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The Eye in Pediatric Systemic Disease

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Alex V. Levin, MD, MHSc, FRCSC
Pediatric Ophthalmology and Ocular Genetics
Wills Eye Hospital
Thomas Jefferson University
Philadelphia, PA, USA

Robert W. Enzenauer, MD, MPH, MBA, MSS
Department of Ophthalmology
University of Colorado School of Medicine
Children's Hospital Colorado
Anschutz Medical Campus
Aurora, CO, USA

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Preface

This book truly is a "labor of love." When we were pediatric ophthalmology fellows at The Hospital for Sick Children in Toronto from 1989 to 1990, we were both already board-certified pediatricians. Going to SickKids was like being children in a candy shop. With our interest in pediatric systemic disease and love of children, combined with our interest in ophthalmology, the possibilities seemed endless. Our Fellowship Director and mentor, Dr. Donald Morin, taught us much and pushed us towards excellence. He made it seem like any goal could be achieved. When we came up with the idea for a comprehensive textbook on the ocular manifestations of pediatric systemic disease, he was encouraging but warned us about the enormity of the effort. He had written one of the great pediatric ophthalmology textbooks, *The Eye in Childhood*, and was well published in many areas. As an academic pediatric ophthalmologist, he knew the rigors of putting a project like this together. Yet, he believed in us, and also knew that there was no similar publication on the market. So, along with our co-fellow, Dr. James Elder, who has authored two of the chapters in this book, we set forward trying to make the book a reality.

Some chapters were drafted, others never began. Time passed. Our careers developed, we went to separate parts of the world, we raised our families, and the project found its way to the "back burner." It was not till recent years that we got the idea of bringing the project back to life. There was no other book available like the one we were planning. Our goal is an encyclopedic reference to be used by non-ophthalmologists and ophthalmologists. For the pediatricians and other non-ophthalmologists, it would be a place where they can learn about the ocular manifestations of diseases they see. For the ophthalmologists, it was a place where they can learn more about the systemic disorders that present to them with ocular findings. Readers might be asking questions such as: "What are the eye findings of this disease that need to be considered? Is the eye finding in my patient a manifestation of the disease? What tests should I be ordering? For what should I be screening?" And for those who want to delve further, the chapters are heavily referenced to provide an entry point into the literature regarding any detail the reader wishes to explore. Although the book is not an atlas, key pictures of findings specific for diseases, rather than generic ocular findings, are provided. Our comprehensive approach is designed to fill the gaps in each reader's knowledge outside their own specialty.

So we recruited new authors and contacted some of the old authors. We believe strongly in the importance of collaboration between pediatricians and pediatric ophthalmologists. Therefore, every chapter has at least one author who is a pediatric ophthalmologist as well as one coauthor who is a non-ophthalmologist with expertise in the field being discussed. We encouraged the use of trainees and other collaborators to write each chapter understanding the huge amount of work that was required. We carefully vetted the chapters and edited them thoroughly to ensure accuracy as well as a comprehensive approach. Each chapter covers many disorders. We decided to allow redundancy between chapters as the approach between authors of different disciplines to a given disease, which covers more than one organ system, might offer unique perspective. Each disease is discussed where possible in sections: definition, history, epidemiology, systemic manifestations, ophthalmic manifestations, diagnosis, and management. We believe the result is unique and uniquely useful.

Everyone who contributed to this book learned in the process. We hope that readers will also experience an expansion of their horizons as they step outside their daily lives of practice to reach into the world of the disciplines with whom they collaborate. We hope that this textbook will become the "go to" source for physicians from all areas, who deal with children, and are trying to understand the ocular manifestations of pediatric systemic disease. We look forward to having physicians come together through this book and establishing appropriate consultation patterns and collaborations. Together, we will all benefit the children we care for. Dr. Morin has unfortunately passed away, but this book is dedicated to everything he believed in: learning, supportive training, collaboration, and above all, thoughtful informed care of the child.

Philadelphia, PA Alex V. Levin, MD, MHSc, FRCSC
Aurora, CO Robert W. Enzenauer, MD, MPH, MBA, MSS

Contents

Contributors

Mariam Ahmad, MD Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA

Fathiya Al-Murshedi, MD, MSc, FCCMG, FRCPC, CIP Clinical Biochemical Genetics, Department of Genetics, Sultan Qaboos University Hospital, Al Khoudh, Muscat, Oman

Khalid Al-Thihli, MD, FRCPC, FCCMG Biochemical Genetics, Genetics Department, Genetics and Developmental Medicine Clinic, Sultan Qaboos University Hospital, Al Khod, Muscat, Oman

Sana Al-Zuhaibi, MD, FRCSC Department of Ophthalmology, Sultan Qaboos University Hospital, Muscat, Oman

Abigail Angulo, MD Developmental-Behavioral Pediatrics, Child Development Unit, Children's Hospital Colorado, Anschutz Medical Campus, Aurora, CO, USA

Sarah K. Bartz, MD Children's Hospital Colorado Endocrinology, Aurora, CO, USA

Rebecca Sands Braverman, MD Children's Hospital Colorado Ophthalmology, Aurora, CO, USA

Edward P. Buchanan, MD Department of Surgery, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, USA

MyMy C. Buu, MD Pediatrics, Division of Pulmonary Medicine, Stanford University School of Medicine, Palo Alto, CA, USA

Cara Elise Capitena, MD Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA

Edward W. Cheeseman, Jr., MD Pediatric Ophthalmologist, Department of Ophthalmology, Medical University of South Carolina, Mt. Pleasant, SC, USA

Eun Young Choi, BS Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, USA

Logan Christensen, MD Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA

Melissa L. Cirillo, MD Division of Neurology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Michael Clarke, MB, BChir, FRCS, FRCOphth, PhD Newcastle Eye Centre, Royal Victoria Infirmary, Newcastle Upon Tyne, UK

Jason Coryell, MD, MS Oregon Health and Science University, Casey Eye Institute, Portland, OR, USA

Andrew Court, MBBS, FRACP, FRANZCP Consultant Child and Adolescent Psychiatrist Consultation and Liaison Psychiatry, Royal Children's Hospital, Parkville, VIC, Australia

Donna Curtis, MD, MPH Department of Pediatric Infectious Diseases, Children's Hospital Colorado, Aurora, CO, USA

Brita S. Deacon, MD University of Arkansas for Medical Sciences/Arkansas, Children's Hospital, Little Rock, AR, USA

Peter C. Dyke II, MD Division of Pediatric Cardiology, Department of Child Health, University of Missouri Health Care, Columbia, MO, USA

Jane C. Edmond, MD Department of Ophthalmology, Baylor College of Medicine, Texas Childern's Hospital, Houston, TX, USA

Lawrence F. Eichenfield, MD UC San Diego School of Medicine, San Diego, CA, USA

James E. Elder, MBBS, FRANZCO, FRACS Department of Ophthalmology, Royal Children's Hospital, Parkville, VIC, Australia

Robert W. Enzenauer, MD, MPH, MBA, MSS Department of Ophthalmology, University of Colorado School of Medicine, Children's Hospital Colorado, Anschutz Medical Campus, Aurora, CO, USA

Jeremie Heath Estepp, MD Department of Hematology, St. Jude Children's Research Hospital, Memphis, TN, USA

Emily R. Gallagher, MD, MPH Department of Pediatrics, Craniofacial Center, Seattle Children's Hospital, Seattle, WA, USA

Anuradha Ganesh, MD, MRCOphth Pediatric Ophthalmology, Strabismus, and Ocular Genetics, Sultan Qaboos University Hospital, Muscat, Oman

Tara J. Guretzky, MD Kids Eye Care of Maryland, Rockville, MD, USA

Winita Hardikar, MBBS, FRACP, PhD Department of Gastroenterology, Royal Children's Hospital, Parkville, VIC, Australia

Laura J. Heinmiller, MD Pediatric Ophthalmology and Ocular Genetics, Wills Eye Hospital, Philadelphia, PA, USA

Mary Ellen Hoehn, MD Department of Ophthalmology, Hamilton Eye Institute, University of Tennessee Health Science Center, Memphis, TN, USA

Jeffry Hogg, MBBS, MRes Newcastle Eye Centre, Royal Victoria Infirmary, Newcastle Upon Tyne, UK

Dorothea Jenkins, MD Department of Pediatrics, Medical University of South Carolina, Charleston, SC, USA

Jennifer L. Jung, MD Department of Ophthalmology, Children's Hospital of Colorado, University of Colorado School of Medicine, Aurora, CO, USA

Arcot Sadagopan Karthikeyan, DNB, FRCS Pediatric Ophthalmology, Strabismus and Ocular Genetics, CMER (Shenzhen) Dennis Lam Eye Hospital, Shenzhen, China

Pediatric Ophthalmology and Ocular Genetics, Aravind Eye Care System, Madurai, Tamil Nadu, India

Lumbini Eye Institute, Shree Rana Ambika Shah Eye Hospital, Siddharthanagar, Nepal

Daniel J. Karr, MD Oregon Health and Science University, Casey Eye Institute, Portland, OR, USA

Mahima Keswani, MD Division of Kidney Diseases, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Marin H. Kollef, MD, FACP, FCCP Division of Pulmonary and Critical Care Medicine, Washington University School of Medicine, St. Louis, MO, USA

Nancy F. Krebs, MD, MS Department of Pediatrics, Section of Nutrition, University of Colorado School of Medicine, Aurora, CO, USA

Sudhi P. Kurup, MD Division of Ophthalmology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Kara C. LaMattina, MD Department of Pediatric Ophthalmology and Ocular Genetics, Wills Eye Hospital, Philadelphia, PA, USA

Guillermo Lay-Son, MSc, MD Clínica Alemana-Universidad del Desarrollo, Santiago, Chile

Sabra Lofgren Leitenberger, MD Oregon Health and Science University, Casey Eye Institute, Portland, OR, USA

Alex V. Levin, MD, MHSc, FRCSC Pediatric Ophthalmology and Ocular Genetics, Wills Eye Hospital, Thomas Jefferson University, Philadelphia, PA, USA

Clara Lin, MD Department of Pediatrics-Rheumatology, University of Colorado School of Medicine, Children's Hospital Colorado Anschutz Medical Campus, Aurora, CO, USA

Gregg Lueder, MD Saint Louis Children's Hospital, Washington University School of Medicine, One Children's Place, Saint Louis, MO, USA

Mariah N. Mason, MD, PhD Oregon Health and Science University, Casey Eye Institute, Portland, OR, USA

Kathryn M. McCans, MD Cooper University Hospital, Camden, NJ, USA

Emily A. McCourt, MD Department of Ophthalmology, Children's Hospital Colorado, Aurora, CO, USA

John T. McDonnell, MD Castle Medical Center, John A. Burns School of Medicine, University of Hawaii, Kailua, HI, USA

Rebecca B. Mets-Halgrimson, MD, MPH Division of Ophthalmology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Rebecca Freedman Neustein, BA Emory University School of Medicine, Atlanta, GA, USA

Radha Ram, MD Division of Ophthalmology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Adele S. Schneider, MD, FACMG Jefferson Medical College, Philadelphia, PA, USA

Genetics Division, Einstein Medical Center Philadelphia, Philadelphia, PA, USA

Veeral S. Shah, MD, PhD Department of Ophthalmology, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, USA

Lance M. Siegel, MD, FAAO, FAAP Children's Eye Institute, Upland, CA, USA

Jasleen Singh, MD Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO, USA

Pediatric Ophthalmology and Adult Strabismus, Children's Hospital of Colorado, University of Colorado-Denver, Aurora, CO, USA

Allison R. Soneru, MD Division of Ophthalmology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Kirstin Tawse, MD Division of Ophthalmology, Children's Hospital of Colorado, Aurora, CO, USA

David S. Walton, MD Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, USA

R. Christopher Walton, MD Department of Ophthalmology, University of Tennessee College of Medicine, Memphis, TN, USA

Naomie Warner, DO, MHA Pediatric Ophthalmology and Ocular Genetics, Wills Eye Hospital, Philadelphia, PA, USA

Herbert G. Whitley, MD, MA Department of Pediatrics, Carilion Clinic Children's Hospital, Pediatric Cardiology, Roanoke, VA, USA

Gar-Yun Wong, MB, BS Newcastle Eye Centre, Royal Victoria Infirmary, Newcastle Upon Tyne, UK

WanWan Xu, MD Division of Ophthalmology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Amy S. Xue, MD Department of Surgery, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, USA

Sylvia H. Yoo, MD Ophthalmology, New England Eye Center at Tufts Medical Center, Boston, MA, USA

Mario Zanolli, MD Clínica Alemana-Universidad del Desarrollo, Santiago, Chile

1 Normal Postnatal Ocular Development

Laura J. Heinmiller and Alex V. Levin

Although detailed normative data regarding the volumetric and topographical analysis of the eyeball and its contents are available [1] this discussion will be confined to the clinically relevant dimensions.

Visual Acuity

Fixation

Perhaps the most frequent question which parents ask pertaining to their infant's eyes is "What does my baby see?" The answer to this question depends in part on the type of method used to assess visual acuity. The majority of babies should show some fixational behavior at term birth. At 4 weeks, the baby looks at their mother's face while breast feeding [2]. When the mother moves her face, the child will follow it visually. This movement is interrupted if the mother turns her face away so that only her profile is presented [2]. By 2 months the baby is following better but the pursuit movements tend to be jerky rather than smooth [2]. Smooth pursuit eye movements show the most maturation from 2 to 6 months old, and reaching almost an adult-like gain by 18 months old [3]. Pieh and coworkers found that tracking time was highest when a larger stimulus of 4.78° of visual angle was applied ($p<0.022$) and when the stimulus was moved at a medium stimulus velocity of 15 degree/s ($p<0.0002$) [3].

Often, the human face is a better stimulus of fixation than a light source [2]. Goren et al. were able to show that 9 min old infants had a preference for a face-like stimulus over a scrambled face image. Both of these were preferred by the infant over a blank face image [4]. One and four month old infants show greater pupillary dilation (a substitute measure for arousal and interest) to faces than to other nonsocial patterns [5]. By 12 weeks of age only 5 % will not fixate on a light although 13 % do not fixate well [6]. Actually, by 12 weeks, half appear to fixate clinically but do not accommodate to focus as judged by the appropriate change in the red reflex [6]. By 6 months, almost 100 % will both fixate and focus normally with either eye although some researchers believe that full adult fixational behavior is not achieved until 1 year [6]. Both eyes do not have to develop normal fixational behavior symmetrically [6]. By 6 months, only 4 % of children will have be a fixational abnormality in one eye due to an underlying ocular problem [6].

Optokinetic Nystagmus (OKN)

More objective values for visual acuity in infants depend largely on the method used. In a comparative review of the literature, Dobson and Teller found that visual acuity in the first month of life measured 20/200–300 by observation of optokinetic nystagmus (OKN), visual evoked potentials (VEP) or preferential looking responses [7]. By 6 months the vision improved to 20/100–200 by OKN and preferential looking but to 20/25 by VEP [7]. Normal values for grating acuity and OKN have been developed for the first 3 years of life [8]. The range of normal values is very wide in the first 6 months. Visual development, as measured by these tools, appears to accelerate in the second year of life [8].

Visual Evoked Potential (VEP)

VEP can be used to measure visual acuity although the reliability of this technique has been questioned [9]. The data depends in part on the type of VEP used [7]. With sweep VEP,

L.J. Heinmiller, M.D.
Pediatric Ophthalmology and Ocular Genetics, Wills Eye Hospital, 840 Walnut Street, Ste. 1210, Philadelphia, PA 19107, USA
e-mail: laura.heinmiller@gmail.com

A.V. Levin, M.D., M.H.Sc., F.R.C.S.C. (✉)
Pediatric Ophthalmology and Ocular Genetics, Wills Eye Hospital, Thomas Jefferson University, 840 Walnut Street, Ste. 1210, Philadelphia, PA 19107, USA
e-mail: alevin@willseye.org

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Table 1.1 Visual acuity in infants by method [11, 12]

Method	OKN	VEP	Preferential looking (tellar cards)	Otago photoscreener
Full term newborn	20/400	20/100–20/200	20/200–20/545	–
2–3 months	20/400	20/80	20/285	20/20–20/25
4 months	20/200	20/80	20/167	–
5–6 months	20/100	20/20–20/40	20/100–20/120	20/20
1 year	20/60	20/20	20/50	–

OKN optokinetic nystagmus, *VEP* visual evoked potential

a pattern of vertical lines of varying width move across the visual field in a continuous fashion, usually on a video monitor. As the lines get thinner, they also become proportionately closer together until the subject can no longer perceive that lines are present. Results of this technique are often reported in cycles/degree which must then be approximately translated into the standard Snellen acuity values (20/x where x = 600/cycles/degree). This simple conversion may not be entirely accurate as it does not take into account other factors such as retinal-neural processing and contrast sensitivity. But if one accepts this technique, visual acuities ranging from 20/133 in the first month to 20/30 by the end of the first year can be found [9]. Norcia and Tyler have cautioned that these values should be used as the lower boundary of infant performance rather than absolute limits [9]. Further investigations using a dual-frequency technique VEP in infants 10–39 weeks old showed that both central and peripheral visual acuity improved by a factor of 2.6 and 2.2 respectively with central acuity higher by a factor of 2.3 [10].

Current Consensus on Ages for Maturity of Visual Acuity

Depending on which method is used to test visual acuity there can be large variations in the expected norms throughout the first years of life (Table 1.1) [11, 12].

Preferential Looking/Tellar Acuity Cards

Using Tellar Acuity cards, the visual acuity in full-term newborns was estimated at 20/200 [11].

Otago Photoscreener

Molteno and coworkers made estimations of visual acuity using the Otago photoscreener, a system which uses the variations in the red reflex to assess fixation, accommodation, refractive error, and ocular alignment [6]. They estimated that the visual acuity at 3 months ranges from 6/6 to 6/15, at 6 months almost 70 % are 6/6 with a further 15 % having 6/9 in the worse eye, and by 1 year over 90 % have at least 6/9 vision in both eyes [6]. A summary of visual acuity in infants by method can be found in Table 1.1 [11, 12].

Contrast Sensitivity

Contrast Sensitivity begins to develop through the first 3 months of life [12]. Fiorentini and coworkers showed that infants aged 2.5–6 months exhibited contrast sensitivity by VEP at a mean luminance of 6 and 0.06 cd/m^2. They showed that scotopic contrast sensitivity develops earlier than photopic contrast sensitivity, and by 4–5 months old are nearly at the level of an adult [13]. Contrast sensitivity develops similarly in the central and peripheral visual fields [10].

Globe Size

Axial Length

The axial length of the globe increases in a direct relationship with age until approximately 8 years old with a stronger correlation for hyperopes as compared to myopes [14]. The eyeball increases 2.86–3.25 fold between birth and adulthood [1, 15]. The most rapid portion of this growth occurs in the first 40 weeks of postnatal life [16]. Stafford and coworkers found the maximum axial length at term, as measured by ultrasound (A scan), to be 18.6 mm with a mean of 17.0 ± 0.65 standard deviation [17]. Other authors have found similar values [16]. Formulas are available for more detailed analysis of the ocular growth patterns [16]. Axial growth of the eye occurs in three phases: from birth to 18 months a rapid period from mean of 16 to 20.3 mm; a 1.1 mm increase between years 2 and 5; and 1.3 mm of growth thereafter leveling off at age 13 [18].

Saggital, Transverse and Vertical Size

At birth, the mean saggital, transverse, and vertical diameters of the globe are 17.5, 17.1, and 16.5 mm respectively representing approximately 71 % of the adult equivalents [1]. The anterior segment of the infant globe is roughly 75–80 % that of adults. The posterior segment is less than half of the aver-

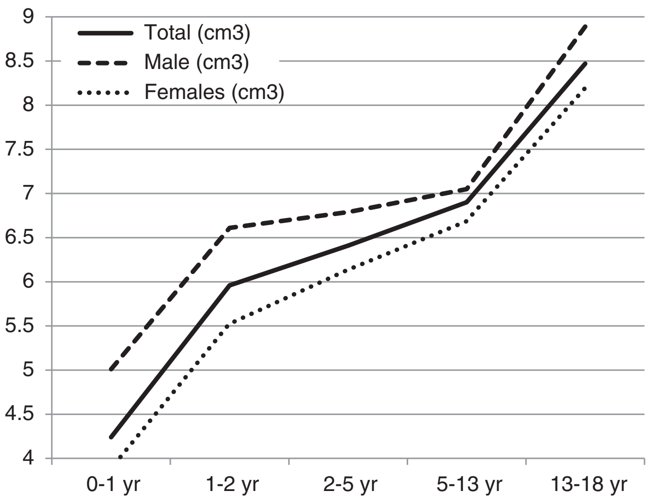

Fig. 1.1 Ocular volume with CT scan in children [21]

age adult. The total sclera surface in infants averages 822 mm^2 which is about 1/3 that of the average adult [19]. Therefore, a majority of the change in globe size stems from the expansion of sclera surface in the posterior segment with 50 % of growth occurring in the first 6 months of life, reaching adult averages at around 13 years [19].

Volume

Through childhood, the ocular volume increases about 300 %; from 2.5 to 7.5 cm^3 [20]. Hahn and Chu performed a study showing ocular volume measured by CT scan and found that rapid eye growth occurs during the first 24 months of life and peaks between the ages of 18 and 24 years old [21]. Figure 1.1 illustrates these findings [21].

Refractive Error

Cycloplegic Retinoscopy

The refractive error of the eye may be measured by a variety of techniques. It is standard to use some form of cycloplegic retinoscopy in children. As the differences in the absolute level of cycloplegia which is obtained through various cycloplegic regimens is small, we will discuss the development of refractive error in the normal infant based on the reported values obtained through various cycloplegic regimens as if they were equal. However, retinoscopy in infants and young children without the use of cycloplegia may be prone to significant error. Data collected under these circumstances will not be included. Likewise, the definition of amblyopia may vary between authors. We have chosen as our definition a two line difference between each eye based on projected acuity charts, visual acuity in an eye with 6/9 acuity or worse, or any other objective test result (e.g. visual evoked potential, preferential looking) which indicates an equivalently significant difference between the eyes.

Trend Towards Emmetropia

In general, there is a trend towards emmetropia throughout early childhood regardless of the initial refractive error [22]. The main changes towards emmetropia occur in the first 2 years [23, 24]. Further studies have shown that hyperopia decreases with age along with astigmatism found in infants. In a prospective study on childhood myopia ranging from −0.25D to −3.50 diopters, Ehrlich and coworkers showed that emmetropization was found to occur by 3 years old. The rate of change in myopia from age 8.5 to 38.5 months occurred at a relatively constant rate of +0.44 diopters per year [25]. Ultimately, emmetropization occurs through a combination of passive and active means. Passive means include a growth in axial length, reduction in the power of the lens, a mild reduction in power of the cornea as the radius lengthens and a lengthening of the anterior chamber [26]. The active component relies on the feedback given by the image clarity of the retina, for which the exact mechanism is unclear [27].

Spherical Equivalent Anisometropia

In 88.5 % of children, there is no significant difference between the spherical equivalent of the right and left eye [28]. One group found only 1 % of 519 children less than 48 months old to have anisometropia [29]. This group also established 99th percentile curves for normal refraction. They found the range to decrease with age, staying fairly stable after the first year. In a cross-sectional study of healthy children under the age of 5 years old, Kuo and coworkers showed that 95 % of the children had less than 1.50 D of anisometropia [24]. Deng and Gwiazda measured refractive error in children ages 6 months ($n=1120$), 5 years ($n=395$) and 12–15 years ($n=312$) and found the mean difference in refraction between the two eyes was similar at 6, 14 months (0.11 D) and 5 years (0.15 D), increasing to 0.28 D at 12–15 years [30]. The prevalence of <1.00 D of spherical equivalent anisometropia, was 1.96 %, 1.27 %, and 5.77 % respectively [30]. Infants with significant astigmatism (≥1.00 D) in one or both eyes have an increased risk of anisometropia ($p<0.05$) [30].

Hyperopia

Over the first 3 years of life, the average spherical equivalent in normal children is −0.75 to +3.00 diopters [28, 31]. Only 7–8 % will have hyperopia (farsightedness) in excess of 2.75 diopters during this time period [28, 32] with only 2 %