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In a country town south of London, late in the summer of 1969, George Harrison strummed on his acoustic guitar the timeless melody of "Here Comes the Sun", later to be published in the classic album, "Abbey Road". I suspect all of us have listened to this song and album. This song reflected his relief at the arrival of spring, as well as a reprieve from business and legal tensions. This was his epic respite from "a long, cold, lonely winter". This song has guided and unified our world with hope for better days to come.

In November 2001, on the day after Harrison's death, loyal fans gathered in Central Park, New York to sing "Here Comes the Sun" in his honor. This song has been adapted by several artists including Jon Bon Jovie with an acoustic rendition in 2021. This piece is everlasting and ever-meaningful to all walks of life, representing better days ahead.

Similarly, on a quiet street in London at Saint Bartholomew's Hospital in the early 1990s was a pediatric oncologist named Judith Kingston. She had a wise idea to employ a chemotherapy regimen known to be effective for neuroblastoma, and she tailored it for a similar neurologically-derived eye tumor, called retinoblastoma. Thus, she treated 14 children with advanced retinoblastoma with intravenous vincristine, etoposide, and carboplatin and found remarkable tumor response.[1] She is considered the "pioneer" of chemotherapy for retinoblastoma. Her observations of the power of this regimen for retinoblastoma trickled out to the rest of the retinoblastoma community and changed the world's approach to this often-fatal malignancy, slowly turning the tables with tumor control, globe salvage, and reduction in tumor-related death. According to her collaborator, John Hungerford, a retinoblastoma expert, Dr. Kingston's contribution "has been paramount to the current worldwide treatment of this tumor in thousands of children".[2] And so the harmonious melody goes on. This regimen was quickly integrated into several major retinoblastoma centers in London, Toronto, Los Angeles, and Philadelphia and favorable results were published.[1,3–5] Soon, the world was employing systemic chemotherapy for retinoblastoma and repeatedly matching the unexpected and remarkable success. A new era had arrived.[6]

Retinoblastoma has had dark, cold days with blindness, metastatic disease, and death from this heritable malignancy in multiple family members at a young age. Over time and mostly due to the impact of intravenous chemotherapy, rays of sunshine have shimmered with hope for a cure. Over the past nearly 30 years, retinoblastoma teams have developed alternative delivery routes and regimens of chemotherapy, dating back to the initial days of intravenous chemotherapy in the early 1990s to later innovations with intra-arterial delivery of chemotherapy in 2008, intravitreal chemotherapy in 2012, and intra-aqueous chemotherapy in 2017.[7-9] The sun has definitely broken through foggy skies for retinoblastoma care.

In this issue of the journal, we learn from Bas et al[10] of the control offered by systemic chemotherapy over 20 years in 964 eyes of 554 patients based on patient age at diagnosis, showing that younger patients demonstrated more lasting control than older patients. A separate analysis of this cohort has demonstrated that first-line intravenous chemotherapy showed globe salvage with avoidance of external beam radiotherapy by year 2 for Group A (96%), Group B (91%), Group C (91%), Group D (71%), and Group E (32%) ($P < 0.001$) and this control typically lasted to 20-year follow up.[9]

Other retinoblastoma topics covered in this issue focus on advanced retinoblastoma, including metastatic disease, trilateral disease, invasive into the optic nerve and/or choroid, and others, with management using stem cell therapy after high-dose chemotherapy by Clarissa et al. These authors comprehensively reviewed 4 online databases to find 35 studies using this technique, leading to survival in 68%. However, they emphasized that control of metastatic disease to the central nervous system was poorer with only 23% survival. Another retinoblastoma-related report in this issue by Zhao et al explores long-term ensuing years after local retinoblastoma control is achieved in patients at risk for second cancers. They reviewed 24-year experience with a broad spectrum of second cancers including sarcomas and carcinomas that were detected at median interval of 37 years after diagnosis of retinoblastoma, leading to mortality is 46% by 5 years and 66% by 10 years. In undeveloped countries, children still succumb to retinoblastoma, whereas in

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developed countries most children survive retinoblastoma, but those with germline mutation can die from the second cancer. Lifelong monitoring is critical.

Yes, we have much more to investigate and understand, but for now, we can appreciate the sunshine we have gained in timely and effective primary treatment of the eye using intravenous chemotherapy for bilateral retinoblastoma, powerful intra-arterial chemotherapy for unilateral retinoblastoma, reliable intravitreal or intra-aqueous chemotherapy for seeding, and enucleation for eyes with advanced disease. We have achieved tremendous progress over the past 30 years with local globe control, but there is much more work to do in addressing more invasive tumors, metastasis, and second cancers. As the song goes, "Here comes the sun"—let us use this light to better "perceive" the nuances of retinoblastoma and its systemic implications. Retinoblastoma is not simply a childhood malignancy, it is a malignancy for life.

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