

# Progress in Screening and Treatment of Common Congenital Eye Diseases

Yan Li, Haotian Lin\*

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510060, China

## Abstract

Congenital eye illnesses are caused by congenital ocular malformations and are a primary cause of poor visual acuity and blindness in infants. Early diagnosis and treatment of congenital eye illnesses are of great significance for affected infants, their families, and even society as a whole. This study describes the current situation for prenatal and infant screening for congenital eye diseases and briefly summarizes novel progress in the treatment of the five most common eye diseases (congenital dacryocystitis, congenital cataract, retinopathy of prematurity, congenital glaucoma and retinoblastoma). Current programs are now aimed at improvements in the prevention and treatment of congenital eye diseases in China. (*Eye Science* 2013; 28:157–162)

**Keywords:** congenital eye disease; screen; treatment

Childhood blindness is a major public health problem and congenital eye diseases are the leading cause of blindness in children. Approximately 1.5 million children around the globe are blind. Based on estimates of the duration of blindness in years (survival after onset of blindness in years), childhood blindness causes a heavier burden economically and socially than does adult blindness. In response to this global issue, the World Health Organization launched VISION 2020 and set elimination of childhood blindness as the paramount strategic goal worldwide.

Early diagnosis and treatment of congenital eye diseases play a pivotal role in reducing and eliminating childhood blindness. Some countries have set up

relatively mature general screening system for childhood eye diseases, but these are not available in nations such as China, which has a large population and an unbalanced allocation of medical resources due to high cost and strict requirement for professional expertise. An effective and systematic network comprising screening, monitoring, and inpatient to outpatient transfer for childhood eye diseases is still lacking in China, even though tentative screenings have been conducted in several regional hospitals. Certain misunderstandings and misconceptions remain regarding the timing and procedures of treatment. Standard criteria and paths of clinical diagnosis and treatment have rarely been established, which prevents affected children from receiving early diagnosis and standard treatment. This study presents a review of the current situation of screening of congenital eye diseases and describes advances in the progress of treatment of congenital eye diseases.

## Current situation of screening of congenital eye diseases

The initial 4–6 months of the embryonic period are crucial to fetal eye development and the infantile period is a pivotal stage for visual development after birth<sup>1</sup>. Hence, screening for congenital eye diseases inevitably includes two stages: prenatal screening and infantile screening. From the perspective of embryonic development, the optimal timing of prenatal screening should be 6 months during pregnancy. At present, prenatal screening has not been initiated in China and is even rarely reported in developed countries due to its high cost, strict requirement for specialized techniques, and low detection rates. In China, screening for congenital eye diseases is mainly concentrated on infant screening. Although the American Association of Ophthalmology has

DOI: 10.3969/j.issn.1000-4432.2013.03.010

**Funding:** The Fundamental Research Funds for the Central Universities; Cultivation Projects for Young Teaching Staff of Sun Yat-sen University (12ykpy61)

\* **Corresponding author:** Haotian Lin, E-mail: gddlht@gmail.com

compiled standard guidelines for clinical evaluation of childhood eye diseases, these guidelines are not directly applicable to the current situation of clinical practice and screening in China due to large regional variations. In this study, we examined this point from the aspects of screening subjects, operators, procedures, and content.

The first step is the selection of screening subjects and operators. Previous studies found that approximately 39% of screening subjects are newborns (including premature infants) from Obstetrics and Gynecology Departments of regional general hospitals, approximately 45% are newborns (including premature infants) from Maternal and Child Health Services Centers, and the remaining are outpatients from Ophthalmology Departments of general hospitals and infants from kindergartens, aged from 24 h to 6 years after birth<sup>1-10</sup>. In addition, more than 95% of screening operators are ophthalmologists, pediatricians, and infant pediatricians undergoing professional training<sup>2</sup>.

The second step is to establish screening procedures<sup>5</sup>. Previous reports indicated that the experts were responsible for designing screening plans and record forms, conducting preliminary evaluation of screening subjects, and consecutive evaluation of eye disease screening in eligible infants. The suspected cases were asked to pay a return visit depending on the course of disease. Those infants with a high risk of eye diseases—including premature infants, low-birth-weight infants with a high concentration of inspired oxygen, and those with a familial history of congenital eye diseases, regardless of whether they passed or failed initial screening—should be included for subsequent follow-up. The cases with definite diagnosis should undergo immediate intervention and those with complex conditions and requiring surgery should be switched to Department of Ophthalmology for further diagnosis and treatment.

The third step is related to screening contents, which is the core of screening process, as shown in Table 1.

**Table 1** Current situation and items of screening for infantile congenital eye diseases in China

Screening item	Current situation <sup>1-11</sup>
Inquiry into medical history	During the initial screening, the patients were surveyed about risk factors of congenital eye diseases (such as premature delivery, oxygen inspiration, low birth weight, and familial history) via direct consultation and questionnaire surveys.
Light stimulation	Through light stimulation using a flashlight, the visual acuity of the infants is roughly evaluated by observing infants' reactions.
External eyes	A headband magnifier or hand-held slit lamp is utilized to conduct a complete examination of the orbit, eyelid, conjunctiva, lacrimal apparatus, cornea, iris, and pupil. Intraocular pressure is measured by finger pressing.
Red reflex	Direct ophthalmoscope: refraction is adjusted to +6 to +12 diopter (D), direct ophthalmoscope is performed through dilated pupils at 10 to 15 cm from the eyeball to observe whether red reflex in pupil area is normal or abnormal. The presence of dark spots, the weakening or disappearance of unilateral red reflex, or the incidence of white light reflex are equally defined as abnormal.
Mydriasis test	Subjects found to be abnormal or have risk factors receive conventional mydriasis to examine the fundus.
Evoked potentials	Subjects confirmed to be abnormal in light stimulation, red reflex, and fundus examination or who are ineligible for hearing screening should undergo simultaneous auditory and visual evoked potential examination.
Visual electrophysiology	Subjects with abnormal red reflex and fundus examination should be considered to receive visual evoked potentials or electroretinography, <i>etc.</i>
Pediatric refractometer	Infants who participate in the screening should receive a Pediatric refractometer test to identify infantile ametropia, refractive media diseases, and even strabismus, <i>etc.</i>
B-mode ultrasound	B-mode ultrasound is cheap, practical, and easy to perform, and can be applied to newborns and infants suspected to have pathological fundus changes and intraocular tumors.

The fourth point is the screening results. Discrepancies in geographic regions and screening criteria cause the screening outcomes to vary significantly among studies, as shown in Table 2. In addition, patients' compliance with follow-up is affected by a

variety of factors including the understanding of diseases, economic conditions, climate conditions, and route of transportation, *etc.* The return-visit and follow-up rates are relatively low in China<sup>2-4</sup>. Table 2 shows the data for each study obtained from prelimi-

nary screening.

**Table 2** Statistical analysis of the incidence of congenital eye diseases determined by preliminary screening in Chinese newborns and infants

Diseases	Incidence <sup>1-7</sup>
Congenital dacryocystitis	5%–11%
Congenital cataract	4‰–6‰
Retinopathy of prematurity	2‰–6‰
Primary congenital glaucoma	0.1‰–0.4‰
Retinoblastoma	0.05‰–3.3‰
Ametropia, strabismus and amblyopia	1.5%–18%
Congenital persistent pupillary membrane	0.2%–4.7%
Congenital microphthalmia	0.01%
Congenital ptosis	0.013%–4.5%

## Progress in treatment of congenital eye diseases

On the basis of multiple factors, such as incidence, blindness rate, and prevention and treatment efficacy of congenital eye diseases, a summary is presented of the novel progress in the timing of lacrimal duct recanalization in congenital dacryocystitis cases, the timing of congenital cataract surgery, the timing of IOL implantation and selection of IOL power, and the selection of congenital glaucoma surgery, medication and gene therapies of retinopathy of prematurity as well as retinoblastoma, *etc.*

### Treatment of congenital dacryocystitis

Congenital dacryocystitis has the highest incidence of the infantile congenital eye diseases and is mainly characterized as an obstruction of the lower opening of nasolacrimal duct by congenital membrane tissues, or obstruction of the nasolacrimal duct or a nasal deformity-induced obstruction or tearing and bacterial retention in the lacrimal sac, which leads to secondary infection. At present, antibiotic eyedrops combined with massage of the lacrimal sac are widely recommended as early treatments. Huiling Yang *et al.*<sup>12</sup> found that gram-positive cocci and gram-negative bacilli, which are common pathogenic bacteria, act as the main pathogenic bacteria of congenital dacryocystitis. They also noted that cepheems and quinolones are effective drugs. If conservative treatment fails, lacrimal duct irrigation and antibiotic administration into lacrimal duct should be performed.

Lacrimal duct recanalization may be attempted following  $\geq 3$  times of lacrimal duct irrigation; recurring cases following after repeated recanalization are considered to be refractory infantile dacryocystitis and probably should receive lacrimal intubation to restore normal function<sup>13</sup>.

The timing of lacrimal duct recanalization varies significantly among clinicians. Some scholars have suggested that conservative therapy rather than lacrimal duct recanalization should be conducted in infants younger than 6 months. Opposing opinions hold that lacrimal duct recanalization should be performed within the 6-month age period because the cure rate of lacrimal duct recanalization declines over time. Lacrimal duct recanalization has been reported as likely to cause severe trauma within the 3-month age group, whereas conservative therapy yields high efficacy; hence, early lacrimal duct recanalization is not recommended<sup>35</sup>. Currently, the optimal time for performing lacrimal duct recanalization is accepted as 3–6 months of age<sup>13</sup>. In short, most ophthalmologists attempt to treat congenital dacryocystitis using a simple and efficacious approach.

### Treatment of congenital cataract

Congenital cataract is one of the primary causes of childhood blindness. However, the blind rate of congenital cataract declines along with the advancement of surgical technique. Surgery is the most widely accepted and effective treatment of congenital cataract, but attention should be paid to the following aspects:

- 1) The timing of surgery. The infantile fixation reflex is developed before 1 year of age, especially during the 2–3 months after birth. Maldevelopment of the fixation reflex during this period may lead to nystagmus and aggravate childhood amblyopia<sup>14</sup>. Previous studies reported that fundus examination or optometry is not possible in patients with lens opacity with a diameter of  $> 3$  mm. For children with bilateral onset receiving surgery in the fellow eye, presenting with strabismus or accompanied by nystagmus and alternative complications, cataract extraction within 3 months after birth yielded the most favorable outcomes regarding visual function. The timing of cataract surgery for unilateral patients can be

moved up<sup>15</sup>.

2) Surgical approach. At present, phacoemulsification, posterior capsulorhexis combined with anterior vitrectomy, and lens-in-the-bag implantation are ideal surgical treatments for congenital cataract, and significantly increase visual acuity and reduce the recurrence of cataract<sup>16</sup>.

3) The timing of IOL implantation and selection of IOL power. IOL implantation can be performed with much care and caution in 1-year-old children with unilateral congenital cataract. It is safe and efficacious to conduct IOL implantation for children >3 years of age with bilateral congenital cataract<sup>17</sup>. The rapid development in terms of IOL material, design and implantation techniques means that IOL implantation can be performed at a much younger age than previously. A minority of scholars insist that IOL implantation can be performed in patients of any age with unilateral congenital cataract and in patients over 6 months of age with bilateral congenital cataract<sup>36</sup>. Other authors held neutral opinions and no consensus has been reached on selection of IOL power. The majority of Chinese ophthalmologists proposed that IOL implantation can be conducted with great caution in children aged <3 years old. Undercorrection of -2.00D IOL power was recommended for those aged 3-4 years, -1.00D refractive undercorrection for those aged 5-7 years, and full refractive correction for children aged  $\geq 8$  years. For patients with unilateral cataract, the calculation of IOL power should refer to the refraction of the fellow eye, allowing for < 3.00D refractive errors between both eyes<sup>18</sup>.

4) Postoperative recovery of visual function. Delayed treatment of postoperative amblyopia is a major cause of visual damages in children with congenital cataract. The pivotal step of amblyopia treatment is refractive correction. Common methods include frame glasses and corneal contact lenses in accordance with the principle of "low power and refractive undercorrection"<sup>19</sup>. Alternative comprehensive therapies should also be performed as necessary, such as the alternating cover test, training of monocular gaze-shift, afterimage, red flicker, and Haidinger brush, *etc.*<sup>19</sup>. Long-term comprehensive treatments can improve visual acuity and establish

good simultaneous vision, imaging-fusion, and stereopsis.

### **Treatment of retinopathy of prematurity**

The incidence of retinopathy in premature infants has shown recent increases with the prolongation of survival of premature newborns and infants, so that this has become the primary cause of childhood blindness. Consequently, early prevention of retinopathy of prematurity is of great importance. In April 2005, the 'Guidelines for therapeutic use of oxygen and prevention and treatment of retinopathy in premature infants' were issued by Ministry of Health in China<sup>20</sup>, with the aim of reducing the incidence of retinopathy in premature infants. At present, partial lesions of stage I and II retinopathy of prematurity are recognized as having the ability to self-heal, but strict monitoring should be provided<sup>21</sup>. Cryotherapy and laser therapy are recommended for cases of stage III retinopathy of prematurity and those complicated by pathological changes<sup>21</sup>. Surgical treatments, such as the scleral buckling procedure, vitrectomy, and lens excision combined with vitrectomy, should be performed in patients with stage IV or V complicated with retinal detachment<sup>21</sup>.

All of these treatments have many complications and unsatisfactory efficacy. A simple, safe, and effective treatment is urgently needed. At present, novel medication therapy (arginine-glutamine, GM6001, triamcinolone acetonide, intravitreal injection of bevacizumab, *etc.*) and gene therapy remain at the stage of animal experiments. However, the research and development of these medications are aimed at treating the pathogenesis and pathophysiology of retinopathy in premature infants and have the potential for prevention of retinopathy of prematurity<sup>21</sup>.

### **Treatment of congenital glaucoma**

Congenital glaucoma is mainly caused by developmental disorders of the anterior chamber angle and the trabecular meshwork during embryo development. Children have a poor tolerance for glaucoma medications and can experience harmful reactions. Therefore, surgical treatment should be performed immediately when children are diagnosed with congenital glaucoma<sup>22</sup>. Different surgical techniques should be employed according to the clinical mani-

festations of the congenital glaucoma and the severity of the corneal opacity. Subjects with a transparent cornea with a diameter of < 13 mm and clear observations through the chamber angle are recommended to undergo chamber angle surgery as the first operation. Those with corneal opacity with a diameter of > 13 mm and a difficult-to-observe chamber angle primarily undergo external trabeculotomy, trabeculectomy, or external combined trabeculotomy-trabeculectomy. External trabeculotomy combined with trabeculectomy is a primary surgical approach for the treatment of congenital glaucoma; it utilizes the aqueous humor inflow pathway established by trabeculotomy, but also takes advantage of aqueous humor outflow pathway created by trabeculectomy. The combination of these two surgical techniques increases the surgical success rate up to 90.9–100%<sup>32,33</sup> while minimizing the incidence of photophobia, lachrymation, blepharospasm, and other complications. Currently, combined trabeculotomy-trabeculectomy is widely applied in clinical settings<sup>23–27</sup>.

### Treatment of retinoblastoma

Retinoblastoma is the most common intraocular malignant tumor affecting children's visual acuity and can be life threatening. The treatment of retinoblastoma should be individualized in combination with the pathological classification of retinoblastoma. Common treatments include:

1) Eye enucleation + prosthesis implantation: applicable to large sized ocular tumors (>50% of the ocular volume) or tumor invasive eye diseases or tumors unresponsive to alternative treatments<sup>29</sup>. 2) Chemotherapy: applicable to children with bilateral tumors, or extraocular and metastatic tumors. 3) Topical therapies: laser photocoagulation therapy, cryotherapy, radiotherapy, etc. These options are commonly used as adjuvant therapies for eye enucleation and chemotherapy rather than being performed alone, due to their limited range of application and excessive side effects<sup>31</sup>. At present, systemic chemotherapy or topical administration, combined with topical treatment, is the primary conservative option worldwide<sup>31</sup>. 4) Gene and medication therapies (anti-tumor agents and proapoptotic medications, *etc.*) are still in the experimental stage, but they are likely to evolve into novel, effective, and safe treatments a-

gainst retinoblastoma<sup>30</sup>. The goal of retinoblastoma treatment should not be limited to retaining the eyeball and saving lives, but should also aim to improve visual acuity as much as possible.

### Brief summary

Identifying eye diseases in infants is a challenging task because infants spend most of their time sleeping and keeping their eyes closed. This leads to negligence and delays in clinical treatments of eye diseases such as infantile amblyopia and blindness and affects the patients, their families, and even society as a whole<sup>1</sup>. Consequently, improving the prevention and treatment of congenital eye diseases is not the responsibility only of clinical ophthalmologists but it also requires the collective efforts of the entire society.

### Disclosure statement

There is no conflict of interest to declare.

### References

- 1 Guo YL, Dong YR, Shi JN, et al. Ocular diseases screening for neonates: A 3704 cases report. *Chinese Journal of Ophthalmology*, 2006, 42(5): 470–471.
- 2 Nie WY, Wu HR, Qi YS, et al. A Ret study of ocular diseases screening for neonates in China. *Chinese Journal of Ophthalmology*, 2008, 44(6): 497–501.
- 3 Li XF. A 2016 case analysis of ocular diseases screening for neonates in Changchun city. *Maternal & Child Health Care of China*, 2004, 19(14): 26.
- 4 Tian T, Wu ZQ, Fei SL, et al. A 2016 cases analysis of ocular diseases screening for neonates in Changchun city. *Chinese Journal of Strabismus & Pediatric Ophthalmology*, 2008, 16(2): 86–87.
- 5 Zhang M, Li YH, Xie F, et al. Study on the technique of newborn eye-disease screening model. *Chinese Journal of Strabismus & Pediatric Ophthalmology*, 2006, 14(3): 118–122.
- 6 Xiang MD, Zeng FL, Chen YT, et al. The value study of the method of eye disease screen in pediatric ophthalmology. *Journal of Clinical Ophthalmology*, 2006, 14(1): 18–20.
- 7 Sun XT, Chen M, Gong GY. Investigation report of ocular diseases screening for neonates in Zhengzhou city. *Journal of Medical Forum*, 2010, 31(22): 138–140.
- 8 American Academy Of Pediatrics. Eye examination in infants, children, and young adults by pediatricians. *Pediatrics*, 2003, 111: 902–907.

- 9 Hartmann EE, Dobson V, Hainline L, et al. Preschool vision screening: summary of a task force report. *Ophthalmology*, 2001, 108: 479–486.
- 10 Multi-ethnic Pediatric Eye Disease Study Group. Prevalence of amblyopia and strabismus in African American and Hispanic children ages 6 to 72 months the multiethnic pediatric eye disease study. *Ophthalmology*, 2008, 115(7): 1229–1236.
- 11 Zhang W, Qi YS, Han DM, et al. A preliminary study of synchronous evoked potential in newborn-infant auditory and visual function test. *Nation Medical Journal of China*, 2003, 83(16): 1394–1398.
- 12 Yang HL, Tao LJ, Tang XR. Pathogen analysis of neonatal dacryocystitis. *Journal of Clinical Research*, 2008, 25(1): 163–164.
- 13 Ma Z. The treatment experience of infant dacryocystitis. *Journal of Clinical Ophthalmology*, 2004, 12(5): 77–78.
- 14 He SZ. The lens epidemiology. Beijing: People's Medical Publishing House, 2002: 1476.
- 15 Xiao W, Zhao DX, Pu W, et al. Clinical analysis of postoperative complications of infantile congenital cataract surgery. *Int J Ophthalmol*, 2009, 9(5): 861–864.
- 16 Perucho-Martinez S, Tejada-Palacios P, de-la-Cruz-Bertolo J. Congenital cataract: complications and functional results according to different surgical techniques. *Arch Sos Esp Oftalmol*, 2010, 85(1): 16–21.
- 17 Lambert SR, Lynn M, Drews-Botsch C, et al. Optotype acuity and re-operation rate after unilateral cataract surgery during the first 6 months of life with or without IOL implantation. *Br J Ophthalmol*, 2004, 88, 11: 1387–1390.
- 18 Ma Y, Wang JP. The choosing of intraocular lens power for children with congenital cataract and its postoperative influence on children's refractive change and axial growth. *International Eye Science*, 2006, 6(3): 626.
- 19 Xie J. Recent advances in infants with congenital cataracts. *Journal of Clinical Ophthalmology*, 2011, 19(6): 566–568.
- 20 Chinese Medical Association. Guidelines for therapeutic use of oxygen and prevention and treatment of retinopathy in premature infants. *Chinese Journal of Ophthalmology*, 2005, 41(4): 375–376.
- 21 Tan JX, Zhu D. New progress on the treatment of retinopathy of prematurity. *International Journal of Ophthalmology*, 2010, 10(5): 898–900.
- 22 Hu HL, Zhang XL, Du SL, et al. Investigation of 266 Cases (445 eyes) of Congenital Glaucoma. *Chinese Journal of Practical Ophthalmology*, 2007, 25(8): 896–899.
- 23 Ke XF, Liu H, Zhu DN. Treatment of congenital glaucoma with combined trabeculectomy and small trabeculectomy. *Chinese Journal of Practical Ophthalmology*, 2003, 21(10): 757–758.
- 24 Dureau P. Congenital glaucoma and trabeculodysgenesis. Clinical and genetic aspects. *J Fr Ophtalmol*, 2006, 29(2): 198–215.
- 25 Al-Hazmi A, Awad A, Zwaan J, et al. Correlation between surgical success rate and severity of congenital glaucoma. *Br J Ophthalmol*, 2005, 89(4): 449–453.
- 26 Dumitras L, Coviltir V. Short-term results of trabeculectomy in early primary congenital glaucoma. *Oftalmologia*, 2004, 48(3): 46–48.
- 27 Mandal AK, Gothwal VK, Bagga H, et al. Outcome of surgery on infants younger than 1 month with congenital glaucoma. *Ophthalmology*, 2003, 110(10): 1909–1915.
- 28 Peng SX, Zhou WB, Peng DW, et al. The analysis of causes affecting postoperative visual acuity of primary congenital glaucoma. *Chinese Journal of Practical Ophthalmology*, 2000, 18(3): 150–151.
- 29 Rodriguez-Galindo C, Chantada GL, Haik BG, et al. Treatment of retinoblastoma: current status and future perspectives. *Curr Treat Options Neurol*, 2007, 9(4): 294–307.
- 30 Li D, Xia XG. Research advanced on treatment for retino-blastoma. *Recent Advances in Ophthalmology*, 2010, 30(2): 186–188.
- 31 Zhao C, You ZP. New progression in the treatment of retinoblastoma. *International Journal of ophthalmology*, 2009, 9(1): 139–141.
- 32 Li GR, Dong YR, Zhang W, et al. External trabeculectomy in treatment of congenital glaucoma. *Chinese Journal of Practical Ophthalmology*, 2001, 19(12): 923–924.
- 33 Campos-Mollo E, Moral-Cazalla R, Belmonte-Martínez J. Combined trabeculectomy-trabeculectomy as the initial surgical procedure of primary developmental glaucoma. *Arch Soc Esp Oftalmol*, 2008, 83(8): 479–485.
- 34 Li XX. The features and screening Guidelines of retinopathy of prematurity in China. *Chinese Journal of Ocular Fundus Diseases*, 2004, 20(6): 384–386.
- 35 Ye XM, Gao HX, Wu BL, et al. Effect of early lacrimal passage probing on the treatment of congenital nasolacrimal duct obstruction. *Chinese Journal of Strabismus & Pediatric Ophthalmology*, 2005, 13(4): 183–184.
- 36 Wang LH, Ma LX. Recent advances of congenital cataracts. *Chinese Journal of Strabismus & Pediatric Ophthalmology*, 2008, 16(3): 142–143.