophies, infections, and inflammation affecting the cornea. Sight-threatening corneal opacity needs corneal transplantation to restore transparency. Among the human organ transplantation procedures corneal transplantation has best success rate. Quality of the donor cornea, the nature of recipient pathology and availability of appropriate postoperative care are some of the factors that determine the final outcome. Procurement and supply of the donor cornea to the corneal surgeons is the primary goal of eye banks. While this fact is recognized, the need for rigorous quality control in eye banking is not appreciated by the eye bankers and the surgeons in India and the other developing countries. We propose a three tier structure encompassing all the activities of eye banking. The three tiers include eye bank (EB), eye bank training center (EBTC), and eye donation center (EDC). Our plan envisages the establishment of one eye bank for every 20 million people, each of which would to be linked to 40 eye donation centers (EDC)- eye banking units that are involved only in harvesting corneas. Five of the eye banks would serve as eye bank training centers. In addition, each eye bank will develop a hospital cornea retrieval program (HCRP) in 10 major hospitals in the immediate community. Half the harvesting (2000) is achieved by the eye bank directly through the HCRP and the other half (2000) will be through the contribution of eye donation centers, with 50 eyes (25 donors) from each EDC. Surprisingly, the entire eye banking infrastructure for the country could be created at a cost of Rs. 260 million and operating expenses of the eye bank would be covered by the processing fees and donations.*

Key words: *Cornea blindness, corneal transplantation, eye bank, eye bank training center, eye bank donation center, hospital cornea retrieval program.*

INTRODUCTION

We obtain more than 80% of our information from external world by means of visual function. Good vision depends on the cornea and lens as refractive elements; on the retina as a receptor system that converts light into chemical and electrical energy; on transmission of visual signals by the optic nerve to the brain; and on the final synthesis of visual information by the visual cortex. The cornea forms, together with the sclera, the outer shell of the eyeball, occupying the outer two thirds of the ocular coat.

The corneal transparency is maintained by combination of biochemical, histological, and physiological factors unique to this tissue. Therefore, corneal transparency is essential and critical for good vision. Corneal transparency is lost by trauma, infections, degenerations, dystrophies, and inflammatory disease affecting cornea.

The importance of corneal disease as a major cause of blindness in the world today remains second only to cataract, but its epidemiology is complicated and encompasses a wide variety of infectious and inflammatory eye disease. In addition, the prevalence of corneal disease varies from country to country and even from one population to another, depending on many factors, such as availability and general standards of eye care. The major causes of corneal blindness globally include trachoma, corneal ulceration, xerophthalmia, ophthalmia neonatarum, traditional eye medicines, onchocerciasis, leprosy, and ocular trauma[1]. Many of these causes are preventable through effective public health strategies but for those who are blind due to corneal opacification only treatment is corneal transplantation. This surgery needs donor cornea obtained from an eye bank, the diseased cornea is excised & replaced with donor cornea. This procedure has very high success rate among organ transplants. Quality of donor cornea, the nature of recipient of pathology and the availability of appropriate postoperative care are the factors that determine the final outcome of this procedure.

Procurement and supply of the donor cornea to the corneal surgeons is the primary goal of eye banks. While this fact is recognized, the need for rigorous quality control in eye banking is not appreciated by the eye bankers and the surgeons in India and the other developing countries[2, 3]. Scarcity of donor corneas, while a major problem, should not lead to utilization of corneas of undesirable quality. This happens when enthusiasm to start an eye bank is not matched by commitment to institution of quality measures. An “eye bank” is not for profit community organization governed by a Board of Directors or Trustees constituted by the community representatives. Ideally, it should be autonomous and not part of any medical organization.

MAGNITUDE OF CORNEAL BLINDNESS IN INDIA

We conducted the Andhra Pradesh Eye Disease Study[4] (APEDS) in our state which is one of the largest states of India with an estimated population of 76 million in 2001. The age distribution of the population of the state is pyramidal like rest of India, with an estimated 35.6% of total population 15 years of age or less, 25.7% between 16-29 years, and 38.7% 30 years of age or more. The rural population comprises approximately 73% of the total population of the state, and agriculture is the primary occupation.

The objectives of APEDS were to determine the prevalence and causes of blindness and visual impairment, risk factors associated with major eye diseases, barriers to eye care services, and quality of life in the visually impaired. Data on blindness (presenting visual acuity <20/200 or central visual field <20 degrees in the better eye) from APEDS have been reported. The prevalence of blind people in this population was estimated as 1.84%, of which 7% was due to corneal diseases.

The prevalence of corneal blindness was 0.66% (95% CI 0.49 to 0.86; design effect 1.35) in at least one eye, which included 0.10% prevalence of corneal blindness in both eyes, and 0.56% prevalence

Correspondence: Virender S Sangwan, *Associate Director L V Prasad Eye Institute, Head - Cornea & Anterior Segment, Ocular Immunology & Uveitis Service, L.V.Prasad Eye Institute, Kallam Anji Reddy Campus, L.V.Prasad Margsangwan, Banjara Hills, Hyderabad - 500 034 Ph:91-40-30612632, 30612345, Fax: 91-40-23548271,* ***E-mail :*** *vsangwan@lvpei.org*

of corneal blindness in one eye[5]. Extrapolating these data from APEDS to the estimated 76 million population of Andhra Pradesh in the year 2001, 50 160 (95% CI 37724 to 65360) people have corneal blindness in at least one eye, of whom approximately 7600 have corneal blindness in both eyes[5]. According to this study 6.8 (95% CI 5.0 to 8.8) million people in India in 2001 are estimated to have corneal blindness in at least one eye, of which one million people have corneal blindness in both eyes. These rates suggest that 8.4 ((5% CI 6.3 to 10.9) million people of the estimated 1168 million population of India in 2010, and 10.6 (95% CI 8.3 to 13.6) million people of the estimated 1312 million population of India in 2020, would have corneal blindness in at least one eye if the current trends continues[5].

The most frequent causes of single eye corneal blindness included keratitis during childhood (36.7%), trauma (28.6%), and keratitis during adulthood (17.7%)[5]. Nearly 95% of all corneal blindness was avoidable. From all the evidence available, direct and indirect, an annual performance of around 100,000 corneal transplants would have a salutary effect on the problem of reversible corneal blindness in India. Going by the experience of eye banking systems worldwide, meeting this demand would require double that numbers of corneas harvested, i.e. 200,000 corneas per year, which translates to 50 eye banks for the entire country. In country like India, where the basic infrastructure and human resource exits, this should not be a problem.

CURRENT SUPPLY OF DONOR CORNEAS IN INDIA

According to Eye Bank Association of India (EBAI) data there were18641 tissues retrieved across the country in 2000 of which more than 50% were collected by Gujarat, Maharashtra, and Tamil Nadu, in the same year 4381 optical corneal transplants were done[6]. This number has increased to 34520 in year 2008 and 9509 optical corneal transplants were done in year 2008. The EBAI data on corneal tissue retrieval from across the country along with total number of corneal transplants (total of optical, therapeutic, and lamellar grafts) done from 2000 to 2008 are shown in Fig 1. It is very clear from this data that the trends are positive and corneal retrieval is increasing but not enough to meet the perceived need for harvesting 200,000 tissues annually to do 100,000 corneal transplants a year. More than 50% corneal tissue collection is done by Tamilnadu, Gujarat, Maharashtra, Andhra Pradesh, and Karnataka. However, other states are also improving the collection (table 1).

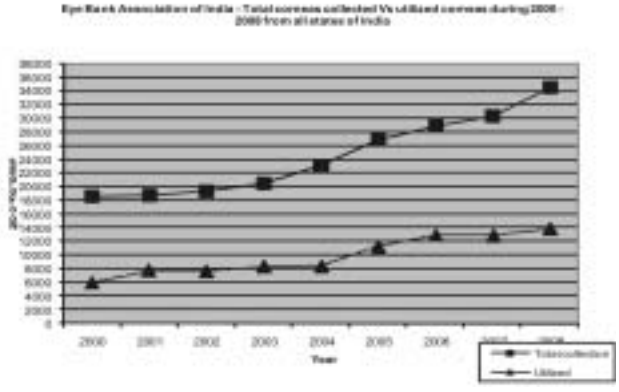

Figure 1:*Figure shows total number of corneas collected annually from different states in India from 2000 to 2008 versus utilization rate of collected tissue. Around 50% of collected tissue is utilized for corneal transplantation due to medical contraindication.*

Table 1: *The table shows total number of corneas collected in year 2008 across India along with utilization. PKP: penetrating keratoplasty.*
Eye Bank of Association of India (EBAI) data of corneal tissue collection for year 2008.

Name of the State	Collection	Optical PKP	Therapeutic PKP	Lamellar Keratoplasty
Andhra Pradesh	4362	1316	763	154
Karnataka	2544	545	163	58
Kerala	868	223	8	2
Pondicherry	359	70	78	5
Tamilnadu	8178	1404	866	249
Maharashtra	4685	1051	415	15
Gujarat	5611	2075	359	31
Punjab	751	324	249	0
Rajasthan	1190	522	50	5
Haryana	1134	413	48	17
Chandigarh	468	164	162	7
Delhi	1598	562	339	39
West Bangal	1688	301	63	125
Orissa	91	48	18	0
Andaman Nikobar	0	0	0	0
Assam	215	122	22	0
Bihar	34	32	0	0
Madhya Pradesh	399	91	33	0
Uttar Pradesh	345	246	33	2
Total	**34520**	**9509**	**3669**	**709**

In 1995-1996, we have performed 283 corneal transplants at L V Prasad Eye Institute; this number has since increased to 1031 in the year 2003-2004 (Corneal retrieval by Ramayamma International Eye Bank is depicted in Figure 2), an almost four fold increase. In the process, we have eliminated the waiting list for corneal transplantation in our institute; we have established the credibility of high quality eye banking in India, the demonstrated success of the concept of Hospital Corneal Retrieval in India, and an assured supply of corneal preservation medium to all eye banks across the country. In addition, we have trained scores of corneal "specialists" (not just corneal "surgeons") and eye banking personnel from around the world. The number -1031- also represented a milestone in the history corneal transplantation since this is the first instance of over 1000 corneal transplants being performed at a single centre anywhere in the world. Since then we have been doing 900-1000 corneal transplants every year. This achievement becomes particularly significant as organ transplantation has so far been considered an insurmountable problem in India. However, unfortunately such an increase in numbers of corneal transplants has not become a national trend.

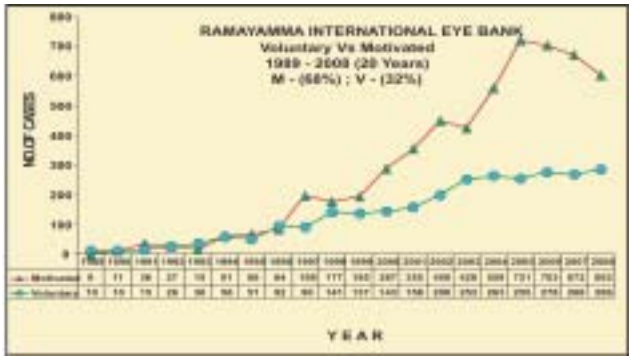

Figure 2: *This chart shows corneal tissue collected by Ramayamma International Eye Bank from 1989 to 2008. It also shows voluntary versus motivated cornea tissue retrieval and steady increase in motivated corneal tissue retrieval due to our Hospital Based Cornea Retrieval Program (HCRP)*

An analysis of the situation is quite revealing. In India, there is no dearth of knowledge, skills and resources to create a world class eye banking and corneal transplantation network. What seems to be missing, however, is a "Proactive National Movement" to translate concepts and plans into time-bound action. There is tremendous gap in demand and supply of corneal tissue and therefore we suggest the three tier eye banking system, which is outlined in next section. The details of the model and medical standards in eye banking in India can be found in handbook published by ministry of health, Government of India[7].

EYE BANKING MODEL

In developing countries such as India, one has to develop a system that is effective, efficient and at once financially relevant. A 3-tier structure encompassing all activities of eye banking will address this issue rather well the determinants will be the infrastructure and manpower available with a profile of functions covered. This system proposed the three tiers of eye donation centers, eye bank and eye banking training center. These should be integrated and will not be effective in isolation.

Hospital Eye Bank: A Hospital Eye bank in an institution that fulfils all the requirements and functions of eye bank except that it restricts collection of tissue within the hospital where the eye bank is located.

Eye Bank Training Centre (EBTC): All of the eye bank functions plus training for all levels of personnel in eye banking and research.

Eye Donation Center (EDC): Eye Donation Center is affiliated to a registered eye bank, which should provide (1) public and professional awareness of eye donation (2) co-ordinate with donor families and hospitals to motivate eye donation (3) to harvest corneal tissue and collect blood for serology (4) to ensure safe transportation of tissue to the parent eye bank. EDC do not need to be registered. The human resource and infrastructure requirement[7] for EBTC, EB, and EDC is listed in Table 2 and 3.

***Table 2**: Table showing manpower requirement for Eye Bank (EB), Eye Bank Training Center (EBTC), and Eye Donation Center (EDC). This table is adapted from Reference # 7*

MANPOWER	EBTC	EB	EDC
Board of Directors	Yes	Yes	No
Medical Director	Yes	Yes	No
Executive Director	Yes	Yes	No
Eye Bank Manager	Yes	Yes	Yes
Eye Bank Technicians	Yes	Yes	Yes
Eye Donations Counselors	Yes	Yes	No
Administrative Secretary	Yes	Yes	No
Telephone Operator	Yes	Yes	No
Panel of Registered Medical Practitioners to enucleate round the clock	Yes	Yes	Yes

Each of these eye banks should be in an autonomous organization, ideally with its own Board and governance structure representing all the stakeholders in the community. All the major functions of an eye bank should be carried out, including public awareness, tissue harvesting, tissue evaluation (including serology and microbiology), tissue preservation and tissue distribution. Equitable distribution is the key to long-term success, since this builds credibility in the community with all its subsequent benefits. The goal is to make safe and high quality corneal tissue accessible to everyone who needs corneal transplantation in the community in an equitable manner. Essentially, this means that all those who are in need for a corneal transplant for visual rehabilitation, irrespective of socio-economic status, gender, religion, or choice of surgeon and institution, should have equal access to the eyes donated to eye banks on a first-come-first-served basis.

***Table 3:** Table showing infrastructure requirement for Eye Bank (EB), Eye Bank Training Center (EBTC), and Eye Donation Center (EDC). This table is adapted from Reference # 7*

INFRASTRUCTURE	EBTC	EB	EDC
Equipment			
Slit Lamp	Yes	Yes	Yes
Refrigerator	Yes	Yes	No
Serology Equipment	Yes	Yes	No
Specular Microscope	Yes	Yes	No
Six sets of instruments for corneal excision and enucleation	Yes	Yes	Yes
Autoclave	Yes	Yes	Yes
Transportation Facility	Yes	Yes	Yes, should have access
Furniture	Yes	Yes	Yes
Computer with email facility	Yes	Yes	Yes
Supportive: (Administrative)			
Two exclusive lines (one with 1919 and another for outgoing calls	Yes	Yes	No
Standard Public information material	Yes	Yes	Yes
Forms for tissue retrieval/consent/…….			
Hospital Cornea Retrieval Programme	Yes	Yes	Yes
Financial sustainability	Yes	Yes	No

This plan then envisages the establishment[8] of one eye bank for every 20 million people, each of which is to be linked to 40 Eye Donation Centres (EDC) – eye banking units that are involved only in harvesting corneas. To meet the demand for training of eye banking personnel, 5 of the eye banks will be identified as training centres. In addition[8], each eye bank will develop a Hospital Cornea Retrieval Programme (HCRP) in 10 major hospitals in the immediate community. Half (2000) the harvesting is achieved by the Eye Bank directly through the HCRP and the other half (2000) will be through the contribution of eye donation centers, with 50 eyes (25 donors) from each EDC (Figure 3).

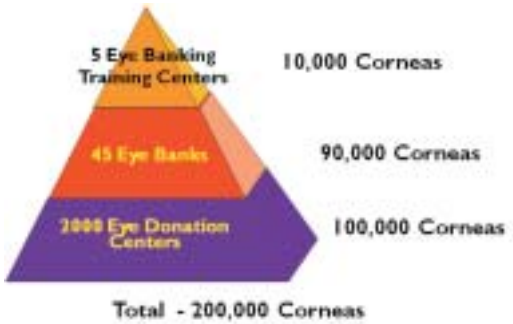

***Figure 3:** The pyramid shows number Eye Bank Training Center (EBTC), Eye Bank (EB) and Eye Donation Center (EDC) and projected number of the corneas required to be processed at each level to meet annual need of 200,000 corneas.*

The overall financial outlay[8] of this plan is surprisingly small. Each eye banking training centre costs around Rs. 50 million, Rs. 30 million for an eye bank and Rs. 50,000 for an eye donation centre. Together the entire eye banking infrastructure for the country can be

created at a cost of Rs. 260 million (Figure 4). This funding can be mobilized from Government, International Non-Governmental Organizations and local sources. The operating expenses of eye banks will be covered by processing fess (those belonging to upper socio-economic groups pay this as part of fees and for the lower socio-economic groups a subsidy may be provided by Government and INGDos) and donations.

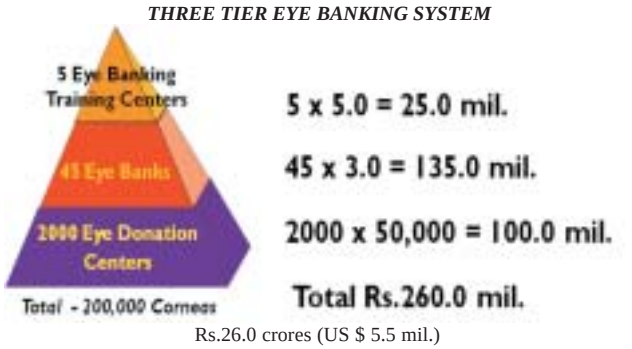

Figure 4: *The pyramid shows number Eye Bank Training Center (EBTC), Eye Bank (EB) and Eye Donation Center (EDC) along with financial requirement to create the system.*

Another aspect that merits attention is the number of well-trained corneal specialists[8]. If an annual target of 100 transplants per surgeon is reasonable, India needs 1000 trained specialists. Against this, the current number is less than 200. There is a need to create more corneal training centers as the existing 4 or 5 centers cannot meet the entire demand.

In summary[8], India needs 50 eye banks, five of which will also be eye banking training centres, 2000 eye donations centres, Cornea Retrieval Programmes in 500 hospitals and 1000 corneal specialists to make a real impact on the problem of this reversible form of corneal blindness. What are the possible next steps to get there? A clear concept and detailed plan must be developed, followed by rigorous implementation of the plan by all concerned in a time-bound fashion. As ophthalmologists, we are obliged to play a leading role in this endevour and have to play only that role that is appropriate for us. Let all of us involved in the fight against corneal blindness work together for a national goal. If we can make that commitment, we can prove that India is definitely up to the task of serious "Eye Banking" and be a role model for other developing countries.

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DRUG PROFILE

Terizidone

Terizidone is WHO categorized group IV anti TB drug. 1 It is an antibiotic effective against mycobacterium tuberculosis and also M. avium for the treatment of tuberculosis, both pulmonary and extra pulmonary. It is classified as a second-line drug, i.e. its use is only considered if one or more first line drugs cannot be used. Terizidone is obtained by combining two molecules of cycloserine and one molecule of terephtalaldehyde and is a broad spectrum antibiotic which greatly improved the disadvantages associated with cycloserine. ***Mechanism of Action:*** Its mode of action is similar to cycloserine i.e. It acts by inhibiting cell wall synthesis by competitively inhibiting two enzymes, L-alanine racemase and D-alanine ligase, thereby impairing peptidoglycan formation necessary for bacterial cell wall synthesis. ***Pharmacokinetics:*** Terizidone is completely and rapidly absorbed after oral administration. Maximum concentration in blood is achieved in 2 to 4 hrs. It was noted that the blood concentration of Terizidone was higher at all time intervals than the concentration attained in the blood after the same doses of cycloserine. Excretion in urine is quicker in the young ones. Its concentration in the urine after 30 hrs of administration sufficiently exceeded its minimum inhibitory concentration. This justifies its use in the treatment of urogenital TB. It was found that the increase in the dose does not cause a proportional increase in the concentration of the drug in the blood. It is well distributed in all body fluids and tissues. The half-life of terizidone was significantly greater than that of cycloserine, it was significantly higher in the elderly than the young patients. The molecule does not have cumulative toxicity and hence better tolerability. ***Indication:*** Terizidone is recommended for tuberculosis both pulmonary or extra pulmonary caused by resistant strains of Mycobacterium tuberculoisis or avium. It is not recommended for use as monotherapy for infections with tuberculosis. As it has higher concentrations in urine it makes it a better choice of drug for urogenital tuberculosis, specially cystitis and epididymoorchitis. ***Precausions and contraindications:*** It is to be used with caution in pateints with psychiatric comorbidities and epilepsy. Also patients who are intolerant to cycloserine. ***Adverse effects:*** Terizidone intensifies the activating effect on ascending section of the reticular formation of brainstem; the effect is lower than cycloserine. Dizziness, slurred speech, headache and convulsions are amongst the few reported side effects. Others include tremors, insomnia, confusion, depression. The most dangerous side effect is suicidal tendency; nausea, vomiting, skin allergies and rashes are also reporeted. When used in higher doses that is more than 1 gm per day liver function disorders, congestive cardiac failure, convulsions and coma are reported. ***Dosage and administartion :*** The usual adult dose ia 15-20 mg/kg per day in three to four divided doses. Maximum recommended dose is 4 capsules a day ie 1gm daily.