UPDATES ON PEDIATRIC RETINA CARE FROM THE PODIUM

The advances in retina are changing how we approach diagnosis and treatment, even for our youngest patients.

LECTURES BY R.V. PAUL CHAN, MD, MSC, MBA, FACS

We had an amazing start to our 49th annual Aspen Retinal Detachments Society Meeting (ARDS). It was a pleasure to bring R.V. Paul Chan, MD, MSc, MBA, FACS, back to the podium to talk about a topic on which he is the world's authority: pediatric retinal diseases. Dr. Chan is one of our youngest and newest chairmen for ARDS and has been a major thought leader in the field of pediatric retina.

Our 50th anniversary meeting is just around the corner on March 5-9. If you haven't already registered, head to https://aspenretina.com for more information. Get ready for more slopes, slides, and socializing.

- Timothy G. Murray, MD, MBA

At the 2021 ARDS meeting in Snowmass, Colorado, Dr. Chan delivered two engaging lectures focused on recent changes that impact how retina specialists diagnose and treat pediatric patients with retinal diseases such as retinopathy of prematurity (ROP). Here, we summarize the discussions.

LASER VERSUS ANTI-VEGF

How do we transition from laser to anti-VEGF for pediatric patients? Many treatment options are available, and it can be a challenging decision when determining which is best for a patient, according to Dr. Chan during his lecture on "Treatment of Pediatric Retina Patients in the Era of Laser and Anti-VEGF." Dr. Chan presented the research and clinical experiences that shape how retina specialists are answering that question.

Where Do We Stand in the Treatment of ROP?

The RAINBOW study prospectively evaluated the use of ranibizumab (Lucentis, Genentech/Roche) for ROP and is now on a 5-year extension study. Data show that patients treated with ranibizumab had good anatomical outcomes.[1]

In addition to the RAINBOW study, there are also the ongoing FIREFLEYE and BUTTERFLEYE studies for 0.4 mg aflibercept (Eylea, Regeneron).[2] "Now, all these questions that we've had for over a decade, what drug, what dose, and so forth, they're being addressed," Dr. Chan stated.

According to Dr. Chan, David K. Wallace, MD, and PEDIG, in collaboration with the DRCR Retina Network, are looking at low-dose bevacizumab (Avastin, Genentech/Roche) and its efficacy for ROP compared with laser in ROP3. They are also looking at more aggressive disease and more posterior disease in ROP4. These studies are underway.

International Endeavors

With the advent of anti-VEGF therapy, our access to treatment has improved where resources may have been limited. "From my own experience and working with my collaborators around the world, anti-VEGF agents have given many children hope for vision when previously they may have gone blind," Dr. Chan shared. "Even though laser is effective, many areas of the world don't have reliable access to laser or pediatric anesthesia. There is an increasing number of children who are being born premature, so there continues to be children at risk of developing ROP around the world."

With anti-VEGF treatment, clinicians can have high success rates in promoting regression of ROP. So, should we change our treatment criteria? Dr. Chan shared his thoughts. "We've went from doing laser for everyone who required treatment to now having anti-VEGF at our disposal for certain cases," Dr. Chan explained. "What we're learning now is that laser is still a good option. I continue to use laser for most cases of zone II, stage 3, plus disease. For aggressive ROP, I consider using anti-VEGF agents." The literature also shows that there can be success in treating with anti-VEGF plus laser at some point, he added.

Still, it's difficult to measure safety in these premature children. ROP is appearing in infants who would not have survived a decade ago, raising the question of increased concern for a safety signal due to the patient's age, he noted.

Back in 2006, clinicians were discussing whether anti-VEGF treatment was ethical in infants. Now, those discussions have turned to what are the ethics of *not* using an anti-VEGF drug, Dr. Chan said. Clinicians have enough experience to offer parents a detailed informed consent about the unknown—a conversation worth having because it works in many situations, especially for ROP. The field must look at redefining the treatment criteria, especially for pediatric retinal diseases.

CLASSIFYING ROP

The International Classification of Retinopathy of Prematurity (ICROP), composed of 34 faculty from six continents, creates a standard nomenclature for classification of ROP. It was first published in 1984, expanded in 1987, and revisited in 2005 and 2021.[3]

In his second talk, Dr. Chan shared the major updates to the ICROP, including redefining and refining classification metrics, such as posterior zone, notch, reactivation, regression, subcategorization of stage 5, and recognition of a plus disease spectrum.

AROP Versus APROP

Often, "what we defined as aggressive *posterior* ROP (APROP) didn't fall posteriorly," Dr. Chan explained. These changes can occur in larger and older preterm infants, and present anterior to the posterior retina. They are aggressive and progress rapidly. The change from APROP to *aggressive* ROP (AROP) focuses more on the tempo of the disease and the appearance of the vascular abnormalities, not necessarily the location. Although it often occurs posteriorly, Dr. Chan shared, the term *AROP* is now preferred.

Reactivation and Regression Patterns

Clinicians have been more familiar with defining reactivation after laser, but there has been some heterogeneity in what they define as reactivation after anti-VEGF treatment. ICROP3 advises the use of two separate terms when describing later phases of ROP: *regression*, which refers to disease involution and resolution; and *reactivation*, which refers to recurrence of acute phase features and can typically be seen more frequently after anti-VEGF treatment.[3]

Plus Disease Spectrum

Clinicians have relied heavily on the standard plus disease photo, Dr. Chan stated, but with better imaging and more experience, plus disease has been recognized as a spectrum. ICROP3 recommends that this spectrum be determined from vessels within zone I, rather than from only vessels within the field of narrow-angle photographs and rather than from the number of quadrants of abnormality.[3,4]

Pre-plus disease is what even expert ROP clinicians often disagree on. This severity scale creates a progressive discussion about the plus disease spectrum.

WATCH IT NOW

ROP in the Era of Anti-VEGF

Stage 5

With improved imaging technology that is more accessible for use with children, clinicians can detect changes earlier, especially in stage 4 disease, Dr. Chan said. ICROP3 has recently added subcategories for stage 5: stage 5A, in which the optic disc is visible by ophthalmoscopy; stage 5B, in which the optic disc is not visible secondary to retrolental fibrovascular tissue or closed-funnel detachment; and stage 5C, in which findings of stage 5B are accompanied by anterior segment abnormalities.[3]

Notch

The ICROP defines three zones of ROP, although we still classify ROP by the most posterior zone. Dr. Chan discussed the definition of *posterior zone II*, which is a region that is 2 disc diameters peripheral to the zone I border and may potentially be a more worrisome disease than ROP in the more peripheral zone II. Zone II is a ring-shaped region extending nasally from the outer limit of zone I to the nasal ora serrata and with a similar distance temporally, superiorly, and inferiorly.[3,4]

The term *notch* describes an incursion by the ROP lesion of 1 to 2 clock hours along the horizontal meridian into a more posterior zone than the remainder of the retinopathy. It is documented as "secondary to notch."

CONCLUSION

Dr. Chan concluded his lecture by affirming the forward momentum of the field, given the new technology, treatments, and 35 years of collective learning. ■

1. Stahl A, Domenico Lepore D, Fielder A. Ranibizumab versus laser therapy for the treatment of very low birthweight infants with retinopathy of prematurity (RAINBOW): an open-label randomised controlled trial. *Lancet*. 2019;394(10208):1551-1559.
2. Stahl A. ROP: Results from the RAINBOW study. Presented at Euretina 2021 Virtual. September 12, 2021.
3. Chiang MF, Quinn GE, Fielder AR, et al. International Classification of Retinopathy of Prematurity, Third Edition. *Ophthalmology*. 2021;128(10):e51-e68.
4. Repka MX. A Revision of the International Classification of Retinopathy of Prematurity. *Ophthalmology*. 2021;128(10):1381-1383.